AMERICAN ACADEMY OF OPHTHALMOLOGY®

Incidence and Risk Factors of Second Eye Involvement in Myopic Macular Neovascularization

Monica Ravenstijn, MD,[1,2] *Caroline C.W. Klaver, MD, PhD,*[2,3,4,5] *Suzanne Yzer, MD, PhD*[4]

Purpose: To report the cumulative incidence and risk factors of second eye involvement after diagnosis of myopic macular neovascularization (MNV) in the first eye.

Design: Retrospective analysis of longitudinal data from a tertiary hospital in the Netherlands.

Participants: Patients with high myopia (spherical equivalent [SE] ≤ -6 diopters [D]), of European ethnicity, who were diagnosed with active MNV lesion in 1 eye between 2005 and 2018. Fellow eyes were free of MNV or macular atrophy at baseline, and data were collected on the SE, axial length, and presence of diffuse or patchy chorioretinal atrophy and lacquer cracks.

Methods: Incidence rate and 2-, 5-, and 10-year cumulative incidences were calculated; hazard ratios (HRs) of second eye involvement were analyzed for potential risk factors using Cox proportional hazard models.

Main outcomes measures: Incidence of second eye involvement after onset of myopic MNV in the first eye.

Results: We included 88 patients over a period of 13 years with a mean age of 58 $\pm$ 15 years, mean axial length of 30 $\pm$ 1.7 mm and SE -14 ± 4 D at baseline. Twenty-four fellow eyes (27%) developed a myopic MNV during follow-up. This resulted in an incidence rate of 4.6 (95% confidence interval [CI], 2.9−6.7) per 100 person-years and a cumulative incidence of 8%, 21%, and 38% at 2, 5, and 10 years, respectively. Mean time until MNV development in the fellow eye was 48 $\pm$ 37 months. Patients aged $<$ 40 years at the initial presentation had a 3.8 times higher risk of bilateral myopic MNV (HR, 3.8; 95% CI, 1.65−8.69; $P = 0.002$). The presence of lacquer cracks in the second eye seemed to increase risk, but this did not reach statistical significance (HR, 2.25; 95% CI, 0.94−5.39; $P = 0.07$).

Conclusions: Our study of high myopes of European descent shows very similar incidence rates for second eye myopic MNV compared with Asian studies. Our findings substantiate the importance for clinicians to monitor closely and create awareness, especially in younger patients.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any materials discussed in this article.

One half of the world's population is estimated to be myopic by 2050, of which a significant proportion will experience severe visual loss during their lifetime.[1−3] Myopic macular neovascularization (MNV) is a sight-threatening complication that occurs in 5% to 11% of patients with high myopia.[4] Myopic MNV often leads to a sudden but progressive decline of the visual acuity resulting in a poor visual prognosis.[5,6] For several years, anti-VEGF injections have been the golden standard of care for treatment of myopic MNV and have significantly improved the visual outcome in these patients, at least in the short term.[7−9] Early diagnosis and treatment have been shown to be beneficial[10] and seem to lower the recurrence rate.[11] Worse baseline best-corrected visual acuity increases the risk of visual impairment and blindness at 10 years,[12,13] because of more prominent chorioretinal atrophy (CRA) and fibrous scarring. It is therefore of great importance to identify MNVs timely in patients at risk of a myopic MNV in the fellow eye.[14]

This study aimed to investigate the incidence rate (IR) of second eye involvement after onset of myopic MNV in the first eye and identify potential risk factors to improve patient-centered clinical management.

