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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

COVID-19 HASTALARINDA RETİNA KALINLIĞININ OPTİK KOHERENS TOMOGRAFİ ANALİZİ

OPTICAL COHERENCE TOMOGRAPHY ANALYSIS OF RETINAL THICKNESS IN COVID-19 PATIENTS

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ÖZET

AMAÇ: Bu çalışmanın amacı COVID-19 enfeksiyonu olan hastalarda retinal değişikliklerin Optik Koherens Tomografi analizini yapmak ve bunları sağlıklı kontrollerle karşılaştırmaktır.

GEREÇ VE YÖNTEM: Bu amaçla, 1 Ekim 2020 ile 1 Mayıs 2021 tarihleri arasında kliniğimize başvuran, 18 ile 68 yaş arasında, COVID-19 pozitif 42 hasta (grup 1) ve 44 sağlıklı yetişkin (grup 2) çalışmaya alındı. Santral foveal kalınlık, koroidal kalınlık (subfoveal) ve peripapiller retina sinir lifi kalınlığı ölçülmüştür. Ölçümler merkezi foveada ve merkezi foveadan 1500 µm nazal ve 1500 µm temporal noktalarda gerçekleştirilmiştir.

BULGULAR: Gruplarda yaş ve cinsiyet dağılımı benzerdir (sırasıyla p=0,610 ve p=0,992). Ancak, santral foveal kalınlık (p<0,001), subfoveal koroid kalınlığı (p=0,001) ve peripapiller retina sinir lifi tabakası kalınlığı (p<0,001) iki grup arasında anlamlı olarak farklıydı.

SONUÇ: Sonuç olarak, polymerase chain reaction pozitif COVID-19 hastalarında santral fovea, foveal altı koroid ve peripapiller retina sinir lifi tabakası kalınlığı sağlıklı kontrollere kıyasla daha yüksektir. COVID-19'un neden olduğu sistemik ve lokal değişikliklerin patogenezini anlamak için, çok sayıda hasta alt grubu ile çok merkezli ve uzun süreli çalışmalar gereklidir.

ANAHTAR KELİMELER: COVID-19, Maküla, Optik Koherens Tomografi, Retina.

ABSTRACT

OBJECTIVE: The aim of this study was to perform Optical Coherence Tomography analysis of retinal changes in patients with COVID-19 infection and compare them with healthy controls.

MATERIAL AND METHODS: For this purpose, 42 COVID-19 positive patients (group 1) and 44 healthy adults (group 2), aged between 18 and 68 years, who were admitted to our clinic between October 1, 2020 and May 1, 2021, were included in the study. Central foveal thickness, choroidal thickness (subfoveal) and peripapillary retinal nerve fiber thickness were measured. Measurements were performed at the central fovea and at 1500 µm nasal and 1500 µm temporal points from the central fovea.

RESULTS: Age and gender distribution were similar in the groups (p=0.610 and p=0.992, respectively). However, central foveal thickness (p<0.001), subfoveal choroidal thickness (p=0.001) and peripapillary retinal nerve fiber layer thickness (p<0.001) were significantly different between the two groups.

CONCLUSIONS: In conclusion, central fovea, subfoveal choroidal and peripapillary retinal nerve fiber layer thickness were higher in polymerase chain reaction positive COVID-19 patients compared to healthy controls. To understand the pathogenesis of systemic and local changes caused by COVID-19, multicenter and long-term studies with a large number of patient subgroups are necessary.

KEYWORDS: COVID-19, Macula, Optical Coherence Tomography , Retina.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a current disease with high mortality rates caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), most commonly affecting the respiratory tract and lungs. The main system affected by the disease is the respiratory system, it may also affect the circulatory system and gastrointestinal system. It may also involve ocular and cutaneous tissues (1).

Scientific publications on ocular involvement have increased as the number of people affected and physician experience has increased. This involvement has a wide range in clinical practice. The early publications focused on the anterior segment involvement (2 - 4) and transmission mechanism of the disease (5), but as time passed, the focus shifted to prevention methods (6).

The most recent publications have focused on the posterior segment involvement of the disease and have tried to observe retinal and choroidal tissue involvement. Previous studies on human eyes have observed that angiotensin-converting enzyme (ACE) 2 receptors are widely distributed in ocular tissues (cornea, retina and retinal pigment epithelium). When the pathogenesis of the disease was investigated, found that the virus exerts its effects through this receptor (7 - 8). Although it has been suggested that retinal involvement may be caused by the direct cytopathic effect of the pathogen, virus-mediated immunity and systemic response may also be the main mechanism (9 - 11).

