

## ORIGINAL ARTICLE

## THE CORRELATION BETWEEN RETINAL NERVE FIBRE LAYER THICKNESS, OPTIC NERVE HEAD PARAMETER, AND RELATED RISK FACTOR IN GLAUCOMA PATIENT

Arif Kusuma Wardhana<sup>1</sup>, Retno Ekantini<sup>2</sup>, Tatang Talka Gani<sup>2</sup>, Krisna Dwi Purnomo Jati<sup>2</sup>

<sup>1</sup>Ophthalmology Resident Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University

<sup>2</sup>Department of Ophthalmology Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University

Email: arif.kusuma.akw@gmail.com

### ABSTRACT

**Introduction & Objective:** To examine the correlation between amount of thickness of retinal nerve fibre layer (RNFL) and the past RNFL thickness, related risk factor (gender, age, myopia, intraocular pressure (IOP), blood pressure). And RNFL parameter (symmetricity and four quadrants RNFL thickness) and optic nerve head parameter (rim area and vertical cup disc ratio).

**Methods:** 39 right eyes of both sex and various age underwent examination including IOP measurement, subjective refraction for determining refractive error, and optical coherence tomography (OCT) for RNFL and ONH analysis. The follow up were done after one year.

**Results:** The RNFL symmetricity, superior, nasal, inferior, temporal RNFL thickness showed significance correlation with RNFL thickness ( $R= 0.487, p= 0.002$ ), ( $R= 0.915, R= 0.749, R= 0.897, R= 0.702$  with  $p<0.001$ ), but not showed significance correlation with rim area and vertical cup disc ratio ( $R= 0.175, p= 0.286$ ) and ( $R= -0.093, p= 0.574$ ). A significance correlation also showed with increasing age, gender, and systolic blood pressure ( $R= -0.387, p= 0.015$ ), ( $R= 0.441, p= 0.005$ ) and ( $R= -0.418, p= 0.008$ ). But not showed significance correlation with history of past RNFL thickness, refractive error, IOP, and diastolic blood pressure ( $R= 0.258, p= 0.113$ ), ( $R= 0.005, p= 0.975$ ), ( $R= -0.234, p=0.152$ ), and ( $R= 0.060, p=0.717$ ).

**Conclusion:** RNFL thickness measurements showed significance correlation with RNFL parameter. It is not clear if past RNFL thickness, refractive error and IOP related with RNFL thickness even showed significance correlation with age, gender, and systolic blood pressure.

**Keywords:** Glaucoma, RNFL thickness, optical coherence tomography, optic nerve head

### INTRODUCTION

Glaucoma is among of major causes of blindness nowadays. And glaucoma is one of leading causes in the world. Glaucoma is characterized by progressive optic disc reduction and related with defect of visual field [1]. Glaucoma usually occurs bilateral and the degrees varies between both eyes [1].

The prevalence itself is estimated around approximately 3.5% among adult and elderly population. The characteristic were high intraocular pressure and open angle glaucoma in most cases [2].

The irreversible vision loss caused by degeneration until loss of retinal ganglion cells and the axons forms the retinal nerve fibre layer (RNFL). The glaucomatous optic nerve

neuropathy include changes in optic disc appearance such as enlargement of optic cup and loss of neuroretinal rims[3].

The objective quantify retinal changes in glaucoma, the loss of retinal ganglion cells manifest in thinning of the retinal nerve

fibre layer (RNFL) around optic nerve head and in the macular region [4].

OCT is an imaging tool that has been used to evaluate RNFL in patients with high resolution, also in glaucoma cases. The RNFL and ONH image are able to obtain by delivery of low coherence near infrared light (850 nm) from a super luminescent diode and subsequent backscattering from the retina [5].

The multiple risk factor showed that include IOP, ocular perfusion pressure, ocular blood flow, myopia, central corneal thickness, and optic disc hemorrhages. Systemic risk factors include age, smoking, African ancestry, family history, genetic factors, systemic hypertension. a nocturnal drop in blood pressure, atherosclerosis, dyslipidemia, type 2 diabetes mellitus (DM), glucose intolerance, obesity, vasospasm, migraine, Raynaud syndrome, stress, and primary vascular dysregulation[6].

## **MATERIALS AND METHODS**

### **Study design**

Retrospective analysis of 39 right eyes primary open angle glaucoma patents from both sex and various age who received RNFL examination (symmetricity and four quadrants RNFL thickness) and optic nerve head examination (rim area and vertical cup disc ratio) by using OCT in our Ophthalmology Departement, Glaucoma Subdivision, in Sardjito General Hospital for 6 months. Exclusion criteria of the study were secondary open angle glaucoma, angle closure glaucoma, non- glaucomatous condition (optic atrophy, papilledema, amblyopia), missing data related IOP, best-corrected visual acuity (BCVA), blood pressure, and past RNFL thickness.

