Original Article

Retinal Predictors of Visual Outcome and Recurrence in Naïve Myopic Choroidal Neovascularization Patients

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Abstract

Purpose: To identify predictive factors for recurrence and to assess variables influencing visual acuity over time.

Methods: This retrospective study analyzed 137 eyes of 128 patients with myopic choroidal neovascularization (mCNV) treated with intravitreal antivascular endothelial growth factor injections (ranibizumab or aflibercept) between June 2017 and June 2022, with a minimum 12-month follow-up. The study cohort was divided into two groups: The recurrence (R) group, which included eyes that experienced a recurrence of mCNV activity, and the nonrecurrence (NR) group, which included eyes without recurrence.

Results: The R group consisted of 56 eyes, whereas the NR group included 81 eyes. Recurrence was significantly associated with lower baseline best-corrected visual acuity (BCVA) (odds ratio [OR]: 1.95; $P = 0.018$), higher central foveal thickness (OR: 0.922; $P = 0.001$), presence of retinal pigment epithelium (RPE) disruption (OR: 2.272; $P = 0.022$), presence of subretinal fluid (OR: 2.83; $P = 0.008$), CNV width (OR: 1.1; $P = 0.041$), and CNV height (OR: 1.3; $P = 0.045$). In the NR group, final BCVA was significantly influenced by age ($P = 0.001$), time to first injection ($P = 0.021$), baseline BCVA ($P = 0.001$), BCVA after initial therapy ($P = 0.001$), RPE disruption ($P = 0.019$), photoreceptor layer disruption ($P = 0.048$), and lesion thickness ($P = 0.033$). In the R group, 12-month BCVA correlated with baseline BCVA ($P = 0.0019$), number of injections ($P = 0.08$), RPE disruption ($P = 0.027$), ellipsoid zone disruption ($P = 0.046$), and CNV height ($P = 0.084$).

Conclusions: Baseline clinical and imaging biomarkers are significantly associated with both recurrence risk and visual outcomes in mCNV. Early identification of these predictive factors may guide treatment strategies and optimize long-term visual prognosis.

Keywords: Antivascular endothelial growth factor, Myopic choroidal neovascularization, Pathological myopia, Prognostic factors, Spectral domain optical coherence tomography

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Introduction

Myopia is a leading cause of legal blindness and visual impairment worldwide, particularly among individuals of working age.[1] It represents the most frequent cause of choroidal neovascularization (CNV) in people under 50 years old and the second most common overall after age-related macular degeneration.[2]

The global burden of myopia is increasing steadily, leading to a rise in cases of high and pathological myopia.[3,4] Pathological myopia is characterized by progressive degenerative changes in the posterior segment of the eye, which may result in structural complications and visual decline.[5] Among these, myopic CNV (mCNV) is one of the most vision-threatening, often leading to permanent central vision loss if left untreated.[6]

It is estimated that around 10% of patients with degenerative myopia will develop mCNV within 10 years, and approximately 30% will develop bilateral involvement.[7] Although mCNV

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may show spontaneous regression in some cases, the natural course often results in fibrotic scarring and macular atrophy, contributing to progressive visual deterioration.[8]

The pathogenesis of mCNV is multifactorial and not yet fully understood, involving mechanical, degenerative, and vascular alterations.[9-11] While intravitreal (IV) antivascular endothelial growth factor (anti-VEGF) agents have become the gold standard in the treatment of mCNV, long-term visual outcomes remain variable.[12,13] In particular, recurrence of neovascular activity is a major challenge, often undermining the functional gains achieved with initial treatment.[14-16] Early intervention has been associated with improved prognosis and a reduced risk of late complications.[5]

Several ocular factors have been associated with mCNV prognosis, including lesion size, location, baseline visual acuity, and age.[14] However, current literature offers limited insight into predictors of recurrence, especially in treatment-naïve populations. Identifying baseline characteristics that influence final best-corrected visual acuity (BCVA) and recurrence risk could support more tailored and effective treatment strategies.

