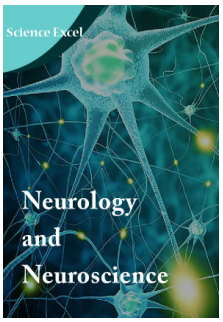
Neurology & Neuroscience

Original Article



Evaluation of the Retina and Optic Discs of Patients with Chronic and Episodic Migraine using Optical Coherence Tomography and Optical Coherence Tomography Angiography

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- Received Date: 07 May 2023
- Accepted Date: 16 May 2023
- Publication Date: 24 May 2023

Abstract

Objective: Migraine is a very common,recurring, usually unilateral, severe, pulsating, and transient headache disorder, which causes temporary disability. Migraine has two main types: with aura and without aura. 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 suggested that the changes foundin the retina and optic disc mightindicate a functional disorder in chronic (with and without aura) and episodic (with and without aura) 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, 16 with aura, 12 without aura) and 32 episodic migraine patients (26 female, 6 male, 21 with aura, 11 without aura), who were diagnosed with migraine and whose migraine types were determinedby 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 optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) at our ophthalmology clinic. A double-blind randomized analysis was performed for the patient data and the data were compared to control group data of similar gender and age groups.

Results: Examining the demographic data, no statistically significant difference was found between the migraine patients and the healthy controls in terms of age, gender, migraine history, and migraine type. However, using Optical Coherence Tomography (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 Optical Coherence Tomography Angiography (OCTA), significant reductions in vessel density (VD) were detected in the foveal, parafoveal, perifoveal areas and in the superficial and deep capillary plexuses (SCP and DCP) of the patients.

Conclusion: It is thought that these findings might be associated with a vasculopathy developing due to a pathology in the autonomic nervous system or impairments in the cerebral, ocular, or systemic circulation. The authors believe that the results achieved in the present study could be useful in the diagnosis, monitoring, and treatment of the disease.

Introduction and Objective

Migraine is a recurrent neurovascular disorder that is typically characterized by unilateral pulsating pain ranging between moderate and severe intensity andmight 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 yet, there are two main theories in the current literature: the trigeminovascular system and the cortical spreading depression (CSD) [2]. Both of thesetheories assume the development of cerebral hypoperfusion. Therefore, the probability of migrainecausing ischemic complications is high. Vascular abnormalities seen in migraine might causeadecreased perfusion in the retina and optic nerve head [3]. It was argued 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 with chronic and episodic migraine

Citation: Yılmaz B, Karnaz A. Evaluation of the Retina and Optic Discs of Patients with Chronic and Episodic Migraine using Optical Coherence Tomography and Optical Coherence Tomography Angiography. Neurol Neurosci. 2023; 4(2):1-11

to those of healthy controls, as well as shedding light on new studieson early diagnosis, monitoring, and treatment of the disease.

Materials and 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 present 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, optical coherence tomography angiography 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 methodology

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 testwas 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 testsand $p < 0.05$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 experimental 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 of 18-30 years, 39.6% in the age group of 31-40 years, and 33.3% in the age group of 41-45 years. No statistically significant difference in age distribution was found between the experimental and control groups ($p>0.05$).

It was determined 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 experimental 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 experimental and control groups ($p>0.05$) (Table 2).

It was determined that only the mean thickness 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) andParaFovea (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 retinawere significantly lower in the experimental 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.

Table 1. *Retina Yüzeysel Katmanının Damar Dansitesi (VD) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sağ Göz)*