### **Glaucoma Diagnosis**

Open angle glaucoma was a kind of progressive optic neuropathy, showed by optic nerve head cupping and defect in visual field in the state of open angle [1]. Some studies showed that lowering IOP slows disease progression and prevent development and the target of IOP should

Vascular factors have been suspected as important role for glaucoma beside IOP. The association between low ocular perfusion pressure and low perfusion of ONH[7].

The correlation between blood pressure and POAG still in development. Previous study shown that diurnal low ocular perfusion pressure and low systolic blood pressure. Systemic hypertension has been associated with visual field visual field progression. The mechanisme is still poorly understand. The evidence is not shown significant relationship [8].

To examine the correlation between amount of thickness of retinal nerve fibre layer (RNFL) and the past RNFL thickness, related risk factor (gender, age, myopia, intraocular pressure (IOP), blood pressure). And RNFL parameter (symmetricity and four quadrants RNFL thickness) and optic nerve head parameter (rim area and vertical cup disc ratio) be individualized [2]. In retinal glaucomatous damage, the particular loss of retinal ganglion cells manifest in thinning of the retinal nerve fibre layer (RNFL) [4]. Measurement of RNFL and optic nerve head examination were using OCT and re- examined 6 months apart. The examination were along basic data including age, gender, examination were IOP (non contact tonometry), BCVA, and blood pressure. The data from right eyes was selected and further analysis were proceed.

### **OCT Examination**

The measurement of RNFL by using Spectral domain optical coherence (SD- OCT). the OCT examination divides the obtained disc into four 90° quadrants (superior, nasal, inferior, and temporal) and averages them as total average thickness. Also the RNFL symmetry and rim area and cup/disc vertical ratio for optic nerve head.

Optic nerve head parameter examination was done by using OCT that consisted of six radial scans centered on ONH. OCT defined by itself to define the edge of optic disc as the end of the retinal pigment epithelium/choriocapillaris and used smoothing with fit to circle to fill the gaps between scans. A straight line connected the edges of the retinal pigment epithelium/choriocapillaris and a parallel line was constructed 150  $\mu\text{m}$  anteriorly. Structures below this line were defined as the disc cup and above this line as the neuroretinal rim. Among the measurements given by the OCT optic nerve head analysis, the following were examined: disc area, cup area, rim area, cup/disc vertical and horizontal ratios, vertical disc diameter [5].

### **RESULTS**

From 360° average RNFL thickness the mean thickness were 86.44  $\mu\text{m}$ . The mean thickness of past RNFL were 92.21  $\mu\text{m}$ . The superiorquadrant thickness were 104.33  $\mu\text{m}$ . The nasal quadrant thickness were 65.72  $\mu\text{m}$ . The inferior quadrant thickness were 105.38  $\mu\text{m}$ . The temporal quadrant thickness were 67.02  $\mu\text{m}$ . The RNFL symmetry were 64.15%.

From optic nerve head parameter, the mean of rim area were 1.20 mm<sup>2</sup>. And cup/disc vertical ratio were 0.64. For the mean age were 48.87. The mean refractive error were -0.21. The mean IOP were 15.38. The mean systole and diastole were 123.28 and 77.18. The RNFL symmetry showed the moderate positive correlation with RNFL thickness (R= 0.487, p= 0.002). Furthermore, the superior, nasal, inferior, temporal RNFL thickness showed positive significance correlation with RNFL thickness (R= 0.915, R= 0.749, R= 0.897,

## Statistics

### Statistical analysis

The numeric data was gathered in Microsoft Excel. Normality was examined using Pearson normality test. Correlation between parameters were evaluated using Pearson correlation factors when appropriate. In the results section of this article, Numeric results are presented as mean, standard deviation, range, and 95% confidence interval. In general, statistical significance was assumed for  $p < 0.05$ .

R= 0.702 with  $p < 0.001$ ). With increasing the thickness of RNFL, the four quadrants thickness were also thicker and strongly correlate. The result did not showed significance positive correlation with rim area and vertical cup disc ratio (R= 0.175,  $p = 0.286$ ). the correlation showed could be positive but the correlation value were weak. The vertical cup disc ratio showed weak negative correlation (R= -0.093,  $p = 0.574$ ). A significance correlation also showed with increasing age, gender, and systolic blood pressure (R= -0.387,  $p = 0.015$ ), (R= 0.441,  $p = 0.005$ ) and (R= - 0.418,  $p = 0.008$ ). but the increasing age showed negative correlation with RNFL thickness. Furthermore, the result did not showed significance correlation with history of past RNFL thickness, refractive error, IOP, and diastolic blood pressure (R= 0.258,  $p = 0.113$ ), (R= 0.005,  $p = 0.975$ ), (R= -0.234,  $p = 0.152$ ), and (R= 0.060,  $p = 0.717$ )

