

COVID-19 Pandemic and Age-Related Macular Degeneration: Real-World Treatment Outcomes

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ABSTRACT

Purpose: Assessment of the effects of COVID-19 pandemic-related treatment interruption on visual and anatomical outcomes in patients with neovascular age-related macular degeneration (AMD).

Methods: Patients with neovascular AMD were included in this retrospective study. The patients were divided into two groups: Group 1 (patients with a follow-up period of 6 months or less before the pandemic) and Group 2 (patients with a follow-up period of longer than 6 months before the pandemic). After the COVID-19 pandemic, the groups were evaluated in terms of reduction in best corrected visual acuity (BCVA) and increase in central macular thickness (CMT).

Results: 66 eyes of 59 patients with AMD were included in this study (n=40 in Group 1, n=26 in Group 2). The mean BCVA change between the last visit before the COVID-19 pandemic and the first visit after the COVID-19 pandemic was logMAR 0.7±0.32 in Group 1 and logMAR 0.2±0.05 in Group 2. The mean CMT change between the last visit before the COVID-19 pandemic and the first visit after the COVID-19 pandemic was 174±94 µm in Group 1 and 68±36 µm in Group 2. There was a significant difference between groups in terms of BCVA reduction and CMT increase (p<0.001).

Conclusion: The treatment interruption associated with the COVID-19 pandemic had a lesser impact on the anatomical and visual outcomes in more stable neovascular AMD patients.

Keywords: covid-19 pandemic, age-related macular degeneration, anti-VEGF agents.

INTRODUCTION

The prevalence of age-related macular degeneration (AMD) is increasing worldwide in relation increased life expectancy.^{1,2} It is a progressive disease that can result in blindness. With early diagnosis of disease and regular follow-up, patients can have a better vision-related quality of life.³ Diagnosis of this disease, which affects central vision, can be made by a detailed fundus examination and is confirmed by fluorescein angiography (FA) and optical coherence tomography (OCT). The choroidal neovascularisation (CNV) which is the main manifestation of neovas-

cular AMD, is detected by FA and OCT. However, OCT is used more frequently than FA in the long-term follow-up of neovascular AMD.^{4,5} Additionally, since OCT is a non-invasive technique, it is also important for the early detection of AMD. Treatment of AMD is mostly related to CNV. Therefore, at present, anti-vascular endothelial growth factor (VEGF) agents are shown as the first-line treatment option.^{6,7} However, since the duration of effectiveness of anti-VEGF agents is limited, repeated injections cause a treatment burden. Because of this, to reduce the number of needed intravitreal injections, different treatment regimens

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(pro re nata - PRN, bimonthly fixed, treat and extend- T&E) have been studied in randomized controlled trials.⁸⁻¹¹ Recent real-world studies have reported that fewer injections are administered for neovascular AMD in real life than in clinical trials.¹²

Regular follow-up for neovascular AMD can not be done in clinical practice due to different reasons. For instance, the COVID-19 pandemic was one of them. The World Health Organization (WHO) declared the COVID-19 pandemic on 11 March 2020. Due to restrictions for COVID-19 pandemic in our country, AMD patients could not have their control visits and injections.

Our aim in this study is to evaluate anatomical and functional results seen in neovascular AMD patients whose treatments were interrupted due to the COVID-19 pandemic.

METHODS

In this study, the medical records of patients who were followed up with the diagnosis of AMD at a tertiary center between January 2018 and October 2023 were reviewed retrospectively. The study conformed to the tenets of the Declaration of Helsinki. Institutional ethics committee approval was obtained for this study (2025/25009).

The detailed ophthalmologic examination files of all the patients were reviewed. Best corrected visual acuity (BCVA) measurement, biomicroscopy, intraocular pressure measurement, funduscopy, optical coherence tomography (OCT, Heidelberg Engineering, Heidelberg, Germany), fluorescein angiography (FA, the integrated software of the Heidelberg Retina Angiography II), number of follow-up visits and total number of intravitreal injections were recorded. BCVA was measured by a standardized Snellen chart. Snellen visual acuity was converted to logMAR (logarithm of the minimum angle of resolution) for statistical analyses. Central macular thickness (CMT, from the inner limiting membrane to the retinal pigment epithelium on the fovea – central 1 mm diameter) and disease activity (subretinal fluid -SRF, ntraretinal fluid-IRF, subretinal hyperreflective material - SRHM) were assessed using OCT.

Review of the medical records revealed that seven patients had been hospitalized due to COVID-19 infection.