Bölge	Grup	N	Ort.	ss	t	p
Whole	Kontrol	48	51,95	2,81	1,604	0,112
	Hasta	60	51,02	3,11		
Sup. Hemi	Kontrol	48	51,92	2,85	1,925	0,057
	Hasta	60	50,38	4,81		
İnf. Hemi	Kontrol	48	51,92	2,88	1,592	0,114
	Hasta	60	50,97	3,24		
Fovea	Kontrol	48	20,24	6,81	0,549	0,584
	Hasta	60	19,54	6,51		
Para.Fovea	Kontrol	48	54,15	3,79	1,806	0,074
	Hasta	60	52,74	4,23		
Para.Sup.Hemi	Kontrol	48	54,29	3,68	1,922	0,057
	Hasta	60	52,80	4,24		
Para.Inf.Hemi	Kontrol	48	54,01	4,15	1,666	0,099
	Hasta	60	52,61	4,52		
Para.Temporal	Kontrol	48	53,89	3,75	1,334	0,185
	Hasta	60	52,87	4,11		
Para.Sup	Kontrol	48	55,11	3,88	1,997	0,048
	Hasta	60	53,53	4,32		
Para.Nasal	Kontrol	48	53,26	4,86	1,364	0,175
	Hasta	60	51,94	5,09		
Para.Inf	Kontrol	48	54,35	4,32	2,039	0,044
	Hasta	60	51,97	7,66		
Peri.Fovea	Kontrol	48	52,66	2,91	1,844	0,068
	Hasta	60	51,58	3,08		
Peri.Sup.Hemi	Kontrol	48	52,63	3,02	2,057	0,042
	Hasta	60	51,41	3,10		
Peri.Inf.Hemi	Kontrol	48	52,69	2,93	1,710	0,090
	Hasta	60	51,68	3,15		
Peri.Temporal	Kontrol	48	48,77	3,42	1,790	0,076
	Hasta	60	47,49	3,89		
Peri.Sup	Kontrol	48	52,68	3,18	1,987	0,049
	Hasta	60	51,43	3,28		
Peri.Nasal	Kontrol	48	56,33	2,69	2,109	0,037
	Hasta	60	55,21	2,81		
Peri.Inf	Kontrol	48	52,98	3,23	1,725	0,087
	Hasta	60	51,85	3,10		
FAZ.Size	Kontrol	48	0,29	0,12	0,323	0,747
	Hasta	60	0,29	0,10		
FAZ.Perimeter	Kontrol	48	2,07	0,45	-0,191	0,849
	Hasta	60	2,08	0,40		
FAZ.FD	Kontrol	48	55,83	3,62	1,236	0,219
	Hasta	60	54,63	5,86		

Table 2. *Retina Yüzeysel Katmanının Damar Dansitesi (VD) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Whole	Kontrol	48	51,83	2,30	0,617	0,539
	Hasta	60	51,51	2,86		
Sup.Hemi	Kontrol	48	51,66	2,26	0,739	0,462
	Hasta	60	51,29	2,80		
Inf.Hemi	Kontrol	48	51,99	2,46	1,423	0,158
	Hasta	60	50,44	7,23		
Fovea	Kontrol	48	20,81	7,04	0,567	0,572
	Hasta	60	19,98	7,97		
Para.Fovae	Kontrol	48	53,47	5,11	-0,067	0,947
	Hasta	60	53,53	3,29		
Para.Sup.Hemi	Kontrol	48	54,08	3,44	0,810	0,420
	Hasta	60	53,53	3,59		
Para.İnf.Hemi	Kontrol	48	54,13	3,22	1,070	0,287
	Hasta	60	53,42	3,53		
Para.Temporal	Kontrol	48	54,05	3,21	0,803	0,424
	Hasta	60	53,53	3,37		
Para.Sup.	Kontrol	48	54,73	3,89	1,061	0,291
	Hasta	60	53,86	4,48		
Para.Nasal	Kontrol	48	52,96	3,72	0,303	0,762
	Hasta	60	52,75	3,49		
Para.İnf.	Kontrol	48	54,70	3,45	0,795	0,429
	Hasta	60	54,13	3,90		
Peri.Fovea	Kontrol	48	52,50	2,32	1,152	0,252
	Hasta	60	51,85	3,49		
Peri.Sup.Hemi	Kontrol	48	52,44	2,24	0,781	0,437
	Hasta	60	52,01	3,51		
Peri.İnf.Hemi	Kontrol	48	52,45	2,91	0,487	0,628
	Hasta	60	52,13	3,67		
Peri.Temporal	Kontrol	48	48,93	2,34	0,890	0,376
	Hasta	60	48,43	3,50		
Peri.Sup.	Kontrol	48	52,56	2,33	0,624	0,534
	Hasta	60	52,18	3,97		
Peri.Nasal	Kontrol	48	55,90	2,79	0,730	0,467
	Hasta	60	55,44	3,59		
Peri.İnf.	Kontrol	48	52,63	2,87	1,237	0,219
	Hasta	60	51,25	7,25		
FAZ.Size	Kontrol	48	0,29	0,12	0,094	0,925
	Hasta	60	0,29	0,12		
FAZ.Perimeter	Kontrol	48	2,06	0,42	-0,379	0,705
	Hasta	60	2,09	0,49		
FAZ.FD	Kontrol	48	56,62	4,23	1,794	0,076
	Hasta	60	55,05	4,76		