**Table 1. Profile Cases of IV MP Pulse Therapy TED Patients**

|                   | Mean   | SD    | Range        | 95% CI |        |
|-------------------|--------|-------|--------------|--------|--------|
|                   |        |       |              | Lower  | Upper  |
| <b>RNFL</b>       |        |       |              |        |        |
| 360° average      | 86.44  | 21.20 | 0 to 113     | 79.19  | 92.74  |
| Past RNFL         | 92.21  | 20.72 | 21 to 142    | 85.82  | 98.56  |
| Superior quadrant | 104.33 | 32.18 | 0 to 159     | 94.18  | 115.13 |
| Nasal quadrant    | 65.72  | 15.77 | 0 to 99      | 60.57  | 70.23  |
| Inferior quadrant | 105.38 | 33.35 | 0 to 151     | 95.00  | 115.49 |
| Temporal quadrant | 67.02  | 19.32 | 0 to 106     | 61.13  | 72.79  |
| RNFL symmetry     | 64.15  | 30.78 | 0 to 96      | 54.03  | 73.20  |
| <b>ONH</b>        |        |       |              |        |        |
| Rim area          | 1.20   | 0.42  | 0.43 to 2.08 | 1.09   | 1.35   |

|                    |          |        |       |               |        |        |
|--------------------|----------|--------|-------|---------------|--------|--------|
| Cup/disc ratio     | vertical | 0.64   | 0.16  | 0.18 to 0.89  | 0.59   | 0.69   |
| <b>Risk factor</b> |          |        |       |               |        |        |
| Age                |          | 48.87  | 15.84 | 15 to 75      | 43.54  | 53.82  |
| Refractive Error   |          | -0.21  | 1.21  | 1.50 to -6.00 | -0.62  | 0.12   |
| IOP                |          | 15.38  | 4.40  | 7 to 26       | 14.08  | 16.82  |
| Sistole            |          | 123.28 | 16.03 | 92 to 147     | 117.95 | 128.38 |
| Diastole           |          | 77.18  | 9.31  | 58 to 92      | 74.33  | 80.10  |

|                |          | <b>RNFL Symetry</b> | <b>Rim area</b> | <b>Vertical cup disc</b> | <b>Superior</b> | <b>Nasal</b> | <b>Inferior</b> | <b>Temporal</b> |
|----------------|----------|---------------------|-----------------|--------------------------|-----------------|--------------|-----------------|-----------------|
| RNFL thickness | <b>R</b> | 0.487               | 0.175           | -0.093                   | 0.915           | 0.749        | 0.897           | 0.702           |
|                | <b>P</b> | 0.002               | 0.286           | 0.574                    | <0.001          | <0.001       | <0.001          | <0.001          |

  

|                |          | <b>Past RNFL thickness</b> | <b>Gender</b> | <b>Age</b> | <b>Sphere</b> | <b>IOP</b> | <b>Sistole</b> | <b>Diastole</b> |
|----------------|----------|----------------------------|---------------|------------|---------------|------------|----------------|-----------------|
| RNFL thickness | <b>R</b> | 0.258                      | 0.441         | -0.387     | 0.005         | -0.234     | -0.418         | 0.060           |
|                | <b>P</b> | 0.113                      | 0.005         | 0.015      | 0.975         | 0.152      | 0.008          | 0.717           |

## DISCUSSION

The reduced RNFL thickness measured by OCT in glaucoma patients correlate with the presence of disease [4]. The result from OCT add another subjective examination such as funduscopy and visual field test.

From the findings that the significant difference in peripapillary and all RNFL quadrants between the glaucomatous and the control. That demonstrating the RNFL parameters can be quantified and detected prior to permanent visual loss. Structural damage of RNFL usually reported before visual loss [3].

Age is known as one of risk factor for POAG due to the prevalence was increased with age. the population in elderly people known as having higher risk for POAG. Aging related with higher IOP, thinner central corneal thickness [9].

With the racial demographic, the elevated IOP become the risk factor of glaucomatous progression an related with several risk factors including the female sex, thicker central corneal thickness, high myopia, high body mass index, high blood pressure, diabetes, and hyperlipidemia [10].

Longer axial length is proven to affect accuracy of OCT scan for thickness. So, we can not distinguish reduced thickness of inner retinal layers (including RNFL) in glaucoma patients with high myopia is due to increasing axial lengths or glaucomatous defects [11].

From the previous study, systolic blood pressure showed correlation with risk of glaucoma. High systolic blood pressure leads to initial optic nerve vascular compromise, which is subsequently further exacerbated by low blood pressure [8].

A hypothesis said that the relationship of hypertension causes vascular harm for optic nerve and lowering of blood pressure limit to blood flow to nerve in vascular dysregulation. The linear trend shows lower hazard compared normal systolic blood pressure[8].

