Neurology Asia 2024; 29(4) : 1077 – 1088

Evaluation of the retina and optic discs of patients with chronic and episodic migraine using optical coherence tomography and optical coherence tomography angiography

[1]Buket Özkara Yılmaz, [2]Ali Karnaz

[1]Department of Neurology, Gaziantep City Hospital, Nizip Public Hospital, Turky; [2]Department of Opthalmology, Gaziantep City Hospital, Nizip Public Hospital, Turkey

Abstract

Objective: Migraine is a very common, recurring, usually unilateral, severe, pulsating, and transient headache disorder, which causes temporary disability. Abnormal retinal and optic disc pathologies in migraine patients were previously reported by using optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). In the present study, it was hypothesized that the changes found in the retina and optic disc might indicate a functional disorder in migraine. It is also emphasized that these changes might be useful for early diagnosis and follow-up of the disease, as well as for the development of new treatments. *Method:* In total, 60 individuals were involved in the present study, including 28 chronic migraine patients (24 female, 4 male) and 32 episodic migraine patients (26 female, 6 male), whose migraine types were determined by using the criteria set by the International Headache Society (IHS) in 2013. The control group consisted of 48 healthy volunteers (34 female, 14 male) aged between 18 and 45 years, who applied to the ophthalmology clinic. The retinas and optic discs of the patients were examined by OCT and OCTA at our ophthalmology clinic. A double-blind randomized analysis was performed for the patient data and the data were compared to control group of similar gender and age. *Results:* Examining the demographic data, no statistically significant difference was found between the migraine patients and the healthy controls in terms of age and gender However, using OCT, it was determined that the mean vertical and horizontal cup-to-disk (c/d) ratios at the optic disc were significantly impaired in patients compared to the control group. Moreover, using OCTA, significant reductions in vessel density were detected in the foveal, parafoveal, perifoveal areas and in the superficial and deep capillary plexuses of the patients.
Conclusion: Migraine patients have statistically significant differences in retinal thickness and vascularity, which is consistent with an increased risk.

Keywords: Migraine, retina, optic coherence tomography, optic coherence tomography angiography

INTRODUCTION

Migraine is a recurrent neurovascular disorder that is typically characterized by unilateral pulsating pain ranging between moderate and severe intensity and might be accompanied by transient neurological, autonomic, cognitive, and emotional symptoms.[1] Having a prevalence of 14.7% (18.8% in women and 10.7% in men), it is the third-most common disease worldwide. Although the pathophysiology of migraine has not been fully understood, there are two main theories in the current literature: the trigeminovascular system and the cortical spreading depression (CSD).[2] Both of these theories assume the development of cerebral hypoperfusion. Therefore, the probability of migraine causing also ischemic complications is high. Vascular abnormalities seen in migraine might cause a decreased perfusion in the retina and optic nerve head.[3] It has been suggested that migraine might be a risk factor for both vascular and neuronal density loss in these regions.[4] The present study aims to determine the effects of migraine on the retina and optic disk by comparing the data obtained from Optical Coherence Tomography (OCT) and Optical Coherence Tomography Angiography (OCTA) in patients

Address correspondence to: Buket Özkara Yılmaz, Gaziantep City Hospital, İbni-Sina Mah., Şahinbey/Gaziantep, Turkey. email: buketozkara4188@hotmail.com
Date of Submission: 4 May 2023; Date of Acceptance: 29 March 2024
https://doi.org/10.54029/2024kxm

with chronic and episodic migraine to those of healthy controls.

METHOD

In total, 60 migraine patients (50 women, 10 men) aged between 18 and 45 years, who applied to the neurology clinic and were diagnosed with migraines and had their types determined by using the criteria set by the International Headache Society (IHS) in 2013, were involved in the present study. The control group consisted of 48 healthy volunteers (34 women, 14 men) between the ages of 18 and 45, who applied to the ophthalmology clinic. Neurological and physical examinations were performed for all participants. Following the neurological examination during the routine outpatient controls, optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) were performed for migraine patients. Images of the patients' retina and optic disc were taken by using OCT and OCTA and were compared to those of the control group.