Criteria for inclusion in the study were: (1) diagnosis of neovascular AMD, (2) History of receiving at least three

intravitreal injections before COVID-19 lockdown, (3) treatment interruption for at least six months due to the COVID-19 lockdown, (4) Availability of complete ophthalmological records for a minimum follow-up period of one year after the COVID-19 lockdown.

Exclusion criteria for the study were: (1) Presence of any other ocular or retinal disease that may affect visual acuity, (2) loading dose not completed before COVID-19 lockdown.

Patients were grouped according to the duration of follow-up before the COVID-19 pandemic. Group 1 included patients with less than 6 months of follow-up before the pandemic, while group 2 included patients with longer than 6 months of follow-up before the pandemic.

Anti-VEGF agents (bevacizumab, ranibizumab, aflibercept) were injected into the vitreous space through the pars plana. A standard protocol was followed for intravitreal injection.

STATISTICAL ANALYSIS

Statistical analysis was conducted with SPSS 28.0 (IBM Software, Chicago, IL). The normality of numerical variables was assessed using the Shapiro-Wilk test. Numerical variables are presented as the mean (standard deviation), while categorical variables are presented as the count (percent). The differences between the groups were evaluated using Mann-Whitney U test. Categorical variables were compared using the Chi-square test $P < 0.05$ was considered statistically significant.

RESULTS

A total of 66 eyes of 59 patients with AMD were included in the study ($n=40$ in group 1, $n=26$ in group 2). No significant differences were found between the groups regarding age, gender, BCVA and CMT (Table 1). Patients in Group 1 had a mean±SD age of 73.2 ± 5.5 years and 18 (45%) were female and those in Group 2 had a mean±SD age of 70.4 ± 6.3 years and 9 (35%) were female.

The mean follow-up period of patients before COVID-19 lockdown was 5.9 ± 0.7 months in Group 1 and 15.3 ± 4 months in Group 2 ($p<0.001$, Table 1). The mean number of injections before COVID-19 lockdown was 3.8 ± 0.5 in Group 1 and 9.0 ± 1.2 in Group 2 ($p<0.001$, Table 1).

In both groups, patients were treated with a PRN regimen following bevacizumab loading doses. Aflibercept injec-

tions were administered in 77.5% of patients in Group 1 and 69.2% of patients in Group 2, while ranibizumab injections were given in 22.5% and 30.8% of patients, respectively.

76.9% of patients in Group 2 did not require any intravitreal injection during the last 3 months prior to the COVID-19 pandemic. The mean duration of treatment interruption related to the COVID-19 pandemic was 12.5±2.9 months in Group 1 and 11.9±2.4 months in Group 2. There was no difference between the groups in terms of duration of treatment interruption (p=0.97).

The mean BCVA change between the last visit before the COVID-19 pandemic and the first visit after the COVID-19 pandemic was logMAR 0.7±0.32 in Group 1 and logMAR 0.2±0.05 in Group 2. There was a significant difference

between the groups in terms of BCVA reduction (p<0.001, Table 2).

The mean CMT change between the last visit before the COVID-19 pandemic and the first visit after the COVID-19 pandemic was 174±94 µm in Group 1 and 68±36 µm in

Group 2 (Figure 1, 2). There was a significant difference between groups in terms of CMT increase (p<0.001, Table 2).

At the first visit after the COVID-19 pandemic, SRF was observed in 34 (85%) cases, IRF in 24 (60%) cases, SRHM in 10 (25%) cases and macular hemorrhage in 8 (20%) cases in

Group 1, whereas in Group 2, SRF was detected in 12 (46%) cases, IRF in 9 (34%) cases, SRHM in 2 (7.6%) cases and macular hemorrhage in 1 (3.8%) case.

Table 1. Baseline Characteristics of the Study Patients

	Group 1 Mean (SD)	Group 2 Mean (SD)	P Value
Age (years)	73.2 (5.5)	70.4 (6.3)	0.23*
Female sex (%)	18 (45.0)	9 (34.6)	0.08*
BCVA (logMAR)	0.57 (0.41)	0.62 (0.35)	0.62**
CMT (µm)	394.4 (97.1)	371.4 (98.6)	0.35**
Follow-up (months)	5.95 (0.7)	15.3 (0.4)	<0.001*
Number of Injections	3.8 (0.5)	9.0 (1.2)	<0.001*

BCVA, best corrected visual acuity; CMT, central macular thickness; SD, standard deviation. * Mann-Whitney U test **independent two sample t test

