ORIGINAL ARTICLE

COMPARISON OF ONH, MACULA STRUCTURE AND HFA PATTERN IN HIGH MYOPIA AND EMETROPIA EYES WITH/WITHOUT GLAUCOMA

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ABSTRACT

Introduction: *Axial length elongation contributes a challenge in myopia eyes due to morphological and visual field abnormalities. OCT instruments do not embed a normative database from high myopia. The study is aimed to compare Cirrus OCT and HFA parameters on high myopia and emetropia with/without glaucoma.*

Methods: *This cross-sectional, prospective study was conducted at Sardjito General Hospital from 1st April 2021 to 11th May 2021. Patients with high myopia was enrolled with Spherical Equivalent (SE) ≥ -6D, 20 – 55 years of age. All participants underwent a complete ophthalmologic examination. Inclusion criteria: BCVA 20/40 or better, reliable visual field results.*

Result: *From 22 eyes, there were no significant difference of age between high myopia with glaucoma/HMG (n=5), high myopia/HM (n=6), emetropia with glaucoma/EG (n=5), emetropia/E (n=6) with mean age was 36±3.2 y.o and 60% were male with SE -8.5±1.03D. Among ONH parameters, there were no differences between groups. In HMG, HM, EG, E group, median avgRNFL was 85um, 96.5um, 105um, 110um respectively. Thus, median vertical CD is 0.48, 0.40, 0.58, 0.55 in HMG, HM, EG, E group respectively. Whilst median GCIPL and visual index were 75um, 78.5um, 85um, 89.5um in HMG, HM, EG, E group respectively and had significantly different 0.012 ($p<0.05$) between groups. Median visual field index was 92%, 97%, 98% in HMG, HM, EG group respectively with significantly different 0.04 ($p<0.05$).*

Conclusion: *The GCIPL and visual field index are significantly different between high myopia and emetropia with/without glaucoma*

Keywords: Glaucoma, myopia, OCT

INTRODUCTION

Based on population study[1], Asians are the highest rates of myopia in the world. The cut-off value of high-axial myopia is ranging from refractive error – 6 to – 8 diopters (D) of refractive error or 26–26.5 mm of axial length. Myopia is an independent risk factor for glaucoma. Subjects with myopia have a two- to threefold increase in the risk of developing glaucoma compared to nonmyopic eyes, and the risk of developing glaucoma increases with the increasing degree of myopia. The papil condition on high myopia patients is tilting, large ovalness index, deformation of the disc, pale disc, shallow and large cup, large peripapillary

Ophthalmol Ina 2023;Vol. 49(1):10-17

crescent, and occasional optic disc hypoplasia. It confounds the diagnosed glaucoma in high myopia eyes.[2]

In the last decade, Optical Coherence Tomography (OCT) has been widely used for assessing retina and optic nerve by providing quantitative and qualitative assessment of macula and retinal nerve fiber layer (RNFL). Even though clinicians need to determine glaucoma diagnosis in patients with high myopia before using it, Spectral domain-optical coherence tomography (SD-OCT) imaging gives more advantage than time domain-optical coherence tomography (TD-OCT), such as the increasing of depth resolution and faster acquisition.[1] Only few studies were reported on the utilization of SD-OCT in high myopia eyes with concomitant glaucoma. In order that, this study is aimed to compare Cirrus OCT and HFA parameters on high myopia and emetropia on patient with/without glaucoma.

METHODS

This cross-sectional study included patients presenting to the outpatient service of Sardjito General Hospital between 1st April 2021 and 11th May 2021, who satisfied the inclusion and exclusion criteria described below. Patients with high myopia with Spherical Equivalent ≥ -6D and 20 - 55 years of age were enrolled. Written informed consent was obtained from participants before enrolment. In present study, the SD-OCT system used GCIPL, RNFL, ONH, three-dimensional optic disc parameters and angiography.