All participants in the study underwent a full ophthalmic examination, including visual acuity, intraocular pressure (IOP) measurement, and anterior and posterior segment examinations. OCT and OCTA imaging were performed using an OptovueRTVue XR Avanti spectral domain OCT device with AngioVue software version 3.5 (Optovue Inc., Fremont, CA, USA).

For both eyes, OCTA images were obtained from a 6 x 6 mm cube of the macula and a 4.5 x 4.5 mm cube of the optic nerve. The retinal vascular network was analyzed using the perfusion density (PD). The quantitative analysis of PD was performed using PD maps of the macula (ETDRS schema) and optic nerve head (S/I and TSNIT charts). By using macular OCTA scans, the foveal avascular zone (FAZ) area on the superficial capillary plexus (SCP) and PD values of the entire SCP, SCP inner (0.5-1.5 mm) and outer (1.5-3.00 mm) ETDRS sectors, nine ETDRS sectors, the entire deep capillary plexus (DCP), and DCP inner and outer ETDRS sectors were collected. PD values of the retinal peripapillary capillary plexus (RPCP) were also recorded for the superior/inferior (S/I) sectors and optic nerve head (TSNIT) sectors.

OCT and OCTA parameters of chronic and episodic migraine patients were compared to those of healthy control groups. The perfusion densities of the outer (1.5-3.00 mm) ETDRS sectors, nine ETDRS sectors, the entire deep capillary plexus (DCP), and DCP inner and outer ETDRS sectors were obtained. The PD values of the foveal avascular zone and the entire SCP and inner SCP (0.5-1.5 mm retinal peripapillary capillary plexus) on the superficial capillary plexus (SCP) were also recorded for upper and lower sectors and TSNIT sectors.

Statistical analysis

The distributions of individuals constituting the study group by various demographic characteristics were determined by preparing frequency tables, whereas crosstabs were used in determining the distributions of some characteristics of migraine patients by categorical variables. The Chi-square test was used in determining if the frequency distributions in the crosstabs were statistically different, while Fisher's exact Chi-square test was used in the analysis of 2x2 crosstabs.

The normality of the distribution of the measurement results for the parameters used in the study was tested by using the Kolmogorov-Smirnov test and considering the skewness-kurtosis coefficients. Differences between the mean values of the groups were examined using the independent groups t-test to determine if the differences were statistically significant. The significance level was set at 0.05 for two-tailed hypothesis tests and $p < 0.05$was accepted that there was a statistically significant difference between the mean values of the groups.

RESULTS

The patient group consisted of 83.3% women and 16.7% men with migraine, whereas the control group consisted of 70.8% female and 29.2% male healthy individuals. There was no statistically significant difference between the gender distributions of the study and control groups ($p>0.05$). Among the migraine patients, 28.3% were in the age group of 18-30 years, 46.7% in the age group of31-40 years, and 25.0% in the age group of41-45 years. In the control group, however, 27.1% of the participants were in the age group of18-30 years, 39.6% in the age group of31-40 years, and 33.3% in the age group of41-45 years. No statistically significant difference in age distribution was found between the experimental and control groups ($p>0.05$).

It was found that the mean vascular densities in the parafoveal (para.sup, para.inf) and perifoveal (peri.sup.hemi, peri.sup, peri.nasal) subregions of the superficial layer of the right eye retina were significantly lower in the experimental group when compared to the control group ($p<0.05$). There

was no statistically significant difference in the mean vascular densities in other subregions of the superficial layer of the right eye retina between the study and control groups (p>0.05) (Table 1).

No statistically significant difference was found in the mean vascular density values in all subregions of the superficial layer of the left eye retina between the study and control groups (p>0.05) (Table 2).

