Bruchs Membrane Opening Area Measurement in Healthy Nepalese Eyes

Ranju Kharel Sitaula,[1] Ganga Sagar Shah[1]

[1]Department of Ophthalmology, B. P. Koirala Lions Centre for Ophthalmic Studies, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal.

ABSTRACT

Background: Bruch's membrane opening area is the circular area around the disc of Bruch's membrane, which is devoid of Bruch's membrane and can be assessed by capturing the retinal imaging system by Spectral-domain optical coherence tomography. BMOA can be a new landmark in analyzing the glaucomatous optic nerve head, myopic optic disc, optic neuropathy and uveitic disc edema. This is the first study from South Asia to evaluate the normal Bruch's membrane opening area among Nepalese eyes.

Methods: This hospital-based, cross-sectional, quantitative, observational study cross-sectional study was conducted in a tertiary eye care hospital in Nepal. Healthy immunocompetent Nepalese participants of both genders and different age groups were enrolled. The mean average Bruch's membrane opening area of each eyes, the difference in Bruch's membrane opening area between the two eyes and the gender of varying age groups were analyzed.

Results: Around 162 eyes (81 participants) were analyzed. The mean age was 56.69±17.5years. The mean average Bruch's membrane opening area of the right and left eye was 2.53±0.58 mm2 and 2.50 ±0.58 mm2. There was no significant difference in the Bruch's membrane opening area in either eye in both genders of any age group.

Conclusion: The Bruch's membrane opening area does not differ significantly according to the laterality, gender and age group in Nepalese eyes.

Keywords: Bruchs membrane opening; Bruchs membrane opening area; Nepal; optical coherence tomography.

INTRODUCTION

Bruch's membrane plays a vital role as a structural and functional support to the retinal pigment epithelium. Bruch's membrane opening(BMO) is the area devoid of Bruch's membrane through which the optic nerve and central retinal branch of the ophthalmic artery and vein pass.[1,2] Bruch's membrane opening area(BMOA) is the circular area around the disc of Bruch's membrane, which is devoid of Bruch's membrane and can be assessed by capturing the retinal imaging system by Spectral-domain optical coherence tomography(SD-OCT).[3] The mean BMOA in Japanese people have been reported as 2.06±0.45 mm^2 but BMO area increases with axial length and decreases with age. The measurement of BMOA can be useful for early diagnosis and detection of progression of many optic nerve head-related diseases like glaucomatous disc, myopic disc, optic neuropathy, and uveitis disc edema.[3,4] So, we conducted this naïve study to identify the normal Bruch's membrane opening area among Nepalese eyes of different genders and age groups with the aim of determining the baseline BMOA reference value in our population.

METHODS

It is a hospital-based, cross-sectional, quantitative, observational study done at B. P. Koirala Lions Centre for Ophthalmic Studies (BPKLCOS), Institute of Medicine, and Tribhuvan University. The study received approval from the Institutional Review Committee (IRC no 417 (6-11) and followed all tenants of the Declaration of Helsinki.

The patients between 20-70 years of age visiting the eye department for refractive error assessment between May 2020 to May 2021 were enrolled in the study. The verbal screening of participation and questioning of medical and ocular history was done. It was ensured that none had any ocular problems like retinal, corneal, or optic nerve disease, instead all had open angles, a best corrected acuity of 6/9 or better, refractive error up to 3.0 diopters (D) and intraocular pressure <

Correspondence: Dr Ranju Kharel Sitaula, Department of Ophthalmology, B. P. Koirala Lions Centre for Ophthalmic Studies, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. **Email: helloranju50@gmail.com.**

21mmHg. Patients less than 20 years and above 70 years got excluded as it could affect the normal choroidal anatomy and BMOA decreases with age as reported in a Japanese study(−2.9% or 0.06 mm2/decade).

A total of 162 eyes of 81 healthy Nepalese participants of both genders and different age groups meeting the above criteria within the given time frame were enrolled. Informed written consents from the participants were obtained prior to enrollment.

All cases underwent retinal imaging and optic nerve head (ONH) analysis by SD-OCT Spectralis® (Heidelberg Engineering, German software version 6.0). The SD-OCT identifies BMO which has automated segmentations which has simplified the planimetry and morphometry of this area.[5] BMOA analysis was done automatically by the machine inbuilt software by a single experienced operator under standard operating procedures in a stepwise pattern. In the first step, the fovea and the BMO were recognized by an automated positioning system. In the second step, a 24 equidistant radial B-scan locating 48 (red dot points in Figure 1) endpoints of the Bruch's membrane points at 7.5 degrees apart from each other center of ONH was obtained. Area reading and analysis was done on its own in terms of mm^2 (blue arrow in Figure 1). Thus, BMOA is automatically calculated and expressed in mm^2 in each eye.