From other studies, by using around 9390 participants from sixty-three studies show that mean RNFL thickness clinically informative in diagnosing glaucoma patients, especially inferior and superior give more information than temporal and nasal sector [12].

For ONH parameters, the sensitivities better in vertical cup/disc ratio than disc area with same specificity among them. Vertical cup/disc ratio superior among all ONH parameters [12].

The size of neuroretinal rim and cup are used for differential diagnosis of glaucoma so the disc estimation is important for assessment [13].

## REFERENCES

1. J.W.Nam, Y.S.Kang, M.S.Sung, and S.W. Park, "Clinical Evaluation of Unilateral Open- Angle Glaucoma: A Two-Year Follow-Up Study," *Chonnam Med. J.*, vol. 57, no. 2, p. 144, 2021, doi: 10.4068/cmj.2021.57.2.144.
2. M. bunod ophthalmic solution 0.024%. a new treatment option for open-angle glaucoma and ocular hypertension Fingeret, I. B. Gaddie, and M. Bloomenstein, "Latanoprostene bunod ophthalmic solution 0.024%: a new treatment option for open- angle glaucoma and ocular hypertension," *Clin. Exp. Optom.*, vol. 102, no. 6, pp. 541–550, 2019, doi: 10.1111/cxo.12853.
3. R. L. Bartlett *et al.*, "Quantifying biomarkers of axonal degeneration in early glaucoma to find the disc at risk," *Sci. Rep.*, vol. 12, no. 1, pp. 1–15, 2022, doi: 10.1038/s41598-022-12036-4.
4. M. Lever, C. Halfwassen, J. D. Unterlauff, N. E. Bechrakis, A. Manthey, and M. R. R. Böhm, "Retinal nerve fibre layer thickness measurements in childhood glaucoma: the role of scanning laser polarimetry and optical coherence tomography," *Graefe's Arch. Clin. Exp. Ophthalmol.*, vol. 259, no. 12, pp. 3777–3786, 2021, doi: 10.1007/s00417-021-05276-z.
5. G. Savini, M. Zanini, V. Carelli, A. A. Sadun, F. N. Ross-Cisneros, and P. Barboni, "Correlation between retinal nerve fibre layer thickness and optic nerve head size: An optical coherence tomography study," *Br. J. Ophthalmol.*, vol. 89, no. 4, pp. 489–492, 2005, doi: 10.1136/bjo.2004.052498.
6. A. Balasopoulou *et al.*, "Symposium Recent advances and challenges in the management of retinoblastoma Globe - saving Treatments," *BMC Ophthalmol.*, vol. 17, no. 1, p. 1, 2017, doi: 10.4103/ijo.IJO.
7. K.E.Kim, S.Oh, S.U.Baek, S.J.Ahn, K.H.Park, and J. W. Jeoung, "Ocular Perfusion Pressure and the Risk of Open-Angle Glaucoma: Systematic Review and Meta-analysis," *Sci. Rep.*, vol. 10, no. 1, pp. 1–12, 2020, doi: 10.1038/s41598-020-66914-w.
8. C. Macri *et al.*, "Blood Pressure Measures and Incident Primary Open-Angle Glaucoma," *Investig. Ophthalmol. Vis. Sci.*, vol. 63, no. 13, 2022, doi: 10.1167/iovs.63.13.3.
9. N. Zhang, J. Wang, Y. Li, and B. Jiang, "Prevalence of primary open angle glaucoma in the last 20 years: a meta-analysis and systematic review," *Sci. Rep.*, vol. 11, no. 1, pp. 1–12, 2021, doi: 10.1038/s41598-021-92971-w.
10. A. Belamkar, A. Harris, F. Oddone, A. Verticchio Vercellin, A. Fabczak-kubicka, and B. Siesky, "Asian Race and Primary Open-Angle Glaucoma: Where Do We Stand?," *J. Clin. Med.*, vol. 11, no. 9, 2022, doi: 10.3390/jcm11092486.
11. W. Wen, Y. Zhang, T. Zhang, and X. Sun, "Consistency between optical coherence tomography and Humphrey visual field for evaluating glaucomatous defects in high myopic eyes," *BMC Ophthalmol.*, vol. 20, no. 1, pp. 1–9, 2020, doi: 10.1186/s12886-020-01724-2.
12. M. Michelessi *et al.*, "Optic nerve head and fibre layer imaging for diagnosing glaucoma," *Cochrane Database Syst. Rev.*, vol. 2015, no. 11, 2015, doi: 10.1002/14651858.CD008803.pub2.
13. Joseph P. Califonia, "基因的改变 NIH Public Access," *Bone*, vol. 23, no. 1, pp. 1–7, 2008.