It was found that only the mean thickness

Table 1: T-test results of the comparison of the vascular density (VD) means of the retinal superficial layer according to the patient and control groups (Right eye)

Region	Group	N	Mean	Sd.	t	p
Whole	Control	48	51.95	2.81	1.604	0.112
	Patient	60	51.02	3.11		
Sup. Hemi	Control	48	51.92	2.85	1.925	0.057
	Patient	60	50.38	4.81		
İnf. Hemi	Control	48	51.92	2.88	1.592	0.114
	Patient	60	50.97	3.24		
Fovea	Control	48	20.24	6.81	0.549	0.584
	Patient	60	19.54	6.51		
Para.Fovea	Control	48	54.15	3.79	1.806	0.074
	Patient	60	52,74	4,23		
Para.Sup.Hemi	Control	48	54.29	3.68	1.922	0.057
	Patient	60	52.80	4.24		
Para.Inf.Hemi	Control	48	54.01	4.15	1.666	0.099
	Patient	60	52.61	4.52		
Para.Temporal	Control	48	53.89	3.75	1.334	0.185
	Patient	60	52.87	4.11		
Para.Sup	Control	48	55.11	3.88	1.997	**0.048**
	Patient	60	53.53	4.32		
Para.Nasal	Control	48	53.26	4.86	1.364	0.175
	Patient	60	51,94	5,09		
Para.Inf	Control	48	54.35	4.32	2.039	**0.044**
	Patient	60	51.97	7.66		
Peri.Fovea	Control	48	52.66	2.91	1.844	0.068
	Patient	60	51.58	3.08		
Peri.Sup.Hemi	Control	48	52.63	3.02	2.057	**0.042**
	Patient	60	51.41	3.10		
Peri.Inf.Hemi	Control	48	52.69	2.93	1.710	0.090
	Patient	60	51.68	3.15		
Peri.Temporal	Control	48	48.77	3.42	1.790	0.076
	Patient	60	47.49	3.89		
Peri.Sup	Control	48	52.68	3.18	1.987	**0.049**
	Patient	60	51.43	3.28		
Peri.Nasal	Control	48	56,33	2,69	2.109	**0.037**
	Patient	60	55.21	2.81		
Peri.Inf	Control	48	52.98	3.23	1.725	0.087
	Patient	60	51.85	3.10		
FAZ.Size	Control	48	0,29	0,12	0,323	0,747
	Patient	60	0.29	0.10		
FAZ.Perimeter	Control	48	2.07	0.45	-0.191	0.849
	Patient	60	2.08	0.40		
FAZ.FD	Control	48	55.83	3.62	1.236	0.219
	Patient	60	54.63	5.86		

Table 2: T-test results of the comparison of the vascular density (VD) means of the retinal superficial layer according to the patient and control groups (Left eye)

Region	Group	N	Mean	sd.	t	p
Whole	Control	48	51.83	2.30	0.617	0.539
	Patient	60	51.51	2.86		
Sup.Hemi	Control	48	51.66	2.26	0.739	0.462
	Patient	60	51.29	2.80		
Inf.Hemi	Control	48	51.99	2.46	1.423	0.158
	Patient	60	50.44	7.23		
Fovea	Control	48	20.81	7.04	0.567	0.572
	Patient	60	19.98	7.97		
Para.Fovae	Control	48	53.47	5.11	-0.067	0.947
	Patient	60	53.53	3.29		
Para.Sup.Hemi	Control	48	54.08	3.44	0.810	0.420
	Patient	60	53.53	3.59		
Para.İnf.Hemi	Control	48	54.13	3.22	1.070	0.287
	Patient	60	53.42	3.53		
Para.Temporal	Control	48	54.05	3.21	0.803	0.424
	Patient	60	53.53	3.37		
Para.Sup.	Control	48	54.73	3.89	1.061	0.291
	Patient	60	53.86	4.48		
Para.Nasal	Control	48	52.96	3.72	0.303	0.762
	Patient	60	52.75	3.49		
Para.İnf.	Control	48	54.70	3.45	0.795	0.429
	Patient	60	54.13	3.90		
Peri.Fovea	Control	48	52.50	2.32	1.152	0.252
	Patient	60	51.85	3.49		
Peri.Sup.Hemi	Control	48	52.44	2.24	0.781	0.437
	Patient	60	52.01	3.51		
Peri.İnf.Hemi	Control	48	52.45	2.91	0.487	0.628
	Patient	60	52.13	3.67		
Peri.Temporal	Control	48	48.93	2.34	0.890	0.376
	Patient	60	48.43	3.50		
Peri.Sup.	Control	48	52.56	2.33	0.624	0.534
	Patient	60	52.18	3.97		
Peri.Nasal	Control	48	55.90	2.79	0.730	0.467
	Patient	60	55.44	3.59		
Peri.İnf.	Control	48	52.63	2.87	1.237	0.219
	Patient	60	51.25	7.25		
FAZ.Size	Control	48	0.29	0.12	0.094	0.925
	Patient	60	0.29	0.12		
FAZ.Perimeter	Control	48	2.06	0.42	-0.379	0.705
	Patient	60	2.09	0.49		
FAZ.FD	Control	48	56.62	4.23	1.794	0.076
	Patient	60	55.05	4.76		

