

Comparison of Optic Disc Morphology Between Glaucomatous and Non-Glaucomatous Myopic Eyes Using Swept-Source Optical Coherence Tomography (SS-OCT)

Wan Nuramalin Wan Abd Manas¹, Mohd Radzi Hilmi^{2,*}, James Stuart Wolffsohn³

¹Department of Optometry and Visual Sciences, Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Pahang, Malaysia

²Integrated Omics Research Group (IORG), Kulliyah of Allied Health Sciences, International Islamic University Malaysia, Pahang, Malaysia

³Ophthalmic Research Group, Aston University, Birmingham, UK.

ABSTRACT

Background: The rising global prevalence of myopia is a growing concern for clinicians, as it predisposes patients to severe ocular pathologies including glaucoma. Myopia can be associated with clinical features that resemble glaucomatous damage, which make an accurate glaucoma diagnosis challenging, particularly among patients with normal intraocular pressures. This study aimed to compare the optic disc morphology, macular retinal ganglion cell layer and retinal nerve fiber layer (RNFL) between non-glaucomatous and glaucomatous myopic eyes using swept-source optical coherence tomography (SS-OCT). **Methods:** 100 participants were recruited which included 50 glaucomatous eyes and 50 non-glaucomatous eyes. All participants underwent standard optometric examination which includes best-corrected visual acuity (BCVA), standard retinoscopy, slit-lamp biomicroscopy, intraocular (IOP) measurement, visual field testing using automated perimetry and fundus examination using SS-OCT. The SS-OCT modalities used for optic nerve head measurements (rim area, disc area, vertical cup-to-disc ratio and cup volume) was 3D Disc 6.0×6.0 mm mode while 3D Macula 7.0×7.0 mm mode was used for macula area measurements. **Results:** The disc area, rim area, vertical cup-to-disc ratio, cup volume, macular ganglion cell layer and total retinal nerve fibre layer thickness were all found comparable between glaucomatous and non-glaucomatous groups (all $P > 0.05$). **Conclusion:** This study found no significant differences in the optic disc parameters and macular ganglion cell layer of glaucomatous and non-glaucomatous myopic eyes.

Keywords:

glaucoma; myopia; optic disc; ganglion cell layer; retinal nerve fiber layer

INTRODUCTION

Myopia is a common visual impairment worldwide, with increased prevalence were noted especially in developing countries including Malaysia. Developing countries and asian countries has been noted as having higher probability of having myopia (Melo et al., 2006; Sung et al., 2016). Changes in behaviours and predominant near work among younger generation has been noted as one of main contributors of myopia (Sun et al., 2023). The association of myopia and primary open angle glaucoma (POAG) is well established (Jonas et al., 2020; Zhang et al., 2022). Many studies had confirmed the association were even more prominent in higher degree of myopia (Xu et al., 2007; Kuzin et al., 2010; Perera et al., 2010; Czudowska et al., 2010).

Glaucoma is a group of disorders with characteristic of progressive degeneration of the optic nerve, with loss of retinal ganglion cells, thinning of the retinal nerve fiber layer (RNFL), and increasing excavation of the optic disc (Schuster et al, 2020). The pathophysiology of glaucoma is complex with increased in intraocular pressure (IOP) and low perfusion pressure leads to increase in gradient across the lamina cribrosa (LC), which cause papillary hypoperfusion. This process leads to changes in structural and remodelling of LC, which cause disruption of axonal transport in the optic nerve fibres. Previous studies had suggested that optic disc (Zhang et al., 2022; Sugihara et al., 2021), macular retinal ganglion cell layer (Nouri-Mahdavi et al., 2013; Seo et al., 2017) and retinal nerve fiber layer (RNFL) (Knight et al., 2012; Yamashita et al., 2013) are important structures in detecting glaucoma.

* Corresponding author.