Table 2. Clinical Data of the Study Patients

	Group 1 Mean (SD)	Group 2 Mean (SD)	P Value
BCVA (logMAR)			
Last pre-pandemic visit	0.30 (0.23)	0.31 (0.23)	0.877*
First post-pandemic visit	1.07 (0.40)	0.53 (0.22)	<0.001*
BCVA change	0.77 (0.32)	0.22 (0.05)	<0.001**
CMT (µm)			
Last pre-pandemic visit	250.7 (38.3)	425.1 (95.7)	0.049*
First post-pandemic visit	234.6 (26.9)	292.0 (28.0)	<0.001*
CMT change	174 (94)	39 (16)	<0.001**

BCVA, best corrected visual acuity; CMT, central macular thickness; SD, standard deviation. * Mann-Whitney U test **independent two sample t test

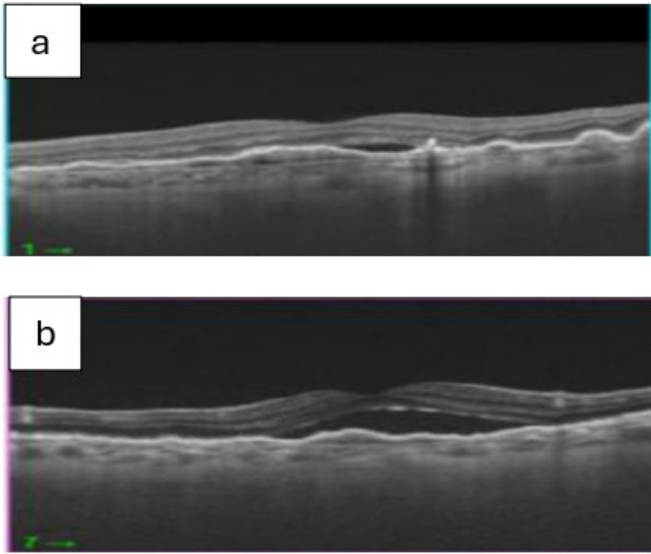


Figure 1. OCT image of a case in Group 1. a) At the last visit before the COVID-19 pandemic b) At the first visit before the COVID-19 pandemic

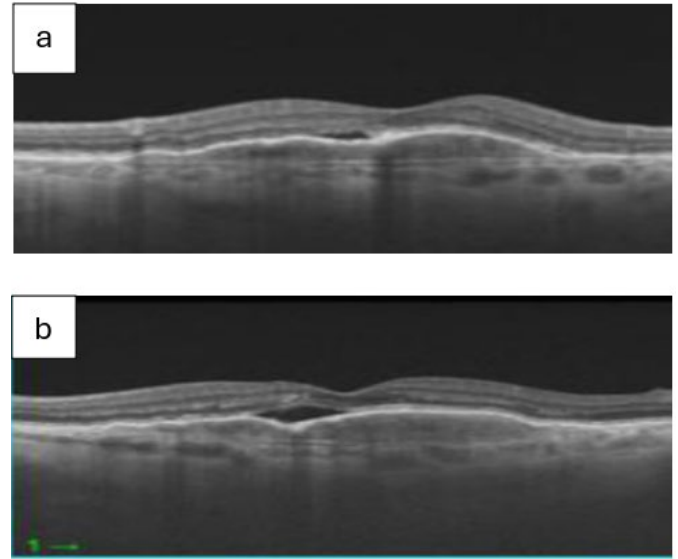


Figure 2. OCT image of a case in Group 2. a) At the last visit before the COVID-19 pandemic b) At the first visit before the COVID-19 pandemic

DISCUSSION

In our study, patients who had received more intensive treatment prior to the COVID-19 pandemic and had achieved a more stable (defined as a lower need for intravitreal injections and less variability in visual acuity and OCT findings) condition were found to be less affected by treatment discontinuation.

Neovascular AMD is the most common of advanced AMD.¹³ In neovascular AMD, therapeutic strategies are primarily targeted at choroidal neovascularization, which is defined by new vessels that arise from the choriocapillaris, passing through the Bruch's membrane and into sub-retinal pigment epithelium or subretinal space. The clinical manifestations of neovascular AMD include intra or sub-retinal fluid accumulation, macular hemorrhage, and pigment epithelial detachment. Since VEGF plays a pivotal role in the development of neovascularization, anti-VEGF agents are utilized as the mainstay of treatment in neovascular AMD.¹⁴ Intravitreal anti-VEGF injections may be administered using either a reactive or proactive approach, aiming to achieve macular drying and improvement in visual acuity.¹⁵

