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Systemic Oxidative Stress Level as a Pathological and Prognostic Factor in Myopic Choroidal Neovascularization

Jiying Wang, MD, PhD,[1] *Hiroshi Kunikata, MD, PhD,*[1,2] *Masayuki Yasuda, MD, PhD,*[1] *Noriko Himori, MD, PhD,*[1] *Fumihiko Nitta, MD, PhD,*[1] *Toru Nakazawa, MD, PhD*[1,2,3,4]

Purpose: To investigate the association of systemic oxidative stress level with myopic choroidal neovascularization (mCNV) and its clinical outcomes.

Design: Retrospective case-control study.

Participants: This retrospective study included 52 eyes of 52 healthy participants (mean age: 62.5 years), 30 eyes of 30 patients (mean age: 59.6 years) with high myopia (HM) but without mCNV, and 23 eyes of 23 patients (mean age: 61.8 years) with HM and mCNV who received intravitreal anti-VEGF antibody injections (IVIs) using a pro re nata regimen during the 6-month follow-up after the first IVI.

Methods: Clinical findings, including oxidative stress parameters, such as diacron reactive oxygen metabolites (dROMs), biological antioxidant potential (BAP), and the BAP/dROM ratio (B/d ratio), were analyzed.

Main Outcome Measures: Clinical features and oxidative stress parameters.

Results: Both BAP and the B/d ratio were significantly lower in the HM/mCNV group than in the HM/no mCNV group ($P = 0.002$ and $P = 0.012$, respectively) and than in the control group ($P = 0.001$ and $P = 0.026$, respectively). In a multiple logistic regression analysis, axial length (odds ratio 1.878, $P = 0.042$) and the B/d ratio (odds ratio 0.470, $P = 0.026$) were significantly associated with mCNV. Dividing the patients into high and low B/d ratio groups (with a cutoff of 5.2) showed that subfoveal choroidal thickness (SFCT) was lower ($P = 0.002$) and the number of IVI treatments was higher ($P = 0.029$) in the low B/d ratio group than in the high B/d ratio group. In multiple regression analyses, only the B/d ratio was significantly associated with SFCT ($\beta = 0.684$, $P = 0.006$).

Conclusions: The oxidative stress level in eyes with HM differed according to mCNV, SFCT, and the number of IVI treatments. Measuring oxidative stress parameters might be useful in eyes with HM both for assessing the risk of developing mCNV and determining disease activity.

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Myopic choroidal neovascularization (mCNV) is a prominent vision-threatening complication of high myopia (HM), a condition characterized by excessive elongation of the eyeball.[1] High myopia involves significant ocular changes, such as thinning of the choroid and retina, that increase the eye's vulnerability to pathological changes, including mCNV.[1,2] Although mCNV is currently treated with anti-VEGF antibodies, the incidence of mCNV has been steadily rising all over the world, particularly in Asia,[3,4] necessitating a deeper exploration of its pathogenesis and prognostic factors.

Lately, systemic oxidative stress has emerged as a potential key player in mCNV development and clinical outcomes.[5–7] Oxidative stress originates from an imbalance between the production of reactive oxygen species and the body's antioxidant defenses. It is known to cause tissue damage and inflammation, leading to pathophysiology in various ocular diseases, including age-related macular degeneration and diabetic retinopathy.[8–11] Although oxidative stress may help explain the altered regulatory pathways in myopia and the incidence of associated eye diseases, its role in mCNV remains unclear.

In recent years, systemic oxidative stress has become easy to measure on an outpatient basis with techniques such as blood sampling, and its relationship with ocular diseases is becoming clearer.[12–17] We believe that oxidative stress is closely involved in the pathogenesis of mCNV and anticipate that oxidative stress markers could be used to predict mCNV progression and determine its treatment strategies. Therefore, we set out to investigate systemic oxidative stress parameters in patients with mCNV and the association of these parameters with clinical findings, including treatment outcomes.

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Methods

Setting and Design

This was an institutional case series. Participants were recruited from patients referred to the Department of Ophthalmology at Tohoku University Hospital and individuals registered in the Tohoku Medical Megabank Organization at Tohoku University. This study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Tohoku University School of Medicine. All participants gave written informed consent.