This study aims to evaluate the parameters influencing final BCVA and to identify predictive factors for disease recurrence in treatment-naïve patients with mCNV receiving IV anti-VEGF therapy.

Methods

This is a retrospective observational study conducted on a group of näive eyes with a diagnosis of mCNV treated with IV injections of ranibizumab or aflibercept. A minimal follow-up period of 1 year from the last IV injection was considered. The patients were recruited at the Eye Clinic, Department of Medical, Surgical Sciences, and Health of the University of Trieste, during a period of 5 years from June 2017 to June 2022. The study followed the guidelines of the Declaration of Helsinki, and each patient provided informed consent for personal data to be used for research purposes. This retrospective study was conducted using anonymized data and therefore did not require approval from the ethics committee in accordance with local regulations. Inclusion criteria were patients aged ≥18 years; diagnosis of treatment-naïve subfoveal, juxtafoveal, or extrafoveal mCNV; no other previous retinal surgery or laser treatments; optical coherence tomography (OCT) with high image signal quality ($Q > 28$). Exclusion criteria were reduction in visual acuity due to other causes, ocular or systemic, unrelated to mCNV; BCVA at the time of diagnosis >1.3 logMAR; ocular surgeries during the follow-up period; and follow-up period of <1 year from the end of IV treatment.

Diagnosis of mCNV was made at the first visit following a comprehensive ophthalmological evaluation, including BCVA, fundus examination, OCT, fluorescein angiography, and indocyanine green angiography. At subsequent follow-up visits, each patient underwent BCVA testing, fundus examination, and OCT. BCVA and various OCT data were recorded at diagnosis, following the first cycle of IV therapy (t1) and after 12 months from the end of the initial IV treatment (t2).

BCVA was performed at each visit using an Early Treatment Diabetic Retinopathy Study chart and then converted into logarithm scale (logMAR). OCT scans were performed using spectral domain OCT (SD-OCT), with dual-beam eye-tracking technology (Heidelberg Engineering GmbH, Heidelberg, Germany), and analyzed with Heidelberg Eye Explorer (V.1.8.6.0). SD-OCT scans were analyzed for all quantitative and qualitative measurements of the macular region. At each visit, all eyes underwent at least two types of SD-OCT scans (horizontal and vertical 20° ×15° pattern with 19 scans spaced 240 µm apart).

The cohort of eyes was divided into two groups: nonrecurrence (NR) Group, composed of individuals who did not experience disease recurrence, and R Group, composed of individuals who presented a recurrence. Patients were treated with a pro re nata regimen, with monthly follow-up visits. Recurrence was defined as the reappearance of mCNV activity after a discontinuation of anti-VEGF therapy for at least 3 months.[17-19]

Signs of mCNV activity on OCT were considered the appearance of intraretinal microcystic edema/subretinal fluid (SRF) and/or an increase in size of the lesion compared to the previous clinical control.[20]

The parameters evaluated were gender, age, eye, central foveal thickness (CFT), choroidal thickness (CT), scleral thickness (ST), structural changes of retinal pigment epithelium (RPE), ellipsoid zone (EZ), external limiting membrane (ELM); SRF, intraretinal cysts (IRC), subretinal hyperreflective exudation (SHE), hemorrhages, number of IVs performed, time between diagnosis and the first IV expressed in days, recurrence rate, and time between the last IV and recurrence expressed in days.