Methods

In this retrospective study, a total of 106 patients had been diagnosed with myopic MNV between 2005 and 2018 at the Rotterdam Eye Hospital, the Netherlands. The inclusion criteria were high myopia with spherical equivalent (SE) of 6 diopters (D) or worse and axial length of $>$ 26.0 mm; active MNV was confirmed by leakage on fluorescein angiography (92% of the cases) or by OCT angiography combined with signs of active MNV (e.g., subretinal fluid) on spectral domain OCT (8% of the cases). Review of baseline fluorescein angiography and/or OCT angiography confirmed the absence of myopic MNV in the fellow eye. Fellow eyes that had been diagnosed with a myopic MNV (n = 5),

https://doi.org/10.1016/j.oret.2023.06.025
ISSN 2468-6530/23

macular atrophy (n = 4) according to the meta-analysis of pathologic myopia classification system,[15] or patients with monocular vision (n = 9) were excluded. Monocular vision was defined as sight in 1 eye as the result of physically losing an eye or a best-corrected visual acuity of ≥ 1.30 logarithm of the minimum angle of resolution because of trauma or previous ocular disease, such as rhegmatogenous retinal detachment. Patients with secondary MNV because of age-related macular degeneration, intraocular inflammatory diseases (e.g., punctate inner choroidopathy and multifocal chorioretinitis), or central serous chorioretinopathy were also excluded. This resulted in 88 patients suitable for analysis. This study was approved by the ethical review board of the Erasmus Medical Center and the scientific review board of the Rotterdam Eye Hospital and adhered to the principles of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study.

Data Collection

Patient characteristics (gender, age, SE, and, when available, axial length) were ascertained from medical records; phenotypic features (i.e., degree of myopic macular degeneration and presence of lacquer cracks) were determined on multimodal imaging (color fundus imaging, OCT, and fundus autofluorescence), and the treatment regime at first visit was registered. Myopic macular degeneration was defined as the presence of diffuse CRA, patchy CRA, and/or the presence of lacquer cracks; and the degree of myopic macular degeneration was graded according to the meta-analysis of pathologic myopia classification system.[15] Macular neovascularization location was considered subfoveal when any portion of the lesion was located under the fovea; juxtafoveal when any portion was located ≤ 200 μm of the fovea, and extrafoveal when the myopic MNV was located > 200 μm of the fovea.

Table 1. Baseline Patient Characteristics and the Incidence Rate of Second Eye Involvement after First-Onset Myopic MNV

Variables	
Number of eyes	88
Female, n (%)	51 (58)
Age, yrs (mean ± SD)	58 ± 15
Axial length of fellow eye, mm (mean ± SD)*	29.3 ± 2.2
Time to follow-up, mos (mean ± SD)	92 ± 46
Incident MNV, n (%)	24 (27)
Incidence rate per 100 person-yrs (95% CI)	4.6 (2.9–6.7)
Time to fellow eye involvement, mos (mean ± SD)	48 ± 37

CI = confidence interval; MNV = macular neovascularization; SD = standard deviation
*Axial length was available for 46 eyes.

Outcomes and Statistical Analysis

The main outcome was incident MNV in the second eye after a diagnosis of myopic MNV in the first eye. Secondary outcomes were other phenotypic lesions related to myopia in the second eye. Descriptive data were summarized using the mean (standard deviation), median (interquartile range), and percentages where appropriate. The IR of second eye involvement was calculated as the number of incident cases per 100 person-years of follow-up; the 2-, 5-, and 10-year cumulative incidences were calculated as (cumulative incidence = $1 - e^{(-IR \times time)}$). Cox proportional hazard analysis was used to estimate hazard ratios (HRs) for the determinants age, gender, number of intravitreal injections, SE, and axial length in the fellow eye and the presence of lacquer cracks and CRA. A P value of < 0.05 was considered statistically

