Prognostic Value of Myopic Disc Deformation in Myopic Choroidal Neovascularization: A 6-year Follow-up Study

Ye Eun Han

Asan Medical Center

Yoon Jeon Kim (✉ anne215@gmail.com)

Asan Medical Center

Hyun Seung Yang

Seoul Shinsegae Eye Center, Eui Jung Bu, Gyeonggi-do

Byung Gil Moon

Seoul Shinsegae Eye Center, Eui Jung Bu, Gyeonggi-do

Joo Yong Lee

Asan Medical Center

June-Gone Kim

Asan Medical Center

Young Hee Yoon

Asan Medical Center

Research Article

Keywords:

Posted Date: March 7th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1388633/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Purpose: To evaluate the clinical characteristics of myopic choroidal neovascularization (mCNV) with myopic disc deformations and explore whether myopic disc features are associated with the prognosis of mCNV.

Methods: Patients with subfoveal mCNV who received anti-vascular endothelial growth factor (VEGF) and followed for > 3 years were included. Myopic disc deformations were quantified as the tilt ratio (the longest/shortest disc diameter), area of the β -zone peripapillary atrophy (PPA), and β -PPA/disc area ratio (PDR). We compared the clinical characteristics in terms of myopic disc features and identified the prognostic factors using Cox regression analysis.

Results: Among a total of 80 eyes (50 with disc tilt), 29 (36.3%) eyes developed macular atrophy during 80.7 ± 34.8 months. Patients with disc tilt required more frequent anti-VEGF ($P=0.044$) and had worse final visual acuity (VA) ($P=0.011$) and a higher incidence of macular atrophy ($P=0.015$). Larger PDR, which had a strong correlation with large tilt ratio ($P=0.006$), showed significant correlations with longer axial length ($P=0.006$), worse VA ($P=0.012$), and thinner subfoveal choroidal thickness ($P=0.015$). Large PDR was a risk factor for macular atrophy ($HR=2.257$, $P<0.001$) and poor visual outcome ($HR=1.407$, $P=0.015$).

Conclusion: Subfoveal mCNV with myopic disc deformations had worse functional and structural outcomes.

Introduction

Myopic choroidal neovascularization (CNV) is a vision-threatening complication¹ of degenerative myopia, and develops in at least 5–11% of patients with a high degree of myopia². The progressive and excessive elongation of the eyeball causes various degenerative changes involving the sclera, choroid, and retina, and many cases with myopic CNV develop macular atrophies and scarring that lead to legal blindness^{3,4}. The exact mechanism for the development and progression of myopic CNV is unknown, but a combination of mechanical and hemodynamic factors with genetic predisposition is a likely culprit⁵. In previous studies, old age, large CNV size, subfoveal location of the CNV, thin subfoveal choroidal thickness, longer axial length, and poor baseline BCVA were identified as poor prognostic factors for myopic CNV^{6–8}.

In myopia, morphological changes of the optic disc such as optic disc tilt, torsion, and formation of PPA occur^{9,10}. Specifically, disc tilting and PPA formation are known to be accompanied by mechanical scleral stretching and posterior deformation secondary to axial elongation^{11,12}. In addition, a recent study¹³ demonstrated that the foveal avascular zone area as well as peripapillary microvasculature decreased with increases in the disc tilt of highly myopic eyes. This suggests that optic disc features might be associated with not only macular structural distortion but also macular microvasculatures in highly

myopic eyes. In this context, we hypothesized that optic disc deformity and its related disc features could be potential prognostic factors for myopic CNV, considering that they are related to both the mechanical and hemodynamic factors.

Hence, in this study, we aimed to evaluate the clinical characteristics and outcomes of myopic CNV according to the presence of disc tilt. We also explored which disc-related parameters are significantly associated with the clinical outcomes of myopic CNV and investigated the prognostic values of myopic disc tilt and its related disc features for myopic CNV.