Patients

The characteristics of the participants at the initial visit are shown in Table 1. The study included a control group of 52 eyes of 52 healthy Japanese individuals (17 males and 35 females; mean age: 62.5 ± 9.7 years, age range: 46−77 years) with a mean axial length of 24.02 ± 0.30 mm (range: 23.53−24.44 mm) and an HM/no mCNV group of 30 eyes of 30 Japanese individuals (10 males and 20 females; mean age: 59.6 ± 12.4 years, age range: 44−84 years) with a mean axial length of 28.17 ± 0.85 mm (range: 27.00−29.63 mm) but without mCNV; these participants were recruited from individuals undergoing standard medical check-ups at the Tohoku University Tohoku Medical Megabank Organization. The study also included an HM/mCNV group of 23 eyes of 23 Japanese patients (7 males and 16 females; mean age: 61.8 ± 17.7 years, age range: 27−82 years) with a mean axial length of 28.89 ± 1.59 mm (range: 26.00−30.70 mm) and mCNV, all of whom had received intravitreal anti-VEGF antibody injections (IVIs) of ranibizumab (Lucentis; Novartis Pharma K.K.) or ranibizumab biosimilar 1 (ranibizumab BS; Senju Pharmaceutical Co., Ltd) for the first time at the initial visit, and then followed with a pro re nata regimen during the 6-month follow-up after the first IVI at the Department of Ophthalmology at Tohoku University Hospital.

The exclusion criteria were clinical evidence or a history of ocular disease other than mild cataract or refractive error; evidence from OCT or fundus photography suggesting glaucoma, such as an abnormal loss of circumpapillary retinal nerve fiber layer thickness or a cup-to-disc ratio of >0.4, respectively; a history of intraocular surgery; and a history of smoking, hypertension, hyperlipidemia, liver function disorders, or diabetes mellitus.

Ophthalmic Evaluations

Ophthalmic examinations included fundus photography (swept-source OCT, Topcon Corporation), best-corrected visual acuity (BCVA), and axial length (IOL-Master, Carl Zeiss Meditec AG), central retinal thickness, and subfoveal choroidal thickness (SFCT) measurements with OCT (Topcon 3D OCT-2000, Topcon Corporation).

Oxidative Stress Measurements

For oxidative stress measurement, blood samples were collected after ≥3 hours of fasting. Next, oxidative stress markers, including diacron reactive oxygen metabolites (dROMs) and biological antioxidant potential (BAP), were measured with a free radical analyzer (Free Carpe Diem, Wismerll Co., Ltd). The BAP/dROM ratio (B/d ratio) was calculated from the measured values of dROMs and BAP. Details of these analysis procedures have been described previously.[12]

Statistical Analysis

The data are presented as mean ± standard deviation. The *t* test and Fisher exact test were used to determine the significance of differences in parameters between groups. Multiple logistic regression analyses were performed to determine independent variables contributing to the presence of mCNV in the HM groups with and without mCNV. Multiple regression analyses were also performed to determine independent variables affecting SFCT in the HM/mCNV group. Statistical analyses were performed using R Studio software (version 4.2.1, R Foundation for Statistical Computing). The significance level was set at $P < 0.05$.

Results

Table 1 shows clinical findings in the participants at the initial visit. Age, gender, and dROMs showed no significant differences among all the groups (Table 1). Axial length showed no significant differences between the HM/mCNV and HM/no mCNV groups ($P = 0.057$). Biological antioxidant potential and the B/d ratio showed no significant difference between the control and HM/no mCNV groups ($P = 0.436$ and $P = 0.265$, respectively); however, both BAP and the B/d ratio were significantly lower in the HM/mCNV group than in the control group ($P = 0.001$ and $P = 0.026$, respectively), and they were also lower in the HM/mCNV group than in the HM/no mCNV group ($P = 0.002$ and $P = 0.012$, respectively).

Table 2 shows the results of multiple logistic regression analyses of independent variables contributing to the presence of mCNV in the eyes with HM. The analysis using age, gender, axial length, and BAP as explanatory variables showed that BAP was an independent factor contributing to the presence of mCNV (odds ratio 0.996, 95% confidence interval 0.992−0.999, $P = 0.008$). Another analysis using age, gender, axial length, and the B/d ratio as explanatory variables showed that axial length (odds ratio 1.878, 95% confidence interval 1.077−3.685, $P = 0.042$) and the B/d ratio (odds ratio 0.470, 95% confidence interval 0.227−0.870, $P = 0.026$) were independent factors contributing to the presence of mCNV.