E-mail address: mohdradzihilmi@iium.edu.my

However, there are limited evidence on comparison of optic disc characteristics in non-glaucomatous and glaucomatous myopic patients in Malaysia population. Thus, this study aimed to compare the morphological

METHODS

100 participants were recruited in this prospective cross-sectional study, based on their visits in a university-based Optometry clinic. All patients were briefed and informed about all procedures and their consent obtained prior to data acquisition. This study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the institution ethical board (IREC 2019-KAHS(U)). The inclusion criteria includes aged 20 - 50, spherical equivalent refraction (SER) from -0.50 to -7.00 DS (Jonas et al., 2002) and axial length between 22 to 26 mm. For the control/non-glaucomatous group, additional criteria were set which includes IOP < 20 mmHg, absence of glaucomatous optic neuropathy, nerve fiber layer defects and glaucomatous VF defects (Schuster et al., 2020). While for glaucomatous group, presence of glaucomatous optic neuropathy and VF damage. Patients with significant ocular surface diseases such as recurrent pterygium, corneal opacity or irregularity were excluded (Che Azemin et al., 2016; Hilmi et al., 2019; Hilmi et al., 2020). A condition in which fundus photography could not be measured due to obstruction of the central cornea were also excluded (Hilmi et al., 2019; Noor Syahira et al., 2020).

All participants underwent standard optometric examination which includes best-corrected visual acuity (BCVA) measurement using LogMAR chart, slit-lamp biomicroscopy, Goldmann Applanation Tonometry (GAT) and anterior chamber angle was measured using anterior OCT (CASIA-2; Tomey Corporation, Nagoya, Japan). Visual field (VF) testing were done using automated perimetry Humphrey Field Analyzer (HFA III)(Zeiss Meditec Inc, Jena, Germany) utilising 30-2 testing modality (Okimoto et al., 2015). The evaluations were carried out on all eyes, excluding those that were unreliable (fixation loss < 20%; false-positive and false-negative, <15%). Abnormal visual field was defined by the presence of at least one abnormal hemifield (Yohannan et al., 2017).

Fundus examinations were done using SS-OCT (DRI Triton, Topcon, Nagoya, Japan). The morphological features of optic disc, macular retinal ganglion cell layer and RNFL were measured using specific modality of SS-

features of optic disc, macular retinal ganglion cell layer and RNFL in non-glaucomatous and glaucomatous myopic eyes using swept-source optical coherence tomography (SS-OCT).

OCT. For optic nerve head measurements (rim area, disc area, vertical cup-to-disc ratio and cup volume) 3D Disc 6.0×6.0 mm mode was used and for macula area measurements 3D Macula 7.0×7.0 mm mode was used (Wichrowska et al., 2022). All procedures were completed within the same day and the diagnosis was confirmed by a senior consultant ophthalmologist. All data were presented as mean and standard deviation. The normality of the data was analysed using Shapiro-Wilk test. Differences in parameters between two groups then were compared by using independent t-tests. The alpha significance level was set at $P < 0.05$. All statistical analyses were performed using IBM SPSS (Predictive analytics software) (version 12, SPSS Inc., Chicago, IL, USA).

RESULTS

This study included 100 eyes of 50 glaucomatous participants and 50 non-glaucomatous. All data were normally distributed. The mean age and SER for both glaucomatous and non-glaucomatous were comparable with 25.5 ± 5.34 years and 23.2 ± 6.53 years respectively ($P = 0.766$), while the SER was -2.55 ± 1.34 D and -2.42 ± 1.29 D respectively ($P = 0.453$). In light of the intended parameters, this study found no significant difference in all parameters (Disc area, Rim area, Vertical CDR, Cup volume, Macular ganglion cell, total RNFL thickness).

For the optic nerve head parameters, the mean disc area for both glaucomatous and non-glaucomatous group were $1.98 \pm 0.43\text{mm}^2$ and $1.96 \pm 0.42\text{mm}^2$ respectively, $P = 0.812$). The mean rims area for both glaucomatous and non-glaucomatous group were $1.27 \pm 0.26\text{mm}^2$ and $1.28 \pm 0.23\text{mm}^2$ respectively, $P = 0.844$). Meanwhile for mean vertical CDR for both glaucomatous and non-glaucomatous group were 0.54 ± 0.14 and 0.52 ± 0.13 respectively, $P = 0.566$). And lastly, the mean cup volume for both glaucomatous and non-glaucomatous group were $(0.20 \pm 0.12 \text{ mm}^3)$ and $(0.15 \pm 0.15\text{mm}^3)$ respectively, $P=0.081$). For the retinal layer parameters, the mean macular ganglion cell layer for both glaucomatous and non-glaucomatous group were $63.95 \pm 3.03\mu\text{m}$ and $64.84 \pm 3.57\mu\text{m}$ respectively, $P = 0.213$). Lastly, the mean total retinal nerve fiber layer for both glaucomatous and non-glaucomatous group were $106.41 \pm 4.99\mu\text{m}$ and $108.45 \pm 8.47\mu\text{m}$ respectively, $P = 0.171$). All findings were summarised in Table 1.