All participants underwent a complete ophthalmologic examination, including assessment of medical and family history, visual acuity testing with refraction, anterior segment evaluating with slit lamp biomicroscopy, intraocular pressure measurement with Non-Contact Tonometery, visual field test with HFA 24-2 SITA Standard, dilated pupil for funduscopic examination and OCT ONH and Macula. Inclusion criteria for all participants were as follows: best corrected visual acuity 20/40 or better, healthy anterior segment appearance on slit lamp biomicroscopy examination, reliable visual field results (fixation loss ≤20%, false positives ≤ 15%, false negative ≤15%) and reliable OCT ONH result with signal strength >7. Subjects were then excluded if any other disease affecting the visual field (neuroopthalmological disease, uveitis, retinal and choroidal disease, trauma) was found. As the purpose of this study, participants were categorized as showing high myopia with glaucoma (HMG), high myopia without glaucoma (HM), emetropia with glaucoma (EG) and emetropia without glaucoma (E). The HM and E eyes were those with IOP ≤21 mmHg and normal visual field results. The HMG and EG eyes displayed glaucomatous abnormal visual field results and IOP ≤21 mmHg, this condition classified into normotension glaucoma on high myopia group and primary open angle

glaucoma under treatment on emetrop group. Diagnosis of glaucoma depends on a glaucomatous VF defect which done minimal twice examination, that was defined as either a cluster of two independent points depressed by ≥10 dB in the comparison visual field or three adjacent points depressed by ≥5 dB. The grading criteria for glaucomatous defects were adapted from the Ocular Hypertension Treatment Study visual field criteria are nasal step, early arcuate, advanced arcuate with additional myopic related defects added including generalized sensitivity loss, paracentral defect, central defect, and differentiated visual field defect due to myopia itself at least 2 abnormal edge point around the blind spot (enlarged blind spot), minimum criteria for a defect but no pattern (suspicious for abnormal).

Instrumentation

The study used SD-OCT (Zeiss, Cirrus HD-OCT 5000/500) with New PanoMap Analysis which wide-field structural damage assessment for glaucoma. Ganglion cell was analyzed based on the macular cube 512x128 or 200x200 scan. This analysis provides quantitative and qualitative evaluation of the ganglion cell layer (GCL) plus inner plexiform layer (IPL). RNFL and ONH analyses based on the 6mm x 6mm data cube were captured by the optic disc cube 200x200 scan. Macular thickness analysis based on the 6mm x 6mm data cube was captured by the macular cube 512x128 or 200x200 scan. This analysis provides qualitative and quantitative evaluation of the retina.

This study uses Humphrey Field Analyzer 3 from Zeiss with central 24-2 SITA Standard test pattern. Visual field indices based on visual field index (VFI), mean deviation (MD) and pattern standard deviation (PSD).

Statistical Analysis

Data from both eyes which are eligible for analysis will be selected and used for following analysis. First, baseline characteristics were reported in counts and mean ± SD values and frequencies and percentages for categorical variables (Table 1). Second, the distribution of diagnostic parameters measured with SD-OCT was presented using median with 25^{th} and 75^{th} percentiles. Third, the defect of visual field measured with HFA 24-2 SITA Standard was presented using median with 25^{th} and 75^{th} percentiles (Table 2). Finally, categorical variable was used for assessing the high myopia and glaucoma on diagnostic parameters.

Ophthalmol Ina 2023;Vol. 49(1):10-17

Table 1. Baseline characteristics of four groups

	Overall n=22	HMG Group n=5	HM Group n=6	EG Group n=5	E Group n=6	p-value
Age (years), mean ± SD	33.31 ± 10.39	36.20 ± 7.35	24.19 ± 4.81	34.95 ± 13.90	38.65 ± 9.36	0.056*
Sex						
Female, n (%)	9 (40.9)	5 (100)	2 (33.3)	2 (40)	0 (0)	N/A
Male, n (%)	13 (59.1)	0 (0)	4 (66.7)	3 (60)	6 (100)	
Refraction, spherical equivalent (D), median (IQR)	-7.0 (-9.5, -6.6)	-7.0 (-8.5, -6.4)	-7.3 (-11.6, 6.6)	-	-	0.461*

Abbreviations: HMG, high myopia with glaucoma; HM, high myopia without glaucoma; EG, emetropia with glaucoma; and E, emetropia without glaucoma.
Baseline characteristics were compared using the unpaired t-test or chi square test, as appropriate, between the groups.
*Independent-samples Kruskal-Wallis Test

Table 2. The parameters of OCT ONH, macular retinal nerve fiber layer, and HFA pattern on four groups