The HM/mCNV group was divided into 2 groups by the median B/d ratio (5.2) for further investigation (Table 3); 13 eyes were included in a group with a B/d ratio <5.2 and 10 eyes were included in a group with a B/d ratio ≥5.2. All cases of mCNV had subfoveal localization, confirmed with fundus photography and in baseline OCT scans (representative cases are shown in Figure 1). There were no significant differences between the 2 groups in mean age ($P = 0.252$), gender ($P = 0.168$), axial length ($P = 0.961$), central retinal thickness at the initial visit ($P = 0.865$), BCVA at the initial visit ($P = 0.295$), BCVA after the 6-month follow-up ($P = 0.417$), BCVA improvement during the 6-month follow-up ($P = 0.258$), the number of eyes with regressed mCNV after the first IVI during the 6-month follow-up ($P = 0.403$), or the number of eyes with recurrent mCNV after the first IVI during the 6-month follow-up ($P = 0.480$). However, SFCT at the initial visit was lower (58.38 ± 30.21 μm vs.

Table 1. Characteristics of the Subjects

		HM		P Value		
				Control vs. HM		*HM*
	Control	*No mCNV*	*mCNV*	*No mCNV*	*mCNV*	*No mCNV vs. mCNV*
Number of patients	52	30	23	-	-	-
Number of eyes	52	30	23	-	-	-
Age (yrs)	62.5 ± 9.7	59.6 ± 12.4	61.8 ± 17.7	0.140	0.430	0.311
Gender (M:F)	17:35	10:20	7:16	0.861*	0.401*	0.822*
Axial length (mm)	24.02 ± 0.30	28.17 ± 0.85	28.89 ± 1.59	-	-	0.057
dROM (U.CARR)	378.94 ± 62.33	364.80 ± 58.69	377.65 ± 63.82	0.152	0.418	0.264
BAP (μM)	2133.06 ± 194.80	2125.60 ± 210.43	1925.91 ± 248.65	0.436	0.001	0.002
B/d ratio	5.80 ± 1.21	5.97 ± 1.14	5.25 ± 1.07	0.265	0.026	0.012

BAP = biological antioxidant potential; B/d ratio = biological antioxidant potential/diacron reactive oxygen metabolite ratio; dROM = diacron reactive oxygen metabolite; F = female; HM = high myopia; M = male; mCNV = myopic choroidal neovascularization; U.CARR = Carratelli units.
Unmarked *P* value: *t* test.
*Fisher exact test.

108.00 ± 35.79 μm, $P = 0.002$) and more IVI treatments were required for the stabilization of mCNV (2.00 ± 0.91 vs. 1.30 ± 0.48, $P = 0.029$) in the B/d ratio <5.2 group compared with the B/d ratio ≥5.2 group (Table 3, Fig 1).

The results of multiple regression analyses are shown in Table 4. The analysis using age, gender, axial length, and BAP as explanatory variables showed that there were no independent contributing factors to SFCT in the HM/mCNV group. Another analysis using age, gender, axial length, and the B/d ratio as explanatory variables showed that the B/d ratio was an independent contributing factor to SFCT in the HM/mCNV group ($\beta = 0.684$, $P = 0.006$).

Discussion

We set out to investigate the association of systemic oxidative stress level with mCNV and its clinical outcomes. Both BAP and the B/d ratio were significantly lower in the HM/mCNV group than in the HM/no mCNV group, and both factors were also lower than in the control group. In a multiple logistic regression analysis, the B/d ratio was negatively associated with mCNV. Grouping HM/mCNV patients according to whether they had a B/d ratio <5.2 or ≥5.2 showed that SFCT was lower and the number of IVI treatments was higher in the first group than in the second group. In multiple regression analyses, only the B/d ratio was positively associated with SFCT.

