Evolution of Macular Bruch Membrane Defects of Patchy Chorioretinal Atrophy in Pathologic Myopia Based on a Recent Classification System

José M. Ruiz-Moreno, Mariluz Puertas, Ignacio Flores-Moreno, Jorge Ruiz-Medrano, Elena Almazán-Alonso, Maria Garcia-Zamora

Abstract

Purpose: The purpose of this study was to analyze the progression of macular Bruch membrane defects (BMD) in highly myopic patients with patchy atrophy (PA); and study its correlation with the enlargement of PA and ATN grading.

Setting/Venue: Puerta de Hierro-Majadahonda University Hospital, Madrid, Spain.

Patients and Methods: This was a cross-sectional, noninterventional study. A series of 451 highly myopic eyes with spherical equivalent > −6.0 D and/or >26 mm of axial length (AL) were included. All patients underwent a complete ophthalmological examination and swept-source optical coherence tomography (SS-OCT), and were graded using the ATN system by 2 masked retina experts that assessed the atrophic (A), tractional (T), and neovascular (N) components. SS-OCT b-scans were employed to study PA and macular BMD at baseline and at a 1-year follow-up, in patients with good foveal fixation.

Results: Out of total 451 eyes, 126 eyes (27.9%) had PA (53 patients; 75.4% women). Mean T and N in eyes with PA were 1.1 ± 1.3 and 0.08 ± 0.2, respectively. Sixty-eight of them had >1-year follow-up with a good foveal fixation and enough image quality. From them, BMD were found in 44 eyes (64.7%) at baseline and increased to 59 eyes (86.7%) at a 1-year follow-up. The mean great linear dimension of PA and macular BMD increased with a median of 384.5 ± 462.5 μm (IR 68.0–660.2) and 265.6 ± 418.1 μm (IR 0–331.7), respectively. At 1-year, PA and BMD sizes increase, and were statistically significant (p < 0.001). There was a positive correlation between the growth of macular BMD and the growth of PA (r = 0.490, p < 0.00). T grading correlated significantly with PA growth (p < 0.05). Conclusions: Macular BMD increase its prevalence and its size over time in highly myopic patients with PA. There is a positive correlation between BMD and PA area growth. New studies with a larger sample size, longer follow-up, and AL elongation correlation are necessary to corroborate our findings.

Introduction

Myopia is an increasingly prevalent disorder that affects 1.6 billion people worldwide, and it is estimated to reach 2.5 billion people by 2020, 27–33% of them suffer with high myopia. The prevalence of high myopia ranges from...
from 1% to 4%. East Asia seems to hold the highest rates with 6.8–21.6% of affected population [1]. High myopia is defined by an axial length (AL) ≥26.0–26.5 mm and/or a spherical equivalent (SE) ≥−6.0 diopters (D) [2–4]. Pathologic myopia (PM) was described as the structural changes that caused vision loss in the context of high myopia [5, 6]. Ohno-Matsui et al. [7] reported the definition of PM based on the presence of diffuse atrophy and/or staphyloma. It is widely accepted that posterior staphyloma and axial elongation play an important role in the changes leading to vision loss [8], but axial elongation cannot be considered the only criterion for the definition [9].

Complications in relation to PM are the leading cause of blindness in East Asia [10–13]. Of patients, 12.2% with severe vision loss [14] suffer from PM in Japan, while 6.7 million people are estimated to show a similar condition in China [15]. PM sits in fourth place of the leading causes of legal blindness in Spain [16], where 2–3% of the population suffers from this disease, and its prevalence is increasing every year [17]. Meanwhile, in Europe it is estimated to cause up to 7.8% of cases of blindness according to different series [18].

