Comparison of Retinal Nerve Fibre Layer versus Bruch Membrane Opening-Minimum Rim Width as an Optical Coherence Tomography-based Marker for Glaucoma in Myopia

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ABSTRACT

Objective: To compare the reliability of Bruch Membrane Opening-Minimum Rim Width (BMO-MRW) Optical Coherence Tomography (OCT) with Retinal Nerve Fibre Layer (RNFL) in myopic patients.

Study Design: Cross-sectional study.

Place and Duration of Study: LRBT Free Base Eye Hospital, Karachi, from May 2019 to July 2020.

Methodology: Moderate myopes with refractive errors between -3 to -6 diopters were examined by 2 glaucoma consultants separately, who performed fundoscopy to evaluate the optic nerve head, checked IOP and assessed CCT and visual fields to stratify the eyes into myopic normal and myopic glaucomatous eyes. All eyes were imaged with SD OCT of Spectralis version 1.10.2.0 of Heidelberg Engineering. Two scanning patterns, one for BMO-MRW and the other for RNFL thickness analysis, were performed.

Results: Fifty eyes of 50 patients were diagnosed with glaucoma in 50% (25 out of 50 patients). OCT RNFL detected glaucoma in 72% (36 out of 50 patients). While OCT BMO-MRW detected glaucoma in 56% (28 out of 50 patients). There was strong agreement between the consultant's judgements and BMO-based test ($\kappa = 0.800$, $p < 0.001$), but the association was comparatively weaker with RNFL-based prediction ($\kappa = 0.480$, $p < 0.001$). Specificity was better with OCT BMO-MRW (85.7%) than RNFL (66.7%). There were lower false positive rates with BMO-MRW (14.3%) than RNFL (33.3%).

Conclusion: OCT BMO-MRW is a better indicator of glaucomatous damage in moderately myopic eyes as compared to OCT RNFL analysis.

Key Words: *Glaucoma, Myopia, Optical Coherence Tomography (OCT), Bruch Membrane Opening-Minimum Rim Width (BMO-MRW), Retinal Nerve Fibre Layer (RNFL).*

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INTRODUCTION

Myopia is the most common refractive error in South Asia and worldwide. The global epidemiological burden of myopia has been estimated to be about 28%, and it is expected to rise to 53% by 2050.[1,2] A significant proportion of myopic patients may eventually develop various vision-threatening conditions like glaucoma, myopic macular degeneration, retinal detachment, and early cataract.[3] Glaucoma is the foremost cause of irreversible blindness worldwide.[4,5]

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Diagnosing glaucoma in myopic patients can be a challenge, as optical coherence tomography-retinal nerve fibre layer (OCT-RNFL) thickness, and ONH (Optic nerve head) analysis, routinely performed as part of glaucoma diagnosis are not optimally reliable in myopic patients.[6] In most cases, tilted disc morphology, peripapillary atrophy, decreased average RNFL thickness, and variability between the clinical disc margin and the actual disc margin in myopic eyes account for this discrepancy.[7,8] Changes in retinal pigment epithelium and choriocapillaris, and corresponding Bruch membrane alterations at the site of peripapillary atrophy may be the reason why OCT fails in optimally identifying the optic disc margin.[9,10]

OCT BMO-MRW (OCT Bruch Membrane Opening-Minimum Rim Width) is a relatively new modality which aids in diagnosing glaucoma in such patients.[11] This test relies on an anatomically consistent landmark, the BMO, which is clinically and photographically invisible, but can be consistently detected by spec-

tral domain imaging (SD-OCT). BMO-MRW is the shortest distance from the BMO to the internal limiting membrane. It is a more realistic and consistent measure of rim tissue.[12] The incorporation of an anatomic positioning system (APS) in the SD OCT software further prevents errors in analysis by overcoming the effect of fovea axis change as well as any errors caused by head tilt.[13]

The purpose of this study was to determine whether OCT-BMO-MRW supersedes OCT-RNFL in detecting glaucoma in myopic eyes.

METHODOLOGY

This cross-sectional study was carried out at LRBT Hospital, after approval by the hospital Ethical Review Committee. Written and informed consent was taken from all participants. Moderate myopes, with refractive errors between -3 diopters and -6 diopters referred to the glaucoma clinic for assessment, were recruited for the study. The inclusion criteria was age 18 to 60 years, BCVA ≥ 6/18 and astigmatism <3 dioptres.

Exclusion criteria were retinal disease (including degenerative myopia), any optic nerve disease other than glaucoma, significant peripapillary atrophic areas that may cause artefacts in analysis, significant media opacity to preclude visualisation of the optic nerve head and history of retinal laser (pan retinal photocoagulation or 360° laser).