Table 2. Multiple Logistic Regression Analyses of Independent Variables Contributing to the Presence of mCNV

Variables			
Response	*Explanatory*	**Adjusted OR (95% CI)**	**P Value**
mCNV	Age (yrs)	1.001 (0.958-1.041)	0.956
	Gender	0.880 (0.219-3.386)	0.853
	Axial length (mm)	1.805 (1.046-3.512)	0.053
	BAP (μM)	0.996 (0.992-0.999)	0.008
	Age (yrs)	0.995 (0.951-1.042)	0.843
	Gender	1.226 (0.275-5.410)	0.785
	Axial length (mm)	1.878 (1.077-3.685)	0.042
	B/d ratio	0.470 (0.227-0.870)	0.026

BAP = biological antioxidant potential; B/d ratio = biological antioxidant potential/diacron reactive oxygen metabolite ratio; CI = confidence interval; mCNV = myopic choroidal neovascularization; OR = odds ratio.

Oxidative Stress as a Factor Affecting the Presence of mCNV

The current results show that both BAP and the B/d ratio were significantly lower in individuals with HM/mCNV compared with those with HM/no mCNV and the control group, suggesting a strong connection between systemic oxidative stress and the presence of mCNV, regardless of the lack of association with only HM. Furthermore, a logistic regression analysis revealed that the B/d ratio was significantly associated with the presence of mCNV. The B/d ratio has been previously reported to represent an index of potential antioxidant capacity.[18] Thus, individuals with a lower B/d ratio, which is indicative of higher systemic oxidative stress due to diminished antioxidant capacity, have a higher likelihood of developing mCNV. Furthermore, local oxidative stress in the eye has previously been reported to be closely involved with mCNV.[19–24] Thus, though several theories, including mechanical, hemodynamic, and heredodegenerative theories, have been proposed to interpret the pathogenesis of mCNV,[1,25,26] the current results suggest that systemic oxidative stress could also potentially be a key player in mCNV and that the B/d ratio may be a promising predictive marker for mCNV risk.

Although the current study did not find any difference in systemic oxidative stress levels between the control and HM/no mCNV groups, past studies have made various findings on local oxidative stress in the eyes. Oxidative stress was reported to increase in the retinal pigment epithelium in eyes with pathological myopia, which may cause higher hypoxia-inducible factor-1 levels, because mitochondrial reactive oxygen species stabilize hypoxia-inducible factor-1 by reducing

Table 3. Characteristics of Patients with mCNV Grouped by B/d Ratio

	All	B/d Ratio <5.2	B/d Ratio ≥5.2	*P* Value
Number of patients	23	13	10	-
Number of eyes	23	13	10	-
Age (yrs)	61.8 ± 17.7	65.5 ± 19.0	57.0 ± 15.5	0.252
Gender (M:F)	7:16	2:11	5:5	0.168*
Axial length (mm)	28.89 ± 1.59	28.90 ± 1.79	28.87 ± 1.40	0.961
CRT at initial visit (μm)	263.57 ± 43.99	262.08 ± 37.62	265.50 ± 53.25	0.865
SFCT at initial visit (μm)	79.96 ± 40.67	58.38 ± 30.21	108.00 ± 35.79	0.002
BCVA at initial visit (logMAR)	0.50 ± 0.41	0.54 ± 0.45	0.45 ± 0.38	0.295
BCVA after 6MFU (logMAR)	0.17 ± 0.33	0.18 ± 0.26	0.15 ± 0.41	0.417
BCVA improvement during 6MFU (logMAR)	0.33 ± 0.24	0.36 ± 0.30	0.30 ± 0.14	0.258
Number of IVI treatments during 6MFU	1.70 ± 0.82	2.00 ± 0.91	1.30 ± 0.48	0.029
Number of eyes with regressed mCNV after first IVI during 6MFU (%)	12 (52.2%)	5 (38.5%)	7 (70.0%)	0.403*
Number of eyes with recurrent mCNV after first IVI during 6MFU (%)	7 (30.4%)	5 (38.5%)	2 (20.0%)	0.480*

BCVA = best-corrected visual acuity; B/d ratio = biological antioxidant potential/diacron reactive oxygen metabolite ratio; CRT = central retinal thickness; F = female; IVI = intravitreal anti-VEGF antibody injection; logMAR = logarithm of minimum angle of resolution; M = male; mCNV = myopic choroidal neovascularization; 6MFU = 6-month follow-up; SFCT = subfoveal choroidal thickness.
Unmarked *P* value: *t* test.
*Fisher exact test.