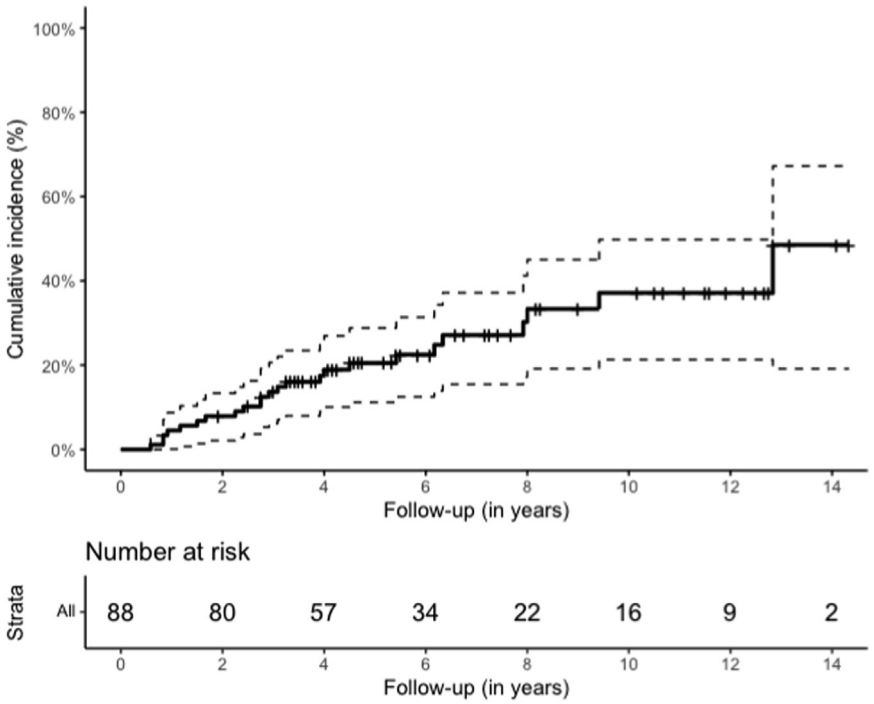

Figure 1. Cumulative incidence of second eye involvement per year after diagnosis of myopic macular neovascularization in the first eye.

Table 2. Incidence Rate and Cumulative Incidence of Second Eye Involvement after Diagnosis of Myopic MNV in the First Eye

Study	Patient Characteristics					Incidence Rate			Cumulative Incidence[#], per Time Point (%)		
	Number	Gender, Female (%)	Ethnicity	Age, yrs	Axial Length, mm	Events, n (%)	Number of Person-yrs	Incidence Rate[§]	2 Yrs	5 Yrs	10 Yrs
Current study	88	51 (58)	European	58 ± 15	29.3 ± 2.2	24 (27)	525	4.6	8	21	38
Ohno-Matsui et al (2003)[16]	46[*]	—	Asian	48 ± 15[†]	29.8 ± 1.7[†]	16 (34)	350[‡]	4.6[‡]	9[‡]	20[‡]	37[‡]
Mallone et al (2022)[17]	30	20 (66)	European	64 ± 8[†]	30.7 ± 1.2[†]	8 (27)	300[‡]	2.7[‡]	5[‡]	12[‡]	23[‡]

IR = incidence rate; MNV = macular neovascularization.
*Forty-six of 218 fellow eyes at baseline had a history of myopic MNV.
†Data from all patients, subgroups were not specified.
‡Number of person-years was calculated using the following formula: mean duration of follow-up × the number of cases.
§Data were extracted from available results and used to calculate the incidence rate and cumulative incidence. The incidence rate equals (events per number of person-years)/100, expressed as rate per 100 person-years.
#Cumulative incidence = $1 - e^{(-IR \times time)}$.

significant. All analyses were conducted using R software version 4.0.3 (http://www.R-project.org/).

Results

Study Population

This study included 88 patients with high myopia and unilateral MNV who received the diagnosis, treatment, and control visits between January 2005 and December 2018. The mean age at myopic MNV onset was 58 ± 15 years; 51 (58%) of patients were female (Table 1). At baseline, mean SE was higher in the eye with myopic MNV than in the fellow eyes (−13.6 ± 4.1 D vs. −12.6 ± 5.5 D; $P = 0.02$); this corresponded to a longer mean axial length (30.0 ± 1.7 mm in the first eye vs. 29.3 ± 2.2 mm in the second eye; $P = 0.003$). Fundus changes at the first presentation in the first eye were diffuse CRA in 36 (43%) of 84 eyes, patchy CRA in 27 (32%) of 84 eyes, and lacquer cracks in 34 (41%) of 82 eyes. In the fellow eyes, fundus changes at the initial presentation were diffuse CRA in 22 (25%) of 87 eyes, patchy CRA in 16 (18%) of 87 eyes, and lacquer cracks in 18 (22%) of 83 eyes. In 37 patients (45%), both eyes showed at least diffuse CRA. Eighty-four eyes (95%) were directly treated with anti-VEGF therapy, and the median (interquartile range) number of injections bevacizumab was 2 (1−5). Photodynamic therapy was initially conducted in 4 eyes before the availability of anti-VEGF therapy. Myopic MNV was located subfoveally in 44 (50%) eyes, juxtafoveally in 30 (34%) eyes, and extrafoveally in 11 (13%) eyes. The mean duration of follow-up was 92 (standard deviation, 46) months; 1 patient (1%) had been followed-up at < 2 years, 25 patients (28%) had been followed-up between 2 and 4.9 years, 30 patients (34%) had been followed-up between 5 and 7.9 years, and 32 patients (36%) had been followed-up at ≥ 8 years. The total number of person-years was 525.

