Long-term Multicenter Analysis of Axial Length and ATN Grading in Myopic Choroidal Neovascularization

Análise Multicêntrica a Longo Prazo do Comprimento Axial e da Classificação ATN na Neovascularização Coroideia Associada à Miopia

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ABSTRACT

INTRODUCTION: High myopia is a major cause of visual impairment, particularly when complicated by choroidal neovascularization (CNV). While progress has been made in understanding myopic maculopathy (MM), a clear definition and its relationship with axial length (AL) is still evolving, with AL emerging as a key factor.

We aimed to evaluate the relationship between AL, treatment, and maculopathy progression in myopic eyes with CNV, based on the atrophy-traction-neovascularization (ATN) classification system.

METHODS: A multicenter retrospective analysis was conducted, including patients with treated myopic CNV and at least 5 years of follow-up from two centers: Unidade Local de Saúde (ULS) de Coimbra and ULS de São João. Patients were grouped by AL as follow: non-pathologic myopia (nPM, AL <28 mm), pathologic myopia (PM, AL ≥28 mm), and severe PM (sPM, AL ≥29.5 mm). A multivariate linear regression was used to predict maculopathy progression

RESULTS: Forty-two eyes (73.8% women) of 42 patients were analyzed: 12 eyes in nPM, 11 in PM, and 19 in sPM. The mean follow-up was 127.57±43.77 months (10.6 years). The patients of sPM group were younger at diagnosis (50.84±12.86 years) compared to the patients of PM group (62.68±11.19 years) (p=0.045). The mean center choroidal thickness (CCT) for all patients was 79.9 ± 47.6 µm, and significantly thinner in the sPM (p=0.025) and in eyes with posterior staphyloma (p=0.033). Worse final BCVA was correlated with increasing age and the atrophic (A) component at baseline (r=-0.34, p=0.029; r=-0.41, p=0.007). CCT also showed a negative correlation with the A component at baseline (r=-0.38, p=0.036). Age at diagnosis (B=0.28, p=0.016) and the presence of staphyloma (B=1.00, p=0.023) were associated with a higher risk of MM progression.

CONCLUSION: The study highlights how the development and progression of chorioretinal atrophy goes beyond simple measurement of AL. In fact, age at diagnosis and posterior staphyloma were significantly associated with MM progression, and choroidal atrophy was associated with atrophy of the retina. This indicates that the tridimensional shape of the eye, and associated changes in the sclera and choroid in the posterior pole may play a more relevant role in

this progression. Our analysis offers insights into MM and underscores the need for close monitoring of these patients.

KEYWORDS: Choroidal Neovascularization; Myopia, Degenerative; Tomography, Optical Coherence.

RESUMO

INTRODUÇÃO: A alta miopia é a principal causa de perda de visão, especialmente quando associada a neovascularização coroideia (CNV). Apesar dos avanços na compreensão da maculopatia miópica (MM), a sua definição e relação com o comprimento axial (CA) não estão estabelecidas. O CA foi proposto como um fator essencial na MM.

O nosso objetivo foi analisar a relação entre CA, tratamento e progressão da MM em olhos míopes com CNV, com base na classificação atrofia-tração-neovascularização (ATN).

MÉTODOS: Estudo multicêntrico retrospetivo que incluiu doentes com CNV miópica tratada e seguimento mínimo de 5 anos de dois centros: Unidade Local de Saúde (ULS) de Coimbra e ULS de São João. Os doentes foram agrupados em: miopia não patológica (nMP, CA <28 mm), miopia patológica (MP, CA ≥28 mm) e severa (sMP, CA ≥29,5 mm). Um modelo de regressão linear foi utilizado para prever a progressão da MM.