Results

A total of 80 eyes with subfoveal myopic CNV were included in the study, and were divided into those without tilted disc ($n = 30$, 37.5%) and those with tilted disc ($n = 50$, 62.5%). The demographic and baseline ocular characteristics are summarized in Table 1. Compared with those without tilted disc, eyes with tilted disc belonged to older patients (56.4 ± 11.5 vs. 45.0 ± 19.5 years, $P = 0.006$) and had longer axial length (30.3 ± 1.6 vs. 28.5 ± 0.6 mm, $P = 0.027$), more myopic refractive errors (-13.4 ± 5.7 vs. -9.8 ± 3.9 diopters, $P = 0.008$), more lacquer cracks (20 vs. 5, $P = 0.045$), thinner subfoveal choroidal thickness (65.7 ± 57.2 vs. 130.8 ± 97.0 μm , $P < 0.001$), and higher proportion of pseudophakia (64% vs. 9%, $P = 0.003$). The proportion of female patients was slightly higher in eyes with tilted disc; however, there were no significant differences regarding systemic diseases, baseline CNV size, and baseline LogMAR BCVA.

Table 1

Baseline demographics and ocular characteristics according to the presence of myopic tilted disc

	Total eyes (n = 80)	Without tilted disc (n = 30)	With tilted disc (n = 50)	P Value
Demographics				
Age, years	52.1 ± 15.9	45.0 ± 19.5	56.4 ± 11.5	0.006
Female, N (%)	49 (61.3)	14 (46.7)	35 (70.0)	0.057
Systemic disease, N (%)				
Diabetes mellitus	5 (6.3)	2 (6.7)	3 (6.0)	0.62
Hypertension	19 (23.8)	5 (16.7)	14 (28.0)	0.29
Ocular characteristics				
Lens status: pseudophakia, N (%)	39 (48.7)	9 (30)	32 (64)	0.003
Axial length, mm	30.0 ± 1.7	28.5 ± 0.6	30.3 ± 1.6	0.027
Refractive errors, diopters	-12.0 ± 5.3	-9.8 ± 3.9	-13.4 ± 5.7	0.008
Presence of lacquer crack, N (%)	25 (31.3)	5 (16.7)	20 (40.0)	0.045
CNV size, mm ²	0.77 ± 0.64	0.65 ± 0.38	0.83 ± 0.75	0.16
sfCT, μm	85.6 ± 83.7	130.8 ± 97.0	65.7 ± 57.2	< 0.001
Baseline BCVA, LogMAR	0.64 ± 0.55	0.52 ± 0.60	0.71 ± 0.51	0.13
<i>CNV = choroidal neovascularization; sfCT = subfoveal choroidal thickness; BCVA = best corrected visual acuity</i>				

After 80.7 ± 34.8 months of follow-up, the mean LogMAR BCVA was changed from 0.64 ± 0.55 to 0.75 ± 0.70 and 29 (36.3%) eyes developed macular atrophy. The two groups showed significant differences in the treatment outcomes as shown in Table 2. Eyes with myopic tilted disc received more intravitreal anti-VEGF injections for the resolution of CNV activities (6.2 ± 5.6 vs. 4.4 ± 2.7 , $P = 0.044$) and had worse final LogMAR BCVA (0.90 ± 0.67 vs. 0.50 ± 0.67 , $P = 0.011$) with significant deterioration during follow-up period (0.20 ± 0.77 vs. -0.03 ± 0.71 , $P = 0.050$) as well as a higher incidence of macular atrophy (24 vs. 5, $P = 0.015$).

Table 2

Treatment outcomes of eyes with myopic choroidal neovascularization according to the presence of myopic tilted disc

	Total eyes (n = 80)	Without tilted disc (n = 30)	With tilted disc (n = 50)	P Value
Total follow-up duration, months	80.7 ± 34.8	77.5 ± 34.4	82.7 ± 35.2	0.52
Total No. of anti-VEGF injections	5.6 ± 4.8	4.4 ± 2.7	6.2 ± 5.6	0.044
Recurrence of mCNV, N (%)	27 (33.8)	9 (30.0)	18 (36.0)	0.63
BCVA at the last visit	0.75 ± 0.70	0.50 ± 0.67	0.90 ± 0.67	0.011
BCVA changes during follow-up	0.12 ± 0.72	-0.03 ± 0.71	0.20 ± 0.77	0.050
Macular atrophy at the last visit	29 (36.3)	5 (16.7)	24 (48.0)	0.015
<i>anti-VEGF = anti-vascular endothelial growth factor; BCVA = best corrected visual acuity; mCNV = myopic choroidal neovascularization</i>				