IR and Cumulative Incidence of Second Eye Involvement

Overall, 24 (27%) fellow eyes developed a myopic MNV during follow-up. From this, we calculated an IR of 4.6 (95% CI, 2.9−6.7) per 100 person-years for second eye involvement (Table 1). This corresponded to a cumulative incidence of 8% (95% CI, 4%−15%) at 2 years, 21% (95% CI, 13%−30%) at 5 years, and 38% (95% CI, 23%−52%) at 10 years (Fig 1, Table 2). Figure 2 shows a representative case of patients with myopia who developed bilateral myopic MNV during follow-up. Table 2 shows the IRs and cumulative incidences of incident MNV in the fellow eye from this study in comparison to previous studies. The baseline age (HR, 0.96; 95% CI, 0.93−0.99; $P = 0.003$) was significantly associated with second eye involvement in this study (Table 3). Patients aged < 40 years at the initial presentation had an increased risk of a MNV in the fellow eyes (HR, 3.8; 95% CI, 1.65−8.69; $P = 0.002$). The presence of lacquer cracks in the second eye seemed to increase risk, but this did not reach statistical significance (HR, 2.25; 95% CI, 0.94−5.39; $P = 0.07$). This was also the case for gender, SE, axial length, presence of fundus changes, MNV location, MNV size, and the number of intravitreal injections (Table 3).

