

Assessment of Vision-Related Quality of Life in Patients with Neovascular Age-Related Macular Degeneration During COVID-19 Pandemic: Retrospective Study

Neovasküler Yaşa Bağlı Makula Dejeneransı Olan Hastalarda COVID-19 Pandemisi Sırasında Görme İlişkili Yaşam Kalitesinin Değerlendirilmesi: Retrospektif Çalışma

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ABSTRACT Objective: To evaluate vision-related quality of life (QoL) using National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) in neovascular age-related macular degeneration (nAMD) patients during coronavirus disease-2019 (COVID-19) pandemic. **Material and Methods:** nAMD patients whose intravitreal injection had to be postponed due to restrictions of COVID-19 lockdown between April and June 2020, NEI-VFQ-25 was administered last visit pre-COVID-19 and first visit during COVID-19. NEI-VFQ-25 scores, best-corrected visual acuity (BCVA) and central macular thickness (CMT) were compared between visits. **Results:** Fifty six patients with nAMD were participated in the study. The composite score of NEI-VFQ-25 was statistically significantly lower at first visit during COVID-19 when compared with at last pre-COVID-19 (95% confidence interval, 2.33-4.24; p=0.000). Decrease in NEI-VFQ-25 composite score was moderately associated with an impairment in BCVA at first visit during COVID-19 and duration of treatment delay after adjusting for age, gender, BCVA at last visit pre COVID-19 and CMT (β coefficient=0.42 and 0.41 and p=0.016 and 0.015). **Conclusion:** Negative impacts of delayed treatment during COVID-19 pandemic were observed by decrease NEI-VFQ-25 composite scores in patients with nAMD observed on psychological well-being and ability of performing daily life activities that depend on visual function.

ÖZET Amaç: Koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] pandemisi sırasında, neovasküler tip yaşa bağlı makula dejeneransı (nYBMD) olan hastalarda Ulusal Göz Hastalıkları Enstitüsü Görme İşlevi Ölçeği-25 [National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25)] kullanarak görme ilişkili yaşam kalitesini değerlendirmektir. **Gereç ve Yöntemler:** Nisan ve Haziran 2020 arasında COVID-19 kısıtlamaları nedeniyle intravitreal enjeksiyonu ertelenen nYBMD hastalarına NEI-VFQ-25 ölçeği COVID-19 öncesi son muayenede ve COVID-19 sırasındaki ilk muayenede uygulandı. Muayeneler arasındaki NEI-VFQ-25 skorları, en iyi düzeltilmiş görme keskinliği (EİDGK) ve santral makula kalınlığı (SMK) karşılaştırıldı. **Bulgular:** Çalışmaya 56 nYBMD'li hasta katıldı. NEI-VFQ-25 bileşik skoru COVID-19 öncesi son muayene ile karşılaştırıldığında COVID-19 sırasındaki ilk muayenede istatistiksel olarak anlamlı daha düşüktü (%95 güven aralığı, 2,33-4,24; p=0,000). Yaş, cinsiyet, COVID-19 öncesi son muayene EİDGK ve SMK için düzeltme yapıldıktan sonra NEI-VFQ-25 bileşik skorundaki azalma COVID-19 sırasındaki ilk muayenede EİDGK'deki azalma ve tedavi gecikme süresi ile orta derecede ilişkiliydi (β katsayısı=0,42 ve 0,41; p=0,016 ve p=0,015). **Sonuç:** nYBMD'li hastalarda bileşik NEI-VFQ-25 bileşik skorundaki azalmayla birlikte psikolojik iyi olma ve görme fonksiyonuna bağlı günlük yaşam aktivitelerini gerçekleştirme yeteneği üzerinde COVID-19 pandemisi sürecindeki gecikmiş tedavinin olumsuz etkileri gözlemlenmiştir.

Keywords: Coronavirus pandemic;
neovascular age-related macular degeneration;
vision-related quality of life

Anahtar Kelimeler: Koronavirüs pandemisi;
neovasküler yaşa bağlı makula dejeneransı;
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After a new charge of the coronavirus family causing severe pneumonia was identified in December 2019, the World Health Organization denominated the disease, coronavirus disease-2019 (COVID-19) and declared COVID-19 as a pandemic on March 11, 2020 with a Public Health Emergency of International Concern.^{1,2}

Age-related macular degeneration (AMD) is one of the leading cause of irreversible blindness in adults over 50 years of age.^{3,4} It mainly affects the central retina and central vision which is essential for performing daily routine activities. Central vision loss in neovascular AMD (nAMD) patients leads to dependency and disability, functional and psychological impairment with considerable decrease in quality of life (QoL).^{5,6}