Table 1: Parameters of glaucomatous and non-glaucomatous myopic eyes

Group	Age (years) Mean (SD)	SER (D) Mean (SD)	Disc Area (mm ²) Mean (SD)	Rim Area (mm ²) Mean (SD)	Vertical CDR Mean (SD)	Cup Volume (mm ³) Mean (SD)	MGC layer (µm) Mean (SD)	RNFL thickness (µm) Mean (SD)
Glaucomatous	25.5 (5.34)	-2.55 (1.34)	1.98 (0.43)	1.27 (0.26)	0.54 (0.14)	0.20 (0.12)	63.95 (3.03)	106.41 (4.99)
Nonglaucomatous	23.2 (6.53)	-2.42 (1.29)	1.96 (0.42)	1.28 (0.23)	0.52 (0.13)	0.15 (0.15)	64.84 (3.57)	108.45 (8.47)
P-value	0.766	0.453	.812	.844	.566	.081	.213	.171

SER: Spherical Equivalent Refraction

SD: Standard deviation

RNFL: Retinal nerve fiber layer

CDR: Cup-to-disc ratio

MGC: Macular ganglion cell

DISCUSSION

The current study intended to compare optic nerve head (disc area, rim area, vertical CDR and cup volume) and retinal layers (MGC layer and RNFL thickness) parameters between glaucomatous and non-glaucomatous myopic eyes using SS-OCT. Based on fundus image obtained, the appearances of the optic nerve head image between glaucomatous and non-glaucomatous eyes were clearly distinct as glaucomatous eye has larger CDR and pale colour compared to non-glaucomatous myopic eye which has normal orange-yellow appearance as in Figure 1 (a) and (b). This study found that there is no significant difference in optic nerve head and retinal layers parameters between glaucomatous and non-glaucomatous myopic eyes. This is in agreement with a previous work (Melo et al., 2006). However, this could be due to the comparison been made based on two different instrument.

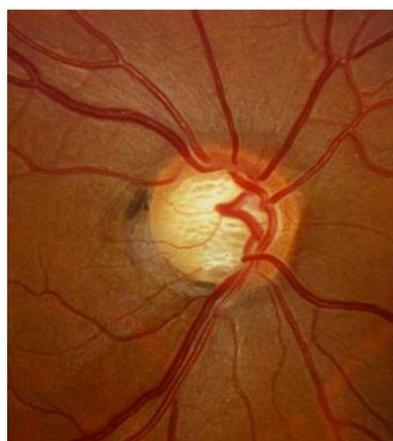


Figure 1 (a) Glaucomatous myopia

We postulate that these indifferences in our findings could be due to the degree of myopia of the

glaucomatous group. Our sample population has lower SER compared to other studies. Previous work (Nakano et al., 2013) had commented that the higher the degree of myopia, more changes in the structural of optic nerve head can be observed. Another possible reason could be this study only comparing the average value of each parameter and not comparing the value in the quadrants. Previous study that take measurements from inferior and superior quadrants reported that peripapillary RNFL values are superior to macular RNFL thickness in giving diagnosis to glaucoma (Sung et al., 2015). This is due to retinal ganglion cell with large axons is more susceptible to damage than the ganglion cell with small axons in macula, however these large axons were commonly seen in the inferior retina (Öztürker et al., 2016; Han et al., 2017). They also reported that the large optic disc or macrodisc can give overestimation of the RNFL thickness as the measurement is taken close to the edge of optic disc, the distance of the scan with the



Figure 1 (b) Non-glaucomatous myopia

optic disc will be less as it is restricted with the large disc size. Also, they also reported that the true analysis of

RNFL and optic disc could be influenced with axial length variation. However, the current study managed to control this factor by only taken participants that within acceptable refractive error and axial length.