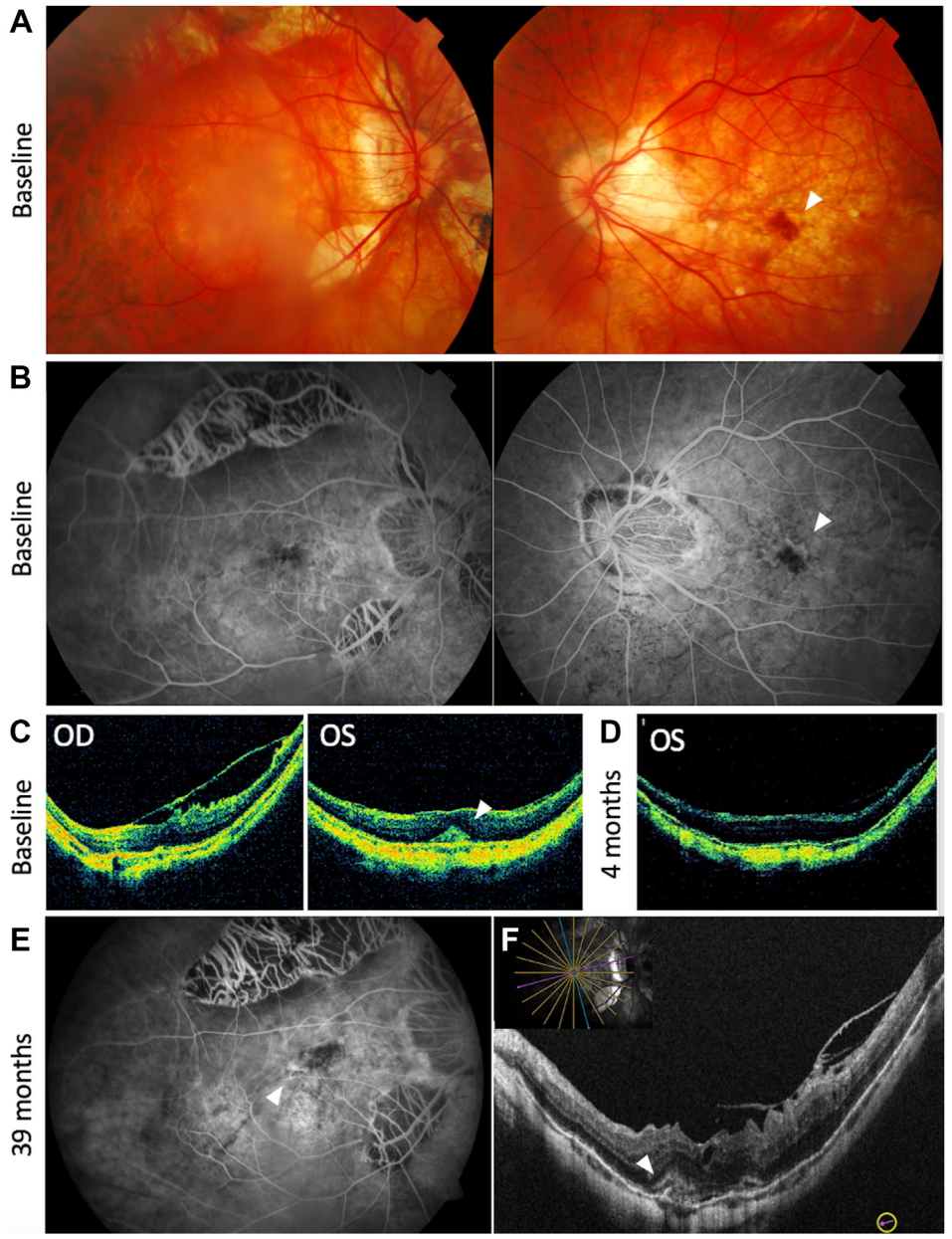

Figure 2. Representative case of a patient with myopia with second eye involvement after first-onset myopic macular neovascularization (MNV). A, Fundus photographs of a 58-year-old man at baseline. The axial length is 32.1 mm in the right eye and 30.6 mm in the left eye, and the left eye shows a retinal hemorrhage (white arrow). B, Fluorescein angiography (FA) showed hyperfluorescence with active leakage in the left eye (white arrow) and no signs of a myopic MNV in the right eye. C, OCT-imaging of the right eye, without signs of a myopic MNV and a subfoveal MNV in the left eye (white arrow). The patient was treated with 4 intravitreal Bevacizumab injections, after which the lesion was resolved as shown in (D). E, At 39 months of follow-up, FA and (F) OCT revealed a myopic MNV in the right eye. The patient was treated with 4 intravitreal Bevacizumab injections. OD = right eye; OS = left eye.

Discussion

This study reports the incidence of second eye involvement after myopic MNV in the first eye. From our data, we calculated a 10-year cumulative incidence of 38%. We found that age of < 40 years was significantly associated with second eye MNV. Other risk factors of myopic MNV, such as lacquer cracks, could not be confirmed in this study.

Prevalences of second eye involvement provided by previous studies range from 5% to 23%,[5,18–20] but data on time of occurrence after the first eye are scarce. This lack of knowledge hampers both useful clinical counseling for the patient as well as practical clinical management for the doctor. To date, 2 studies followed patients with unilateral myopic MNV over time but reported the incidence of second eye involvement as a timeless proportion.