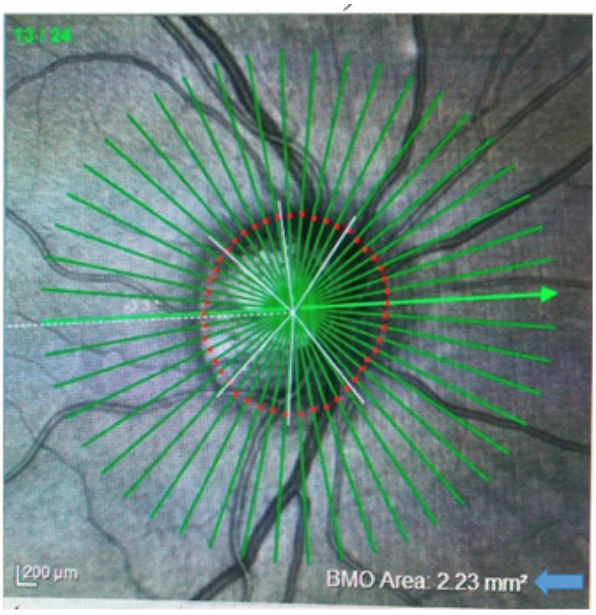

Figure 1. SD-OCT image of 24 radial B scans at 48 endpoints of Bruch's membrane (red dots) over the optic nerve head of the right disc and automatic calculation of BMOA (blue arrow).

RESULTS

During this study period, a total of 162 eyes of 81 participants were analyzed. Out of them, 60.5% were male and 39.5% were female. The mean age of the participants was 56.69 ±17.5 years. The youngest participant was 25 years old and the oldest was 69 years old.

The mean intraocular pressure was 16 mm Hg and 17 mm Hg in each right and the left respectively. The mean BMOA of right eyes was 2.53 ± 0.58 mm^2 and in the left eyes was 2.50 ± 0.58 mm^2 with no significant difference in the BMOA value between either eye.

The mean BMOA of the right eye was 2.53 mm^2 and in the left eye was 2.51 mm^2 as shown in Figure 2.

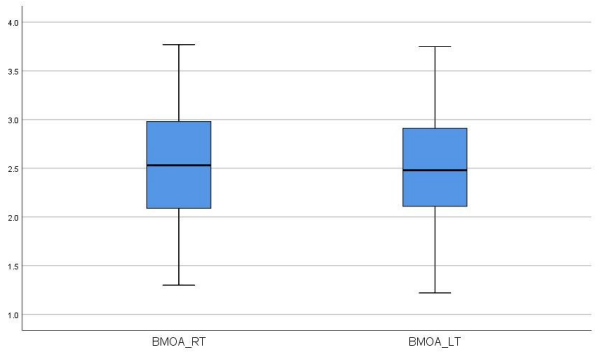

Figure 2. Box and whisker plot showing mean BMO area of right eye and left eye.

The mean BMOA in either eye was compared in both genders (Table 1). The p value between them did not show any significant difference.

Table 1. Comparison of mean Bruch Membrane Opening Area (BMOA) of males and females with laterality.

	Male	*Female*	*p value*
Right eye BMOA	2.52 ± 0.54mm^2	2.55 ± 0.66mm^2	0.836
Left eye BMOA	2.53 ± 0.53mm^2	2.49 ± 0.64mm^2	0.765

Foot note: BMOA-Bruch Membrane Opening Area

The participants were categorized in different age groups, the BMOA of each eye were calculated, compared, and the statistical significance between them was expressed in p value as shown in Table 2.