When we compared the optic disc characteristics (Table 3), we found that eyes with optic disc tilt had a significantly higher PDR at the initial (4.18 ± 3.16 vs. 1.78 ± 2.10 , $P < 0.001$) and final presentation (6.03 ± 5.10 vs. 2.41 ± 2.88 , $P < 0.001$). Regardless of the presence of optic disc tilt, the absolute degree of optic disc tilt (1.42 ± 2.72 to 1.70 ± 0.27) and PDR (3.28 ± 3.03 to 4.66 ± 4.72) were all increased during follow-up. However, the degrees of these changes were significantly larger in eyes with optic disc tilt. In contrast, disc torsion did not show differences between the two groups.

Table 3
Disc morphological characteristics and changes during follow-up according to the presence of myopic tilted disc

	Total eyes (n = 80)	Without tilted disc (n = 30)	With tilted disc (n = 50)	P Value
Disc tilt ratio				
Baseline	1.42 ± 2.72	1.16 ± 0.08	1.57 ± 0.22	< 0.001
Final	1.70 ± 0.27	1.32 ± 0.16	1.95 ± 0.32	< 0.001
Changes during follow-up	0.29 ± 0.44	0.16 ± 0.45	0.38 ± 0.31	0.019
β-zone PPA area/disc area				
Baseline	3.28 ± 3.03	1.78 ± 2.10	4.18 ± 3.16	< 0.001
Final	4.66 ± 4.72	2.41 ± 2.88	6.03 ± 5.10	< 0.001
Changes during follow-up	1.38 ± 2.11	0.63 ± 0.97	1.84 ± 2.46	0.003
Disc torsion				
Baseline	8.05 ± 4.21	7.59 ± 3.83	8.31 ± 4.44	0.47
Final	9.84 ± 5.29	9.41 ± 5.05	10.09 ± 5.47	0.59
Changes during follow-up	1.72 ± 3.21	1.66 ± 3.41	1.75 ± 3.13	0.90
<i>β-zone PPA area/disc area = β-zone peripapillary area to disc area ratio</i>				

Partial correlation coefficient between ocular characteristics and parameters of myopic optic disc deformations (disc tilt ratio and PDR) adjusted for age and sex are shown in Table 4. There was a strong correlation between the tilt ratio and PDR ($r = 0.717$, $P = 0.006$). While the tilt ratio showed borderline correlations with axial length ($r = 0.529$, $P = 0.063$) and subfoveal choroidal thickness ($r = -0.401$, $P = 0.074$), PDR showed significant correlations with axial length ($r = 0.717$, $P = 0.006$), baseline and final LogMAR BCVA ($r = 0.672$, $P = 0.012$ and $r = 0.656$, $P = 0.015$, respectively), and subfoveal choroidal thickness ($r = -0.656$, $P = 0.015$).

Table 4
Partial Correlation Analysis between Disc Tilt Ratio and PPA characteristics and ocular parameters
adjusted for age and sex

	Disc tilt ratio		β -zone PPA area/disc area	
	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value
Axial length	0.529	0.063	0.717	0.006
Baseline BCVA	0.388	0.19	0.672	0.012
Final BCVA	0.213	0.19	0.656	0.015
CNV size	-0.017	0.76	0.163	0.59
Subfoveal choroidal thickness	-0.401	0.074	-0.656	0.015
Disc tilt ratio	NA		0.717	0.006
β -zone PPA area/disc area	0.717	0.006	NA	
<i>BCVA = best corrected visual acuity; CNV = choroidal neovascularization; β-zone PPA area/disc area = β-zone peripapillary area to disc area ratio; NA = not available</i>				