of the superficial layer of the right eye's retina in the ParaFovea (Para.Nasal) sub-region was significantly higher in the experimental group compared to the control group ($p<0.05$) (Table 3). No statistically significant differences were found between the mean thickness values of the other sub-regions in the experimental and control groups ($p>0.05$).

In the left eye, there was no statistically significant difference experimental and control groups in terms of the mean thickness values of all sub-regions in the superficial layer of the retina ($p>0.05$) (Table 4).

It was seen that the mean vascular density values of the whole region (Sup.Hemi, Inf.Hemi) and ParaFovea (Para.Sup. Hemi, Para.Inf. Hemi, Para.Temporal, Para.Sup, Para.Nasal, Para.Inf) and PeriFovea (Peri.Sup.Hemi, Peri.Inf.Hemi, Peri.Sup, Peri.Nasal, and Peri.Inf) sub-regions in the deep layer of the right eye's retina were significantly lower in the study group when compared to the control group ($p<0.05$) (Table 5). No significant difference was found between the groups in terms of the mean vascular density of the Fovea and Perifovea (Peri.Temporal) sub-regions in the deep layer of the right eye's retina ($p>0.05$).

The mean vascular density values in the whole (inf. hemi) and parafovea (para. sup. hemi, para. inf. hemi, para. sup. para. nasal, para. inf.), and perifovea (peri. sup. hemi, peri. inf. hemi, peri. temporal, peri. sup. peri. inf.) sub-regions in the deep layer of the left eye's retina were significantly lower in the study group in comparison to the control group ($p<0.05$) (Table 6). There was no statistically significant difference between the groups in terms of the mean vascular density values of the sup. hemi, fovea, parafovea (para. temporal), and perifovea (peri. nasal) sub-regions in the deep layer of the left eye's retina ($p>0.05$).

There was no statistically significant difference between the groups in terms of the mean thickness values of all sub-regions of the deep layer of the right eye retina ($p>0.05$) (Table 7).

Similar to the right eye, there also was no statistically significant difference between the groups in terms of the mean thickness values of all sub-regions of the deep layer of the left eye retina ($p>0.05$) (Table 8).

It was determined that there was no statistically significant difference between the groups in terms of the mean values of RNFL densities in the right eye in any of the sub-regions ($p>0.05$) (Table 9).

Similarly, it was determined that there was no statistically significant difference between the groups in terms of the mean RNFL values in the left eye ($p>0.05$) (Table 10).

It was found that the mean vertical cup-disc ratio of the right eye's optic disc in the patient

Table 3: T-test results of the comparison of the thickness means of the retinal superficial layer according to the patient and control groups (Right eye)

Region	Group	N	Mean	sd.	t	p
Fovea	Control	48	52.46	8.08	-0.298	0.766
	Patient	60	52.95	8.84		
Para.Temporal	Control	48	102.83	5.37	-0.913	0.364
	Patient	60	104.12	8.47		
Para.Sup.	Control	48	113.63	5.03	-1.075	0.285
	Patient	60	115.08	8.25		
Para.Nazal	Control	48	109.31	7.04	-1.986	**0.049**
	Patient	60	112.92	11.65		
Para.İnf.	Control	48	114.83	6.52	-0.195	0.846
	Patient	60	115.12	8.20		
Peri.Temporal	Control	48	88.88	8.99	0.101	0.920
	Patient	60	88.70	8.99		
Peri.Sup	Control	48	99.02	5.98	-1.150	0.253
	Patient	60	100.67	8.34		
Peri.Nasal	Control	48	114.94	10.31	-1.348	0.180
	Patient	60	117.72	10.90		
Peri.İnf	Control	48	99.13	6.43	-0.663	0.509
	Patient	60	100.05	7.77		

