Differences of Retinal Nerve Fibre Distributions Between High Myopes and Emmetropes – A Population Based Study

Ka Wai Jasper Wong (jasperwongkw@gmail.com)
Clinical Assistant Professor, Department of Ophthalmology, University of Hong Kong
https://orcid.org/0000-0003-4039-5468
Bukhari Mohammad Abdullah
University of Hong Kong
Jimmy Shiu Ming Lai
University of Hong Kong
Ian Yat Hin Wong
University of Hong Kong

Research article

Keywords: OCT machines, Diagnosing glaucoma, retinal nerve fibre layer (RNFL)

Posted Date: August 18th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-56691/v1

Abstract

Background

Diagnosing glaucoma in patients with high myopia is still a challenge despite the rapid develop of optical coherence tomography (OCT) in the past 2 decades. One of the reasons was the different geographic anatomies of the retinal nerve fibre layer (RNFL) among the high myopes and the emmetropes. This often resulted in errors when RNFL thicknesses were analysed. As diagnosis of glaucoma relied on the detection of focal RNFL thinning in OCT, this could lead to wrong diagnosis. This study aimed to compare the distributions of superotemporal and inferotemporal retinal nerve fibre bundles among these 2 groups of population.

Methods

Retrospective case-control study. Myopic group comprised subjects with a spherical equivalent of ≤-6D and axial length ≥ 26 mm, whereas non-myopic control group consisted of subjects with a spherical equivalent of 0 ± 0.5D and axial length 24 ± 0.5 mm. Cirumpapillary OCT images were retrieved from all subjects and the distances between the peaks of the 2 retinal nerve fibre bundles was measured.

Results

One-hundred-thirty-four highly myopic eyes from 74 subjects were included in the myopic group and 188 non-myopic eyes from 94 subjects were recruited as control group. The mean inter-peak distance of the myopic group 8.89 ± 1.00 mm and that of the non-myopic group was 6.81 ± 0.61 mm. The mean inter-peak distance was significantly larger in the myopic group ($p < 0.0001$).

Conclusions

Retinal nerve fibres arranged differently in high myopes with a tendency of more temporally arranged superotemporal and inferotemporal retinal nerve fibre bundles. Direct comparison of RNFL thickness with built-in normative database made by most of the OCT machines might lead to false positive diagnoses of glaucoma in patients with high myopia.

Background

Myopia is one of the most common ocular abnormalities reported worldwide[1]. High myopia, or pathological myopia, is of particular concern as it is not only a refractive problem, but also increases ones' risks of various ocular diseases such as retinal detachment, myopic maculopathy and primary open angle glaucoma[2]. Glaucoma is the commonest cause of irreversible blindness affecting more than

60 million populations[3]. One with high myopia possesses more than 3 times risks of glaucoma[4]. Due to its irreversibility, early diagnosis and close disease monitoring is crucial to prevent permanent visual loss.

Before the era of optic coherence topography (OCT), clinicians relied on an increased in cup-to-disc ratio (CDR) and the characteristic visual field loss demonstrated by Humphrey perimetry to diagnose glaucoma. The rapid development of OCT over the past 2 decades has revolutionized glaucoma diagnosis and the way glaucoma were managed. OCT allowed high resolution cross-sectional imaging of the retina, enabling segmentation and accurate measurements of different retinal layers. This empowered clinicians to diagnose glaucoma earlier and more accurately monitoring disease progression by detecting focal thinning of peripapillary retinal nerve fibres layer (RNFL). Various studies have proven that RNFL thinning, when compared with one's age-matched normative data, has been one of the most sensitive parameters for glaucomatous optic neuropathy (GON) diagnosis and monitoring[5–9].

Nevertheless, diagnosing glaucoma and monitoring glaucoma progression in patients with high myopia is still a substantial challenge[10]. High myopes usually have a different optic disc morphology compared with their non-myopic counterparts. They tend to have tilted optic discs with more oval configurations and peripapillary atrophies[11,12]. Therefore, their CDR might not be easily discerned. Disagreements in CDR could occur even between different experienced glaucoma specialists, let alone general ophthalmologists.