the activity of prolyl hydroxylases.[27] In patients with age-related macular degeneration (both with/without CNV), increased expression of hypoxia-inducible factor-1 α in the retinal pigment epithelium when it is exposed to oxidative stress also promotes the development of CNV.[24] Mice that lack a hypoxia response element in their VEGF promoters also develop significantly less CNV at Bruch's membrane rupture sites than wild-type mice.[28] Furthermore, the level of

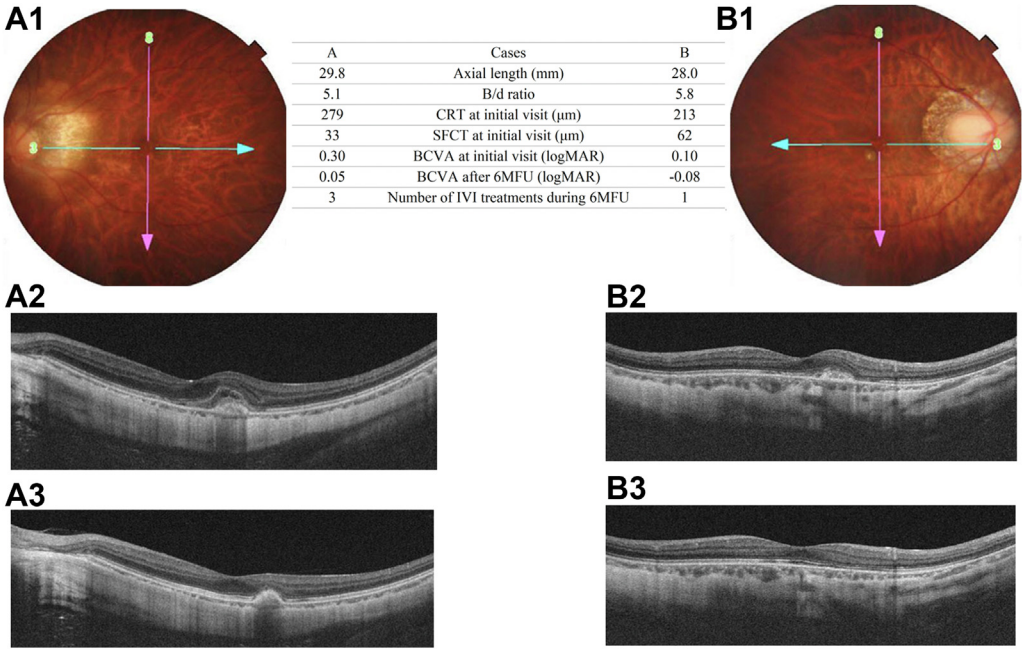

Figure 1. Typical cases of HM with mCNV that have different B/d ratios. The characteristics of each case are indicated in the table (upper center). Case A (**A**1, 2, 3): an 82-year-old woman with a B/d ratio of 5.1. Her left eye had mCNV, as demonstrated in a color fundus photograph (**A**1) and an OCT image (**A**2) at the initial visit. Three IVI treatments were required for the stabilization of the mCNV during the 6MFU. There were no exudative changes, only a small pigment epithelial detachment, as demonstrated in an OCT image after the 6MFU (**A**3). Case B (**B**1, 2, 3): a 78-year-old man with a B/d ratio of 5.8. His right eye had mCNV, as demonstrated in a color fundus photograph (**B**1) and an OCT image (**B**2) at the initial visit. The mCNV completely regressed after only 1 IVI treatment during the 6MFU. There were no exudative changes or any recurrence, as demonstrated in an OCT image after the 6MFU (**B**3). 6MFU = 6-month follow-up; BCVA = best-corrected visual acuity; B/d ratio = biological antioxidant potential/diacron reactive oxygen metabolite ratio; CRT = central retinal thickness; HM = high myopia; IVI = intravitreal anti-VEGF antibody injection; logMAR = logarithm of minimum angle of resolution; mCNV = myopic choroidal neovascularization; SFCT = subfoveal choroidal thickness.