RESULTADOS: Quarenta e dois olhos (73,8% mulheres) de 42 doentes foram divididos: 12 no grupo nMP, 11 no MP e 19 no sMP. O seguimento médio foi de 127,57±43,77 meses (10,6 anos). O grupo sMP apresentou doentes mais jovens (50,84±12,86 anos) que o grupo MP (62,68±11,19 anos) (p=0,045). A espessura coroideia central (ECC) média de todos os doentes foi 79,9 ± 47,6 mm, com afinamento significativo na sMP (p=0,025) e nos olhos com estafiloma posterior (p=0,033). Uma pior AV final correlacionou-se com o aumento da idade e com o componente de atrofia (A) inicial (r=-0,34, p=0,029; r=-0,41, p=0,007). A ECC correlacionou-se com o componente A inicial (r=-0,38, p=0,036). A idade ao diagnóstico (B=0,28, p=0,016) e a presença de estafiloma (B=1,00, p=0,023) foram associadas a maior risco de progressão da MM.

CONCLUSÃO: Este estudo destaca que o desenvolvimento e a progressão da atrofia coriorretiniana não se limita à simples medição do CA. Na verdade, a idade ao diagnóstico e o estafiloma posterior foram significativamente associados à progressão da MM, e a atrofia coroideia foi associada à atrofia da retina. Isso indica que a forma tridimensional do olho, e as alterações na esclera e coroide no polo posterior, podem desempenhar um papel relevante na progressão. A nossa análise oferece novas perspetivas sobre a MM e reforça a necessidade de seguimento rigoroso desses pacientes.

PALAVRAS-CHAVE: Miopia Degenerativa; Neovascularização de Coroide; Tomografia de Coerência Óptica.

INTRODUCTION

Myopic maculopathy (MM) is one of the main causes of visual impairment and blindness worldwide. Its prevalence is expected to rise in response to the increasing global incidence of myopia, thereby amplifying the burden of MM.[1-3] The risk of developing MM increases exponentially with the severity of myopia, which can manifest in various clinical ways.

To address this complexity, the ATN classification system was recently introduced, providing a method to evaluate three key components of MM: atrophy (A), traction (T), and neovascularization (N), using fundus photography and optical coherence tomography (OCT) scans.[3-5] This comprehensive system enhances patient monitoring and unifies clinical reporting, aiding future research. Additionally, employing the ATN system to track the disease progression over time offers critical insights into MM's natural history.[3-5]

Since MM is often progressive and irreversible, early detection and timely treatment are crucial to mitigate its impact. Ophthalmic examination based on axial length (AL) thresholds can serve as a guide to prioritize patients. Recently, Moreno's group proposed specific AL cut-off points for differentiating between high myopia, pathological myopia (PM), and severe PM (sPM).[6] These categories are clinically significant, as eyes diagnosed with PM or severe PM differ substantially in terms of AL, best-corrected

visual acuity (BCVA), age, and ATN classification, all of which impact the potential complications and management strategies for these patients.[6,7]

The aims of this study were: (1) to evaluate the relationship between AL and ATN classification; (2) to identify differences in clinical characteristics (in terms of age, sex, BCVA, spherical equivalent, posterior staphyloma, treatment and central choroidal thickness (CCT)) in eyes with myopic CNV, stratified by AL cut-off values for PM and severe PM; and (3) to analyze the pattern of myopic progression based on ATN scores in a Portuguese cohort.

METHODS

STUDY DESIGN

This is a multicentre, retrospective longitudinal study of patients with myopic CNV at two tertiary hospitais, Unidade Local de Saúde de Coimbra – Hospitais da Universidade de Coimbra, Coimbra, Portugal and Unidade Local de Saúde de São João – Hospitais da Universidade de São João, Porto, Portugal. Participants included in the analysis were followed for a minimum duration of five years. Our study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee.