On the other hand, the RNFL anatomy could be quite different between myopic and non-myopic people. Many studies have been done comparing the thickness of RNFL between myopia and non-myopic populations[13–20]. A number of studies found that people with high myopia have thinner peripapillary RNFL[13,16]. However, seldom had studied the discrepancies of the arrangement of the superotemporal and inferotemporal retinal nerve fibre bundles between high myopes and emmetropes. Some even suggested that the RFNL arrangement might not be correlated with the axial length and spherical equivalent of the eye.[19]

We compared the circumpapillary OCT images from healthy subjects with and without high myopia to study the differences of their RNFL arrangements, particularly on the superotemporal and inferotemporal retinal nerve fibre bundles, between these 2 groups.

Methods

This is a retrospective case-control study. Circumpapillary OCT images were taken from normal Chinese populations who participated in a community eye health screening program conducted in the Southern District of Hong Kong. Subjects with spherical equivalent (SE) of ≤ -6 diopters and axial length (AXL) ≥ 26 mm were classified as the myopic group, whereas similar number of subjects with SE within 2 diopters and AXL of 24 ± 0.5 mm would be randomly selected from the database as non-myopic control group. This study was approved by the Institutional Review Board of the University of Hong Kong / Hospital

Authority Hong Kong West Cluster (HKU/HKWC IRB) and in accordance with the tenets of the Declaration of Helsinki.

Circumpapillary OCT images of the subjects were taken using Spectralis OCT machine (Heidelberg Engineering GmbH, Heidelberg, Germany). Cross-sectional OCT images of a circle of 3.45 mm diameter centred at the optic disc were obtain for each subject by a trained and experienced operator. The 2 humps in the circumpapillary OCT images were identified and the distances between the peak of these 2 humps were measured and compared by an independent investigator.

The inter-peak between the 2 retinal nerve fibre bundles of the 2 groups are compared. Each eye of the subjects was analysed separately. Only the qualified eye would be included for subjects with unilateral high myopia. Independent sample t-tests were performed to compare the inter-peak distances and angular widths between the myopic and non-myopic groups. Statistical significance was defined as $p \leq 0.05$.

Results

Circumpapillary OCT images of 134 highly myopic eyes from 74 subjects and 188 control from 94 subjects were included in this study. The demographics of the subjects were shown in Table 1.

Table 1
Demographics of subjects

	Myopic group	Non-myopic group
Number of subjects	74	94
Male-to-female ratio	31:43	36:58
Mean age	59.7 ± 6.3	65.8 ± 8.5
Number of eyes	134	188
Right eye : left eye ratio	71:63	94:94

The mean AXL of the myopic group was 27.64 ± 1.12 mm and that of the non-myopic group was 23.95 ± 0.35 mm ($p < 0.0001$). The mean SE of the myopic group was − 8.97 ± 2.38D and that of the non-myopic group was 0.12 ± 1.11D ($p < 0.0001$). The mean inter-peak distance was 8.89 ± 1.00 mm for the myopic group and 6.81 ± 0.61 mm for the non-myopic group. The inter-peak distance was significantly larger in the myopic group ($p < 0.0001$). Table 2 showed the results of independent t-test.

Table 2
Comparisons of inter-peak distances and angular widths on circumpapillary OCT images between myopic and non-myopic group.

	Myopic group	Non-myopic group	P value
Axial length (mm)	27.64 ± 1.12	23.95 ± 0.35	< 0.0001
Spherical equivalent (D)	-8.97 ± 2.38	0.12 ± 1.11	< 0.0001
Inter-peak distance (mm)	8.89 ± 1.00	6.81 ± 0.61	< 0.0001

The inter-peak distances represented the circumferential distance from the superotemporal bundle to the inferotemporal bundle through the nasal retina. Therefore, the 2 retinal nerve fibre bundles were more temporally arranged in the retina.

Discussion

In the modern era of ophthalmology, OCT has been an indispensable tool in diagnosing glaucoma. Thinning of the peripapillary RNFL and the ganglion-cell-internal-plexiform-layer (GC-IPL) complex are 2 most reliable indicators in OCT images to suggest GON[20,21]. They have been proven to be sensitive to diagnose early glaucoma and useful in monitoring glaucoma progression as well[7,21–23]. They have been heavily relied on for these purposes as perimetry is notorious in its subjectivity and variability[24], while intraocular pressure (IOP) could not thoroughly reflect the nerve status and observed worsening of CDR would have been too late to intervene.