CFT was measured as the distance between the inner surface of the RPE and the internal limiting membrane at the foveal center [Figure 1A]. CT was measured perpendicularly from the outer border of the RPE to the choroid–scleral interface at the foveal center [Figure 1B]. ST was measured perpendicularly from the choroid–scleral interface to the outer scleral border in the same foveal scan [Figure 1C]. All measurements were

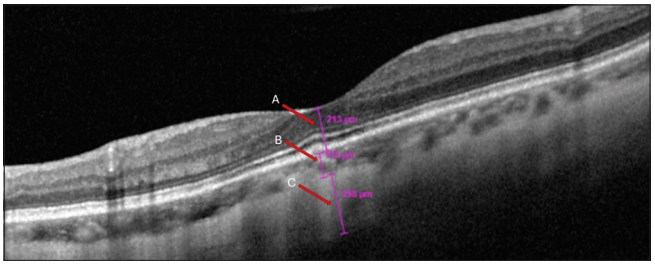

Figure 1: Measurement of central foveal thickness, choroidal thickness, and scleral thickness on an optical coherence tomography image

taken using the built-in caliper tool in the Heidelberg Eye Explorer software, in a high-definition B-scan passing through the foveal center. Each measurement was performed twice by two independent masked graders, and the mean value was used for analysis. In case of disagreement >10 μm, a third senior grader provided the final measurement.

Spherical equivalent refraction (in diopters [D]) and axial length (in millimeters) were also collected. Axial length was measured at baseline using the IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany). Refraction was measured as spherical equivalent using an autorefractor and confirmed by subjective refraction.

The statistical analysis was performed using Jamovi software (version 2.3.28; The Jamovi Project, Sydney, Australia). Continuous variables with a normal distribution were expressed as mean ± standard deviation, continuous variables with a nonnormal distribution are represented as median and interquartile range, and categorical variables were expressed as absolute frequencies and percentages (%). The Shapiro–Wilk test was conducted on all variables to ascertain their adherence to a normal distribution. Binary logistic regression analysis was utilized to establish predictors linked to the reappearance of mCNV at the time of diagnosis. Spearman's correlation analysis was employed to evaluate the relationship between final BCVA and continuous variables among eyes with and without mCNV recurrence. Independent samples *t*-test was applied to examine the association between final BCVA and categorical variables in eyes with and without mCNV recurrence. A significance level of 95% was set for each analysis carried out ($P < 0.05$).

Moreover, in each group, a multivariable linear regression model with final BCVA at 12 months as the dependent variable was performed. The full set of covariates included age, baseline BCVA, CFT, CT, ST, RPE/EZ/ELM disruption, presence of SRF/IRC/SHE, hemorrhages, CNV width and height, number of IV injections, and time from diagnosis to first injection. Heteroscedasticity-robust (HC3) standard errors were used. Analyses were conducted on complete cases. Written informed consent was obtained from all patients involved in the study.

Results

The study cohort comprises 137 eyes from 128 patients, with 69.3% female ($n = 85$) and 30.7% male ($n = 43$). 29% of the subjects were aged ≤65 years at the time of diagnosis, whereas 71% were >65 years. mCNV occurred in 51.1% of cases ($n = 70$) in the right eye and 48.9% ($n = 67$) in the left eye. Nine patients exhibited bilateral lesions (6.56%), and both eyes were included in the study. Of the 137 eyes, 112 (81.8%) were treated with ranibizumab and 25 eyes (18.2%) with aflibercept. In the group treated with ranibizumab, 45 eyes experienced recurrence, whereas 67 eyes were free from disease activity, meaning that in total, 40.2% of the ranibizumab-treated group showed recurrence. On the other hand, 14 eyes treated with aflibercept were free from disease relapse, and 11 eyes showed recurrence, for a total rate of recurrence of 44%. Although these proportions appear similar, the markedly smaller size of the aflibercept group (25 vs. 112 eyes) limits the strength of any direct comparison between the two treatments.

The cohort was divided into two groups: 59.1% ($n = 81$) of eyes did not experience neovascular recurrence and were classified as NR Group, whereas 40.9% ($n = 56$) of eyes experienced recurrence and were then identified as recurrence group (R Group).

The mean spherical equivalent refraction at baseline was –11.8 ± 2.6 D in the NR Group and –12.1 ± 2.4 D in the R Group ($P = 0.42$). The mean axial length was 27.8 ± 1.2 mm in the NR Group and 28.0 ± 1.3 mm in the R Group ($P = 0.30$). No statistically significant differences were found between the two groups for either parameter.