The current atrophic (A) myopic maculopathy classification grants an easy and accurate staging of the degree of atrophy [19]. Based on the International photographic classification and grading system, patchy atrophy (PA) was classified as score 3 [19]. PA is a greyish-white and well-defined atrophy in the posterior fundus region [20–22], and Bruch membrane defects (BMD) are one of the hallmarks of PA [23–25], but the size of BMD is usually smaller than PA [24]. It has been published that 95.2% of eyes with PA show progression of PM, including the growth of the original PA [26]. Due to the inherent elasticity of the Bruch membrane (BM), once a defect is created the defect should be expected to increase over time, but until now this fact has not been proven [25]. The ATN classification was proposed with the objective to provide a simple, reliable, and more complete grading system, including tractional (T) and neovascular (N) components for myopic maculopathy [1]. The aim of this article is to analyze the progression of BMD in patients with PA; and study its correlation with the enlargement of PA, and with the ATN grading in a series of highly myopic eyes.

Methods

This was a cross-sectional, noninterventional study in adhesion to the tenets of the Declaration of Helsinki for research involving humans. Its protocol was reviewed and approved by the Ethics Committee of Puerta de Hierro-Majadahonda University Hospita-
test or Mann-Whitney test, depending on normality. Pearson correlation was used to determine the correlations. The results were expressed in terms of \( r \) and \( p \) value. The paired \( t \) test was used to compare PA’s and BMD growth between the initial and final size. All analyses were conducted using a statistical analysis program SPSS, version 26.0 (IBM SPSS, Chicago, IL, USA). A two-tailed \( p \) value <0.05 was considered as statistically significant.

### Results

Among these 451 eyes, 126 (27.9%) had PA (53 patients; 75.4% women). The mean age of this patients was 64.0 ± 13.4 years old (range, 37–97), with mean SE of −16.1 ± 5.7 D (range, −6 to −29.5). Mean BCVA logMAR for PA was 0.62 ± 0.69 (range, 0–3.00); and mean AL was 31.2 ± 2.5 mm (range, 26.5–37.6). Mean T and N in eyes with PA were 1.1 ± 1.3 (range, 0–5) and 0.08 ± 0.2 (range, 0–2), respectively. PA eyes (A3 score) were compared to eyes without atrophy (score ≤A2). Age, AL, SE, BCVA, and components T and N of the ATN classification were significantly different (\( p < 0.001; \chi^2 \) and Student \( t \) tests) (shown in Table 1).

Out of total of these 126 PA eyes, only 68 of them had more than 1-year follow-up with a good foveal fixation and good image quality (>70). Mean BCVA logMAR of these 68 eyes was 0.58 ± 0.65 (range, 0–2.00); mean AL was 30.3 ± 1.6 mm (range, 26.8–32.7). On the first visit, BMD (shown in Fig. 1) were found in 44 eyes (64.7%); and at 1 year, the number of PA eyes with macular BMD (shown in Fig. 2–4) increased to 59 eyes (86.7%). The mean size of BMD at the beginning was 542.3 ± 994.5 μm (range, 61–4,787) versus 854.5 ± 1167.5 μm (range, 68–5,477) at a 1-year follow-up. The mean size (great linear dimension) of PA and macular BMD increased with a median of 384.5 ± 462.5 μm (IR 68.0–660.2) and 265.6 ± 418.1 μm (IR 0–331.7), respectively.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (A3 score)</th>
<th>Group 2 (score ≤A2)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( N )</td>
<td>126</td>
<td>266</td>
<td>0.007</td>
</tr>
<tr>
<td>Age</td>
<td>66.08±12.8</td>
<td>62.0±12.4</td>
<td>0.000</td>
</tr>
<tr>
<td>AL</td>
<td>31.1±2.1</td>
<td>29.06±2.4</td>
<td>0.000</td>
</tr>
<tr>
<td>SE</td>
<td>−19.3±7.6</td>
<td>−13.6±5.9</td>
<td>0.000</td>
</tr>
<tr>
<td>BCVA logMAR</td>
<td>0.76±0.76</td>
<td>0.38±0.54</td>
<td>0.000</td>
</tr>
<tr>
<td>T component</td>
<td>1.06±1.2</td>
<td>0.7±0.9</td>
<td>0.001</td>
</tr>
<tr>
<td>N component</td>
<td>0.08±0.2</td>
<td>0.04±0.2</td>
<td>0.001</td>
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</table>

\( AL \), axial length; \( SE \), spherical equivalent; \( BCVA \), best-corrected visual acuity; \( T \), tractional; \( N \), neovascular.