Nevertheless, diagnosing glaucoma in patients with high myopia has been a challenge despite the rapid advancements of OCT technology in the past 2 decades[10]. There are many OCT manufacturers in the market but most of them produce similar reports by comparing the peripapillary RFNL thickness with their own age-match normative database stored in their systems. The comparisons were made directly by quadrants or clock hours of the optic nerve head (ONH).

Our study demonstrated that the superotemporal and inferotemporal retinal nerve fibre bundles are arranged differently in subjects with high myopia and a long AXL. This could explain the phenomenon that high myopes were often over-diagnosed with glaucoma. Since the retinal nerve fibre bundles, together with the major retinal vessel arcades tend to attain a more temporal distribution, directly compare the RNFL thickness quadrant by quadrant, or by clock hours, could result in misalignment during analysis. Therefore, the OCT systems might mistakenly compare the areas outside the retinal nerve fibre bundles which are usually thinner to the thicker area of fibre bundles in the normative data. This results in false positives if clinician did not interpret the reports very carefully. As most of OCT manufacturers label area of RNFL thinning using red colour, it is also called the “red disease”[25]. On the other hand, if the retinal neve fibre bundles of a high myope with early GON, comparing his RNFL thickness to the supposed thinner non-bundle areas could lead to false negative, which might result in delayed diagnosis and treatment.

To further find out how common are false positive and false negative diagnosis of glaucoma in high myopes, a much larger number of highly myopic subjects with longitudinal observations and thorough assessments would be necessary. In order to solve this potential problem, normative database specific for high myopes would be needed.

Conclusions

For population with high myopia, their retinal nerve fibre bundles were arranged differently when compared to the non-myopic population, with a tendency of more temporally arranged superotemporal and inferotemporal retinal nerve fibre bundles. Direct comparison of RNFL thickness with built-in normative database made by most of the OCT machines might lead to false positive diagnoses of GON in patients with high myopia.

List Of Abbreviations

- Optic coherence topography (OCT)
- Retinal nerve fibre layer (RNFL)
- Cup-to-disc ratio (CDR)
- Glaucomatous optic neuropathy (GON)
- Spherical equivalent (SE)
- Axial length (AXL)
- Ganglion-cell-internal-plexiform-layer (GC-IPL)
- Intraocular pressure (IOP)
- Optic nerve head (ONH)

Declarations

- **Ethics approval and consent to participate**

This study was approved by the Institutional Review Board of the University of Hong Kong / Hospital Authority Hong Kong West Cluster (HKU/HKWC IRB) and in accordance with the tenets of the Declaration of Helsinki.

- **Consent for publication**

Not applicable.

- **Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

- **Competing interests**

The authors declare that they have no competing interests.

- **Funding**

No funding was received for the study.

- **Authors' contributions**

JKW conceptualized the study and wrote the manuscript.

BMA extracted and analysed the data.

JSL revised and proof-read the manuscript.

LYW revised and proof-read the manuscript.

- **Acknowledgements**

Not applicable.

References

1. Pan CW, Ramamurthy D, Saw SM. Worldwide prevalence and risk factors for myopia. Ophthalmic Physiol Opt. 2012;32(1):3–16.
2. Saw SM, Gazzard G, Shih-Yen EC, Chua WH. Myopia and associated pathological complications. Ophthalmic Physiol Opt. 2005;25(5):381–91.
3. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121(11):2081–90.
4. Mitchell P, Hourihan F, Sandbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. Ophthalmology. 1999;106(10):2010–5.
5. Mok KH, Lee VW, So KF. Retinal nerve fiber layer measurement by optical coherence tomography in glaucoma suspects with short-wavelength perimetry abnormalities. J Glaucoma. 2003;12(1):45–9.
6. Medeiros FA, Zangwill LM, Bowd C, Vessani RM, Susanna R Jr, Weinreb RN. Evaluation of retinal nerve fiber layer, optic nerve head, and macular thickness measurements for glaucoma detection using optical coherence tomography. Am J Ophthalmol. 2005;139(1):44–55.
7. Wollstein G, Schuman JS, Price LL, et al. Optical coherence tomography longitudinal evaluation of retinal nerve fiber layer thickness in glaucoma. Arch Ophthalmol. 2005;123(4):464–70.
8. Li S, Wang X, Li S, Wu G, Wang N. Evaluation of optic nerve head and retinal nerve fiber layer in early and advance glaucoma using frequency-domain optical coherence tomography. Graefes Arch Clin

Exp Ophthalmol. 2010;248(3):429–34.