Table 3. Risk of Second Eye Involvement of Myopic MNV for Personal and Retinal Characteristics

Determinants	Events/Total Number	Univariate		Multivariate	
		HR (95% CI)	P	*HR (95% CI)*	P
Age at first-onset, continuous.	24/88	0.96 (0.93–0.99)	0.003	0.97 (0.94–0.99)	0.02
Gender (reference = male)	12/37	1.00	-	-	-
Female	12/51	0.75 (0.33–1.67)	0.48		
Fellow eye					
Refractive error	24/88	0.98 (0.91–1.05)	0.51	-	-
Axial length	13/46	1.17 (0.91–1.52)	0.22		
Fundus changes (reference = none)	13/49	1.00	-	-	-
Diffuse chorioretinal atrophy	8/22	1.71 (0.70–4.17)	0.17	-	-
Patchy chorioretinal atrophy	2/16	0.50 (0.11–2.22)	0.58	-	-
Lacquer cracks (reference = none)	14/65	1.00	-	1.00	
Present	8/18	2.25 (0.94–5.39)	0.07	2.07 (0.86–4.98)	0.11
Eye with first-onset					
Location of MNV (reference = subfoveal)	14/44	1.00	-	-	-
Juxtafoveal	3/30	0.33 (0.10–1.17)	0.09	-	-
Extrafoveal	4/11	0.96 (0.32–2.94)	0.95	-	-
Number of intravitreal injections	21/84	1.01 (0.96–1.07)	0.72	-	-
Size of MNV lesion	19/73	1.74 (0.71–4.31)	0.23	-	-

CI = confidence interval; HR = hazard ratio; MNV = macular neovascularization.

In epidemiology, IR is calculated by dividing the number of new cases in the population at risk by the number of years of observation and is expressed as person-years. The cumulative incidence is calculated as the number of new events divided by the total number of individuals in the population at risk for a given timepoint but can also be inferred from IR. Mallone et al[17] reported that 8 of 30 patients with high myopia developed a myopic MNV in the second eye at 10 years of follow-up; Ohno-Matsui et al[16] followed 46 patients with unilateral MNV and found that 16 (34.8%) developed MNV in the fellow eye after an average follow-up of 7.6 years. We converted these figures to IRs and cumulative incidences and found very similar incidences for our study compared with the study from Japan[16] and somewhat lower figures for the Italian study.[17] The latter involved older patients, which may have contributed to a lower rate.

Older patients in our study population had a lower risk of myopic MNV development in the second eye and impaired VEGF upregulation with age may be an explanation. The structural changes that occur in the retina and choroid of high myopes is known to result from excessive axial elongation, and hypoxia in the retinal pigment epithelial cells and glia cells are hypothesized to trigger VEGF upregulation and angiogenesis. Animal studies have shown that this angiogenetic process is associated with age; for instance, the expression of VEGF in ischemic tissues was lower in the older rabbits than in young ones.[21]

Patchy CRA, lacquer cracks, and thinning of the choriocapillaris and choroid are established risk factors for first-onset myopic MNV.[16,22] Similarly, we found that lacquer cracks were borderline significantly associated with myopic MNV development in the fellow eye in the univariate analysis. This corresponds to the results of Ohno-Matsui et al,[16] who mentioned the close resemblance in phenotype between first and second eye MNV. Current insights are that European and Asian patients show a similar myopic phenotype, with age and axial length as the most important drivers for myopic maculopathy.[23] Also, the genetic drivers of refractive error seem to be highly correlated between European and Asian individuals.[24] Taking these parallels together, it is valid to assume that the risk and presentation of myopic MNV for first and second eyes of patients with high myopia is not determined by ethnicity.

This study has strengths and limitations. Strengths of our study include the long and almost complete follow-up after onset of myopic MNV in the first eye. Another strength is the limited number of exclusion criteria, allowing direct translation of findings to the clinic. A limitation is the retrospective design of the study, which allowed for variability in patient management and cannot exclude selection bias. Nevertheless, our strict requirement of multimodal imaging to exclude MNV in the fellow eye at baseline validated its occurrence during the study period. Another important drawback was the limited number of outcome events, which lowered the statistical power and our ability to find a comprehensive risk profile. Another limitation of retrospective research is the variability in follow-up duration. Loss of follow-up was limited to 7 eyes (8%), of which 1 eye already had a second eye involvement before dropping out. The cumulative incidence in this study can still be an underestimation of the number of second eye involvements. Large, prospective, long-running studies, with perhaps multicenter cohorts, that employ extensive multimodal imaging are needed to further investigate all determinants associated with the risk of myopic MNV.