The purpose of this manuscript was to perform Optical Coherence Tomography (OCT) analysis of retinal changes in patients with COVID-19 infection and to compare them with controls.

MATERIAL AND METHODS

In this cross-sectional study, 42 patients (group 1) between the ages of 18-68 years who were admitted to the Department of Ophthalmology, Mersin State Hospital between October 1, 2020 and May 1, 2021, patients with COVID-19 diagnosed by polymerase chain reaction (PCR) test within the last 3 months , and recovered with follow-up and/or medical treatment were included. Forty-four healthy controls (group 2) who had no known disease and whose demographic data were similar to the patient group were comparatively analyzed. Central foveal thickness (CFT), choroidal thickness (subfoveal, SCT) and peripapillary retinal nerve fiber thickness were measured by Spectral-Domain Optical Coherence Tomography (SD-OCT, Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany). Choroidal thickness was measured using images acquired in enhanced depth imaging (EDI) mode.

The vertical distance between the outermost border of the retinal pigment epithelium and the inner border of the sclera, which appears as a high reflection line, was measured at the central fovea and at points 1500 µm nasal and 1500 µm temporal from the central fovea using a tool provided by the OCT software. Patients receiving treatment in intensive care unit for COVID-19 infection, receiving antiplatelet therapy, smoking, or having systemic disease were excluded. Patients with known retinal and choroidal pathology (myopia, hole, epiretinal membrane and intravitreal anti-VEGF (vascular endothelial growth factor) treatment) and history of previous ocular surgery were excluded.

Ethical Committee

This observational, retrospective, comparative and case-control study was approved by Mersin University Ethical Committee (Date-number: 2020/15-21) and Mersin State Hospital Education Planning Committee. The study protocol was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis of the study data was performed with the statistical package for social sciences (SPSS, version 24, IBM Corporation, USA). Normal distribution was checked by Shapiro-Wilk test. Non-numerical variables are presented as number and percentage, numerical variables are presented as mean ± standard deviation. Student's t test was used to compare the means of two independent groups for the variables that conformed to normal distribution. Relationships between categorical variables were investigated by chi-square analysis. Statistical significance level was accepted as $p<0.05$ for all comparisons.

RESULTS

The participants included in the study were 42 COVID-19 positive (group 1) and 44 healthy (group 2) adults. The mean age of the participants in group 1 was 35,1 ± 8 years. In terms of gender distribution, 20 (47,6%) were male and 22 (52,4%) were female. The mean age of the participants in Group 2 was 34,4 ± 7,03 years, 21 (47,7%) were male and 23 (52,3%) were female. Both groups were similar in terms of demographic data (age and gender) (p=0,610 and p=0,992, respectively) **(Table 1)**.

Table 1: Demographic data of the participants

	Group 1	Group 2	
N	42	44	p
Age	35,1 ± 8	34,4 ± 7,03	0,610
Male (n, %)	20 (47,6%)	21 (47,7%)	0,992
Female (n, %)	22 (52,4%)	23 (52,3%)	

Optical Coherence Tomography (OCT) findings were as follows: central foveal thickness (CFT) 263,5 ± 15,6 µm, subfoveal choroidal thickness (SCT) 420,2 ± 15,6 µm, nasal retinal thickness 371,2 ± 27,6 µm, temporal retinal thickness 366,3 ± 26,3 µm, peripapillary retinal nerve fiber layer (RNFL) thickness 107,4 ± 6,5 µm in group 1. In Group 2, CFT was 226,9 ± 15,3 µm, SCT was 411,6 ± 10,4 µm, nasal retinal thickness was 368,8 ± 16,0 µm, temporal retinal thickness was 366,4 ± 12,2 µm, and peripapillary RNFL thickness was 96,1 ± 4,2 µm. Central foveal thickness (p<0,001), subfoveal (SCT) choroidal thickness (p=0,001) and peripapillary retinal nerve fiber layer thickness (p<0,001) were significantly higher in group 1. However, nasal and temporal retinal thickness were similar between both groups (p=0,308 and p=0,495, respectively)**(Table 2)**.