Table 2. Distribution of Bruch Membrane Opening Area values in different age categories in each eye.				
	Age range in year	Frequency of eye	Mean BMOA ± SD in mm^2	P value
Right Eye	21-30	4	2.55 ± 0.69 mm^2	0.424
	31-40	8	2.83 ± 0.58 mm^2	
	41-50	15	2.57 ± 0.46 mm^2	
	51-60	14	2.63 ± 0.74 mm^2	
	61-70	40	2.42 ± 0.56 mm^2	
Left Eye	21-30	4	2.51 ± 0.44 mm^2	0.342
	31-40	8	2.75 ± 0.58 mm^2	
	41-50	15	2.64 ± 0.51 mm^2	
	51-60	14	2.62 ± 0.67 mm^2	
	61-70	40	2.38 ± 0.59 mm2	

Foot note: BMOA-Bruch Membrane Opening Area

DISCUSSION

Histologically, the optic nerve head is a three-layered opening through which the axons of the retinal ganglion cells pass; the innermost layer is Bruch's membrane opening, the middle layer is the choroidal opening, and the third layer is the scleral canal opening.[7,8] Recently, SD-OCT technology have improved the accurate optical measurement of optic nerve head parameters and Bruch's membrane morphometry, thus adding a new horizon in ophthalmology to assess the retinal and optic nerve head-related pathology without histological dissection in normal disc as well as in macro/micro disc. Qualification and quantification of the relation between structural damage to the ganglion axons in the optic nerve head and functional, perimetric damage have been the principal aims in glaucoma, neuro-ophthalmology and uveitis research.[4]

The BMOA can be vital as this circular area around the disc of Bruch's membrane provides the area for passage of the optic nerve, central retinal arteries and veins to its content. And, it is utmost important to document the baseline BMOA values and compare the change in BMOA values in different ocular pathologies in different races, ethnic groups, genders, and age groups. But there is a paucity of literatures in this aspect.

The mean BMOA in our study participant was identified as 2.51mm^2 +/-0.58. This is higher compared to the BMOA of Japanese population (2.06 +/- 0.45mm^2) and German populations (2.13+/-0.56mm^2).[4,5,8] Though the BMOA in our study is higher compared to the Japanese and German study, we cannot assure at the moment that Nepalese have larger BMOA. We need to conduct BMOA screening in different ethnic groups, different age group and gender of Nepal to reach to a stronger conclusion in future. Thus, there is scarcity of literatures from other parts of the world to compare our people BMOA with other population, gender, age and ethnicities. But the present BMOA value identified in our population can be the landmark value to undergo future studies related to the optic nerve pathologies in South Asian region.

We presume that the enlargement in the size of BMOA can lead to glaucomatous disc, myopic disc, and alpha/beta/gamma zone optic atrophy.[3,4] The mean BMOA is found to be enlarged larger in myopic eye (2.59±0.80 mm^2).[1] Thus, increase in the size of BMOA in subsequent follow-up can help to predict the ongoing ganglion cell loss and timely intervention can prevent retinal nerve fibre atrophy.

Similarly, narrowing of the size of BMOA can lead to optic neuritis, infectious/non-infectious inflammatory disc edema, and vascular occlusion.[3-5,8] Thus, decrease in the size of BMOA can help to early identify the acute compression on the optic nerve and cause optic neuropathy or disc edema in ocular inflammatory conditions like uveitis, and timely intervention with anti-inflammatory agents can reduce the strangulation effect of Bruch membrane opening and prevent the progression of disc edema and vascular occlusions. Moreover, BMO can also be the landmark junction to calculate other ONH morphometric values like Bruch Membrane Opening-Minimum Rim Width (BMO-MRW) which is the vertical width from the endpoint of BMO to the inner limiting membrane. BMO-MRW is useful to monitor the change in MRW in response to glaucoma treatment, to monitor the complication of uveitic glaucoma, and to diagnose myopic glaucoma.[3,9] In addition, although the BMO-OCT cannot directly discern between macro and non-macro discs, its anatomical accuracy in area calculation based on the BMO has persuaded to define a threshold for identifying macro-BMOs.[5]

Thus, the imaging of the retinal nerve fibre layer over the disc and automatic identification and documentation of Bruch membrane opening and its circumferential area can be vital in the prediction and prevention of these optic nerve-related complications as BMOA can aid to identify even small-scale changes in the ONH. So SD-OCT BMOA readings can be considered as the a simple and convenient volumetric diagnostic tool with high

sensitivity/specificity, good reproducibility with ability to detect changes in BMO over time.[10] So, this study opens the door to screen, predict, and monitor the progression of various posterior segment ocular diseases using the novel OCT-based Bruch's membrane parameters.

The strength of this study is the inclusion of healthy subjects with and no ocular disease, who were thus free of confounding factors.