### Table 1. Characteristics and comparison between A3 score and ≤A2 score myopic eyes

Fig. 1. Color image of a left eye with PM with a SS-OCT radial scan through a PA lesion. On the bottom right, SS-OCT images of PA lesion of the color image. White descendent arrows pointing out the breaks in the retinal pigmentary epithelium. The third (right) descedning arrow marks a punctual break in the retinal pigmentary epithelium. The white upward arrows mark the edge of BMD. BMD, Bruch membrane defects; PA, patchy atrophy; SS-OCT, swept-source optical coherence tomography; PM, pathological myopia.

Fig. 2. Color image of a highly myopic right eye with a radial SS-OCT scan through a PA lesion. On the right, the same eye with a SS-OCT radial scan passing through the same atrophy patch in the same place 3 years later with an evident growth of PA. PA, patchy atrophy; SS-OCT, swept-source optical coherence tomography.

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Discussion

By using SS-OCT, the present study revealed that macular BMD, hallmark of PA in highly myopic patients [24], increase their prevalence and size over time, as previously suspected [22], but until now this had not been proven. PA was found in 27.9% of our center’s highly myopic patient database, versus 10.5% found by Ohno-Matsui and colleagues [24], being more common in women (75.4%) just like her study revealed. The mean age was 64.0 ± 13.4 years old, similar to other PA series, 62.2 ± 9.6 [22], 67.9 ± 6.4 [23], and 65.3 ± 11.0 [24]; therefore, age cannot justify this significant difference in prevalence found. Mean AL in our patients (31.2 ± 2.5 mm) was longer than other previously published series (30.3 ± 2.0 mm [22], 29.6 ± 0.3 mm [23]) but shorter than Du et al. [24] (31.7 ± 2.4 mm); therefore, even AL does not seem to justify this difference. Only the high mean age (63.1 ± 13.4 years old), of our database series of myopic patients, very close to the average age of patients with PA (64.0 ± 13.4), would justify the higher prevalence rate of PA in our study, as PA has been shown to increase in number and size with follow-up, but not by the difference with the Ohno-Matsui and colleagues [26] series; nor would the OCT study scan performed justify it, as it was the same in both studies (radial scan). Compared to highly myopic eyes without atrophy (neither patchy nor macular atrophy), we found that these eyes show worse BCVA, are older, longer, and therefore present a higher SE and ATN grading (shown in Table 1), that is, they would also show higher T and N gradings, and not only in A.

In the group of patients (68 eyes) with a good image quality and with a minimum follow-up of 1 year, an increase in the prevalence of BMD has been shown, from 64.7 to 86.7%, similar to that published by Ohno-Matsui...
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and colleagues [24] of 82.9%. As in this publication, we have found a lack of RPE, choriocapillaris, and deep retinal layers, with preservation of retinal nerve fiber layer and parts of the inner plexiform layer and inner nuclear layer in the region of BMD. Large choroidal vessels are preserved in the choroid with hardly any presence of middle-sized vessels (shown in Fig. 1, 3, 4).

The mean size (great linear dimension) of PA grows more than BMD in our series, 384.5 ± 462.5 μm versus 265.6 ± 418.1 μm. As previously mentioned, it has been published that with a longer follow-up (>18 years), 95.2% of the eyes with PA show growth in myopia with an increase in initial PA areas or the appearance of new PA areas [26]. That is to say, in eyes with PA there is growth of myopia, growth of PA plaques, and the possibility of the appearance of macular BMD.

Ohno-Matsui and colleagues [24] found BMD in 82.9% of eyes with PA, being PA without BMD smaller than those with BMD; therefore, if in a follow-up year the presence of PA and their size increases, an increase in BMD could be expected; therefore, our results confirm this suspicion. To avoid the influence that the myopic choroidal neovascularization (mCNV) could have on the appearance of BMD, we have not included in our series BMD under mCNV as in previous studies [23]. Therefore, if there were any signs of mCNV in the area of PA on the initial SS-OCT study, the patient was excluded [22]. Our mean BMD size (803.9 ± 1146.5) was similar to previous series (1,175 ± 1,249 μm) [23].