In NR Group, an average of 2.11 ± 1.31 IV injections were performed during the follow-up period, with 32% ($n = 26$) receiving a single injection, 47% two ($n = 38$), 12% three ($n = 10$), and <9% ($n = 7$) more than three.

The first injection was performed after 20.9 ± 13.1 days from diagnosis. In R Group, an average of 4.52 ± 1.67 IV injections were performed, with 27% ($n = 15$) receiving three or fewer IVs, 73% ($n = 41$) receiving more than three up to a maximum of nine. The first injection was performed after 20.7 ± 18 days from the diagnosis.

The negative binomial regression revealed that patients in the R Group underwent a significantly higher number of IV injections compared with NR Group (incidence rate ratio = 2.13, 95% confidence interval: 1.44–3.15, $P < 0.001$).

71.43% ($n = 40$) of the eyes experienced a single recurrence, whereas 28.57% ($n = 16$) had two recurrences. The NR Group fundus examination revealed hemorrhage associated with myopic lesions in 33 out of 81 cases, whereas in the R Group, 19 out of 56 cases. BCVA progression at each visit is reported in Table 1.

The analysis of CFT was performed by dividing the eyes into three groups based on lesion localization: Group 1: foveal localization, Group 2: juxtafoveal localization (within 200–500 μm from the foveal center), and Group 3: extrafoveal localization (within 2500 μm). Values of CFT in each group are reported in Table 2. Table 3 reports the values of CT and ST, RPE, EZ, and ELM disruption, presence of SRF and IRC, and SHE in both groups. The CNV widths in NR and R Groups are

Table 1: Best-corrected visual acuity (logMAR) progression in nonrecurrence and recurrence Groups were recorded at diagnosis (t0), following the first cycle of intravitreal therapy (t1) and after 12 months from the end of the initial intravitreal treatment (t2)

BCVA	t0	t1	t2
NR Group	0.54±0.35	0.55±0.39	0.54±0.43
R Group	0.55±0.33	0.46±0.3	0.57±0.38

BCVA: Best-corrected visual acuity, NR: Nonrecurrence, R: Recurrence

Table 2: Central foveal thickness in nonrecurrence and recurrence Groups

CFT	Group 1	Group 2	Group 3
NR Group	449±189	252±61.3	227±92.5
R Group	393±113	299±90.7	268±115

Group 1 foveal localization, Group 2 juxtafoveal localization, Group 3 extrafoveal localization (within 2500 µm). CFT: Central foveal thickness, NR: Nonrecurrence, R: Recurrence

Table 3: Choroidal thickness, scleral thickness, disruption of the retinal pigmented epithelium, disruption of the ellipsoid zone, disruption of the external limiting membrane, presence of subretinal fluid intraretinal cysts and subretinal hyperreflective exudation in nonrecurrence and recurrence Groups

OCT characteristics	NR Group	R Group
Choroidal thickness (µ), mean±SD	70±61.6	68.9±52.1
Scleral thickness (µ), mean±SD	329±105	320±90
RPE disruption, *n* (absence: presence)	26:55	27:29
EZ disruption, *n* (absence: presence)	52:29	20:36
ELM disruption, *n* (absence: presence)	48:33	20:36
SRF presence *n*%	41.1	19.8
IRC presence *n*%	25	19.8
SHE presence *n*%	96.4	93.2

OCT: Optical coherence tomography, NR: Nonrecurrence, R: Recurrence, SD: Standard deviation, RPE: Retinal pigment epithelium, EZ: Ellipsoid zone, ELM: External limiting membrane, SRF: Subretinal fluid, IRC: Intraretinal cyst, SHE: Subretinal hyperreflective exudation

994 ± 450 µm and 1101 ± 475 µm, respectively; instead, the CNV height is 221 ± 143 µm and 218 ± 120 µm, respectively.