All participants were examined by two glaucoma specialists separately, who evaluated the optic nerve head by fundoscopy, checked IOP and assessed CCT and visual fields. If there was any disagreement in diagnosis, the patient underwent a re-examination and a consensus was reached between the two consultants. The eyes were then stratified into myopic normal and myopic glaucomatous eyes.

All subjects included in this study underwent imaging of their eyes with SD-OCT using Spectralis (version 1.10.2.0, Heidelberg Engineering). Two scanning patterns were used with the SD-OCT; one for BMO-MRW and the other for RNFL thickness analysis.

Scanning of all eyes was performed by a single skilled operator. For neuroretinal rim analysis by BMO-MRW, the location of BMO and ILM are identified by the system. This distance from BMO to the ILM is referred to as the BMO-MRW. The APS software incorporated within the system creates a fovea-BMO axis by aligning the centre of the fovea with centre of BMO. This ensures accurate scan acquisition. High resolution 15° radial scans centred on the optic disc were performed. This scanning pattern takes into account normative database and ensures that the measurements are according to normal ranges for age. The mean global and sectorial BMO-MRW measurements were recorded.

The second scanning pattern was for RNFL thickness. This was carried out in a circular 3.5mm, 4.1mm, and 4.7mm diameter around the optic disc. The mean global and sectorial RNFL measurements were recorded.

Data was analysed using IBM SPSS software version 25. Frequencies and percentages were calculated for all qualitative data, while mean ± S.D. was used for quantitative data. Cohen's κ test was applied to determine if there was agreement between the consultants' judgment; and the OCT tests on whether or not the patients had glaucoma. A p-value of <0.05 was taken as statistically significant.

RESULTS

Fifty patients were included in the final analysis (one eye per patient). Mean age was 38.4 ± 11.8 years. Mean refraction was -4.4 ± 0.90 diopters. The glaucoma consultants classified 50% (25 out of 50) patients as glaucomatous. In comparison, OCT-RNFL detected glaucoma in 72% (36 out of 50 patients) and OCT-BMO-MRW identified glaucoma in 56% (28 out of 50 patients).

There was strong agreement between the consultants' judgments and BMO-MRW- based test ($\kappa = 0.800$, $p < 0.001$, Table I), but the association was comparatively weaker with RNFL based prediction ($\kappa = 0.480$, $p < 0.001$, Table II). The agreement between the two OCT-based measures was weak ($\kappa = 0.493$, $p < 0.001$). (Table III).

Sensitivity of BMO-MRW was 95.5%, while sensitivity of RNFL was 92.9%. Specificity was seen to be higher by BMO-MRW (85.7%) than by OCT RNFL (66.7%). False positive rates were similarly lower with BMO-MRW (14.3%) than RNFL (33.3%).

DISCUSSION

Over the years, ophthalmologists have strived to add a more significant objective modality to their armamentarium for the assessment of the optic nerve head in glaucoma diagnosis. Optical coherence tomography (OCT) imaging has been instrumental in this regard because of its ability to visualise ocular structures at high resolution.[14] From the earlier time domain (TD) OCT, progress was made to Spectral domain (SD) OCT and swept source (SS) OCT. These newer OCT modalities have a higher scanning speed.[15] Nevertheless, even the newer Fourier domain OCT systems (the SD-OCT and SS-OCT modalities), did not fully enable a diagnosis of glaucoma to be made with certainty in some situations, such as situations when the evaluation of the optic discs in myopic eyes was required.

OCT-based parameters, like RNFL thickness, present a challenge to clinicians, because the normative database does not take into account such a large range of refractive errors and axial lengths encountered with myopia. A number of studies recommend careful interpretation of RNFL data on moderate myopic eyes when applying the currently available OCT devices.[16,17] RNFL thickness measurements even with the APS show lower values in myopes in all sectors. This frequently results in classifying healthy myopic discs as abnormal when compared with the normative database.

Furthermore, with routinely utilised OCT parameters for assessing the optic nerve head, the rim analysis is done, based on localisation of the clinical disc margin, which is not a reliable landmark, especially in discs with a substantial degree of tilt. Such tilted discs are commonly encountered in myopia.

Table I: Agreement between the glaucoma specialist and OCT-based BMO-MRW in diagnosing glaucoma in patients.

		BMO-MRW		Total
		Normal	Glaucoma	
Glaucoma Consultant opinion	Normal	21 (84%)	4 (16%)	25 (100%)
	Glaucoma	1 (4%)	24 (96%)	25 (100%)
Total		22 (44%)	28 (56%)	50 (100%)

Table II: Agreement between the glaucoma specialist and OCT-based RNFL in diagnosing glaucoma in patients.