In conclusion, this study evaluated the IR and cumulative incidence of MNV in the fellow eye of patients with high myopia after onset of myopic MNV in the first eye. The 2-, 5-, and 10- year cumulative incidences were 8%, 21%, and

38%, respectively. An age of < 40 years was a prominent, significant risk factor. Our findings substantiate the importance for clinicians and patients to monitor closely and start treatment immediately in case of symptoms. This will create an optimal starting point for saving sight in patients with high myopia.

Footnotes and Disclosures

Originally received: April 18, 2023.
Final revision: June 27, 2023.
Accepted: June 29, 2023.
Available online: ■■■. Manuscript no. ORET-D-23-00255R2.

[1] Rotterdam Ophthalmic Institute, Rotterdam Eye Hospital, Rotterdam, the Netherlands.

[2] Department Of Ophthalmology, Erasmus Medical Center, Rotterdam, the Netherlands.

[3] Department Of Epidemiology, Erasmus Medical Center, Rotterdam, the Netherlands.

[4] Department of Ophthalmology, Radboud University Medical Center, Nijmegen, the Netherlands.

[5] Institute of Molecular and Clinical Ophthalmology, Basel, Switzerland.

Disclosures:

All authors have completed and submitted the ICMJE disclosures form.

The authors have no proprietary or commercial interest in any materials discussed in this article.

Supported by Oogfonds, Landelijke Stichting voor Blinden en Slechtzienden, Algemene Nederlandse Vereniging Ter Voorkoming Van Blindheid and Stichting Beheer 't Schild through Uitzicht (2019-14), Rotterdamse Stichting Blindenbelangen (20190034) and Stichting Wetenschappelijk Onderzoek Oogziekenhuis (2019S06). Funding from Netherlands Organization for Scientific Research (NWO, grant no.: 91815655), and from European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant no.: 648268) (C.CW.K.). The funding organizations had no role in the design or conduct of this research.

HUMAN SUBJECTS: Human subjects were included in this study. This study was approved by the ethical review board of the Erasmus Medical Center and the scientific review board of the Rotterdam Eye Hospital and adhered to the principles of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study.

No animal subjects were included in this study.

Author Contributions

Conception and design: Ravenstijn, Klaver, Yzer

Data collection: Ravenstijn

Analysis and interpretation: Ravenstijn, Klaver, Yzer

Obtained funding: Klaver, Yzer

Overall responsibility: Ravenstijn, Klaver, Yzer

Abbreviations and Acronyms:
CI = confidence interval; **CRA** = chorioretinal atrophy; **HR** = hazard ratio; **IR** = incidence rate; **MNV** = macular neovascularization; **SE** = spherical equivalent.

Keywords:
Cumulative incidence, Incidence rate, Macular Neovascularization, Myopia Bilateral.

Correspondence:
Suzanne Yzer, MD, PhD, Philips van Leydenlaan 15, 6525 EX Nijmegen, the Netherlands. E-mail: Suzanne.yzer@radboudumc.nl.