To identify the risk factors for poor anatomical and functional outcomes, univariate and multivariate Cox proportional hazard models were conducted including the baseline variables. In the multivariate analysis, larger baseline CNV size (HR = 8.461 [95% CI, 1.722–41.557], $P = 0.009$) and large PDR (HR = 2.257 [95% CI, 1.454–3.505], $P < 0.001$) were found to be significant risk factors for the occurrence of macular atrophy at the last visit (Table 5). Meanwhile, older age (HR = 1.063 [95% CI, 1.010–1.118], $P = 0.020$) and large PDR (HR = 1.407 [95% CI, 1.068–1.853], $P = 0.015$) were associated with poor final visual outcome ($< 20/60$, Snellen mean) (Table 6). Representative images demonstrate the poor anatomical and functional outcomes of subfoveal myopic CNV in eyes with large optic disc tilt and PDR (Fig. 2).

Table 5

Baseline characteristics associated with the occurrence of macular atrophy in eyes with myopic choroidal neovascularization

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	<i>P</i> Value	HR (95% CI)	<i>P</i> Value
Demographic factors				
Age	1.075 (1.031–1.121)	0.001		
Female sex	1.437 (0.441–4.682)	0.55		
Diabetes mellitus	1.001 (0.279–10.197)	0.99		
Hypertension	3.810 (0.903–16.068)	0.069		
Ocular factors				
Baseline BCVA	2.560 (1.009–6.499)	0.048		
Axial length	1.061 (0.839–1.226)	0.19		
CNV size	6.034 (1.732–21.025)	0.005	8.461 (1.722–41.557)	0.009
Subfoveal choroidal thickness	0.990 (0.981–0.998)	0.02		
Presence of optic disc tilt	4.518 (1.387–14.715)	0.012		
β -zone PPA area/disc area	2.216 (1.471–3.338)	< 0.001	2.257 (1.454–3.505)	< 0.001
<i>BCVA = best corrected visual acuity; CNV = choroidal neovascularization; β-zone PPA area/disc area = β-zone peripapillary area to disc area ratio</i>				

Table 6
Baseline characteristics associated with poor visual outcomes in eyes with myopic choroidal neovascularization

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	PValue	HR (95% CI)	PValue
Demographic factors				
Age	1.061 (1.029–1.094)	< 0.001	1.063 (1.010–1.118)	0.020
Female sex	0.849 (0.429–1.681)	0.40		
Diabetes mellitus	0.907 (0.179–3.197)	0.90		
Hypertension	2.009 (1.004–4.021)	0.049		
Ocular factors				
Baseline BCVA	2.086 (1.205–3.610)	0.009		
Axial length	1.053 (0.991–1.226)	0.12		
CNV size	1.596 (1.102–2.311)	0.013		
Subfoveal choroidal thickness	0.982 (0.969–0.994)	0.004		
Presence of optic disc tilt	2.979 (1.117–7.947)	0.029		
β -zone PPA area/disc area	1.225 (1.120–1.338)	< 0.001	1.407 (1.068–1.853)	0.015
<i>BCVA = best corrected visual acuity; CNV = choroidal neovascularization; β-zone PPA area/disc area = β-zone peripapillary area to disc area ratio</i>				

Discussion

Our current study shows that myopic CNV in eyes with disc tilt was predisposed to worse functional and anatomical outcomes as well as worse baseline characteristics compared with those without disc tilt. In particular, high PDR, indicating PPA enlargement and small disc area, was significantly correlated with pathologic ocular changes of myopia and was the common independent prognostic factor for both the occurrence of macular atrophy and poor visual outcomes. To the best of our knowledge, this is the first study to investigate whether the optic disc tilt and PPA-related disc characteristics are associated with functional and structural outcomes of myopic CNV. This is a clinically significant observation as it highlights the importance of paying more attention to myopic CNV patients with disc tilting and PPA despite good visual acuity and mild phenotype at the early stage. Moreover, the disc morphologic features could be intuitively confirmed only using the fundus photo. Thus, PDR may be a useful parameter in the management of myopic CNV.