Table 4: T-test results of the comparison of the thickness means of the retinal superficial layer according to the patient and control groups (Left eye)

Region	Group	N.	Mean	sd.	t.	p.
Fovea	Control	48	52.98	8.42	0.016	0.987
	Patient	60	52.95	10.10		
Para.Temporal	Control	48	101.92	5.82	-0.657	0.513
	Patient	60	102.93	9.37		
Para.Sup.	Control	48	113.19	5.93	-0.093	0.926
	Patient	60	113.37	12.29		
Para.Nasal	Control	48	110.08	7.15	-0.861	0.391
	Patient	60	111.82	12.40		
Para.İnf.	Control	48	114.63	6.54	-0.294	0.769
	Patient	60	115.48	19.35		
Peri.Temporal	Control	48	86.65	5.58	-0.296	0.768
	Patient	60	87.00	6.62		
Peri.Sup.	Control	48	99.19	5.94	-0.529	0.598
	Patient	60	99.97	8.71		
Peri.Nasal	Control	48	116.77	8.74	-0.850	0.397
	Patient	60	118.30	9.71		
Peri.İnf.	Control	48	98.40	7.19	-0.559	0.578
	Patient	60	99.33	9.68		

group was significantly lower than that of the control group ($p<0.05$) (Table 11). Similarly, the mean horizontal cup-disc ratio of the right eye's optic disc in the experimental group was significantly lower than that of the control group ($p<0.05$).

There was no statistically significant difference between the groups in terms of either the mean vertical cup-disc ratio or the mean horizontal cup-disc ratio of the left eye's optic disc ($p>0.05$) (Table 12).

DISCUSSION

Although the pathophysiology of migraine has not been fully understood, it is thought to be a systemic neurovascular disorder, and ischemic events in migraine are not limited to the brain. Other systemic ischemic conditions such as stroke, angina, and myocardial infarction are also observed more frequently in these patients when compared to healthy subjects.[5,6] Two main theories have been proposed for the pathophysiology of migraine, which are the trigeminovascular model and the cortical spreading depression (CSD).[7] In both theories, it is thought that cerebral hypoperfusion develops during an attack. The trigeminovascular system activates during a migraine attack. Vasoactive substances are secreted upon the activation of nociceptive neurons around the blood vessels. This process triggers mast cell degranulation and causes sterile neurogenic inflammation in the dura mater. In addition, the monosynaptic reflex arc between the trigeminocervical complex and the superior salivatory nucleus activates the parasympathetic nerve endings around the dural blood vessels. Following this process, vasodilator agents are released and vasodilation occurs.[8] In summary, migraine attacks alter both intracerebral and extracerebral vascular regulations. Therefore, migraine is likely to cause the development of ischemic complications. Decreased perfusion in the optic nerve head and retina might be observed in migraine due to these vascular changes.

Although the vascular abnormalities observed in cerebral and retrobulbar arteries are temporary, the chronic nature of migraine, which is characterized by recurring attacks, might lead to permanent retinal damage.[9] As can be seen, migraine is considered as a risk factor for ischemic optic neuropathy.[10] Kara *et al*.[11], supporting this hypothesis, investigated retrobulbar circulation and hemodynamic changes among patients having migraine by using color Doppler sonography. They reported that central retinal artery and posterior ciliary artery resistances were higher in migraine patients during headache-free periods. Greven *et al*.[12] reported that 25% of young adults with retinal artery occlusion had a history of migraine, and

Table 5: T-test results of the comparison of the vascular density (VD) means of the retinal deep layer according to the patient and control groups (Right eye)