Questionnaires have been established to determine the psychosocial status of patients and to examine related potential problems. Studies demonstrated that vision-related QoL scores improved with anti-vascular endothelial growth factor (anti-VEGF) therapy and diminished when visual acuity decreased.⁷⁻⁹ Vision-related QoL can be identified using the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25). The reliability and validity of the questionnaire has been defined among patients with AMD.¹⁰ Over 90% of nAMD patients treated with intravitreal injections of anti-VEGF therapy results in vision improvement or stabilization, even though nAMD remains leading cause of blindness due to disease process.¹¹

Patients with nAMD require intravitreal anti-VEGF in a timely manner. Patients with nAMD are at high risk of blindness during disease process and unfavourable impact of COVID-19 outbreak and lockdown on reaching medical needs had affected visual status and treatment regimens. After first COVID-19 positive patient was seen in Türkiye on March 2020, health services had been interrupted temporarily and intravitreal injections in our retina clinic had to be postponed for a meanwhile. In a routine retina visit daily living activities and well-being are not usually assessed and in this aspect, diminished vision related QoL during COVID-19 pandemic was predicted and this study was planned. The aim of this study is in order to determine the impact of delayed

treatment on vision-related QoL among patients with nAMD required intravitreal injection by NEI-VFQ-25, visual acuity and macular thickness changes at last visit pre COVID-19 and at first visit during COVID-19 pandemic.

MATERIAL AND METHODS

Yıldırım Beyazıt University Medical School Committee of Clinic Trials (Ankara, Türkiye) confirmed this study in 15th December 2021 with number of E1-21-2161. Written informed consent was acquired from the subjects in accordance with the Declaration of Helsinki. Between April 2020 and June 2020, 56 patients with nAMD, whose medical treatment had to be postponed because of COVID-19 lockdown were prospectively recruited to this study in retina department of a tertiary referral hospital

NEI-VFQ-25

NEI-VFQ-25 examines vision-related QoL, well-being and social functioning induced by visual deteriorations or restrictions. The questionnaire consists 25 items including 12 subscales: “general vision”, “near and distance vision activities”, “ocular pain”, “vision-related social function”, “vision-related role function”, “vision-related mental health”, “vision-related dependency”, “driving difficulties”, “color vision”, and “peripheral vision”.¹² Toprak et al. has validated the Turkish translation of VFQ-25 and Cronbach’s α for the VFQ-25 total score was 0.97.¹³

This study utilized results of NEI-VFQ-25 scores last visit pre COVID-19 pandemic from medical records and NEI-VFQ-25 taken at intravitreal injection date after lockdown. The inclusion criteria consisted of patients diagnosed with nAMD and arranged to inject intravitreally whose treatment plan was interrupted. Fellow eye of patients had 20/40 or better visual acuity. Patients with any reason of treatment delay apart from lockdown were excluded from the study.

Medical records including best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, fundus examination with a noncontact fundus lens, spectral domain optical coherence tomography (OCT) (SD-OCT; Spectralis HRA-OCT; Heidelberg Engineer-

ing, Heidelberg, Germany) images and results of NEI-VFQ-25 scores were evaluated. Patients with nAMD requiring intravitreal treatment apart from loading dose were determined and completed ophthalmic examination including OCT images and NEI-VFQ-25 at first visit during COVID-19. Central macular thickness (CMT) was calculated in central 1 mm area by OCT images at last visit pre COVID-19 and at first visit during COVID-19.

ANALYSIS

An algorithm ranging from 0 to 100 was used for the calculation of the VFQ-25 scores; higher values demonstrates better visual function in relation to the individual's well-being and the higher QoL. In this study, manual methodology was utilized to create one total score by means of 12 subscale scores as previously described apart from driving difficulties subscale due to restrictions on movement for persons greater than 65 years old in Türkiye during COVID-19 lockdown.¹²

BCVA at last visit pre COVID-19 and at first visit during COVID-19 were determined using Snellen chart and converted to the logarithm of the minimal angle of resolution (logMAR) for statistical analysis. Gain or loss in snellen line was identified by the difference last visit pre COVID-19 and first visit during COVID-19 as for CMT, total and subscale score of NEI-VFQ-25. A paired sample t test was used for comparing BCVA, CMT, composite and subscale of NEI-VFQ-25. Changes in visual acuity, CMT, composite score and subscales of NEI-VFQ-25 were used for univariate correlation analysis. To determine the relation between loss in Snellen line with change in composite or subscale score of NEI-VFQ-25 and macular thickness, Spearman's correlation analysis was used. In this study, a p value < 0.05 was considered statistically significant. All analysis and calculations were performed via IBM SPSS Statistics 22.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

RESULTS

Of 56 patients participated in the study, 26 (46.4%) were female and mean of age was 66.8±5.1 years.