Although the underlying mechanisms of the association between myopic optic disc deformation (disc tilt and PPA)-related parameters and prognosis of myopic CNV are yet to be defined, we propose an

explanation for this observation based on two aspects—structural deformation and hemodynamic change. First, disc tilt and PPA are associated with progressive structural deformation of the eyeball, which is related to well-known prognostic factors for myopic CNV such as old age, longer axial length, and thin choroidal thickness. Recently, eyes with disc tilt were shown to have a thin choroidal thickness and a higher risk for myopic maculopathy¹⁷. In addition, several studies^{18 19} have reported that the development or enlargement of PPA was a risk factor for the progression of myopic maculopathy and the progression from high myopia to pathologic myopia. Specifically, when the deformation of the eyeball is gradually aggravated with progressive eyeball elongation, the choroidal thickness in eyes with large PPA is more prone to further thinning and subsequent myopic chorioretinal atrophic changes.

The second possible explanation is that the differences in clinical course might be caused by perfusion insufficiency in association with peripapillary structural deformities. This speculation is supported by the study by Sung et al.¹³, which reported the differences of retinal microvasculature according to the degree of optic disc tilt in highly myopic eyes. Moreover, choroidal structural changes were considered to be related to choroidal perfusion, although the causal relationship between the two needs to be elucidated in a targeted study. A previous report²⁰ suggested that significant choroidal changes lead to decreases in the choroidal blood flow and that ischemia-induced expression of growth factors caused by choroidal hypoperfusion is possibly related to the development and progression of myopic CNV.

In our present analysis, we found that optic disc tilt and PDR were strongly related to each other in eyes with subfoveal myopic CNV. In addition, both of their degrees had increased during follow-up and these changes in optic disc morphology were more prominent in eyes with optic disc tilt. Interestingly, after adjusting for confounding factors and multivariate analysis, PDR was the most robust risk factor for subfoveal myopic CNV even in consideration with disc tilt. This difference might be due to the fact that PDR is a parameter comprising PPA and optic nerve head changes, (e.g., disc tilt), while the tilt ratio only represents optic nerve head morphologic changes. As an eyeball is elongated, nasalization of the optic nerve head and temporal stretching of sclera occur and lead to disc tilt and PPA, respectively²¹. Since PDR represents both changes, it would be a more potentially useful parameter for delineating degenerative myopic changes.

One of the strengths of this study is that we focused only on subfoveal myopic CNV. Moreover, the follow-up duration and the number of patients were sufficient for the analysis of prognostic factors. Despite these strengths, the present study also has some limitations aside from its retrospective design. First, the tilted optic disc was evaluated in two-dimensional fundus photos, which might not exactly reflect the shape of the three-dimensional optic disc. Lee et al.²² showed that the increases in the ovality index did not represent the changes of posterior polar curvature, but rather a shift of the temporal disc margin. With two-dimensional assessment, we could only make a limited evaluation of the optic disc alterations. Hence, a three-dimensional method to measure the tilt ratio needs to be developed and used in future studies. Second, since distinguishing the inflammatory lesions, i.e. punctate inner choroidopathy and multifocal choroiditis, and myopic CNV is challenging²³, there are possibilities that newly diagnosed CNV

may include the inflammatory atrophic lesions. To minimize such mis-classification, we included the eyes with CNV which had a firm relationship to myopic degenerative changes and excluded the eyes which had inflammatory signs, i.e. late staining of the optic disc margin in FA, late hypofluorescent dots in ICGA, after initial thorough examinations. Third, because the present study was conducted in a single university-affiliated hospital, its results might not be representative of the myopic population as a whole. Moreover, patients with early improvement may not have been included in this study because they were more likely to be lost to follow-up. Yet, the main goal of this study was to compare the clinical characteristics according to the presence of optic disc features, and considering that the limitations listed above were applicable to all of the study patients, the main results were not likely to have been significantly affected by the limitations.

In conclusion, after investigating the morphologic characteristics of the optic disc in patients with subfoveal myopic CNV, we found that the presence of tilted optic disc and larger PPA area were correlated with a higher requirement of anti-VEGF injections and poor functional and anatomical outcomes. Our findings suggest that myopic CNV in eyes with tilted disc features, especially those with a large PPA-to-disc area ratio, should be given high priority for close observation.