Region	Group	N.	Mean	sd.	t	p
Whole	Control	48	56.64	5.83	2.574	**0.011**
	Patient	60	52.63	9.45		
Sup.Hemi	Control	48	56.45	5.77	2.778	**0.006**
	Patient	60	53.14	6.44		
İnf.Hemi	Control	48	56.81	6.10	2.673	**0.009**
	Patient	60	53.53	6.54		
Fovea	Control	48	38.45	7.73	1.487	0.140
	Patient	60	36.29	7.32		
Para.Fovea	Control	48	59.30	3.74	2.868	**0.005**
	Patient	60	57.15	3.97		
Para.Sup.Hemi	Control	48	59.62	3.75	3.058	**0.003**
	Patient	60	57.24	4.22		
Para.İnf.Hemi	Control	48	58.98	3.93	2.270	**0.025**
	Patient	60	57.25	3.94		
Para.Temporal	Control	48	60.22	3.67	2.756	**0.007**
	Patient	60	58.18	3.93		
Para.Sup.	Control	48	59.07	4.02	2.961	**0.004**
	Patient	60	56.59	4.56		
Para.Nasal	Control	48	60.16	4.03	2.623	**0.010**
	Patient	60	58.14	3.96		
Para.İnf.	Control	48	57.83	4.57	2.120	**0.036**
	Patient	60	55.92	4.74		
Peri.Fovea	Control	48	58.17	6.33	2.659	**0.009**
	Patient	60	54.67	7.14		
Peri.Sup.Hemi	Control	48	58.00	6.23	2.842	**0.005**
	Patient	60	54.32	7.04		
Peri.İnf.Hemi	Control	48	58.33	6.65	2.623	**0.010**
	Patient	60	54.73	7.43		
Peri.Temporal	Control	48	58.68	5.63	1.913	0.058
	Patient	60	56.49	6.09		
Peri.Sup.	Control	48	57.53	6.79	2.503	**0.014**
	Patient	60	53.97	7.76		
Peri.Nasal	Control	48	58.23	6.44	2.927	**0.004**
	Patient	60	54.07	7.99		
Peri.İnf.	Control	48	58.60	7.22	2.506	**0.014**
	Patient	60	54.81	8.26		

none of them were acutely symptomatic during the event.

There are only few studies that examine the effects of migraine on retinal vascular structure by using OCTA. Chang *et al*.[4] compared the macular and optic nerve vessel densities (VD) and reported that the foveal avascular zone (FAZ) area was significantly larger, as well as a decreased foveal VD, in migraine patients when compared to healthy control participants. Ulusoy *et al*.[13] reported thinner retinal nerve fiber layer thickness (RSLT) and wider FAZ area in migraine patients. Lower superficial and deeperfoveal VDs were found using OCTA but there was no statistically significant difference in parafoveal VDs.

Table 6: T-test results of the comparison of the vascular density (VD) means of the retinal deep layer according to the patient and control groups (Left eye)

Region	Group	N	Mean	sd.	t	p
Whole	Control	48	56.64	5.83	2.574	**0.011**
	Patient	60	52.63	9.45		
Sup.Hemi	Control	48	56.45	5.77	2.778	**0.006**
	Patient	60	53.14	6.44		
İnf.Hemi	Control	48	56.81	6.10	2.673	**0.009**
	Patient	60	53.53	6.54		
Fovea	Control	48	38.45	7.73	1.487	0.140
	Patient	60	36.29	7.32		
Para.Fovea	Control	48	59.30	3.74	2.868	**0.005**
	Patient	60	57.15	3.97		
Para.Sup.Hemi	Control	48	59.62	3.75	3.058	**0.003**
	Patient	60	57.24	4.22		
Para.İnf.Hemi	Control	48	58.98	3.93	2.270	**0.025**
	Patient	60	57.25	3.94		
Para.Temporal	Control	48	60.22	3.67	2.756	**0.007**
	Patient	60	58.18	3.93		
Para.Sup.	Control	48	59.07	4.02	2.961	**0.004**
	Patient	60	56,59	4.56		
Para.Nasal	Control	48	60,16	4.03	2.623	**0.010**
	Patient	60	58.14	3.96		
Para.İnf.	Control	48	57.83	4.57	2.120	**0.036**
	Patient	60	55.92	4.74		
Peri.Fovea	Control	48	58.17	6.33	2.659	**0.009**
	Patient	60	54.67	7.14		
Peri.Sup.Hemi	Control	48	58.00	6.23	2.842	**0.005**
	Patient	60	54.32	7.04		
Peri.İnf.Hemi	Control	48	58.33	6.65	2.623	**0.010**
	Patient	60	54.73	7.43		
Peri Temporal	Control	48	58.68	5.63	1.913	0.058
	Patient	60	56.49	6.09		
Peri.Sup.	Control	48	57.53	6.79	2.503	**0.014**
	Patient	60	53.97	7.76		
Peri.Nasal	Control	48	58.23	6.44	2.927	**0.004**
	Patient	60	54.07	7.99		
Peri.İnf.	Control	48	58.60	7.22	2.506	**0.014**
	Patient	60	54.81	8.26		