		RNFL		Total
		Normal	Glaucoma	
Glaucoma Consultant opinion	Normal	13 (52%)	12 (48%)	25 (100%)
	Glaucoma	1 (4%)	24 (96%)	25 (100%)
Total		14 (28%)	36 (72%)	50 (100%)

Table III: Agreement between OCT-BMO-MRW and OCT-RNFL in diagnosing glaucoma in patients.

		RNFL		Total
		Normal	Glaucoma	
BMOMRW	Normal	12 (54.5%)	10 (45.5%)	22 (100%)
	Glaucoma	2 (7.1%)	26 (92.9%)	28 (100%)
Total		14 (28%)	36 (72%)	50 (100%)

Shin *et al.* advocated that RNFL thickness analysis should be construed with caution in eyes with tilted optic discs.[18] Reis *et al*. stated that the innermost edge of Bruch's membrane as detected by SD-OCT does not always correspond with the clinically apparent disc margin. That is why it is important to consider these aspects when commenting on the neuroretinal rim.[19]

BMO-MRW analysis has the potential to overcome these problems to some extent because this measurement is made by taking a more consistent and reliable landmark, the BMO, which is identified by the automated delineation software. In these tilted discs with an oblique insertion of the optic nerve, the amount of neuroretinal rim can be better assessed by measuring the minimum distance between the BMO and the internal limiting membrane (BMO-MRW). Hence, the interpretation of test results will not vary on serial investigations because this landmark, in addition to being consistent and reliable, also does not change with age, and is not an operator-dependent measurement.[12,13]

In the current study, OCT based BMO-MRW performed better than OCT-RNFL in identifying glaucoma patients. A strong association was seen between the patient assessment by BMO-MRW and the assessment of those patients by the glaucoma specialists, as indicated by κ value, which was calculated to be 0.8 (with the associated p-value also highly significant). κ value for association between RNFL-based assessment and the glaucoma specialists' assessment was 0.4, which was also fairly strong considered independently, but less so as compared to BMO-MRW.

A number of studies report similar superiority of BMO-MRW-based assessment in glaucoma diagnosis. Toshev *et al*. stated that BMO-MRW assessment with SD-OCT achieved better results in detecting glaucoma as compared to other modalities.[20] BMO-MRW also appeared to be the best predictor of glaucomatous visual field defects according to Mizumoto *et al.*[21] However, in the current study, even though visual fields were checked along with other parameters for a diagnosis of glaucoma, they were not analysed in the statistical calculations.

This study identified a false positive rate of 14.3% by OCT-BMO-MRW and 33.3% by OCT-RNFL. This is comparable to a study carried out by Rebolleda *et al*. in which they reported that the overall false positive rate was significantly lower (8%) using BMO-MRW compared with RNFL (33.3%).[22] Sensitivity of both tests was found to be similar. Sensitivity of OCT-BMO-MRW was found to be 95.5%; whereas, sensitivity of OCT-RNFL was found to be 92.9%. For practical purposes, it can be extrapolated that OCT- RNFL is an equally good modality for picking out diseased cases; however, when it comes to ruling out the disease, OCT-BMO-MRW takes precedence over OCT-RNFL. The values calculated for specificity (85.7% by BMO-MRW and 66.7% by RNFL analysis) in this study showed a similar trend to the specificity of these tests as deduced by Rebolleda *et al*. They reported that specificity was significantly higher by BMO-MRW (95.2%) than RNFL (33.3%) in eyes with moderate myopia.[22]

The overall analysis seems to be in favour of this newer modality as a superior tool in glaucoma assessment for myopic patients. The major limitation of this study was a demographically limited sample population. Moreover, a longer duration of follow-up is required for further validation of glaucoma diagnosis. The authors of this study also propose additional testing in myopic patients (including patients with higher degrees of myopia, degenerative myopia, and significant peripapillary atrophic areas) to further assess the reliability of BMO-MRW in detecting glaucoma in such patients.

CONCLUSION

BMO-MRW is a better indicator of glaucomatous damage in

moderately myopic eyes as compared to RNFL when using OCT-based analysis.

ETHICAL APPROVAL:
This cross-sectional study was carried out at LRBT Hospital, after approval by the hospital Ethical Review Committee.

PATIENTS' CONSENT:
Written and informed consents were taken from all participants.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
NU, MS, SAM, SN, LF, KK: Conceived the study and designed it, were involved in literature search and manuscript writing, did the statistical analysis. and final review and correction of the manuscript.

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