STUDY POPULATION

The study included adult patients with myopic CNV, whether previously treated or currently undergoing treatment. Inclusion criteria comprised high myopia (AL ≥ 26 mm or spherical equivalent (SE) ≥ −6 diopters) with CNV and a follow-up of at least five years. Exclusion criteria were other conditions known to be associated with CNV, including age-related macular degeneration, inflammation, angioid streaks, trauma, and macular dystrophies, as well as diabetic retinopathy and retinal vein occlusion. Despite both eyes being examined for each patient, only the findings from one eye were included in the analysis to avoid inter-eye correlations. Patients/ eyes were divided into three groups according to the AL: non-pathologic myopia (nPM) with AL <28 mm; PM eyes with AL ≥ 28 mm; and sPM with AL ≥ 29.5 mm.

DATA COLLECTION

Baseline characteristics included demographics such as age, sex, and ethnicity. Ocular characteristics comprised: BCVA, subjective refraction, lens status, AL measured by optical biometry (IOL Master, Carl Zeiss, Tubingen, Germany), number of intravitreal treatments, and type of anti-vascular endothelial growth factor (VEGF) administered.

Multimodal imaging included: ultra-widefield color fundus photography (Optos PLC, Dunfermline, United Kingdom), spectral-domain OCT (SD-OCT) (Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany), and fundus autofluorescence (Optos PLC, Dunfermline, United Kingdom). CCT was manually measured from the central retinal pigmented epithelium to the choroid-sclera interface, using the built-in software of the OCT device. Enhance depth imaging scan was not performed or necessary in any case, since the thinner choroid of myopes were seen in all cases. The presence of posterior staphyloma and dome-shaped macula was assessed based on fundus examination and OCT radial images. Curtin classification of staphylomas was used.

ATN GRADING

The ATN staging system was used to classify the MM of all patients and was graded by the first author. In cases of uncertainty, a senior retinal specialist (RS or CF) was consulted to make the final classification decision. The ATN system grades the A (atrophic), T (tractional) and N (neovascular) components, respectively, as follows: A0 (no myopic retinal lesions), A1 (tessellated fundus), A2 (diffuse chorioretinal atrophy), A3 (patchy chorioretinal atrophy) and A4 (complete macular atrophy); T0 (no macular schisis), T1 (inner or outer foveoschisis), T2 (inner and outer foveoschisis), T3 (foveal detachment), T4 (full-thickness macular hole) and T5 (macular hole + retinal detachment); and N0 (no myopic CNV), N1 (macular lacquer crack), N2a (active myopic CNV) or N2s (scar/Fuchs spot).[6]

PROGRESSION OF MYOPIC MACULOPATHY

Progression of MM was defined as the progression of any score in any of the three components of the ATN classification system. Since all patients have myopic CNV and N2a and N2s are dynamic stages, only the A and T components were fully evaluated for progression.

STATISTICAL ANALYSIS

Snellen BCVA measurements were converted to ETDRS letter score for data analysis. The Kolmogorov-Smirnov test was used to assess the normal distribution of the variables. Clinical and demographic data were expressed as mean plus standard deviation for continuous variables, and in absolute numbers and percentages for categorical variables. To compare means and proportions among groups, we used one-way ANOVA for normally distributed samples, the Kruskal-Wallis Test for non-normally distributed samples and Chi-square test for categorical variables. Pearson and Spearman correlations were used to determine the correlations for normally distributed and non-normally distributed variables, respectively. A multivariate linear regression analysis was performed to explore the linear relationships between AL, age, CCT, posterior staphyloma, and the number of treatments to predict MM progression. A value of $p<0.05$ was considered statistically significant. Statistical analysis was performed with SPSS Statistics version 29.0.0 (IBM Corporation, New York).

RESULTS

Forty-two eyes (73.8% women) of 42 patients with high myopia were divided into three groups: 12 eyes in nPM, 11 eyes in PM, and 19 eyes in sPM. The mean follow-up period was 127.57 ± 43.77 months (approximately 10.6 years) and was similar between the groups.