Parameter	Overall n=22	HMG Group n=5	HM Group n=6	EG Group n=5	E Group n=6	p-value*
OCT ONH						
Average RNFL (µm)	104.5 (92.5, 108.3)	85.0 (81, 107.5)	96,5 (90, 107)	105.0 (98.5, 110)	110.0 (102.8, 114.8)	0.086
Vertical CD	0.52 (0.41, 0.65)	0.480 (0.280, 0.755)	0.400 (0.265, 0.485)	0.580 (0.535, 0.660)	0.545 (0.483, 0.665)	0.113
Flux index	0.45 (0.43, 0.46)	0.444 (0.419, 0.447)	0.435 (0.422, 0.458)	0.436 (0.406, 0.468)	0.465 (0.457, 0.475)	0.066
Perfusion (%)	0.45 (0.44, 0.47)	44.9 (44.5, 50.6%)	45.7 (45.3, 47.4%)	44.5 (42.3, 48.3%)	44.5 (43.9, 45.0%)	0.175
Macular retinal nerve fiber layer						
GCIPL (µm)	83.5 (75,8 89.3)	75.0 (68.5, 90.0)	78.5 (74.8, 80.8)	85.0 (83.5, 91.0)	89.5 (86.0, 93.0)	0.012**
HFA Pattern						
Visual Field Index (%)	97.0 (89.8, 98.3)	92.0 (86.5, 96.0)	97.0 (83.5, 97.3)	98.0 (91.5, 99.0)	-	0.040**
MD (dB)	-3.63 (-7.06, -1.47)	-3.72 (-6.69, -2.89)	-5.68 (-9.84, -3.08)	-2.91 (-6.40, -0.54)	-0.30 (-0.51, -0.09)	0.095

Abbreviations: HMG, high myopia with glaucoma; HM, high myopia without glaucoma; EG, emetropia with glaucoma; and E, emetropia without glaucoma.
* Independent-samples Kruskal-Wallis Test
**Statistically significance ($p<0.05$)

RESULTS

Twenty-four patients (22 eyes) were examined from eye outpatient at Dr. Sardjito General Hospital. Afterward, those were categorized as high myopia with glaucoma/HMG group (5 eyes), high myopia/HM group (6 eyes), emetropia with glaucoma/EG group (5 eyes), emetropia/E group (6 eyes). The severity of glaucoma each group are not included in this study because minimal sample and this one of the limitation, the severity level of glaucoma might effect the result. The laterality of eye on HMG and EG was excluded because OCT angiography analysis is unreliable and SE ≤-6.0 respectively. Thus, a total of 22 eyes were included in this study. The characteristics of participants in four groups are summarized in Table 1. There was no significant difference of age between high myopia with glaucoma (HMG) group, high myopia (HM) group, emetropia with glaucoma (EG) group, emetropia (E) group. The mean age of overall population was 33.1±10.39 y.o and about 13 (60%) were male with Spherical Equivalent -7 (IQR: -9.5D – -6.6D).

The parameters of OCT ONH, macular retinal nerve fiber layer, and HFA pattern on four groups are listed in Table 2. Among ONH parameters, there were no differences between groups for RNFL, vertical CD, flux index, perfusion ($p>0.05$). For the macular retinal nerve fiber layer, the GCIPL was significantly different ($p<0.05$) between groups. Among HFA pattern, visual field index was significantly different between groups ($p<0.05$).

The comparisons of system parameters in glaucoma group vs non glaucoma group and high myopia vs emetropia are listed in Table 3. Among ONH parameters there were significantly difference ($p<0.05$) in average RNFL, vertical CD, and perfusion between high myopia group vs emetropia group. For the macular retinal nerve fiber layer, the GCIPL was significantly different ($p<0.05$) between high myopia vs emetropia group. Among HFA pattern, visual field index was significantly different between high myopia vs emetropia group ($p<0.05$). Between glaucoma group and non-glaucoma group, there were no significantly difference in OCT ONH, macular retinal nerve fiber layer, and HFA pattern.