Thus, patients with neovascular AMD can maintain visual function over time. In patients with neovascular AMD,

early intensive intravitreal injection therapy exerts a favorable effect on visual function. In a study conducted in UK, it was found that greater visual improvements in patients who underwent a loading phase at the start of treatment (the first three doses received within 90 days) versus those who did not.¹⁶ In another study on this subject, it was also reported that neovascular AMD patients who received a higher number of anti-VEGF injections during the first year of treatment achieved better long-term visual outcomes.¹⁷ A meta-analysis reported that disease stability was achieved in nearly two-thirds of eyes within the first year of therapy.¹⁸ These findings suggest that early stabilization of the disease appears to be crucial for achieving favorable long-term visual and anatomical outcomes. In addition, neovascular AMD is a chronic, progressive disorder that necessitates long-term and continuous treatment to maintain visual and anatomical stability. If treatment interruption occurs, as experienced during the COVID-19 pandemic, it is likely to adversely affect both visual and anatomical outcomes. Several studies in the literature have investigated this issue.¹⁹⁻²² These studies demonstrate that treatment interruption due to the COVID-19 pandemic had a negative impact on visual and anatomical outcomes in patients with AMD. In the literature, there are no studies evaluating the impact of

treatment interruption according to disease stability in the pre-pandemic period.

In the present study, patients were divided into two groups. Group 1 included those who completed the loading dose, whereas group 2 consisted of more stable patients who received an average of nine injections. Due to COVID-19 pandemic, both treatment groups experienced similar intervals of treatment interruption. However, the decrease in BCVA between the last pre-pandemic visit and the first post-pandemic visit was greater in Group 1, which had lower disease stability. Regarding anatomical outcomes, a significantly greater increase in CMT was observed in Group 1 than in Group 2. Sekeroglu et al. reported that unintended lapses during COVID-19 pandemic resulted with poor functional and structural results for AMD patients, especially for those at the beginning of treatment.²³

In the present study, macular hemorrhage was observed in 20% of the cases in Group 1 and 3.8% of the cases in Group 2 at the first visit after the COVID-19 pandemic. Macular hemorrhage, which is characterized by sudden vision loss, was more frequently observed in the group that was at the initiation phase of anti-VEGF injection therapy. It is possible that patients received anticoagulant therapy during the COVID-19 pandemic, potentially contributing to an increased risk of macular hemorrhage. However, the higher incidence of macular hemorrhage in Group 1 compared to Group 2 suggests a possible association with a more unstable clinical course of the disease. Romano et al reported a high rate of large sub-macular hemorrhages during the early stages of COVID-19 pandemic.²⁴ In another prospective study, subretinal hemorrhage was detected in 14.3% of neovascular AMD patients in the early period following the COVID-19 pandemic.²³

Neovascular AMD is a chronic, progressive condition that necessitates regular follow-up visits and continuous treatment to maintain visual stability. Unintended interruptions in the treatment process may result in adverse structural and functional outcomes. Humanity had experienced an unprecedented situation such as the COVID-19 pandemic, and similar circumstances may occur again in the future. To be better prepared for such circumstances and to ensure the long-term preservation of visual function in neovascular AMD patients, the frequency of follow-up visits should be adjusted based on the stability of the disease.

STUDY LIMITATIONS

The limitations of this study were its retrospective design, relatively small sample size and lack of a control group.

CONCLUSION

In our study, the discontinuation of treatment due to the COVID-19 pandemic had a lesser impact on visual and anatomical outcomes in AMD patients who had received an average of nine injections and were more stable before the pandemic. Larger sample sizes of randomized clinical trials are needed for the assessment.

REFERENCES

- 1- Kawasaki R, Yasuda M, Song SJ, et al. The prevalence of age-related macular degeneration in Asian: a systematic review and meta-analysis. *Ophthalmology* 2010;117:921-7.
- 2- Colijn JM, Buitendijk GHS, Prokofyeva E, et al. Prevalence of age-related macular degeneration in Europe: the past and the future. *Ophthalmology* 2017;124:1753-63.
- 3- Fenwick EK, Cheung CMG, Ong PG, et al. The impact of typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy on vision-related quality of life in Asian patients. *Br J Ophthalmol* 2017;101:591-6.
- 4- Mathew R, Pefkianaki M, Kopsachilis N, et al. Correlation of fundus fluorescein angiography and spectral-domain optical coherence tomography in identification of membrane subtypes in neovascular age-related macular degeneration. *Ophthalmologica* 2014;231:153-9.
- 5- Sadda SR, Liakopoulos S, Keane PA, et al. Relationship between angiographic and optical coherence tomographic (OCT) parameters for quantifying choroidal neovascular lesions. *Graefes Arch Clin Exp Ophthalmol* 2010;248:175-84.
- 6- Martin DF, Maguire MG, Ying GS, et al. CATT Research Group. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N Engl J Med*,2011;364:1897-908.
- 7- Irgat SD, Divarçı SF, Doğan M, et al. Overview of anti-VEGF treatment regimens and new agents in age-related macular degeneration. *Ret-Vit* 2021 ;30 : 212-222.
- 8- Bressler NM, Chang TS, Suner U, et al. Vision-related function after ranibizumab treatment by better – or worse-seeing eye: clinical trial results from MARINA and ANCHOR. *Ophthalmology* 2010 ;117:747-56.
- 9- Silva F, Axer-Siegel R, Eldem, et al. The SECURE study: long-term safety of ranibizumab 0.5 mg in neovascular age-related macular degeneration. *Ophthalmology* 2013;120:130-9.