Through logistic binary regression analysis, the relationship between the factors included in the study and the recurrence of the lesion was evaluated to identify potential predictors of the disease. In the R Group, the factors that seem to be predictive of disease relapse are lower baseline BCVA, higher CFT, RPE disruption, SRF, CNV width, and CNV height. Data are reported in Table 4.

Through Spearman correlation analysis and the Student's *t*-test for independent samples, the correlation between final BCVA and the variables under examination was evaluated in patients without and with recurrence of mCNV.

In the NR Group, final BCVA is significantly influenced by age and by the timing of the initial injection, with a notable impact observed when treatment is initiated within 15 days of diagnosis. Additional significant factors include initial BCVA, BCVA at the first follow-up, RPE disruption, disruption of the photoreceptor layer, and thickness of the lesion. Data are reported in Table 5.

In the R Group, final BCVA is correlated with lower baseline BCVA, higher number of IV injections, RPE disruption, EZ disruption, and CNV height. Data are reported in Table 6.

In the R Group ($n = 55$), the regression model explained 60.3% of the variance in final BCVA. None of the included variables, including baseline BCVA, demographic characteristics, OCT features, or treatment-related parameters, reached statistical significance as independent predictors of final BCVA. Values are reported in Supplementary Table 1.

In the NR Group ($n = 81$), the regression model explained 76.2% of the variance. Similarly, no variable emerged as a significant predictor of final BCVA after adjusting for all covariates. Values are reported in Supplementary Table 2.

Discussion

This study aimed to identify predictive factors for recurrence of mCNV and those influencing final visual acuity in a cohort of treatment-naïve eyes who underwent anti-VEGF therapy, with a minimum follow-up of 12 months. The results provide clinically relevant insights into prognostic markers and may support more tailored therapeutic strategies in patients with mCNV.

A key finding of this analysis is the significantly different therapeutic needs between the two study groups. Eyes without recurrence (NR Group) generally required only one or two injections to achieve disease control, consistent with current guidelines for mCNV treatment. In contrast, over 70% of eyes in the recurrence group (R Group) required more than three injections, suggesting a more aggressive disease course and a higher burden of reactivation. This observation agrees with previous studies by Jain *et al*., which highlighted that a greater number of injections during initial treatment is associated with a higher risk of recurrence.[20]

Moreover, the recurrence rate observed in our study (40.9%) falls within the range reported in the literature, which varies between 23% and 62%.[20-22] Most recurrences occurred within the first 6 months following initial therapy, underlining the importance of close monitoring during the 1st year, a finding supported by Moon *et al.*, who reported that 72.7% of recurrences occurred within 12 months.[22]

The logistic regression analysis identified several OCT-based parameters at baseline as significant predictors of recurrence: lower BCVA, increased CFT, presence of SRF, RPE disruption, as well as greater width and height of the neovascular lesion. These findings suggest that eyes with a more exudative and structurally damaged profile at diagnosis are at higher risk for relapse. Similar OCT features, particularly RPE disruption and SRF, have been recognized in prior studies as markers of disease activity and recurrence potential.[21,23]

Interestingly, although early anti-VEGF administration (within 15 days from diagnosis) was associated with better final BCVA in the NR Group, this timing did not significantly prevent recurrence. This highlights a potential divergence between factors influencing disease reactivation and those driving visual outcomes. However, it is noteworthy that in the NR Group, early treatment correlated with better functional

Table 4: Binary regression analysis

Parameters	OR	*P*
Age	1.019	0.191
Gender	1.36	0.415
Days 1 IV	1.006	0.66
BCVA t0	1.95	0.018*
Hemorrhages	0.768	0.461
Central foveal thickness	0.992	0.001*
Choroidal thickness	1.00	0.988
Scleral thickness	1.00	0.858
RPE disruption	2.272	0.022*
EZ disruption	1.004	0.992
ELM disruption	1.23	0.553
SRF presence	2.83	0.008*
IRC presence	1.35	0.466
SHE presence	1.77	0.502
CNV average width	1.1	0.041*
CNV height	1.3	0.045*