DISCUSSION

Optic disc configuration measurements, such as rim volume and C/D vertical ratio are some important diagnostic parameters for glaucoma. The optic disc of high myopia eyes, which is frequently associated with tilting, peripapillary atrophy, oval configuration may influence the algorithms such as circle size scan and disc margin definition.[3] The relationship between p-RNFL measurement and degree of myopia is controversial. Regarding to p-RNFL

Ophthalmol Ina 2023;Vol. 49(1):10-17

measurement, Hoh *et al*.[4] reported that the mean p-RNFL thickness did not vary on myopia or axial length, others have stated that high myopia had different topographic profiles compared with low myopia.[5]

Table 3. Comparison of system parameters in glaucoma vs non glaucoma, and high myopia vs emetropia

Parameters	Glaucoma n=10	Non-Glaucoma n=12	p-value*	High Myopia n=11	Emetropia n=11	p-value*
OCT ONH						
Average RNFL (µm)	104.5 (84.8, 107.3)	105.0 (96.3, 110.5)	0.381	96.0 (85.0, 107.0)	107.0 (103.0, 113.0)	0.016**
Vertical CD	0.57 (0.44, 0.69)	0.48 (0.38, 0.57)	0.228	0.44 (0.32, 0.56)	0.57 (0.51, 0.66)	0.040**
Flux index	0.440 (0.417, 0.453)	0.457 (0.434, 0.469)	0.123	0.438 (0.423, 0.449)	0.463 (0.436, 0.472)	0.076
Perfusion (%)	0.449 (0.443, 0.483)	0.451 (0.444, 0.458)	0.821	0.456 (0.448, 0.474)	0.445 (0.441, 0.453)	0.047**
Macular retinal nerve fiber layer						
GCIPL (µm)	83.5 (74.5, 90.0)	84.5 (78.3, 89.8)	0.628	76.0 (74.0, 80.0)	89.0 (85.0, 92.0)	0.001**
HFA Pattern						
Visual Field Index (%)	96.0 (89.8, 98.3)	97.0 (87.3, 99.5)	0.573	95.0 (84.0, 97.0)	99.0 (97.0, 100.0)	0.011**
MD (dB)	-3.53, (-5.96. -2.01)	-4.09 (-8.61, -0.82)	0.829	-4.65 (--8.15, -3.34)	-0.70 (-3.80, -0.38)	0.044**

Abbreviations: HMG, high myopia with glaucoma; HM, high myopia without glaucoma; EG, emetropia with glaucoma; and E, emetropia without glaucoma.
* Independent-samples Mann-Whitney U Test
** Statistically significance ($p<0.05$)

Our study is concerned on average RNFL, vertical CD, flux index, and perfusion. The difference was statistically not significant ($p>0.05$) in four groups. Conversely, there was significant different ($p<0.05$) for average RNFL, vertical CD and perfusion in high myopia group vs emetropia group. The present study implies that the OCT ONH parameters are ineffective for detecting glaucoma patients with high myopia, but it can discriminate topographic profiles on high myopia.

The role of macular thickness parameters in detecting glaucoma has been previously reported, as ganglion cells are thickest at the perifovea (constitute 35% of retinal thickness). The higher-resolution SD-OCT system allows measurement of ganglion cell complex, reflected

the death of ganglion cells, and showed good ability to discriminate between glaucoma patients and nonglaucoma subjects in high myopia subgroups.[2] Our study, concerned on GCIPL, there was significant different ($p<0.05$) between four groups, and also between high myopia group and emetropia group. The present study implies that the influence of high myopia on GCIPL may be less than that on ONH parameters.

The highlight of high myopia group vs emetropia group. The OCT parameters were significantly difference 0.016, 0.040, 0.047 in average RNFL, vertical CD, perfusion respectively. The GCIPL and visual field index was significantly different 0.001 and 0.04 ($p<0.05$). The previous study reported that a good level of association was observed between the strength of correlation between points in the VF and the relative location of those test points in the peripheral retina and in corresponding RNFL bundles at the ONH which described the anatomic organization of the ONH and glaucomatous disease process.

Several limitations were applied to this study. First, this study is conducted on limited eye samples. All group has VFI data except for emetrop group. Emetrop group is assumed as normal VFI. However, samples can be still discriminated between high myopia eyes with glaucoma and the others regarding to that limitation. Second, glaucoma was only diagnosed based on HFA pattern to avoid the bias analysis of optic configuration parameters.

CONCLUSION

GCIPL and visual field index are significant difference between eyes with high myopia and emetropia with/without glaucoma. This could be an interesting result because these parameters were compared to the normative database which does not include high myopia. These parameters provide valuable information for assessing high myopia patients with glaucoma. Nevertheless, further research is required using more subject.

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