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS – COMPARISON BETWEEN GROUPS

The mean age in the last appointment was 65.9 ± 12.8 years (range, 24-92 years). Patients in the sPM group were younger at diagnosis of myopic CNV (50.84 ± 12.86 years) compared with PM (62.68 ± 11.19 years) (p=0.045). Moreover, the mean CCT for the whole group was 79.9 ± 47.6, with a significant thinning observed in the sPM compared to the nPM group (p=0.025) and in the eyes with posterior staphyloma (mean CCT 67.3 ± 46.2, p=0.033).

Other baseline characteristics such as sex, BCVA, presence of staphyloma, dome-shaped macula and previous phacoemulsification did not differ between groups. The demographics and clinical characteristics of the study population are summarized in Table 1.

Regarding the A and T components of the ATN grading, the sPM presented with higher baseline A (31.60% of eyes with patchy atrophy) compared to the other groups. Overall, the A component presented notable progression during follow-up, with A3 increasing from 26% of eyes at baseline to 50% at the final assessment. The T component remained stable throughout the follow-up in most eyes, except for 3 patients that progressed from non-traction (T0) to full-thickness macular hole (T4). Considering both factors, MM progression was observed in more than half the population studied (64.30%, n=27). The number and percentage of each stage by AL-cut-offs offs is outlined in Tables 2 and 3 and represented in Figs. 1 to 3.

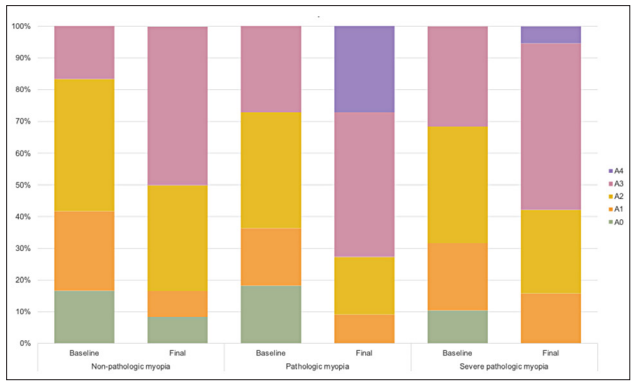

Figure 1. Stacked column chart of A component grading for each group (baseline and final).

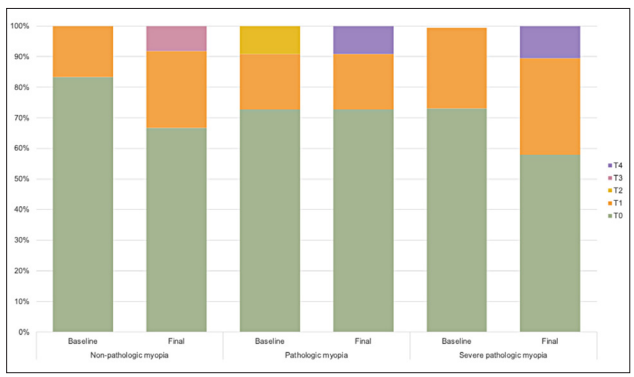

Figure 2. Stacked column chart of T component grading for each group (baseline and final).

Table 1. Clinical and demographic characteristics of patients divided by groups.