*Statistical significance. Predictors of recurrence of myopic choroidal neovascularization at baseline in treatment-naïve patients. Variables included age, gender, days before 1 intravitreal, best-corrected visual acuity, hemorrhages, choroidal thickness, scleral thickness, retinal pigmented epithelium disruption, ellipsoid zone disruption, external limiting membrane disruption, presence of subretinal fluid intraretinal cysts and subretinal hyperreflective exudation. IV: Intravitreal, BCVA: Best-corrected visual acuity, RPE: Retinal pigment epithelium, EZ: Ellipsoid zone, ELM: External limiting membrane, SRF: Subretinal fluid, IRC: Intraretinal cyst, SHE: Subretinal hyperreflective exudation, CNV: Choroidal neovascularization, OR: Odds-ratio

Table 5: Spearman correlation analysis

Characteristics	*Rs*	*P*
Age	0.358	0.001*
Gender		0.845
Days 1 IV	0.255	0.021*
<15 days		0.021*
15–30 days		0.195
>30 days		0.925
BCVA t0	0.699	0.001*
IV number	0.08	0.476
Hemorrhages		0.278
Central foveal thickness	0.166	0.139
Choroidal thickness	0.148	0.187
Scleral thickness	0.042	0.712
RPE disruption		0.019*
EZ disruption		0.048*
ELM disruption		0.479
SRF presence		0.986
IRC presence		0.787
SHE presence		0.763
CNV average width	0.077	0.495
CNV height	0.237	0.033*

*Statistical significance. Factors influencing best-corrected visual acuity (BCVA) in nonrecurrence Group. Variables included age, gender, days before 1 intravitreal (IV), baseline (t0) BCVA, number of IV injection, hemorrhages, choroidal thickness, central foveal thickness, scleral thickness, retinal pigmented epithelium disruption, ellipsoid zone disruption, external limiting membrane disruption, presence of subretinal fluid intraretinal cysts and subretinal hyperreflective exudation, choroidal neovascularization width and height. *Rs* indicates the Spearman rank correlation coefficient. IV: Intravitreal, BCVA: Best-corrected visual acuity, RPE: Retinal pigment epithelium, EZ: Ellipsoid zone, ELM: External limiting membrane, SRF: Subretinal fluid, IRC: Intraretinal cyst, SHE: Subretinal hyperreflective exudation, CNV: Choroidal neovascularization

recovery, emphasizing the importance of prompt initiation of therapy.

Considering that the recurrence rate is nearly the same in the two groups, respectively, 40.2% for ranibizumab and 44% for aflibercept, and that the recurrence rate was the primary risk factor for decreasing in visual acuity, we can affirm that the drug choice did not impact significantly the final BCVA.

Visual acuity outcomes at 1 year were strongly associated with baseline BCVA and BCVA at the first follow-up visit. In the NR Group, BCVA progressively improved over time, while in the R Group, initial improvement was followed by a decline, likely related to the recurrence itself. The integrity of the RPE and EZ was both significantly associated with better visual prognosis, underscoring their critical anatomical and functional roles in visual signal transduction. Disruption of these layers, particularly when combined with high lesion height, was associated with worse visual outcomes.[24,25]

In the multivariate regression models, none of the baseline demographic, anatomical OCT, or treatment-related variables were independently associated with final BCVA, both in the R and in the NR Groups. This result contrasts with the Spearman correlation analysis, where some baseline OCT parameters showed weak associations with visual outcome. The lack of significance in the multivariate setting suggests that these correlations were not independent predictors once the effect of multiple covariates was taken into account. Therefore, while bivariate correlations may highlight potential trends, they do not translate into robust predictors of final visual acuity, reinforcing the notion that long-term prognosis in mCNV is difficult to predict solely on the basis of baseline structural parameters.