- 10- Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, et al. Intravitreal aflibercept injection for neovascular age related macular degeneration: ninety-six-week results of the VIEW studies. *Ophthalmology* 2014;121:193-201.
- 11- Silva R, Berta A, Larsen M, et al. Treat-and-Extend versus monthly regimen in neovascular age-related macular degeneration. *Ophthalmology* 2018;125:57-65.
- 12- Holtz FG, Tadayoni R, Beatty S, et al. Multi-country real-life experience of anti-vascular endothelial growth factor therapy for wet age-related macular degeneration. *Br J Ophthalmol* 2015;99:220-6.
- 13- R. Klein, B.E.K. Klein, S. C. Tomany, S.M. Meuer, G.H. Huang. Ten-year incidence and progression of age-related maculopathy: the Beaver Dam eye study. *Ophthalmology* 2002;109 (10):1767-1779.
- 14- Ammar MJ, Hsu J, Chiang A, Ho AC, Regillo CD. Age-related macular degeneration therapy: a review. *Curr Opin Ophthalmol.* 2020 ; 31 : 215-21.
- 15- Wong TY, Liew G, Mitchell P. Clinical update: New treatments for age-related macular degeneration. *Lancet* 2007 ;370:204-206.
- 16- Hykin P, Chakravarthy, Lotery A et al. A retrospective study of the real-life utilization and effectiveness of ranibizumab therapy for neovascular age-related macular degeneration in the UK. *Clin Ophthalmol.* 2016;19:87-96.
- 17- Finger RP, Puth MT, Schmid M, et al. Lifetime Outcomes of Anti-VEGF Treatment for Neovascular Age-Related Macular Degeneration. *JAMA Ophthalmol* 2020 Dec 1;138(12):1234-1240.
- 18- Garweg JG, Gerhardt C. Disease stability and extended dosing under anti-VEGF treatment of exudative age-related macular degeneration (AMD)- a meta-analysis. *Graefes Arch Clin Exp Ophthalmol.* 2021 Aug;259 (8):2181-2192.
- 19- Rego-Lorca D, Valverde-Megias A, Fernandez-Vigo JI, et al. Long-Term Consequences of COVID-19 Lockdown in Neovascular AMD Patients in Spain: Structural and Functional Outcomes after 1 Year of Standard Follow-Up and Treatment. *J Clin Med.* 2022 Aug 28;11(17):5063.
- 20- Tsiropoulos GN, Vallee R, Gallo CD, et al. The importance of monitoring wet age-related macular degeneration patients during Coronavirus disease 19 pandemic: A retrospective study of assessment of functional and structural outcomes, *J Fr Ophthalmol.* 2022 Oct ;45(8):852-59.
- 21- Yeter DY, Dursun D, Bozali E, et al. Effects of the COVID-19 pandemic on neovascular age-related macular degeneration and response to delayed Anti-VEGF treatment. *J Fr Ophthalmol.* 2021 Mar;44(3):299-306.
- 22- Nanji K, Kennedy K, Fung M, et al. Impact of COVID-19 on a real-world treat and extend regimen with aflibercept for neovascular age-related macular degeneration. *CJO* 2024 ; 05. 027 : 92-99.
- 23- Sekeroglu MA, Hekimsoy HK, Ceran TH, et al. Treatment of neovascular age related macular degeneration during COVID-19 pandemic: The short term consequences of unintended lapses. *European Journal of Ophthalmology* 2022, Vol. 32(2) 1064-1072.
- 24- Romano F, Monteduro D, Airaldi M, et al. Increased number of submacular hemorrhages as a consequence of coronavirus disease 2019 lockdown. *Ophthalmol Retina* 2020;4(12):1209-1210.