Table 2: Optical coherence tomography data of the participants

	Group 1	Group 2	
N	42	44	p
CFT (µm)	263,5 ± 15,6	226,9 ± 15,3	< 0,001
SCT (µm)	420,2 ± 15,6	411,6 ± 10,4	0,001
NRT (µm)	371,2 ± 27,6	368,8 ± 16,0	0,308
TRT (µm)	366,3 ± 26,3	366,4 ± 12,2	0,495
Peripapillary RNFLT (µm)	107,4 ± 6,5	96,1 ± 4,2	< 0,001

CFT: Central foveal thickness, SCT:Subfoveal choroidal thickness, NRT: Nasal retinal thickness, TRT: Temporal retinal thickness, RNFLT: Retinal nerve fiber layer thickness

DISCUSSION

This study showed that patients with a recent history of COVID-19 had increased central foveal thickness, peripapillary retinal nerve fiber thickness and subfoveal choroidal thickness compared to controls. There are very few studies in the literature on retinal and choroidal changes in patients infected with COVID-19. In one study, Invernizzi et al. (2020) showed that "cotton wool spots", retinal hemorrhages, dilated veins and increased vascular tortuosity were present in the retinas of patients with COVID-19. At the conclusion of the study, they stated that the findings of microangiopathy-related retinopathy may be coincidental. However, they also hypothesized that these alterations may have been secondary to COVID-19 or that systemic treatments may have induced microangiopathy (12). In our findings, central foveal thickness was higher in patients with COVID-19 than controls. According to this finding, there are many factors in addition to microangiopathy that determine the retinal thickness level.

One of these possible mechanisms is ischemia. Varga et al. reported paracentral lesions of acute macular neuroretinopathy and acute central maculopathy in the retina of two patients with COVID-19. Both findings may reflect ischemia due to microangiopathy in the retinal capillary beds (13).

Previous studies have demonstrated that posterior segment structures such as the vitreous, inner retinal layers and choroid can be damaged in patients with COVID-19 (14). In a study by Abrishami et al, 17 eyes (28.3%) in the patient group had at least one abnormal finding including hyperreflective lesions in different retinal layers. In addition, dilated choroidal vessels were detected in 41 eyes in the patient group. The mean subfoveal choroidal thickness was significantly higher than in the control group (p<0.001) (15). In a study involving one hundred and sixty participants, increased global RNFL, nasal superior and nasal inferior peripapillary RNFL thickness was reported in COVID-19 patients. In addition, increased ganglion cell layer (GCL) thickness in the outer superior, outer nasal and outer inferior quadrants was reported in COVID-19 patients (16). The foveal thickness change ob-

served in the posterior segment OCT and the retinal nerve fiber thickness change observed in the peripapillary region in our study suggest that COVID-19 has a pathogenesis affecting all retinal regions (vasculitis and/or ischemia).

In a study by Bajka et al. the capillary vessel density of the optic disc was higher in the SARS-CoV-2 group compared to healthy controls (17). In a study reported from our country, macular retinal nerve fiber layer thickness in the outer ring was thinner in the first and second visits compared to healthy controls (p=0.049 and p=0.005). The central and inferonasal quadrants of the peripapillary RNFL thickness were also thinner compared to healthy controls (p=0.001 and p=0.024 for the first visit; p=0.001 and p=0.006 for the second visit). The thickness of the outer nuclear layer in the inner ring was observed to be thinner in the first and second visits compared to healthy subjects (p=0.006 and p=0.001) (18). In an optical coherence tomography angiography (OCTA) study, vessel density measurements in the central fovea, in all quadrants of the superficial and deep retinal layers and in the choriocapillaris showed a significant decrease in the COVID-19 group compared to the healthy control group. Significant reductions in these measurements were more pronounced in the choriocapillaris than in the retinal layers (19). In another study, a baseline saturation of 90% or less in COVID-19 patients was found to result in decreased vessel density in some areas of the superficial and deep capillary plexus and enlargement of the foveal avascular zone (FAZ). In addition, statistically significant retinal thinning was observed in the inner superior (p=0.029), outer superior (p=0.012) and outer temporal (p=0.004) (20). In the OCTA study, an increase in choroidal blood flow was found in patients with COVID-19. This finding was thought to be due to the choroidal vasodilation response to hypoxia in the outer retinal layers. Another reason may be that systemic inflammatory factors induced by the virus increase choroidal blood flow (21). In our study, subfoveal choroidal thickness was higher in the COVID-19 positive group compared to healthy controls. Our findings and literature data suggest that systemic inflammation causes ischemia in the choroid, which leads to vasodilation and increases choroidal thickness. This research has various limitations, including the small number of patients included, its retrospective nature, and its exclusion of active and convalescent patients.

In conclusion, central fovea, subfoveal choroid and peripapillary retinal nerve fiber layer thickness are higher in COVID-19 patients. Multicenter and long-term studies with a large number of patient subgroups are needed to understand the pathogenesis of systemic and local changes caused by COVID-19. Multicenter and long-term studies with a large number of patient subgroups are needed to elucidate the pathogenesis of COVID-19-induced changes.

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