	All cases (n=42)	Non-PM (n=12)	PM (n=11)	Severe PM (n=19)	p-value
Age (y), mean ± SD	65.88 ± 12.79	64.82 ± 11.95	72.55 ± 10.80	62.63 ± 13.48	0.116
Age at diagnosis (y), mean ± SD	55.05 ± 13.09	54.58 ± 12.76	62.68 ± 11.19	50.84 ± 12.86	**0.045**
Sex, n (%)					0.652
Male	11 (26.20)	2 (16.70)	3 (27.30)	6 (31.60)	
Female	31 (73.80)	10 (83.30)	8 (72.70)	13 (68.40)	
Baseline BCVA (ETDRS letters), mean ± SD	53.69 ± 20.30	60.00 ± 15.67	47.27 ± 22.18	53.42 ± 21.54	0.331
Final BCVA (ETDRS letters), mean ± SD	49.17 ± 29.30	46.67 ± 29.80	45.45 ± 28.94	52.89 ± 30.34	0.761
Variance BCVA (ETDRS letters), mean ± SD	-4.52 ± 27.05	-13.33 ± 22.09	-1.82 ± 22.94	-0.53 ± 31.66	0.417
Pseudophakia, n (%)	29 (69.00)	5 (41.70)	9 (81.80)	15 (78.90)	0.052
Dome-shaped macula, n (%)	2 (4.80)	2 (16.70)	0	0	0.072
Axial length (mm), mean ± SD	29.61 ± 2.39	27.00 ± 0.64	28.77 ± 0.41	31.75 ± 1.68	**<0.001**
SE (diopters), mean ± SD	-13.38 ± 6.02	-8.28 ± 2.97	-11.25 ± 4.74	-17.50 ± 5.09	**<0.001**
Center choroidal thickness (mm), mean ± SD	74.26 ± 47.59	104.55 ± 44.25	63.29 ± 33.81	54.54 ± 46.10	**0.025**
Posterior staphyloma, n (%)	38 (90.50)	9 (75.00)	11 (100)	18 (94.70)	0.087
Type I	12 (28.60)	3 (25.00)	2 (18.20)	7 (36.80)	
Type II	8 (19.00)	0	1 (9.10)	7 (36.80)	
Type III	15 (35.70)	6 (50.00)	7 (63.60)	2 (10.50)	
Type VII	2 (4.80)	0	0	2 (10.50)	
Type IX	1 (2.40)	0	1 (9.10)	0	
Follow-up (months), mean ± SD	127.57 ± 43.77	122.25 ± 47.19	114.82 ± 37.63	138.32 ± 44.47	0.332

BCVA – best corrected visual acuity; PM – pathological myopia; SD – standard deviation; SE – spherical equivalent.

Table 2. Baseline ATN scores for all groups.

	All cases (n=42)	Non-PM (n=12)	PM (n=11)	Severe PM (n=19)
Baseline A				
A0, n (%)	6 (14.30)	2 (16.70)	2 (18.20)	2 (10.50)
A1, n (%)	9 (21.40)	3 (25.0)	2 (18.20)	4 (21.10)
A2, n (%)	16 (38.10)	5 (41.70)	4 (36.40)	7 (36.80)
A3, n (%)	11 (26.20)	2 (16.70)	3 (27.30)	6 (31.60)
A4, n (%)	0	0	0	0
Baseline T				
T0, n (%)	32 (76.20)	10 (83.30)	8 (72.70)	14 (73.70)
T1, n (%)	9 (21.40)	2 (16.70)	2 (18.20)	4 (26.30)
T2, n (%)	1 (2.40)	0	1 (9.10)	0
T3, n (%)	0	0	0	0
T4, n (%)	0	0	0	0
T5, n (%)	0	0	0	0
Baseline N				
N0, n (%)	0	0	0	0
N1, n (%)	2 (4.80)	0	1 (9.10)	1 (5.30)
N2, n (%)	40 (95.20)	12 (100)	10 (90.90)	18 (94.70)

A – atrophic; N – neovascular; PM – pathological myopia; T – tractional.

Table 3. Final ATN scores for each group.