In previous studies, macular parameters such as RSLT thickness, choroidal thickness, ganglion cell layer (GCL) thickness, and foveal thickness among migraine patients were evaluated by making use of the OCT findings. Gipponi *et al*.[14] reported a decrease in RSLT thickness in the upper retinal quadrant of migraine patients when compared to normal subjects, regardless of the duration or frequency of the disease. Reggio *et al*.[15] reported a thinner RSLT in migraine patients in comparison to the control group. Acer *et al*.[16] found no significant difference between patients and controls in terms of GCL and macular thickness. Salman *et al*.[17] also determined that

Table 7: T-test results of the comparison of the thickness means of the retinal deep layer according to the patient and control groups (Right eye)

Region	Group	N	Mean	sd.	t	p
Fovea	Control	48	203.25	11.89	-0.592	0.555
	Patient	60	204.77	14.20		
Para.Temporal	Control	48	210.96	8.20	0.421	0.674
	Patient	60	210.10	12.06		
Para.Sup	Control	48	212.65	8.56	-0.193	0.847
	Patient	60	213.02	10.87		
Para.Nasal	Control	48	214.81	7.80	0.762	0.448
	Patient	60	213.23	13.48		
Para.İnf	Control	48	209.40	8.44	1.298	0.197
	Patient	60	206.83	11.40		
Peri.Temporal	Control	48	184.65	8.17	0.317	0.751
	Patient	60	184.02	11.62		
Peri.Sup	Control	48	187.48	7.87	-0.720	0.473
	Patient	60	188.78	10.39		
Peri.Nasal	Control	48	185.96	8.86	0.235	0.815
	Patient	60	185.50	10.97		
Peri.İnf	Control	48	178.04	8.10	0.698	0.487
	Patient	60	176.77	10.37		

there was no statistically significant difference between the RSLT thickness of the migraine group and the control group. In the present study, there also was no significant difference in RSLT and the thickness of the superficial and deep retinal layers between the groups. These controversial results are thought to be related to focal perimetric changes and differences in the sensitivity of retinal axons

Table 8: T-test results of the comparison of the thickness means of the retinal deep layer according to the patient and control groups (Left eye)

Region	Group	N	Mean	sd.	t	p
Fovea	Control	48	202.92	11.70	-1.214	0.228
	Patient	60	206.50	17.57		
Para.Temporal	Control	48	209.96	8.35	0.177	0.859
	Patient	60	209.58	12.59		
Para.Sup	Control	48	212.96	8.25	-0.692	0.490
	Patient	60	214.57	14.29		
Para.Nasal	Control	48	214.65	7.79	-0.160	0.874
	Patient	60	215.05	17.58		
Para.İnf	Control	48	208.54	7.65	0.204	0.839
	Patient	60	208.03	15.85		
Peri.Temporal	Control	48	183.42	7.70	-0.089	0.930
	Patient	60	183.58	11.06		
Peri.Sup	Control	48	187.79	7.77	-1.013	0.314
	Patient	60	189.67	11.41		
Peri.Nasal	Control	48	185.77	8.94	0.254	0.800
	Patient	60	185.27	11.21		
Peri.İnf	Control	48	176.98	7.64	-0.693	0.490
	Patient	60	178.37	12.95		

Table 9: T-test results of the comparison of retinal nerve fiber density (RNFL) means by patient and control groups (Right eye)

Region	Group	N	Mean	sd.	t	p
Peripapille	Control	48	114.31	9.37	-1.315	0.191
	Patient	60	117.63	15.35		
Suphemi	Control	48	112.92	9.31	-1.526	0.130
	Patient	60	117.33	18.23		
İnfhemi	Control	48	116.04	11.17	-1.297	0.197
	Patient	60	121.10	25.08		
Superior	Control	48	131.75	11.98	-1.228	0.222
	Patient	60	135.50	18.24		
İnferior	Control	48	146.77	17.10	-0.667	0.506
	Patient	60	150.03	30.24		
Nasal	Control	48	104.69	12.13	-0.747	0.456
	Patient	60	106.82	16.48		
Temporal	Control	48	76.17	8.85	-0.691	0.491
	Patient	60	78.35	22.37		