The mean follow-up duration was 31.89±15.01 months and the mean duration of postponement was 12.2±1.6 weeks. Sociodemographic features of the study group was also shown in Table 1.

The mean BVCA of treated eye was 0.69±0.46 logMAR at last visit pre COVID-19 and 0.84±0.47 logMAR at first visit during COVID-19 and worse at first visit during COVID-19 than at last visit pre COVID-19 (p=0.004); mean BCVA of fellow eye was 0.23±0.1 logMAR and no change was observed between visits. The mean CMT of treated eye and fellow eye were significantly increased at first visit during COVID-19 than at last visit pre COVID-19 (p=0.007 and p=0.002).

The reliability rate of scales were high that Cronbach's α coefficients of composite score at last visit pre COVID 19 and first visit during COVID-19 on the NEI-VFQ-25 were 0.826 and 0.841. The NEI-VFQ-25 subscale and composite scores were compared between last visit pre COVID-19 and first visit during COVID-19 (Table 2). There were statistically significant reduction in the subscale of general health, general visual health, ocular pain, near vision, distance vision, peripheral vision and vision-related social functioning, mental health and dependency and also the composite score of NEI-VFQ-25 at first visit during COVID-19 compared to at last visit pre COVID-19 (p<0.05, in each comparison) (Table 2).

TABLE 1: Sociodemographic characteristics.

All patients (n=56)	
Age (years)	66.8±5.1
Gender (female/male)	26/30
Duration of follow-up (months)	31.8±15
Marital status (n, %)	
Married	50 (89.3%)
Divorced	6 (10.7%)
Education	
Illiterate	4 (7.1%)
Elementary school	18 (32.1%)
High school	34 (60.7%)
Duration of postponement (weeks)	12.2±1.6
Number of persons living with (n, %)	
≤2	49 (87.5%)
≥3	7 (12.5%)

TABLE 2: Comparison of mean BCVA, central macular thickness, subscale and composite score of NEI-VFQ-25 between last visit pre COVID-19 and first visit during COVID-19.

	Last visit pre COVID-19	First visit during COVID-19	p value
BCVA (logMAR)			
Treated eye	0.69±0.46	0.84±0.47	0.004
Fellow eye	0.23±0.1	0.21±0.16	0.980
Central macular thickness (µm)			
Treated eye	480.2±238.7	535.5±254.2	0.007
Fellow eye	278.7±36.9	283.9±32.5	0.002
NEI-VFQ-25			
General health	45.9±18.9	40.1±15.5	0.002
General visual health	54.2±14.1	50.3±13.7	0.002
Ocular pain	49.5±12.8	46.6±13.1	<0.001
Near vision	61.3±14.5	55.±15.8	<0.001
Distance vision	52.8±14.8	50±15.4	0.009
Vision-related			
Social functioning	56.6±16.1	52.9±16.5	<0.001
Mental health	46±9.1	42.9±9.9	<0.001
Role difficulties	39.2±12	37±11.4	0.077
Dependency	43.4±12.4	40.7±12.8	0.001
Color vision	62.±17.1	60.7±15.7	0.261
Peripheral vision	51.7±20.7	47.3±23.1	0.001
Composite score	51.4±9	48±9.4	<0.001

BCVA: Best-corrected visual acuity; NEI-VFQ-25: National Eye Institute Visual Function Questionnaire-25; logMAR: Logarithm of the minimal angle of resolution.

Decrease in NEI-VFQ-25 composite score was moderately associated with an impairment in BCVA at first visit during COVID-19 and duration of treatment delay after adjusting for age, gender, BCVA at last visit pre COVID-19 and CMT (β coefficient=0.42 and 0.41 and $p=0.016$ and 0.015). Reduction in near activities subscale score was moderately correlated with worsening in visual acuity during treatment delay (β coefficient=0.339 $p=0.011$). There was no association between decrease in NEI-VFQ-25 composite score and increase in CMT (β coefficient=-0.128, $p=0.346$), after adjusting for all baseline factors.

DISCUSSION

Patients with retinal diseases required intravitreal injection had to face delayed treatment and visual impairment during COVID-19 pandemic. In this study negative impacts of delayed treatment during COVID-19 pandemic were observed by increase of

NEI-VFQ-25 composite scores in patients with nAMD observed on psychological well-being and ability of performing daily life activities that depend on visual function.

Government restrictions on movement for elderly persons older than 65 years old in our country to limit any potential exposure to coronavirus and patients with retinal diseases who need to visit retina clinics were vulnerable populations due to their age or comorbid diseases had resulted in hitch of intravitreal treatments in retina clinics. While considering the course of retinal diseases and delayed treatment due to COVID-19 pandemic may induce reduction in vision, this study demonstrated visual impairment, macular thickening and diminution in all scores of NEI-VFQ-25 subscales apart from role difficulties and color vision.