	All cases (n=42)	Non-PM (n=12)	PM (n=11)	Severe PM (n=19)
Final A				
A0, n (%)	1 (2.40)	1 (8.30)	0	0
A1, n (%)	5 (11.90)	1 (8.30)	1 (9.10)	3 (15.80)
A2, n (%)	11 (26.20)	4 (33.30)	2 (18.20)	5 (26.30)
A3, n (%)	21 (50.00)	6 (50.00)	5 (45.50)	10 (52.60)
A4, n (%)	4 (9.50)	0	3 (27.30)	1 (5.30)
Final T				
T0, n (%)	27 (64.30)	8 (66.70)	8 (72.7)	11 (57.90)
T1, n (%)	11 (26.20)	3 (25.00)	2 (18.20)	6 (31.60)
T2, n (%)	0	0	0	0
T3, n (%)	1 (2.40)	1 (8.30)	0	0
T4, n (%)	3 (7.10)	0	1 (9.10)	2 (10.50)
T5, n (%)	0	0	0	0
Final N				
N0, n (%)	0	0	0	0
N1, n (%)	0	0	0	0
N2, n (%)	42 (100)	12 (100)	11 (100)	19 (100)
N2a, n (%)	9 (21.40)	3 (25.00)	3 (27.30)	3 (15.80)
N2b, n (%)	33 (78.60)	9 (75.00)	8 (72.70)	16 (84.20)

A – atrophic; N – neovascular; PM – pathological myopia; T – tractional.

FUNCTIONAL OUTCOME AND TREATMENT NEEDS

In the last visit, 31.0% (n=13) of patients reached visual gain (BCVA >5 L), 19.0% (n=8) of patients maintained visual acuity (range, -5 to + 5L, inclusive), while the remaining half of patients lost more than 5 letters (50%, n=21). Interestingly, the mean change in VA between baseline and the final visit was higher in nPM (-13.33 ± 22.09) compared to PM (-1.82 ± 22.94) and sPM (-0.53 ± 31.66) (p>0.05).

The total number of anti-VEGF injections was higher in

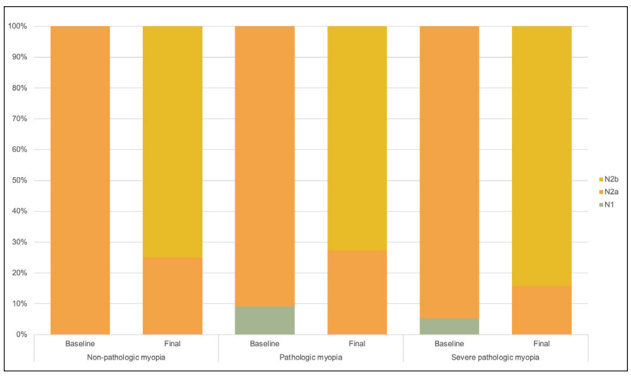

Figure 3. Stacked column chart with N component grading for each group (baseline and final).

the PM group compared to the sPM (23.09 ± 13.72 *vs* 14.89 ± 7.77, respectively) (p>0.05), with most patients having ranibizumab followed by aflibercept. Recurrence rate of CNV was higher in the sPM (73.70%, n=14 *vs* 63.60%, n=7 in PM *vs* 50.00%, n=6 in nPM), while fellow eye involvement was comparable between groups. Treatment characteristics for each group are presented in Table 4.

UNIVARIATE ANALYSIS

Final BCVA was negatively correlated with age (r=-0.34, p=0.029), the A component at baseline (r=-0.41, p=0.007) and in the last appointment (r=-0.35, p=0.023). Additionally, CCT was negatively correlated with A baseline (r=-0.38, p=0.036), while age was linearly correlated with final A component (r=0.36, p=0.018) and SE (r=0.41, p=0.034).

In our study, AL was inversely correlated with the CCT (r=-0.457, p=0.001). Yet, it was not correlated with age or with any component of the ATN grading. Posterior staphyloma was present in 90.5% of eyes and was associated with higher AL (r=0.32, p=0.038), and lower CCT (r=-0.40, p=0.026), but no correlation was found with AT components (Table 1).

MULTIVARIATE ANALYSIS

The multivariate linear regression model was significant in the overall (F (5,25) = 3.02, p=0.029), but not all predictors were. Age at diagnosis (B=0.28, p=0.016) and staphyloma (B=1.00, p=0.023) were significantly associated with a higher prediction of MM progression. Yet, the number of treatments, AL and CCT did not significantly affect the progression.