From a structural point of view, choroidal and STs did not differ significantly between the two groups, suggesting these parameters may not be reliable predictors of either recurrence or visual outcomes in this specific context. However, a larger and thicker lesion at baseline (in terms of CNV width and height) was associated with both recurrence and visual loss, supporting the idea that more advanced or active lesions should prompt a more intensive treatment approach.

Importantly, we propose that a subgroup of patients presenting with baseline predictors of recurrence, namely poor initial BCVA, increased CFT, presence of SRF, large CNV dimensions, and RPE disruption, could benefit from a more intensive induction therapy (i.e., two or three anti-VEGF injections upfront), as opposed to the single-injection strategy often applied in standard practice. This is supported by our finding that in the recurrence group, a higher number of injections was significantly associated with better final BCVA,

Table 6: Spearman correlation analysis

Characteristics	*Rs*	*P*
Age	0.157	0.249
Gender		0.567
Days 1 IV	0.08	0.56
<15 days		0.233
15–30 days		0.183
>30 days		0.698
BCVA t0	0.419	0.001*
IV number	0.235	0.08*
Hemorrhages		0.527
Central foveal thickness	0.019	0.887
Choroidal thickness	0.04	0.770
Scleral thickness	0.06	0.632
RPE disruption		0.027*
EZ disruption		0.046*
ELM disruption		0.578
SRF presence		0.461
IRC presence		0.688
SHE presence		0.216
CNV average width	0.06	0.641
CNV height	0.13	0.034*

*Statistical significance. Factors influencing best-corrected visual acuity (BCVA) in recurrence Group. Variables included age, gender, days before 1 intravitreal (IV), baseline (t0) BCVA, number of IV injection, hemorrhages, choroidal thickness, central foveal thickness, scleral thickness, retinal pigmented epithelium disruption, ellipsoid zone disruption, external limiting membrane disruption, presence of subretinal fluid, intraretinal cysts and subretinal hyperreflective exudation, choroidal neovascularization width and height. *Rs* indicates the Spearman rank correlation coefficient. IV: Intravitreal, BCVA: Best-corrected visual acuity, RPE: Retinal pigment epithelium, EZ: Ellipsoid zone, ELM: External limiting membrane, SRF: Subretinal fluid, IRC: Intraretinal cyst, SHE: Subretinal hyperreflective exudation, CNV: Choroidal neovascularization

suggesting that aggressive early treatment may help mitigate the functional impact of relapse.

Taken together, these findings support a risk-stratified treatment approach in mCNV. OCT biomarkers, particularly CFT, lesion size, and outer retinal integrity, should be carefully evaluated at baseline to guide treatment intensity and monitoring frequency. Moreover, early functional response (i.e., BCVA at first follow-up) may serve as an additional prognostic indicator and help tailor management in the longer term.

This study has several limitations. First, its retrospective design limits the ability to establish causal relationships. Second, the minimum follow-up of 12 months may not fully capture late recurrences or long-term visual outcomes. Third, the possibility of selection bias cannot be excluded. Nonetheless, the relatively large sample size and the use of standardized imaging and treatment protocols strengthen the validity of our findings. In addition, the unequal distribution of patients between treatment groups, with a substantially larger proportion treated with ranibizumab compared to aflibercept, may have reduced the statistical power to detect potential differences in recurrence rates. Consequently, the absence of a statistically significant difference should be interpreted with caution.

Our findings highlight specific baseline features, such as lower BCVA, increased CFT, presence of SRF, and RPE disruption, as predictive of mCNV recurrence and worse visual outcomes. Larger and thicker lesions are more likely to recur and are associated with poorer vision, emphasizing the importance of individualized treatment plans. Incorporating OCT biomarkers and early functional responses into clinical decision-making may improve long-term visual prognosis in patients with mCNV.