The depth and thickness of lamina cribrosa (LC) are also useful to differentiate between glaucomatous and non-glaucomatous eyes. Previous works (Hata et al. 2014; Yoshikawa et al. 2018) had commented that the depth of LC were deeper, with its thickness were found lesser in glaucomatous compared to non-glaucomatous eyes. This happen could be due to the measurement of LC depth could be including the Bruch membrane opening (BMO) and also influenced by the thickness of choroid. However, in this current study, choroid thickness was not measured. This study found that the macular ganglion cell were comparable between glaucomatous and non-glaucomatous eyes. This is contrary with other studies. Previous study (Rao et al., 2016; Nakano et al, 2013) commented that the difference could be due to lack of sensitivity of the test in differentiating or detecting glaucoma in low myopia, not as in high myopia group. This could reflect limitation in this current study as our study sample were relatively low myopia.

Further investigations are suggested in relation between optic disc morphology and glaucoma with/without myopia. Longitudinal study on the timeline of structural changes in the optic nerve head may help differentiate myopia-related optic disc changes from glaucomatous damage. Age-related differences in optic disc morphology also can be further explored as both aging and myopia influence the optic disc, and age-related changes may exacerbate glaucoma risk. Regional variations in the optic disc and peripapillary area also another area could be worth to explore as certain regions of the optic disc (e.g., inferior-temporal) are more vulnerable to glaucomatous damage.

CONCLUSION

This study found no significant differences in the optic disc parameters and macular ganglion cell layer of glaucomatous and non-glaucomatous myopic eyes.

ACKNOWLEDGEMENT

This research was not funded by any grant

REFERENCES

Che Azemin, M.Z., Mohd Tamrin, M.I., Hilmi, M.R., Mohd Kamal, K. (2016). Inter-grader reliability of a supervised pterygium redness grading system. *Advance Science Letter*, 22(10), 2885-2888.

Czudowska, M. A., Ramdas, W. D., Wolfs, R. C., Hofman, A., De Jong, P. T., Vingerling, J. R., & Jansonius, N. M. (2010). Incidence of glaucomatous visual field loss: a ten-year follow-up from the Rotterdam Study. *Ophthalmology*, 117(9), 1705–1712. <https://doi.org/10.1016/j.ophtha.2010.01.034>

Han, S., Sung, K. R., Park, J., Yoon, J. Y., & Shin, J. W. (2017). Sub-classification of myopic glaucomatous eyes according to optic disc and peripapillary features. *PloS one*, 12(7), e0181841. <https://doi.org/10.1371/journal.pone.0181841>

Jonas, J. B., Martus, P., & Budde, W. M. (2002). Anisometropia and degree of optic nerve damage in chronic open-angle glaucoma. *American journal of ophthalmology*, 134(4), 547–551. [https://doi.org/10.1016/s0002-9394\(02\)01644-6](https://doi.org/10.1016/s0002-9394(02)01644-6)

Jonas, J. B., Wang, Y. X., Dong, L., & Panda-Jonas, S. (2020). High Myopia and Glaucoma-Like Optic Neuropathy. *Asia-Pacific journal of ophthalmology (Philadelphia, Pa.)*, 9(3), 234–238. <https://doi.org/10.1097/APO.0000000000000288>

Knight, O. J., Girkin, C. A., Budenz, D. L., Durbin, M. K., Feuer, W. J., & Cirrus OCT Normative Database Study Group (2012). Effect of race, age, and axial length on optic nerve head parameters and retinal nerve fiber layer thickness measured by Cirrus HD-OCT. *Archives of ophthalmology (Chicago, Ill. : 1960)*, 130(3), 312–318. <https://doi.org/10.1001/archophthalmol.2011.1576>

Kuzin, A. A., Varma, R., Reddy, H. S., Torres, M., Azen, S. P., & Los Angeles Latino Eye Study Group (2010). Ocular biometry and open-angle glaucoma: the Los Angeles Latino Eye Study. *Ophthalmology*, 117(9), 1713–1719. <https://doi.org/10.1016/j.ophtha.2010.01.035>

Melo, G. B., Libera, R. D., Barbosa, A. S., Pereira, L. M., Doi, L. M., & Melo, L. A., Jr (2006). Comparison of optic disk and retinal nerve fiber layer thickness in nonglaucomatous and glaucomatous patients with high myopia. *American journal of ophthalmology*, 142(5), 858–860. <https://doi.org/10.1016/j.ajo.2006.05.022>