Change in visual acuity is often used to measure the clinical effectiveness of intravitreal injection treatment in retinal diseases. However, visual acuity

and clinical measurements for assessing effectiveness of treatment are inadequate to determine the changes in psychological well-being and the ability to perform daily living activities that depend on visual function.¹⁴ The NEI-VFQ investigates psychological aspects of visual impairment in nAMD patients and has been shown to be responsive to change in vision over time.^{15,16} In this current study, we observed a decrease of NEI-VFQ-25 composite score was moderately associated with worse BCVA at first visit during COVID-19 compared to before corroborating findings from previous studies.¹⁴⁻¹⁶ To the best of our knowledge, there is no study that have determined whether COVID-19 pandemic has impact on vision-related QoL in patients with nAMD.

In this study, we found that CMT was significantly increased in patients with nAMD required intravitreal injection at first visit during COVID-19 when compared with at last visit pre COVID-19. Although BCVA and CMT were found to be closely related in nAMD, there was no significant correlation between NEI-VFQ-25 composite score and increase in CMT in our study.¹⁷ The increased macular thickness observed over the study period did not have a sufficient impact on the functional aspects of daily living. However, decrease in near activities subscales was moderately correlated with worsening in visual acuity during delayed treatment. These results reflect the impact of pandemic on indoor activities rather than outdoor activities and was verified by restrictions on movement for elderly patients. The relationship between long term effects of COVID-19 pandemic and vision related QoL for patients with nAMD warrants further investigation. Nevertheless when considering the exposure of COVID-19 and vulnerability of elderly patients for COVID-19, patients with nAMD had to postpone their mandatory medical treatment. This study demonstrated that NEI-VFQ-25 would be an aid instrument for assessing impact of COVID-19 pandemic on psychological well-being and the ability to perform daily living activities that depend on visual function, in addition to visual impairment and increase in macular thickness among patients with nAMD need medical treatment. The results of our study should take into account for scheduling time of intravitreal injections during COVID-19 pandemic.

Awareness of vision-related QoL for nAMD patients among clinicians was low. Thus, management of treatment on patients with nAMD need to be based on factors concerned to vision-related quality of health and life especially during COVID-19 pandemic. As demonstrated in our study, delayed intravitreal treatments resulted in decreasing vision with diminishing composite score of NEI-VFQ-25.

Although visual acuity in worst eye was statistically decreased and no change was observed in best eye in our study, scores of vision related QoL was decreased when compared scores last visit before pandemic and first visit during COVID-19. This could be explained with the phenomena of visual inhibition that visual impairment of worst eye affects vision and also health related QoL.^{18,19}

LIMITATIONS

The patients participated in this study were diagnosed with nAMD and small sample size were limitations of our study that restricted the generalization of our findings to whole patients with retinal diseases. Government restrictions on movement for patients greater than 65 years old was not covered all cities in our country, therefore accessibility of medical need was not interrupted in all regions of our country or worldwide. Restrictions for COVID-19 were varied according to country specific factors such as population, local restrictions, number of infections and deaths and duration of lockdown were other limitations of the study. The COVID-19 pandemic is still going on, these results also need to be confirmed and investigated in future studies with larger population.

CONCLUSION

In conclusion, the unprecedented COVID-19 pandemic was associated with visual impairment and reduced vision related QoL among patients with nAMD whose medical treatment had to be postponed during COVID-19 pandemic. These results also recommend that protecting visual acuity in the worst eye of patients with nAMD may contribute to vision-related QoL. Our study managed to capture negative impacts of delayed treatment on both vision, CMT and vision-related QoL during COVID-19 pandemic. Our study

has also suggested to consider vision related QoL besides a routine retina examination.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members

of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: İnci Elif Erbahçeci Timur; **Design:** İnci Elif Erbahçeci Timur; **Control/Supervision:** İnci Elif Erbahçeci Timur; Nagihan Uğurlu; **Data Collection and/or Processing:** Mehmet İçöz, Şule Gökçek İçöz; **Analysis and/or Interpretation:** İnci Elif Erbahçeci Timur; Sema Yüzbaşıoğlu, Esra Dağ Şeker; **Literature Review:** Esra Dağ Şeker; **Writing the Article:** İnci Elif Erbahçeci Timur; Esra Dağ Şeker; **Critical Review:** Esra Dağ Şeker; **References and Fundings:** İnci Elif Erbahçeci Timur; **Materials:** İnci Elif Erbahçeci Timur.

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