Methods

Study Patients

This was a retrospective observational case series study conducted at Asan Medical Center, a tertiary referral center in Seoul, Republic of Korea. We reviewed the medical records of all consecutive treatment-naïve patients with subfoveal myopic CNV treated with anti-vascular endothelial growth factor (anti-VEGF) and regularly followed for more than three years between January 2007 and September 2020. All procedures were conducted in accordance with the tenets of the Declaration of Helsinki, and the study design was approved by the Institutional Review Board (IRB) of Asan Medical Center (Seoul, Korea; IRB No. 2020 – 1421). Due to the retrospective design of the study and the use of de-identified patient data, the IRB of Asan Medical Center waived the need for written informed consent from patients and control subjects.

Subfoveal myopic CNVs were defined as CNVs that developed in eyes with degenerative myopia. Degenerative high myopia was defined as eyes with a spherical equivalent refractive error of more than –8.0 diopters or an axial length longer than 26.5 mm. The presence of CNVs was mainly determined by using spectral domain optical coherence tomography (SD-OCT) and fluorescein angiography (FA) and were considered to be subfoveal if any portion of the CNV involved the center of the fovea. The criteria for exclusion were as follows: history of intraocular surgeries other than cataract surgery; history of intraocular treatments (e.g., photodynamic therapy, laser photocoagulation, and intravitreal injection) due to other ocular pathologies; history of ocular trauma, inflammation, or infection; and media opacities that could affect visual acuity.

Ocular Examination and Treatments

At the initial and following visits to the clinic, all patients underwent complete ophthalmologic examinations, including a review of the ophthalmologic history, measurement of the best-corrected visual acuity (BCVA), slit lamp biomicroscopy, and funduscopy examinations through dilated pupils by retinal specialists. OCT images were taken at every visit using Spectralis (Heidelberg Engineering GmbH, Heidelberg, Germany). Axial length was measured at baseline; FA and indocyanine green angiography (ICGA) were performed to assess the CNV activities at baseline and as needed. Macular status, including the lacquer crack, CNV size, subfoveal choroidal thickness, and macular atrophy, was assessed using SD-OCT, FA, and ICGA. Macular atrophy was defined as hypofluorescent area in fundus autofluorescence images and defective retinal pigment epithelium in OCT images.

Treatment using anti-VEGF injections was given on an “1 + PRN” protocol. CNV was defined as active if leakage on FA or intra-/sub-retinal fluid or fuzzy margin of CNV on OCT was observed. If CNV activity was resolved on the next follow-up OCT after one injection, no further injection was given until recurrences were observed. However, if CNV activity remained, additional injections were given until CNV was stabilized. Recurrence of myopic CNV was defined as the reactivation of CNV activity at least 3 months after the initial resolution of the fluid.

Optic Disc Feature Measurements

The optic disc parameters which include the longest diameter (LD) and shortest diameter (SD), and the areas of the disc and β -zone peripapillary atrophy (β -PPA) were measured from fundus photography using the ImageJ software (version 1.52; Wayne Rasband, National Institutes of Health, Bethesda, MD, USA) (Fig. 1). The optic disc was classified as a tilted disc when its tilt ratio (i.e., LD to SD ratio) was greater than 1.30¹⁴. The optic disc was defined as having torsion when the degree of torsion (i.e., angle between the vertical meridian and the long axis of the disc) was greater than 15°¹⁵. The margins of the optic disc (i.e., inner border of Elschnig’s sclera ring) and β -zone peripapillary atrophy (i.e., inner crescent of chorioretinal atrophy with visible sclera and choroidal vessels) were manually demarcated and their areas were measured in pixel areas. To minimize the effects of photographic magnification error according to axial length, we used the β -PPA-to-disc area ratio (PDR) to represent the size of the β -PPA¹⁶. Measurements were made by two independent examiners (YEH and YJK) and the averaged data were used in the final analysis. Interclass correlation coefficient value for disc tilt ratio was 0.970 (95% confidence interval, 0.953 to 0.981) and PDR was 0.964 (95% confidence interval, 0.943 to 0.977).