DISCUSSION

This is the first study to longitudinally evaluate the relationship between the proposed ATN grading system and AL and other clinical characteristics in a Portuguese cohort of myopic CNV patients followed in two tertiary hospitals.

In this study we adopted the new, simple and comprehensive ATN classification system, focusing on three main components of the MM. This reliable and reproducible method of classification was crucial for ensuring consistent grading during follow-up and enabling comparisons with other studies.[3,4,8] We found that atrophy and higher grades of myopic tractional maculopathy were more frequently observed in eyes with AL greater than 28 mm. Moreover, while most patients showed an expansion of atrophic areas, the predominant progression pattern in longer eyes was a transition from diffuse chorioretinal atrophy (A2) to patchy atrophy (A3). Yet, surprisingly, AL was not correlated with any component of the ATN grading system in our analysis, which can be attributed to the small patient sample size but also highlights the controversial nature of this relationship.

Conversely, age demonstrated a positive linear correlation exclusively with the A component, consistent with previous studies.[6,8-10] This finding suggests that older myopic patients, particularly those with additional risk factors, are more predisposed to developing advanced stages of atrophic maculopathy. Additionally, CCT was negatively correlated with baseline A, implying that choroidal thinning may play a critical role in the early stages of atrophic myopic maculopathy.[11,12] The precise mechanism underlying this association remains unclear, although it may be related to changes in the choroidal vascular structure and associated ischemic environment in the outer retina, as previously suggested by animal studies.[1]

In addition, CCT was inversely correlated with AL, consistent with the understanding that myopic eyes typically have thinner choroids due to mechanical stretching from axial elongation.[8,11,16] Previous studies have also demonstrated that thinner choroids are associated with incomplete resolution of myopic CNV,[17] which may account for the lower CCT, higher frequency of anti-VEGF injections, and 63.6% recurrence rate observed in the PM group. How-

Table 4. Treatment characteristics for each group.

	All cases (n=42)	Non-PM (n=12)	PM (n=11)	Severe PM (n=19)	*p*-value
Type of anti-VEGF, n (%)					0.281
Ranibizumab	35 (83.33)	10 (83.33)	8 (72.72)	17 (89.47)	
Aflibercept	18 (42.86)	4 (33.33)	7 (63.64)	5 (26.32)	
Bevacizumab	8 (19.05)	2 (16.67)	1 (9.09)	5 (26.32)	
Total number treatment, mean ± SD	18.38 ± 11.35	19.58 ± 12.88	23.09 ± 13.72	14.89 ± 7.77	0.149
Recurrence, n (%)	27 (64.30)	6 (50.00)	7 (63.60)	14 (73.70)	0.407
Fellow eye involvement, n (%)	21 (50.00)	5 (41.70)	6 (54.50)	10 (52.60)	0.788

VEGF – vascular endothelial growth factor; PM – pathological myopia; SD – standard deviation.

ever, the sPM had even more recurrences but needed fewer injections, which is an interesting result. We can hypothesize that with extremely thin choroids, such as those observed in this group, there is a lower neovascular potential associated with choriocapillaris insufficiency, translating to less aggressive CNVs, more amenable to control with fewer anti-VEGF agents.[6,17] This potential association between treatment needs and choroidal morphology deserves further investigation to elucidate its underlying mechanisms.

