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ORIGINAL ARTICLE

Evaluation of the choroidal vascular structure in patients with migraine

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ABSTRACT

Objectives: This study aimed to compare the posterior segment structures of the eye, including the macula, choroid, and choroidal vascularity index, in patients with migraine with those of healthy individuals.

Patients and methods: In this case-control study, 51 right eyes of 51 patients (42 females, 9 males; median age: 36 years; range, 22 to 47 years) diagnosed with migraine (migraine group) and 36 right eyes of 36 healthy volunteers (control group) (30 females, 6 males; median age: 35 years;; range, 22 to 49 years) were included between January 2022 and December 2022. Optical coherence tomography images were evaluated in the enhanced deep imaging mode. Choroid, macular thickness, and choroidal vascularity index values were statistically compared between the groups.

Results: Choroidal vascularity index values were found to be significantly higher in patients with migraine than in controls (67.4±3.9 *vs.* 65.7±2.0; p=0.025). There was no statistically significant difference in subfoveal macular thickness (p>0.05). Subfoveal choroidal thickness and total choroidal area were significantly lower in patients with migraine (p<0.001 and p=0.039, respectively). No statistically significant correlation was detected in macula and choroid measurements according to migraine duration, attack frequency, and presence of aura (p>0.05).

Conclusion: The findings suggested that migraine caused changes in the choroidal tissue and vascular structure. The effects of migraine on the eye should be considered in the follow-up and treatment of both migraine and other diseases affecting the choroid.

Keywords: Choroid, choroid vascularity index, macula, migraine.

Migraine is a chronic neurovascular disorder that occurs in individuals with a genetic predisposition with recurrent, unilateral, throbbing, and severe headache attacks, usually caused by intrinsic or environmental factors.[1] While the prevalence of migraine is 12 to 15% in the general population, it is reported that the lifetime frequency in adults is approximately three times more common in females than in males, and migraine mainly affects females aged 20 to 45 years.[2,3]

Migraine symptoms are thought to be caused by changes in the vascular tone of cerebral blood vessels.[4,5] Although the contraction and dilatation of the cerebral and retrobulbar arteries is a temporary phenomenon, recurrent attacks of migraine can lead to permanent cerebral and retinal damage.[6] The choroid, a blood-dense tissue, is directly affected by changes in perfusion pressure.[7] Migraine has been reported to be a risk factor for ischemic complications of the retina and optic nerve.[8,9] The main goal of migraine treatment is to reduce the number of attacks and the impact of these complications.[10]

Optical coherence tomography (OCT) is a reliable, noninvasive imaging technique that provides cross-sectional imaging of the

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retina.[11] In recent years, many studies have evaluated changes in retinal and choroidal thickness in patients with migraine.[12,13] Choroidal vascular index (CVI) is a new quantitative OCT parameter defined by Agrawal et al.[14] to measure the vascular state of the choroid. This study aimed to evaluate the structural parameters of the choroid and macula and the vascular structure of the choroid in migraine patients by calculating the CVI value.

PATIENTS AND METHODS

This case-control study was carried out at the Kırıkkale University Faculty of Medicine, Departments of Neurology and Ophthalmology, between January 2022 and December 2022. Fifty-one patients diagnosed with migraine (migraine group) (42 females, 9 males; median age: 36 years; range, 22 to 47 years) and 36 age- and sex-matched healthy volunteers (control group) (30 females, 6 males; median age: 35 years; range, 22 to 49 years) were included in the study. The right eyes of the patients and the volunteers were evaluated. Patients with migraine were divided into two subgroups: those with (n=13) and without aura (n=38). The exclusion criteria were as follows: being over 50 years of age, refraction more than ±6.0 diopters, systemic (e.g., diabetes mellitus, hypertension, heart diseases, and other central nervous system diseases) or ocular (e.g., corneal or lenticular disorders, glaucoma, uveitis, optic neuropathy, retinal vascular diseases, and age-related macular degeneration) disease, use of antihypertensives, calcium channel blockers, or beta-blockers, intraocular surgery, and smokers. Additionally, patients who consumed caffeine or alcohol or used analgesic drugs, triptans, or ergot alkaloids 24 h before the examination were excluded. The study protocol was approved by the Kırıkkale University Clinical Research Ethics Committee (date: 29.04.2021, no: 05/08). Written informed consent was obtained from all participants. The study was performed in accordance with the principles of the Declaration of Helsinki.