Hata, M., Miyamoto, K., Oishi, A., Makiyama, Y., Gotoh, N., Kimura, Y., Akagi, T., & Yoshimura, N. (2014). Comparison of optic disc morphology of optic nerve atrophy between compressive optic neuropathy and glaucomatous optic neuropathy. *PloS one*, 9(11), e112403. <https://doi.org/10.1371/journal.pone.0112403>

- Hilmi, M.R., Khairidzan, M.K., Ariffin, A.E., Norazmar, N.A., Maruziki, N.N., Musa, N.H., Nasir, M.S., Azemin, M.Z.C., Azami, M.H., Abdul Rahim, M.A.S. (2020). Effects of Different Types of Primary Pterygium on Changes in Oculovisual Function. *Sains Malaysiana*, 49(2), 383-388. <http://dx.doi.org/10.17576/jsm-2020-4902-16>
- Hilmi, M.R., Maruziki, N.N., Khairidzan, M.K., Azemin, M.Z.C., Norazmar, NA, Nasir MS, Musa NH 2019. Topographic Changes As Predictor For Determining Anterior Corneal Curvature Stabilization Point Subsequent To Pterygium Excision Using Controlled Partial Avulsion Fibrin Glue Technique. *International Journal Of Allied Health Sciences*, 3(2), 734-740.
- Hilmi, M.R., Musa, N.H., Khairidzan, M.K., Azemin, M.Z.C., Maruziki, N.N., Norazmar, N.A., Nasir, M.S. (2019). Changes In Apical Corneal Curvature In Unilateral Primary Pterygium And Normal Adults Using Simulated-K And Corneal Irregularity Measurement. *International Journal Of Allied Health Sciences*, 3(2), 588-594.
- Nakano, N., Hangai, M., Noma, H., Nukada, M., Mori, S., Morooka, S., Takayama, K., Kimura, Y., Ikeda, H. O., Akagi, T., & Yoshimura, N. (2013). Macular imaging in highly myopic eyes with and without glaucoma. *American journal of ophthalmology*, 156(3), 511–523.e6. <https://doi.org/10.1016/j.ajo.2013.04.028>
- Nouri-Mahdavi, K., Nowroozizadeh, S., Nassiri, N., Cirineo, N., Knipping, S., Giacconi, J., & Caprioli, J. (2013). Macular ganglion cell/inner plexiform layer measurements by spectral domain optical coherence tomography for detection of early glaucoma and comparison to retinal nerve fiber layer measurements. *American journal of ophthalmology*, 156(6), 1297–1307.e2. <https://doi.org/10.1016/j.ajo.2013.08.001>
- Noor Syahira, C.R., Mohd Radzi, H., Khairidzan, M.K., Muziman, M.S.M.M. (2020). Association of net pterygium tissue mass (dryweight) in determining changes in oculovisual functions and anterior corneal curvature relative to pterygium types. *International Journal of Allied Health Sciences*, 4(1), 1042-1048.
- Okimoto, S., Yamashita, K., Shibata, T., & Kiuchi, Y. (2015). Morphological features and important parameters of large optic discs for diagnosing glaucoma. *PloS one*, 10(3), e0118920. <https://doi.org/10.1371/journal.pone.0118920>
- Öztürker, Z. K., Eltutar, K., Karini, B., Erkul, S. Ö., Osmanbaşoğlu, Ö. A., & Sultan, P. (2016). Optic nerve head topography and retinal structural changes in eyes with macrodisks: a comparative study with spectral domain optical coherence tomography. *Clinical ophthalmology (Auckland, N.Z.)*, 10, 1737–1742. <https://doi.org/10.2147/OPHTH.S102789>
- Perera, S. A., Wong, T. Y., Tay, W. T., Foster, P. J., Saw, S. M., & Aung, T. (2010). Refractive error, axial dimensions, and primary open-angle glaucoma: the Singapore Malay Eye Study. *Archives of ophthalmology (Chicago, Ill. : 1960)*, 128(7), 900–905. <https://doi.org/10.1001/archophthamol.2010.125>
- Rao, H. L., Kumar, A. U., Bonala, S. R., Yogesh, K., & Lakshmi, B. (2016). Repeatability of Spectral Domain Optical Coherence Tomography Measurements in High Myopia. *Journal of glaucoma*, 25(5), e526–e530. <https://doi.org/10.1097/IJG.0000000000000385>
- Schuster, A. K., Erb, C., Hoffmann, E. M., Dietlein, T., & Pfeiffer, N. (2020). The Diagnosis and Treatment of Glaucoma. *Deutsches Arzteblatt international*, 117(13), 225–234. <https://doi.org/10.3238/arztebl.2020.0225>
- Seo, S., Lee, C. E., Jeong, J. H., Park, K. H., Kim, D. M., & Jeoung, J. W. (2017). Ganglion cell-inner plexiform layer and retinal nerve fiber layer thickness according to myopia and optic disc area: a quantitative and three-dimensional analysis. *BMC ophthalmology*, 17(1), 22. <https://doi.org/10.1186/s12886-017-0419-1>
- Sugihara, K., Takai, Y., Kawasaki, R., Nitta, K., Katai, M., Kitaoka, Y., Yokoyama, Y., Omodaka, K., Naito, T., Yamashita, T., Mizoue, S., Iwase, A., Nakazawa, T., & Tanito, M. (2021). Comparisons between retinal vessel calibers and various optic disc morphologic parameters with different optic disc appearances: The Glaucoma Stereo Analysis Study. *PloS one*, 16(7), e0250245. <https://doi.org/10.1371/journal.pone.0250245>
- Sung, M. S., Kang, Y. S., Heo, H., & Park, S. W. (2016). Characteristics of Optic Disc Rotation in Myopic Eyes. *Ophthalmology*, 123(2), 400–407. <https://doi.org/10.1016/j.ophtha.2015.10.018>
- Sun, M. T., Tran, M., Singh, K., Chang, R., Wang, H., & Sun, Y. (2023). Glaucoma and Myopia: Diagnostic Challenges. *Biomolecules*, 13(3), 562. <https://doi.org/10.3390/biom13030562>
- Wichrowska, M., Wichrowski, P., & Kocięcki, J. (2022). Morphological and Functional Assessment of the Optic Nerve Head and Retinal Ganglion Cells in Dry vs Chronically Treated Wet Age-Related Macular Degeneration. *Clinical ophthalmology (Auckland,*