The Beijing Eye Study found BMD in eyes from over 28.27 mm of AL, and BMD presence was significantly associated with longer AL [23]. In our series, BMD appeared in eyes with at least 27.76 mm, but we have found no association between BMD growth and traction ATN classification; however, there is a significant correlation between T, N, and A grading (Table 2). Eyes with longer AL tend to show alterations that translate into higher A, T, and N gradings [27].

BM, unlike the choroid and sclera, does not get thinner with increasing AL in highly myopic eyes in a histomorphometry study [28]. The posterior sclera [29] and choroid [30] are thinner in highly myopic eyes than in emmetropic eyes. Thickness of the BM is not reduced; it remained unclear why BM may develop a rupture without previous thinning. Fang et al. [26] show growth of PA with AL elongation. In other words, an increase in AL would increase the stress on the BM and facilitate its breakage. It would be important to check in a long series of cases with a longer follow-up, how this increase in AL coincides with an increase in BMD in number and size.

There are several limitations to our study: first, it does not reflect the general myopic population, as our patient database is biased, being comprised of patients who come to the myopia unit of our hospital. Second, we would need not only consider the measurement of the greater linear dimension of PA and BMD, but an exact measurement of the surface of both, which would allow us to know better about their evolution. The presence of islands of BMD in the PA areas makes this situation more difficult to assess. Third, it is not always easy to identify BMD; sometimes the inner sclera reflects due to atrophy of the choroid covering BMD, but in case of doubt a senior ophthalmologist was consulted. Fourth, we do not have the measure of AL growth accurately enough to analyze whether the increase in AL coincides with the increase in BMD. This would need to be done in future studies.

### Conclusion

In conclusion, macular BMD are a hallmark of PA in high myopic patients, with an increasing prevalence and size over time. There is a positive correlation between BMD and PA area growth. New studies with a larger series, longer follow-up, and correlation with AL are necessary to corroborate our findings.

### Statement of Ethics

This was a cross-sectional, noninterventional study in adherence to the tenets of the Declaration of Helsinki for research involving humans. Its protocol was reviewed and approved by the Ethics Board.

### Table 2. BMD and PA mean sizes on the first visit and at a 1-year follow-up

<table>
<thead>
<tr>
<th></th>
<th>First visit</th>
<th>One-year follow-up</th>
<th>Increase</th>
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<tbody>
<tr>
<td>BMD, (n)</td>
<td>64.7% (44/68)</td>
<td>86.7% (59/68)</td>
<td>22.06%</td>
</tr>
<tr>
<td>Mean size, μm</td>
<td>538.3±937.1</td>
<td>803.9±1146.5</td>
<td>265.6±418.1</td>
</tr>
<tr>
<td>PA mean size, μm</td>
<td>2,593.4±2303.3</td>
<td>2,977.9±2357.6</td>
<td>384.5±462.5</td>
</tr>
</tbody>
</table>
Conflict of Interest Statement

The authors declare that there is no conflict of interest to disclose.

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References


Author Contributions

Substantial contributions to conception and design of the work; or the acquisition, analysis, or interpretation of data for the work: José M. Ruiz-Moreno, Mariluz Puertas, and Ignacio Flores-Moreno. Drafting the work or revising it critically for important intellectual content: Jorge Ruiz-Medrano, Ignacio Flores-Moreno, and Elena Almazan-Alonso. Final approval of the version to be published: José M. Ruiz-Moreno, Mariluz Puertas, Jorge Ruiz-Medrano, and Elena Almazan-Alonso. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: José M. Ruiz-Moreno, Mariluz Puertas, Ignacio Flores-Moreno, Jorge Ruiz-Medrano, and Elena Almazan-Alonso.

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