9. Mansoori T, Viswanath K, Balakrishna N. Ability of spectral domain optical coherence tomography peripapillary retinal nerve fiber layer thickness measurements to identify early glaucoma. Indian J Ophthalmol. 2011;59(6):455–9.
10. Tan NYQ, Sng CCA, Jonas JB, Wong TY, Jansonius NM, Ang M. Glaucoma in myopia: diagnostic dilemmas. Br J Ophthalmol. 2019;103(10):1347–55.
11. Li Z, Guo X, Xiao O, et al. Optic Disc Features in Highly Myopic Eyes: The ZOC-BHVI High Myopia Cohort Study. Optom Vis Sci. 2018;95(4):318–22.
12. Fledelius HC, Goldschmidt E. Optic disc appearance and retinal temporal vessel arcade geometry in high myopia, as based on follow-up data over 38 years. Acta Ophthalmol. 2010;88(5):514–20.
13. Choi SW, Lee SJ. Thickness changes in the fovea and peripapillary retinal nerve fiber layer depend on the degree of myopia. Korean J Ophthalmol. 2006;20(4):215–9.
14. Rauscher FM, Sekhon N, Feuer WJ, Budenz DL. Myopia affects retinal nerve fiber layer measurements as determined by optical coherence tomography. J Glaucoma. 2009;18(7):501–5.
15. Kang SH, Hong SW, Im SK, Lee SH, Ahn MD. Effect of myopia on the thickness of the retinal nerve fiber layer measured by Cirrus HD optical coherence tomography. Invest Ophthalmol Vis Sci. 2010;51(8):4075–83.
16. Kim MJ, Lee EJ, Kim TW. Peripapillary retinal nerve fibre layer thickness profile in subjects with myopia measured using the Stratus optical coherence tomography. Br J Ophthalmol. 2010;94(1):115–20.
17. Kim NR, Lee ES, Seong GJ, et al. Comparing the ganglion cell complex and retinal nerve fibre layer measurements by Fourier domain OCT to detect glaucoma in high myopia. Br J Ophthalmol. 2011;95(8):1115–21.
18. Wang G, Qiu KL, Lu XH, et al. The effect of myopia on retinal nerve fibre layer measurement: a comparative study of spectral-domain optical coherence tomography and scanning laser polarimetry. Br J Ophthalmol. 2011;95(2):255–60.
19. Zhao Z, Jiang C. Effect of myopia on ganglion cell complex and peripapillary retinal nerve fibre layer measurements: a Fourier-domain optical coherence tomography study of young Chinese persons. Clin Exp Ophthalmol. 2013;41(6):561–6.
20. Malakar M, Askari SN, Ashraf H, Waris A, Ahuja A, Asghar A. Optical coherence tomography assisted retinal nerve fibre layer thickness profile in high myopia. J Clin Diagn Res. 2015;9(2):NC01–03.
21. Schulze A, Lamparter J, Pfeiffer N, Berisha F, Schmidtmann I, Hoffmann EM. Diagnostic ability of retinal ganglion cell complex, retinal nerve fiber layer, and optic nerve head measurements by Fourier-domain optical coherence tomography. Graefes Arch Clin Exp Ophthalmol. 2011;249(7):1039–45.
22. Jeoung JW, Choi YJ, Park KH, Kim DM. Macular ganglion cell imaging study: glaucoma diagnostic accuracy of spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2013;54(7):4422–9.

23. Nouri-Mahdavi K, Hoffman D, Tannenbaum DP, Law SK, Caprioli J. Identifying early glaucoma with optical coherence tomography. Am J Ophthalmol. 2004;137(2):228–35.
24. Holmin C, Krakau CE. Variability of glaucomatous visual field defects in computerized perimetry. Albrecht Von Graefes Arch Klin Exp Ophthalmol. 1979;210(4):235–50.
25. Chong GT, Lee RK. Glaucoma versus red disease: imaging and glaucoma diagnosis. Curr Opin Ophthalmol. 2012;23(2):79–88.