In migraine patients, the duration of the disease, the frequency of headache (attacks/month), and the presence of aura were questioned and recorded by a neurologist. The biomicroscopic examination, intraocular pressure measurement, gonioscopy, and fundoscopic examination of all participants were performed. Macular and choroidal thickness measurements were taken with OCT (Retinascan Advanced RS-3000; NIDEK, Gamagori, Aichi, Japan). Macular and choroidal thicknesses were measured in three regions: the central fovea, 750 µm nasal to the central fovea, and 750 µm temporal to the central fovea. Choroidal thickness was determined as the distance between the posterior edge of the retinal pigment epithelium and the choroidoscleral junction. The CVI value was found by using the ImageJ software version 1.50a (National Institutes of Health, Bethesda, MD, USA), a Java-based image processing software, with the ratio of choroidal lumen area (LA) to total choroidal area (Figure 1).

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were given as mean ± standard deviation (SD) values. Visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov test) were performed for all data samples to check the normality of distribution. The chi-square test was used in the analysis of categorical variables. Correlations were assessed with Pearson correlation analysis. The independent sample t-test was used to compare two independent groups. A p-value <0.05 was considered statistically significant.

RESULTS

There was no statistically significant difference in age and sex distribution between the two groups (p=0.781 and p=0.906, respectively; Table 1). The CVI was significantly higher in migraine patients compared to the control group (p=0.025). While

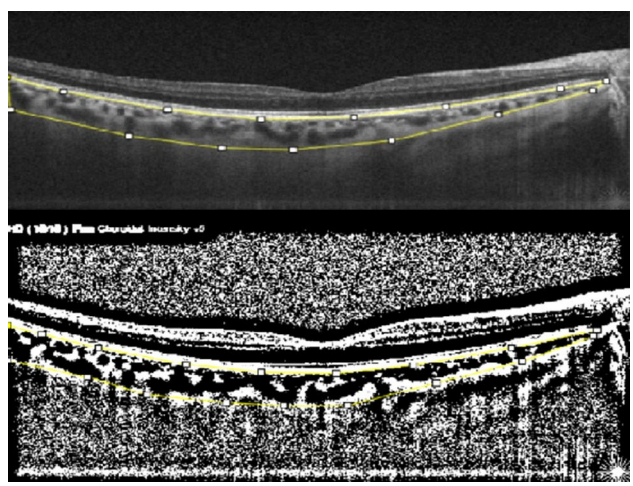

Figure 1. Optical coherence tomography image showing choroidal vascular index calculation with the ImageJ software.

TABLE 1
Demographic characteristics and macular and choroidal thickness measurements of migraine and control groups

	Migraine group					Control group					
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	*p*
Age (year)				36	22-47				35	22-49	0.781
Sex											0.906
Female	42	82				30	83				
Male	9	18				6	17				
Total choroid area (mm^2)			2.1±0.4					2.3±0.4			0.039
Choroid lumen area (mm^2)			1.4±0.3					1.5±0.3			0.250
Choroid stromal area (mm^2)			0.7±0.2					0.8±0.1			<0.001
Choroidal vascular index (%)			67.4±3.9					65.7±2.0			0.025
SMT (μ)				231	210-319				226	197-264	0.430
SMT temporal (μ)			266±42.5					271.5±25.5			0.501
SMT nasal (μ)			274.8±26.8					281.8±22.7			0.205
SCT (μ)			320.5±64.2					370.1±59.7			<0.001
SCT temporal (μ)			317.6±59.0					357±61.2			0.003
SCT nasal (μ)			309.8±64.1					352.3±61.1			0.003

SD: Standard deviation; SMT: Subfoveal macula tickness; SCT: Subfoveal choroid thickness.