- N.Z.), 16, 2373–2384. <https://doi.org/10.2147/OPHTH.S372626>
- Xu, L., Wang, Y., Wang, S., Wang, Y., & Jonas, J. B. (2007). High myopia and glaucoma susceptibility the Beijing Eye Study. *Ophthalmology*, 114(2), 216–220. <https://doi.org/10.1016/j.ophtha.2006.06.050>
- Yamashita, T., Asaoka, R., Tanaka, M., Kii, Y., Yamashita, T., Nakao, K., & Sakamoto, T. (2013). Relationship between position of peak retinal nerve fiber layer thickness and retinal arteries on sectoral retinal nerve fiber layer thickness. *Investigative ophthalmology & visual science*, 54(8), 5481–5488. <https://doi.org/10.1167/iovs.12-11008>
- Yohannan, J., Wang, J., Brown, J., Chauhan, B. C., Boland, M. V., Friedman, D. S., & Ramulu, P. Y. (2017). Evidence-based Criteria for Assessment of Visual Field Reliability. *Ophthalmology*, 124(11), 1612–1620. <https://doi.org/10.1016/j.ophtha.2017.04.035>
- Yoshikawa, Y., Shoji, T., Kanno, J., Kimura, I., Hangai, M., & Shinoda, K. (2018). Optic disc vessel density in nonglaucomatous and glaucomatous eyes: an enhanced-depth imaging optical coherence tomography angiography study. *Clinical ophthalmology (Auckland, N.Z.)*, 12, 1113–1119. <https://doi.org/10.2147/OPHTH.S167222>
- Zhang, F., Liu, X., Wang, Y., Wang, Q., Zheng, M., Chang, F., & Mao, X. (2022). Characteristics of the optic disc in young people with high myopia. *BMC ophthalmology*, 22(1), 477. <https://doi.org/10.1186/s12886-022-02719-x>