References

1. Tideman JWL, Snabel MCC, Tedja MS, et al. Association of axial length with risk of uncorrectable visual impairment for Europeans with myopia. *JAMA Ophthalmol*. 2016;134:1355−1363.
2. Haarman AEG, Enthoven CA, Tideman JWL, et al. The complications of myopia: a review and meta-analysis. *Invest Ophthalmol Vis Sci*. 2020;61:49. https://doi.org/10.1167/IOVS.61.4.49.
3. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123:1036−1042. https://doi.org/10.1016/j.ophtha.2016.01.006.
4. Wong TY, Ferreira A, Hughes R, et al. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularization: an evidence-based systematic review. *Am J Ophthalmol*. 2014;157:9−25.e12.
5. Hayashi K, Ohno-Matsui K, Yoshida T, et al. Characteristics of patients with a favorable natural course of myopic choroidal neovascularization. *Graefe's Arch Clin Exp Ophthalmol*. 2005;243:13−19.
6. Yoshida T, Ohno-Matsui K, Yasuzumi K, et al. Myopic choroidal neovascularization: a 10-year follow-up. *Ophthalmology*. 2003;110:1297−1305.
7. Onishi Y, Yokoi T, Kasahara K, et al. Five-year outcomes of intravitreal ranibizumab for choroidal neovascularization in patients with pathologic myopia. *Retina*. 2019;39:1289−1298.
8. Kasahara K, Moriyama M, Morohoshi K, et al. Six-year outcomes of intravitreal bevacizumab for choroidal neovascularization in patients with pathologic myopia. *Retina*. 2017;37:1055−1064.
9. Ruiz-Moreno JM, Montero JA, Araiz J, et al. Intravitreal antivascular endothelial growth factor therapy for choroidal neovascularization secondary to pathologic myopia: six years outcome. *Retina*. 2015;35:2450−2456.
10. Ikuno Y, Ohno-Matsui K, Wong TY, et al. Intravitreal aflibercept injection in patients with myopic choroidal neovascularization: the MYRROR study. *Ophthalmology*. 2015;122:1220−1227.
11. Moon BG, Cho AR, Lee J, et al. Improved visual outcome and low recurrence with early treatment with intravitreal antivascular endothelial growth factor in myopic choroidal neovascularization. *Ophthalmologica*. 2017;237:128−138.
12. Ravenstijn M, Klaver CCW, Yzer S. Long-term treatment outcomes after bevacizumab therapy for macular neovascularization in White patients with high myopia. *Retina*. 2023;43:444−453.

13. Cicinelli MV, La Franca L, De Felice E, et al. Long-term incidence and risk factors of macular fibrosis, macular atrophy, and macular hole in eyes with myopic neovascularization. *Ophthalmol Retin*. 2022;6:1231−1240.
14. Iacono P, Parodi MB, Selvi F, et al. Factors influencing visual acuity in patients receiving anti-vascular endothelial growth factor for myopic choroidal neovascularization. *Retina*. 2017;37:1931−1941.
15. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International photographic classification and grading system for myopic maculopathy. *Am J Ophthalmol*. 2015;159:877−883.e7.
16. Ohno-Matsui K, Yoshida T, Futagami S, et al. Patchy atrophy and lacquer cracks predispose to the development of choroidal neovascularisation in pathological myopia. *Br J Ophthalmol*. 2003;87:570−573.
17. Mallone F, Giustolisi R, Franzone F, et al. Ten-year outcomes of intravitreal bevacizumab for myopic choroidal neovascularization: analysis of prognostic factors. *Pharmaceuticals (Basel)*. 2021;14:1042. https://doi.org/10.3390/PH14101042.
18. Leveziel N, Caillaux V, Bastuji-Garin S, et al. Angiographic and optical coherence tomography characteristics of recent myopic choroidal neovascularization. *Am J Ophthalmol*. 2013;155:913−919.e1.
19. Tan NW, Ohno-Matsui K, Koh HJ, et al. Long-term outcomes of ranibizumab treatment of myopic choroidal neovascularization in East-Asian patients from the Radiance study. *Retina*. 2018;38:2228−2238.
20. Chhablani J, Paulose RM, Lasave AF, et al. Intravitreal bevacizumab monotherapy in myopic choroidal neovascularisation: 5-year outcomes for the PAN-American Collaborative Retina Study Group. *Br J Ophthalmol*. 2018;102:455−459.
21. Rivard A, Fabre JE, Silver M, et al. Age-dependent impairment of angiogenesis. *Circulation*. 1999;99:111−120.
22. Wakabayashi T, Ikuno Y. Choroidal filling delay in choroidal neovascularisation due to pathological myopia. *Br J Ophthalmol*. 2010;94:611−615.
23. Haarman AEG, Tedja MS, Brussee C, et al. Prevalence of myopic macular features in Dutch individuals of European ancestry with high myopia. *JAMA Ophthalmol*. 2022;140:115−123.
24. Tedja MS, Haarman AEG, Meester-Smoor MA, et al. IMI − myopia genetics report. *Invest Ophthalmol Vis Sci*. 2019;60:M89−M105.