TABLE 2
Correlation analysis of macular and choroidal measurements according to attack frequency and disease duration

	TCA	LA	SA	CVI	SMT	SCT
Frequency of headache (attacks/month)						
Correlation	0.241	**0.314***	−0.011	0.259	−0.159	**0.334***
p	0.088	**0.025**	0.941	0.066	0.265	**0.017**
Duration of disease						
Correlation	0.068	0.078	0.011	0.266	0.091	−0.039
p	0.636	0.586	0.941	0.060	0.525	0.788

TCA: Total choroid area; LA: Lumen area; SA: Stromal area; CVI: Choroid vascular index; SMT: Subfoveal macular thickness; SCT: Subfoveal choroid thickness.

TABLE 3
Macular and choroidal thickness measurements of the subgroups formed according to the presence of aura

	Migraine with aura			Migraine without aura			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	*p*
Age (year)		34	26-41		36	22-47	0.336
Choroid lumen area (mm^2)	1.5±0.3			1.5±0.3			0.414
Choroid stromal area (mm^2)		0.7	0.3-1		0.7	0.2-0.8	0.607
Choroidal vascular index (%)	68.1±4.3			67.9±2.5			0.125
SMT (μ)		235	214-319		222	210-247	**0.027**
SMT temporal (μ)	280.2±26			268.4±24.9			**0.002**
SMT nasal (μ)	287±28.2			268.5±22.8			0.258
SCT (μ)	317.1±68.4			339.2±45.6			0.595
SCT temporal (μ)	314±58.1			335.2±49.1			0.368
SCT nasal (μ)	310.8±68.1			323.9±54.3			0.291

SD: Standard deviation; SMT: Subfoveal macula tickness; SCT: Subfoveal choroid thickness.

macular thickness and LA were similar between the groups (p>0.05), total choroidal area, choroidal stromal area, and subfoveal choroidal thickness (SCT) were significantly lower in the migraine group (p=0.039, p<0.001, and p<0.001, respectively). There was no significant difference in macular thickness between groups (Table 1).

The correlation analysis was used to evaluate the effect of attack frequency and disease duration on ocular findings. A statistically significant, weak positive correlation was found between the frequency of attacks and LA and SCT (p=0.025, r=0.314, and p=0.017, r=0.334, respectively). No correlation was found for the effect of disease duration on ocular findings (Table 2).

There was no statistically significant difference between patients with migraine with and without aura in terms of frequency of attacks and duration of disease (p=0.062 and p=0.570, respectively). The subfoveal macula tickness was found to be significantly higher in the group with aura (p=0.027). No significant difference was found between the groups in terms of CVI and choroidal thickness (p>0.05; Table 3).

DISCUSSION

Migraine is a common disease with many systemic vascular changes. Its pathophysiology is not well-understood, but the vasogenic theory links migraine symptoms to prolonged vasospasm followed by vasodilation. In this study, we investigated the effects of migraine on the choroid, which is one of the most blood-dense tissues of the body. Agrawal et al.[14] defined the CVI value obtained by the ratio of choroidal LA and total choroid area to each other in 345 healthy eyes in 2016. According to Agrawal et al.,[14] this ratio is a quantitative OCT parameter that provides information about the vascularity of the choroid. In our study, we evaluated choroid vascularity in migraine patients with CVI.

In this study, CVI was found to be significantly higher in patients with migraine compared to healthy controls. The CVI, calculated as the ratio of the choroidal LA to the total choroidal area, was high as a result of a decrease in the choroidal stroma without a significant change in the LA. This finding showed that there was no change in choroidal vascularity in patients with migraine, and they developed thinning or atrophy of the choroidal stroma. Contrary to our study, Temel et al.[15] examined the thickness of the CVI and retinal nerve fiber layer (RNFL) in patients with migraine and found that both of them decreased.

Tasli et al.[16] examined the vascular structure of the retina with OCT angiography in patients with migraine. According to this study, the vascular density decreased in the deep and superficial plexus of the macula in patients with migraine without aura, and the foveal avascular zone was enlarged. On the other hand, there was no change in the optic disc vascular density. In our study, we evaluated the migraine group according to the presence of aura, and there was no difference in the CVI between the groups. However, subfoveal macula tickness was significantly higher in the group with aura.