Statistical Analysis

The following variables were analyzed in each patient: i) demographic variables (i.e., age, sex, and systemic diseases), ii) ocular characteristics (i.e., BCVA and disc parameters at the first and the last visit, axial length, refractive error, lens status, CNV size, presence of lacquer crack, subfoveal choroidal thickness, and presence of macular atrophy), and iii) ocular treatment-related variables (i.e., number and timing of ocular treatments and recurrence of CNV).

Descriptive statistics of the baseline characteristics are presented in numbers and percentages for categorical variables and mean $\pm$ standard deviation for continuous variables. For comparison of the presence of disc tilt, Student's *t*-test or Mann–Whitney *U* test was used depending on the normality of their distribution. Chi-squared test was used to compare categorical data. Partial correlation analysis was used to investigate the disc tilt, β -PPA, and ocular parameters adjusted for age and sex. Cox proportional hazards model was used to identify factors associated with the occurrence of macular atrophy and poor visual prognosis ($< 20/60$, Snellen mean). Univariate analyses were performed for each variable and those with *P* values < 0.1 were included in the multivariate analysis with forward elimination process. HRs with 95% confidence intervals (CIs) were calculated. All statistical analyses were performed using the IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

Declarations

Data availability

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

Contributions

Study concept and design (Y.J.K, J.Y.L, J.G.K, and Y.H.Y); data acquisition, management, analysis, and interpretation (Y.E.H and Y.J.K); manuscript draft (Y.E.H and Y.J.K), revision, review and approval (Y.J.K, H.S.Y, B.G.M, J.Y.L, J.G.K, and Y.H.Y)

Ethics declarations

Competing interests

The authors declare no competing interests

References

1. Wong TY, Ferreira A, Hughes R, Carter G, Mitchell P. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: an evidence-based systematic review. *Am J Ophthalmol* 2014;**157**:9-25.e12.
2. Hayashi K , *et al.* Long-term pattern of progression of myopic maculopathy: a natural history study. *Ophthalmology* 2010;**117**:1595-611, 611.e1-4.
3. Chan NS, Teo K, Cheung CM. Epidemiology and Diagnosis of Myopic Choroidal Neovascularization in Asia. *Eye Contact Lens* 2016;**42**:48-55.
4. Ohno-Matsui K, Ikuno Y, Lai TYY, Gemmy Cheung CM. Diagnosis and treatment guideline for myopic choroidal neovascularization due to pathologic myopia. *Prog Retin Eye Res* 2018;**63**:92-106.