The presence of posterior staphyloma is a key factor in the development of MM, observed in 90.5% of eyes in this population sample. It was associated with higher AL and lower CCT, consistent with the understanding that posterior staphyloma is a fundamental lesion in pathological myopia and a critical factor in choroidal thinning in highly myopic eyes.[18] Eyes without staphyloma were found primarily in the nPM group, reinforcing the concept that staphyloma is essential in the pathogenesis of MM. Although no direct correlation was identified between posterior staphyloma and the ATN components, multivariate linear regression analysis revealed that staphyloma was significantly predictive of MM progression. The exact role of posterior staphyloma in the progression of MM remains unclear, though recent studies have highlighted its potential impact.[18,19] For instance, Zhou *et al*[18] concluded that posterior staphyloma is related to a reduction in choroidal stroma and vessels, leading to a thinner choroid and choroidal structural remodeling, which may be associated with myopia progression. Other studies suggest that the progression of maculopathy occurs relatively quickly because staphyloma facilitates this progression.[20]

In this longitudinal study with a mean follow-up over 10 years, MM progression was observed in 57% of eyes analyzed and was associated, in multivariate analysis, with age at diagnosis and the presence of staphyloma. This aligns with the retrospective findings of Fang *et al*,[21] who reported a 58.6% progression with a mean follow-up of 18 years. However, our progression rate was higher than a recent study using the same ATN classification, which reported 42% progression rate.[6] We attribute this discrepancy to factors such as the longer follow-up period in our study, the older age of our patient population, and the presence of CNV, which predisposes to atrophy development and enlargement.

The PM group presented worse baseline BCVA compared to other groups. This discrepancy may be attributed to the relatively older age of this group and the previously noted age-dependent progression of atrophic changes. Additionally, the mean change in VA between baseline and the final visit was greater in eyes with an AL less than 28 mm (nPM group), a group that also showed significant progression to patchy atrophy, increasing from 16.7% to 50%. Consequently, as expected, final BCVA was negatively correlated with both age and the baseline A component, reinforcing that visual outcomes in myopic patients with CNV are strongly influenced by age, as well as the development and progression of atrophy surrounding regressed CNV tissue.[15] Notably, our study included only patients with myopic CNV (N > 2), and the type or duration of treatment did not significantly differ between groups. Therefore, the impact of intravitreal anti-VEGF therapy on the progression of chorioretinal atrophy was not possible to elucidate in our analysis.

As for limitations, first, the relatively low n in each group might underscore important associations in the analysis. Second, due to the inclusion criteria, no eyes were classified as N0, limiting the statistical power of the N component analysis. Consequently, extrapolation of these findings should be approached with caution, considering the specific characteristics of this study population. Third, the complexity of measuring CCT in highly myopic eyes introduced variability in measurement times, which may have affected the consistency of the results. Yet, standardizing the timing of OCT scan acquisition in clinical practice is challenging. Fourth, the ATN classification does not account for the enlargement of preexisting areas of diffuse or patchy atrophy, possibly leading to an underestimation of MM progression. Finally, additional studies are needed to validate the axial length cut-off points observed in this study. Despite this, our study is the first and only to analyze the ATN system in a Portuguese cohort of myopic CNV patients, exploring its relationships with CCT, AL, age, and posterior staphyloma. Furthermore, the long-term follow-up, combined with detailed demographic and clinical characterization, along with a classification based on expert evaluation of multimodal imaging, further strengthens our findings.

In conclusion, the association between chorioretinal atrophy and AL remains controversial, and other factors such as age, and mechanical conformational changes caused by the presence of a staphyloma and the thinning of the choroid, appear to be more important in the progression of MM and atrophy development. Patients with these characteristics should be advised of their risk of progression. In addition, treatment needs were not different between groups, and the functional prognosis of myopic CVN was mainly dependent on the progression of macular atrophy and not simply on AL stratification.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

TM: Conceptualization, formal analysis, data collection, writing original draft.

AMF and ML: Data collection, writing and review.

ML: Data collection, writing and review.

CF: Conceptualization, formal analysis, writing, review and editing.

AC: Conceptualization, writing, review and editing.

RS: Conceptualization, formal analysis, writing, review and editing.

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TM: Conceitualização, análise formal, recolha de dados, redação do rascunho original.

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CF: Conceitualização, análise formal, redação, revisão e edição.

AC: Conceitualização, redação, revisão e edição.

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Todos os autores leram e aprovaram o manuscrito.

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