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Conflicts of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or nonfinancial interest (such as personal or professional relationships, afliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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Supplementary Table 1: Multivariate regression analysis (Recurrence Group)

Characteristics	Coefficient (β)	95% CI (lower–upper)	*P*
Age	−0.002	−0.006 to 0.01	0.601
Gender	0.083	−0.123 to 0.29	0.417
Days 1 IV	−0.005	−0.012 to 0.003	0.248
BCVA t0	−0.257	−0.644 to 0.131	0.187
IV number	−0.007	−0.061 to 0.046	0.782
Hemorrhages	0.106	−0.095 to 0.306	0.292
Central foveal thickness	0	−0.001 to 0.001	0.442
Choroidal thickness	0.001	−0.002 to 0.003	0.594
Scleral thickness	0	−0.001 to 0.002	0.595
RPE disruption	−0.185	−0.434 to 0.064	0.14
EZ disruption	0.012	−0.142 to 0.166	0.871
ELM disruption	0.012	−0.142 to 0.166	0.871
SRF presence	−0.171	−0.383 to 0.04	0.109
IRC presence	0.057	−0.235 to 0.349	0.695
SHE presence	−0.317	−0.895 to 0.26	0.273
CNV average width	0	0	0.716
CNV height	0	−0.001 to 0.001	0.539

*Statistical significance. Factors influencing best-corrected visual acuity (BCVA) in the recurrence Group. Variables included age, gender, days before first intravitreal (IV) injection, baseline (t0) BCVA, BCVA at t1, number of IV injections, presence of hemorrhages, choroidal thickness, central foveal thickness, scleral thickness, retinal pigmented epithelium disruption, ellipsoid zone disruption, external limiting membrane disruption, presence of subretinal fluid, intraretinal cysts, subretinal hyperreflective exudation, and choroidal neovascularization location, width, and height. CI: Confidence interval, IV: Intravitreal, BCVA: Best-corrected visual acuity, RPE: Retinal pigment epithelium, EZ: Ellipsoid zone, ELM: External limiting membrane, SRF: Subretinal fluid, IRC: Intraretinal cyst, SHE: Subretinal hyperreflective exudation, CNV: Choroidal neovascularization

Supplementary Table 2: Multivariate regression analysis (Nonrecurrence Group)

Characteristics	Coefficient (β)	95% CI (lower–upper)	*P*
Age	0.002	−0.004 to 0.007	0.504
Gender	−0.001	−0.125 to 0.123	0.983
Days 1 IV	0.002	−0.003 to 0.007	0.506
BCVA t0	0.01	−0.284 to 0.304	0.946
IV number	−0.017	−0.063 to 0.03	0.475
Hemorrhages	−0.033	−0.162 to 0.096	0.609
Central foveal thickness	0	0	0.194
Choroidal thickness	0.001	−0.001 to 0.002	0.373
Scleral thickness	0	−0.001 to 0.001	0.998
RPE disruption	0.088	−0.065 to 0.241	0.254
EZ disruption	0.141	−0.243 to 0.525	0.465
ELM disruption	−0.077	−0.376 to 0.222	0.609
SRF presence	−0.015	−0.172 to 0.141	0.847
IRC presence	0.07	−0.088 to 0.227	0.379
SHE presence	−0.08	−0.346 to 0.186	0.55
CNV average width	0	0	0.444
CNV height	0	0 to 0.001	0.136

*Statistical significance. Factors influencing best-corrected visual acuity (BCVA) in the nonrecurrence Group. Variables included age, gender, days before first intravitreal (IV) injection, baseline (t0) BCVA, BCVA at t1, number of IV injections, presence of hemorrhages, choroidal thickness, central foveal thickness, scleral thickness, retinal pigmented epithelium disruption, ellipsoid zone disruption, external limiting membrane disruption, presence of subretinal fluid, intraretinal cysts, subretinal hyperreflective exudation, and choroidal neovascularization location, width, and height. CI: Confidence interval, IV: Intravitreal, BCVA: Best-corrected visual acuity, RPE: Retinal pigment epithelium, EZ: Ellipsoid zone, ELM: External limiting membrane, SRF: Subretinal fluid, IRC: Intraretinal cyst, SHE: Subretinal hyperreflective exudation, CNV: choroidal neovascularization