Table 4. Multiple Regression Analyses of Independent Variables Contributing to SFCT in Patients with mCNV

Response	Explanatory	β	*P* Value
SFCT at initial visit (μm)	Age (yrs)	−0.215	0.334
	Gender	0.074	0.734
	Axial length (mm)	0.105	0.635
	BAP (μM)	0.365	0.106
	Age (yrs)	−0.085	0.672
	Gender	−0.283	0.210
	Axial length (mm)	−0.093	0.644
	B/d ratio	0.684	0.006

β = standard partial regression coefficient; BAP = biological antioxidant potential; B/d ratio = biological antioxidant potential/diacron reactive oxygen metabolite ratio; mCNV = myopic choroidal neovascularization; SFCT = subfoveal choroidal thickness.

VEGF in the aqueous humor was reported to be significantly higher in eyes with HM/mCNV than in eyes with HM/no mCNV.[29–31] It has been hypothesized that loss of SFCT may lead to hypoxic retinal changes, resulting in secretion of VEGF and the occurrence of mCNV.[32] Thus, given the past and current results, we believe that the pathogenesis of mCNV could be explained by a mutual association between oxidative stress, hypoxia, and VEGF.

Oxidative Stress as a Factor Affecting SFCT

Subfoveal choroidal thickness reflects structural changes in the eye and could be a critical anatomical parameter in mCNV as previously reported.[33–35] Our multiple regression analyses indicated that only the B/d ratio significantly contributed to SFCT in eyes with HM and mCNV. This observation is of clinical significance, suggesting that oxidative stress levels directly influence structural changes in the choroid, which, in turn, might affect the presence and progression of mCNV. Subfoveal choroidal thickness in eyes with mCNV was previously reported to be significantly lower than in contralateral eyes.[36] Lower SFCT at baseline has also been reported to indicate a poorer anatomic outcome after intravitreal anti-VEGF treatment in eyes with mCNV.[36,37] Additionally, SFCT has been reported to be lower in eyes with recurring mCNV than in those without recurrence, and associations were found between SFCT and 1-year recurrence rates.[37] Thus, SFCT might reflect disease activity, and knowledge of SFCT might aid decision making regarding retreatment for mCNV in recurrent cases.[36] In the current study, a lower B/d ratio, that is, lower antioxidant capacity, led to lower SFCT in eyes with HM and mCNV, which may have contributed to the pathogenesis of mCNV. Together with current and previous studies, lower SFCT is a key risk factor for active mCNV, which could be caused by higher oxidative stress levels, as indicated by a lower B/d ratio.

Oxidative Stress as a Factor Affecting Clinical Outcomes in mCNV

In the current study, the relationship between oxidative stress levels and the clinical outcomes of mCNV was assessed by dividing patients into groups based on a B/d ratio threshold of 5.2. Notably, there were no differences in axial length, BCVA, or central retinal thickness at baseline; however, SFCT was significantly lower and the number of IVIs during the 6-month follow-up period was significantly higher in the group with lower antioxidant capacity (i.e., those with a lower B/d ratio). This finding underscores the influence of oxidative stress on the clinical course of mCNV. In treatment for mCNV, we used a pro re nata regimen for the IVIs to keep their total number as low as possible. In fact, when comparing 1-loading and 3-loading approaches in treatment for mCNV, it has been reported that the total number of IVIs is lower with 1-loading than 3-loading even though BCVA results are similar, although there are more additional treatments with the 1-loading approach.[38,39] In the present study, there were no differences in final BCVA, the rate of resolution after a single IVI, or the rate of recurrence between the groups; however, IVI treatment requirements significantly increased in the group with a B/d ratio <5.2. Therefore, it is reasonable to infer that higher oxidative stress levels contribute to more aggressive and treatment-resistant mCNV. This may be because patients with mCNV with a lower B/d ratio experience more extensive oxidative damage to the retinal pigment epithelium and choroid than those with a higher B/d ratio, necessitating multiple interventions to stabilize the condition.