Table 10: T-test results of the comparison of retinal nerve fiber density (RNFL) means by patient and control groups (Left eye)

Region	Group	N	Mean	sd.	t	p
Peripapille	Control	48	114.77	10.83	-0.749	0.456
	Patient	60	116.55	13.31		
Suphemi	Control	48	114.75	11.43	-0.875	0.384
	Patient	60	116.75	12.10		
İnfhemi	Control	48	114.85	11.84	-0.801	0.425
	Patient	60	117.17	16.97		
Superior	Control	48	135.94	17.21	-0.084	0.933
	Patient	60	136.20	15.09		
İnferior	Control	48	145.10	17.67	-0.064	0.949
	Patient	60	145.37	23.40		
Nasal	Control	48	102.56	11.11	-1.742	0.084
	Patient	60	108,20	20.08		
Temporal	Control	48	76.21	8.23	-0.739	0.462
	Patient	60	78.00	16.38		

Table 11: T-test results of the comparison of cup disc ratios in optic disc according to patient and control groups (Right eye)

Parameter	Group	N	Mean	sd.	t	p
Verticalc/d	Control	48	0.35	0.20	2.715	**0.008**
	Patient	60	0.24	0.24		
Horizontalc/d	Control	48	0.30	0.17	2.513	**0.013**
	Patient	60	0.21	0.20		

Table 12: T-test results of the comparison of cup disk ratios in optic disc according to patient and control groups (Left eye)

Parameter	Group	N	Mean	sd.	t	p
Verticalc/d	Control	48	0.31	0.22	1.218	0.226
	Patient	60	0.26	0.22		
Horizontalc/d	Control	48	0.26	0.19	0.678	0.499
	Patient	60	0.24	0.19		

to ischemia.[18,19]

Karaca *et al*.[20] analyzed choroidal thickness in 32 migraine patients during the headache-free period. They concluded that migraine causes a decrease in choroidal thickness, as well as vasoconstriction and ischemia, during the headache-free period. As a result of these studies, it was concluded that migraine is a vasoconstrictive disease even during headache-free periods. In the present study, it was determined that the vascular densities (VD') of the foveal, parafoveal, perifoveal, superficial capillary plexus (SCP), and deep capillary plexus (DCP) were low in the patient group when compared to the control group during the headache-free period. This finding suggests that the low vascular density (VD') in the study groups during headache-free periods might be because of the vasoconstriction originating from the autonomic nervous system dysfunction.

Ao *et al*.[21] reported significant changes in the thickness of the RSLT and choroid and emphasized that they might be associated with cortical spreading depression. Phelps and Corbett[22] revealed that the incidence of low-tension glaucoma in migraine patients was higher and it was attributed to the narrowing of retrobulbar arteries. Grosberg *et al*.[23] evaluated 46 patients having retinal migraine and they found permanent visual loss due to long-term vascular damage in 21 (46%) of those 46 patients. The mean age of their patient cohort was 25 years (range 7-54 years) and they had a very low incidence of vascular risk factors.

As mentioned in these studies, repeated vasospasm and focal ischemia during attacks can lead to optic nerve and retinal damage, ultimately contributing to ocular diseases such as ischemic optic neuropathy and glaucoma. In our study, the lower vertical and horizontal cup-to-disc (c/d) ratio at the optic nerve head compared to the control group supports the vascular theory in migraine pathophysiology.

The limitations of the study was that the findings of migraine patients were not divided into chronic-episodic, with and without aura.

In conclusion, it is thought that OCT and OCTA findings in migraine patients might be associated with an increased risk of ocular vascular events. OCT and OCTA may provide potential benefits as a non-invasive, rapid, and relatively inexpensive biomarkers in migraine patients.

DISCLOSURES

Ethics: Ethical approval was obtained from the Ethics Committee of the Medical Faculty of Kocaeli University (Decision Number: 2020/271).

Financial support: None

Conflict of interest: None

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