Recently, there have been many reports of ocular disorders caused by choroidal thickness change. It was reported that choroidal thickness decreased due to high myopia, retinal dystrophy, and age, while choroidal thickness increased in central serous chorioretinopathy and Vogt-Koyanagi-Harada disease.[17-23] Peripapillary choroidal thickness was found to be lower in patients with glaucoma compared to healthy controls.[24] In addition, a number of recent OCT studies were conducted on the hemodynamic effects of chemicals, namely sildenafil and cigarette smoke, on the choroid.[25,26] In our migraine group, in which these conditions were excluded, choroidal thickness was found to be significantly lower in migraine patients, which was attributed to the loss of choroidal stroma area.

The vasogenic theory, which considers migraine as a form of vascular dysregulation, assumes that migraine headache is caused by rebound vasodilation of the cranial vessels after a temporary vasoconstriction. Karalezli et al.[27] found reduced choroidal thicknesses in patients with migraine. In the same study, they found increased choroidal thickness compared to the control group in the measurements they took during an acute migraine attack. The authors suggested that rebound vasodilation during the acute attack could be the underlying mechanism of choroidal thickening in migraine patients. Similarly, Karaca et al.[28] showed that choroidal thickness significantly decreased in patients with migraine. In our study, we evaluated patients only during the attack-free period and found that their choroidal thickness was significantly reduced.

Demircan et al.[29] evaluated RNFL and the thickness of the macula and choroid in migraine

patients. The mean RNFL and choroidal thicknesses were found to be significantly reduced in patients with migraine compared to the control group. Zengin et al.[30] showed that there was a thinning of the choroid at all points in the migraine group compared to the control group, and they did not detect a significant difference between patients with migraine with and without aura. Yurtogulluları et al.[31] showed that the ganglion cell layer thickness was reduced in migraine patients compared to healthy individuals. Ao et al.[12] found that the macula was thinner in patients with migraine with and without aura than in the control group. In our study, we found that the choroidal thicknesses were similar in patients with and without aura, and the subfoveal macular thickness was greater in migraine patients with aura.

Ekinci et al.[32] observed that RNFL and ganglion cell layer thickness values were significantly lower in patients with migraine with aura compared to the control group in a study involving 90 patients with migraine with and without aura and 30 healthy controls. However, although choroidal thinning was observed in both groups, they could not find a significant difference. In a study in which magnetic resonance imaging of patients with migraine was examined, it was found that brain activation in the visual cortex and lateral geniculate was higher in patients with migraine with aura than in patients with migraine without aura and controls.[33] Therefore, the study associated aura with hyperactivation in the visual cortex in patients with migraine.

Feng et al.[34] showed a positive correlation between the duration of diagnosis and RNFL in patients with migraine followed for a long time. In contrast, Reggio et al.[35] found a negative correlation between RNFL and the frequency of migraine attacks. According to our data, there was no significant difference in CVI and macular thickness in patients with more frequent attacks or longer duration of migraine. In correlation analyses, LA and SCT were found to be higher in patients with a higher frequency of attacks. Theoretically, the pathophysiology of the disease suggests that a higher frequency of attacks or longer duration of migraine may cause more changes in measured thickness values. Therefore, studies with more extended follow-up periods and larger samples are needed to investigate the relationship between the duration and severity of migraine and macular and choroidal thickness values.

The current study had some limitations. The relatively small sample size may have limited the power of statistical analyses. The cross-sectional nature of the study did not allow the evaluation of longitudinal changes. The CVI is not an accurate measure of blood flow rate; thus, it cannot provide sufficient information about dynamic blood flow. The strength of our study was that it evaluated changes in the retina and choroid in the migraine group compared to the control group, taking into account tissue structure and vascular status.

In conclusion, our findings demonstrated a relative increase in CVI associated with stromal area loss in patients with migraine. Therefore, in the follow-up and treatment of other diseases affecting the choroid and vascular structure, the presence of migraine should be considered, and the effects of migraine on these tissues should be taken into account.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, design, data collection and/or processing, literature review: E.D., A.G.A.D., B.S., N.Ö.; Control/supervision, critical review, analysis and/or interpretation: B.S., N.Ö.; Writing the article, refereces and fundings: E.D., B.S.

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