In mCNV, various factors other than oxidative stress have been reported to be associated with the prognosis. It has been reported that younger patients and those with favorable indocyanine green findings (a dark rim) and favorable OCT findings (integrity of the lesion-adjacent external limiting membrane and the lesion-adjacent ellipsoid zone) have a good prognosis, while those with hemorrhage have a poor prognosis.[40,41] Furthermore, a dome-shaped macula was reported not to be a negative prognostic factor in response to anti-VEGF therapy in mCNV after 2 years. However, in eyes with a dome-shaped macula, mCNV tends to be extrafoveal, thus ensuring a good visual prognosis from the earliest stage of the disease.[42] In addition to these various clinical findings, oxidative stress levels may be considered as an additional factor to predict the course of treatment in mCNV.

Limitations

The current study has some limitations. Firstly, it was retrospective, which may have introduced bias and confounding variables; the sample size was relatively small; and the study was conducted with a specific population (only Japanese individuals), which may limit the generalizability of the findings to other populations. Secondly, the analysis was based mainly on systemic oxidative stress parameters, and it did not provide information on localized oxidative stress within the eye. Exploring local oxidative stress markers within the ocular tissues, particularly the retina and choroid, might also offer a more comprehensive understanding of disease mechanisms. However, the ideal treatment would be to reduce the development of mCNV by systemically controlling oxidative stress with oral medication or supplements. Antioxidant therapies,

such as supplements containing food-derived antioxidants, have been reported to potentially be important as retinal neuroprotection treatments.[43,44] Thus, control of systemic oxidative stress might be promising as a candidate therapeutic strategy for mCNV, as also suggested by the results of the Age-Related Eye Disease Study, which indicated that there were benefits from taking supplements used for slowing the progression of age-related macular degeneration, though this is still under debate.[45,46] Thirdly, although oxidative stress is considered a significant factor in mCNV, it may not be the sole cause of disease progression and the treatment response. Thus, further studies with larger and more diverse cohorts are needed to validate the current results and explore their potential implications for clinical practice.

The results of this study provide valuable insights into the role of oxidative stress in mCNV. Oxidative stress, as indicated by a decreased B/d ratio, appears to be a significant factor associated with the presence of mCNV. This finding has the potential to serve as a predictive marker for identifying individuals with HM at a higher risk of developing mCNV. Furthermore, the study highlights the impact of oxidative stress on the structural changes of the choroid, as individuals with a lower B/d ratio had lower SFCT. This suggests that oxidative stress directly influences anatomical changes in eyes with mCNV. Additionally, patients with higher oxidative stress, as indicated by a lower B/d ratio, had a greater need for IVI treatments, reflecting the clinical severity of mCNV. These findings emphasize the potential clinical utility of measuring systemic oxidative stress parameters to assess the risk, structural changes, and treatment requirements for mCNV. Thus, oxidative stress appears to play a crucial role in the pathogenesis and prognosis of mCNV. The results of this study open up possibilities for further research, diagnostic tools, and treatment strategies for individuals at risk of mCNV.

Footnotes and Disclosures

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[1] Department of Ophthalmology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.

[2] Department of Retinal Disease Control, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.

[3] Department of Ophthalmic Imaging and Information Analytics, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.

[4] Department of Advanced Ophthalmic Medicine, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.

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All authors have completed and submitted the ICMJE disclosures form.

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Author Contributions:

Conception and design: Wang, Kunikata, Yasuda, Himori, Nitta, Nakazawa

Data collection: Wang, Kunikata, Yasuda, Himori, Nitta

Analysis and interpretation: Wang, Kunikata, Yasuda, Nakazawa

Obtained funding: Kunikata, Yasuda, Nakazawa

Overall responsibility: Wang, Kunikata, Yasuda, Himori, Nitta, Nakazawa

Abbreviations and Acronyms:
BAP = biological antioxidant potential; **BCVA** = best-corrected visual acuity; **B/d ratio** = biological antioxidant potential/diacron reactive oxygen metabolite ratio; **dROM** = diacron reactive oxygen metabolite; **HM** = high myopia; **IVI** = intravitreal anti-VEGF antibody injection; **mCNV** = myopic choroidal neovascularization; **SFCT** = subfoveal choroidal thickness.

Keywords:
High myopia, Myopic choroidal neovascularization, Systemic oxidative stress, Intravitreal anti-VEGF antibody injection, Subfoveal choroidal thickness.

Correspondence:
Hiroshi Kunikata, MD, PhD, Department of Ophthalmology, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai, Miyagi, 980-8574, Japan. E-mail: drkunikata@gmail.com.

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