5. Cheung CMG, *et al.* Myopic Choroidal Neovascularization: Review, Guidance, and Consensus Statement on Management. *Ophthalmology* 2017;**124**:1690-711.
6. Kim YM, Yoon JU, Koh HJ. The analysis of lacquer crack in the assessment of myopic choroidal neovascularization. *Eye (Lond)* 2011;**25**:937-46.
7. Farinha CL, *et al.* Choroidal thickness after treatment for myopic choroidal neovascularization. *Eur J Ophthalmol* 2013;**23**:887-98.
8. Calvo-Gonzalez C, Reche-Frutos J, Donate J, Fernandez-Perez C, Garcia-Feijoo J. Intravitreal ranibizumab for myopic choroidal neovascularization: factors predictive of visual outcome and need for retreatment. *Am J Ophthalmol* 2011;**151**:529-34.
9. Samarawickrama C, *et al.* Myopia-related optic disc and retinal changes in adolescent children from singapore. *Ophthalmology* 2011;**118**:2050-7.
10. How AC, *et al.* Population prevalence of tilted and tortorted optic discs among an adult Chinese population in Singapore: the Tanjong Pagar Study. *Arch Ophthalmol* 2009;**127**:894-9.
11. Hayashi K, *et al.* Spectral-domain optical coherence tomography of β -zone peripapillary atrophy: influence of myopia and glaucoma. *Invest Ophthalmol Vis Sci* 2012;**53**:1499-505.
12. Park HY, Jung Y, Park CK. Posterior staphyloma is related to optic disc morphology and the location of visual field defect in normal tension glaucoma patients with myopia. *Eye (Lond)* 2015;**29**:333-41.
13. Sung MS, Lee TH, Heo H, Park SW. Association Between Optic Nerve Head Deformation and Retinal Microvasculature in High Myopia. *Am J Ophthalmol* 2018;**188**:81-90.
14. Tay E, *et al.* Optic disk ovality as an index of tilt and its relationship to myopia and perimetry. *Am J Ophthalmol* 2005;**139**:247-52.
15. Park HY, Choi SI, Choi JA, Park CK. Disc Torsion and Vertical Disc Tilt Are Related to Subfoveal Scleral Thickness in Open-Angle Glaucoma Patients With Myopia. *Invest Ophthalmol Vis Sci* 2015;**56**:4927-35.
16. Lee J, Lee JE, Kwon J, Shin JW, Kook MS. Topographic Relationship Between Optic Disc Torsion and β -Zone Peripapillary Atrophy in the Myopic Eyes of Young Patients With Glaucomatous-appearing Visual Field Defects 2018;**27**:41-9.
17. Chen Q, *et al.* Impact of the Morphologic Characteristics of Optic Disc on Choroidal Thickness in Young Myopic Patients. *Invest Ophthalmol Vis Sci* 2019;**60**:2958-67.
18. Fang Y, *et al.* Progression of Myopic Maculopathy during 18-Year Follow-up. *Ophthalmology* 2018;**125**:863-77.
19. Yan YN, *et al.* Ten-Year Progression of Myopic Maculopathy: The Beijing Eye Study 2001-2011. *Ophthalmology* 2018;**125**:1253-63.
20. Wakabayashi T, Ikuno Y. Choroidal filling delay in choroidal neovascularisation due to pathological myopia. *Br J Ophthalmol* 2010;**94**:611-5.
21. Park HL, Kim YC, Jung Y, Park CK. Vertical disc tilt and features of the optic nerve head anatomy are related to visual field defect in myopic eyes. *Sci Rep* 2019;**9**:3485.

22. Lee KM, Kim M, Kim SH. Case report: what gives the myopic tilted disc an oval appearance? *BMC Ophthalmol* 2020;**20**:20.
23. Dolz-Marco R, Fine HF, Freund KB. How to Differentiate Myopic Choroidal Neovascularization, Idiopathic Multifocal Choroiditis, and Punctate Inner Choroidopathy Using Clinical and Multimodal Imaging Findings. *Ophthalmic Surg Lasers Imaging Retina* 2017;**48**:196-201.

Figures

Figure 1

Measurement of the optic disc tilt and the β -PPA-to-disc area ratio (PDR)

Blue lines indicate the shortest diameter (SD) and the longest diameter (LD) of the optic disc. The disc tilt ratio was defined as the LD-to-SD ratio. The optic disc area (demarcated by the *yellow line*) and β -zone peripapillary area (β -PPA, demarcated by the *green line*) were automatically calculated in pixel area using the Image J software. The β -PPA-to-disc area ratio (PDR) was used to minimize the effects of photographic magnification error and represent the β -PPA.

Figure 2

Color fundus photo, optical coherence tomography, fundus autofluorescence images showing progression of macular atrophy and poor visual outcome of subfoveal myopic choroidal neovascularization (CNV) in an eye with myopic disc deformation (a), compared to that without disc deformation (b).

(a) A 65-year old female patient with an axial length of 28.7 mm. At baseline (the upper row), visual acuity was 0.63 in snellen with the large optic disc tilt ratio (1.9) and the β -PPA-to-disc area ratio (PDR) (3.7) were noted. During 6 years of follow-up, the patients underwent 2 recurrences and received a total of 9 injections. At the last visit (the lower row), visual acuity was deteriorated to counting finger with the development of extensive CNV-related macular atrophy. (b) A 65-year old female patient with an axial length of 28.1 mm. At baseline (the upper row), visual acuity was 0.32 in snellen with the small optic disc tilt ratio (1.05) and the β -PPA-to-disc area ratio (PDR) (0.61) were noted. During 6.5 years of follow-up, the patients experienced no recurrence and received a total of 3 injections. At the last visit (the lower row), visual acuity was maintained at 0.4 in snellen with little occurrence of macular atrophy.