Finally, we recommend the wise adoption of BMO and BMOA in clinical practice for objective assessment of early screening of disc enlargement in glaucoma suspect timely detection of α/ß zone atrophy in myopic eyes and early detection of disc edema in uveitis eyes and neuro-ophthalmological disorders. Thus, BMO morphometrics can aid to discriminate optic nerve pathology patients from normal controls.[3]

However, lack of the larger population for the study, unable to explore the BMOA in different age, gender, race, geography and ethnicities are the limitation on the study.

CONCLUSIONS

The normal BMOA in our healthy population is 2.51mm^2 +/-0.58 and it did not differ significantly in regards to the ocular laterality, gender and age group. This value of BMOA can be used as the reference value to assess the BMOA in various eye disease in Nepal.

ACKNOWLEDGEMENTS

We are thankful to Mr. Suresh Raj Sharma, the imaging unit technician for the Optical Coherence Tomography, clinical photography, and documentation of the cases.

CONFLICT OF INTEREST

None

REFERENCES

1. Reis AS, O'Leary N, Yang H, Sharpe GP, Nicolela MT, Burgoyne CF, Chauhan BC. Influence of clinically invisible, but optical coherence tomography detected, optic disc margin anatomy on neuroretinal rim evaluation. Investigative ophthalmology & visual science 2012; 53: 1852-60. doi:https://doi.org/10.1167/iovs.11-9309
2. Abràmoff MD, Lee K, Niemeijer M, Alward WL, Greenlee EC, Garvin MK, Sonka M, Kwon YH. Automated segmentation of the cup and rim from spectral domain OCT of the optic nerve head. Investigative ophthalmology & visual science 2009; 50: 5778-84. doi:https://doi.org/10.1167/iovs.09-3790
3. Enders P, Schaub F, Adler W, Hermann M, Dietlein T, Cursiefen C, Heindl L. Bruch's membrane opening-based optical coherence tomography of the optic nerve head: a useful diagnostic tool to detect glaucoma in macrodiscs. Eye 2018; 32: 314-23. doi: doi.org/10.1038/eye.2017.306
4. Enders P, Longo V, Adler W, Horstmann J, Schaub F, Dietlein T, Cursiefen C, Heindl LM. Analysis of peripapillary vessel density and Bruch's membrane opening-based neuroretinal rim parameters in glaucoma using OCT and OCT-angiography. Eye 2020; 34: 1086-93.doi: https://doi.org/10.1038/s41433-019-0631-8
5. Cazana IM, Böhringer D, Reinhard T, Evers C, Engesser D, Anton A, Lübke J. A comparison of optic disc area measured by confocal scanning laser tomography versus Bruch's membrane opening area measured using optical coherence tomography. BMC ophthalmology 2021; 21: 1-7.doi: https://doi.org/10.1186/s12886-020-01799-x
6. Strouthidis NG, Yang H, Downs JC, Burgoyne CF. Comparison of clinical and three-dimensional histomorphometric optic disc margin anatomy. Investigative ophthalmology & visual science 2009; 50: 2165-74. doi:https://doi.org/10.1167/iovs.08-2786
7. Jonas JB, Holbach L, Panda-Jonas S. Peripapillary ring: histology and correlations. Acta Ophthalmologica 2014; 92: e273-e9.doi: https://doi.org/10.1111/aos.12324
8. Araie M, Iwase A, Sugiyama K, Nakazawa T, Tomita G, Hangai M, Yanagi Y, Murata H, Tanihara H, Burgoyne CF. Determinants and characteristics of bruch's membrane opening and bruch's membrane opening–minimum rim width in a normal Japanese population. Investigative Ophthalmology & Visual Science 2017; 58: 4106-13. doi: https://doi.org/10.1167/iovs.17-22057
9. Chauhan BC, O'Leary N, AlMobarak FA, Reis AS, Yang H, Sharpe GP, Hutchison DM, Nicolela MT, Burgoyne CF. Enhanced detection of open-angle glaucoma with an anatomically accurate optical coherence tomography–derived neuroretinal rim parameter. Ophthalmology 2013; 120: 535-43. doi: https://doi.org/10.1167/iovs.17-22057
10. Belghith A, Bowd C, Medeiros FA, Hammel N, Yang Z, Weinreb RN, Zangwill LM. Does the location of Bruch's membrane opening change over time? Longitudinal analysis using San Diego Automated Layer Segmentation Algorithm (SALSA). Investigative ophthalmology & visual science 2016; 57: 675-82. doi: https://doi.org/10.1167/iovs.11-9309