Table 3. *Retina Yüzeysel Katmanının Kalınlık (Thickness) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sağ Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Fovea	Kontrol	48	52,46	8,08	-0,298	0,766
	Hasta	60	52,95	8,84		
Para.Temporal	Kontrol	48	102,83	5,37	-0,913	0,364
	Hasta	60	104,12	8,47		
Para.Sup.	Kontrol	48	113,63	5,03	-1,075	0,285
	Hasta	60	115,08	8,25		
Para.Nazal	Kontrol	48	109,31	7,04	-1,986	0,049
	Hasta	60	112,92	11,65		
Para.İnf.	Kontrol	48	114,83	6,52	-0,195	0,846
	Hasta	60	115,12	8,20		
Peri.Temporal	Kontrol	48	88,88	8,99	0,101	0,920
	Hasta	60	88,70	8,99		
Peri.Sup	Kontrol	48	99,02	5,98	-1,150	0,253
	Hasta	60	100,67	8,34		
Peri.Nasal	Kontrol	48	114,94	10,31	-1,348	0,180
	Hasta	60	117,72	10,90		
Peri.İnf	Kontrol	48	99,13	6,43	-0,663	0,509
	Hasta	60	100,05	7,77		

Table 4. *Retina Yüzeysel Katmanının Kalınlık (Thickness) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Bölge	Grup	N.	Ort.	ss.	t.	p.
Fovea	Kontrol	48	52,98	8,42	0,016	0,987
	Hasta	60	52,95	10,10		
Para.Temporal	Kontrol	48	101,92	5,82	-0,657	0,513
	Hasta	60	102,93	9,37		
Para.Sup.	Kontrol	48	113,19	5,93	-0,093	0,926
	Hasta	60	113,37	12,29		
Para.Nasal	Kontrol	48	110,08	7,15	-0,861	0,391
	Hasta	60	111,82	12,40		
Para.İnf.	Kontrol	48	114,63	6,54	-0,294	0,769
	Hasta	60	115,48	19,35		
Peri.Temporal	Kontrol	48	86,65	5,58	-0,296	0,768
	Hasta	60	87,00	6,62		
Peri.Sup.	Kontrol	48	99,19	5,94	-0,529	0,598
	Hasta	60	99,97	8,71		
Peri.Nasal	Kontrol	48	116,77	8,74	-0,850	0,397
	Hasta	60	118,30	9,71		
Peri.İnf.	Kontrol	48	98,40	7,19	-0,559	0,578
	Hasta	60	99,33	9,68		

Table 5. *Retina Yüzeysel Katmanının Damar Dansitesi (VD) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Bölge	Grup	N.	Ort.	ss.	t	p
Whole	Kontrol	48	56,64	5,83	2,574	0,011
	Hasta	60	52,63	9,45		
Sup.Hemi	Kontrol	48	56,45	5,77	2,778	0,006
	Hasta	60	53,14	6,44		
İnf.Hemi	Kontrol	48	56,81	6,10	2,673	0,009
	Hasta	60	53,53	6,54		
Fovea	Kontrol	48	38,45	7,73	1,487	0,140
	Hasta	60	36,29	7,32		
Para.Fovea	Kontrol	48	59,30	3,74	2,868	0,005
	Hasta	60	57,15	3,97		
Para.Sup.Hemi	Kontrol	48	59,62	3,75	3,058	0,003
	Hasta	60	57,24	4,22		
Para.İnf.Hemi	Kontrol	48	58,98	3,93	2,270	0,025
	Hasta	60	57,25	3,94		
Para.Temporal	Kontrol	48	60,22	3,67	2,756	0,007
	Hasta	60	58,18	3,93		
Para.Sup.	Kontrol	48	59,07	4,02	2,961	0,004
	Hasta	60	56,59	4,56		
Para.Nasal	Kontrol	48	60,16	4,03	2,623	0,010
	Hasta	60	58,14	3,96		
Para.İnf.	Kontrol	48	57,83	4,57	2,120	0,036
	Hasta	60	55,92	4,74		
Peri.Fovea	Kontrol	48	58,17	6,33	2,659	0,009
	Hasta	60	54,67	7,14		
Peri.Sup.Hemi	Kontrol	48	58,00	6,23	2,842	0,005
	Hasta	60	54,32	7,04		
Peri.İnf.Hemi	Kontrol	48	58,33	6,65	2,623	0,010
	Hasta	60	54,73	7,43		
Peri.Temporal	Kontrol	48	58,68	5,63	1,913	0,058
	Hasta	60	56,49	6,09		
Peri.Sup.	Kontrol	48	57,53	6,79	2,503	0,014
	Hasta	60	53,97	7,76		
Peri.Nasal	Kontrol	48	58,23	6,44	2,927	0,004
	Hasta	60	54,07	7,99		
Peri.İnf.	Kontrol	48	58,60	7,22	2,506	0,014
	Hasta	60	54,81	8,26		

Table 6. *Retina Derin Katmanının Damar Dansitesi (VD) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Whole	Kontrol	48	56,64	5,83	2,574	0,011
	Hasta	60	52,63	9,45		
Sup.Hemi	Kontrol	48	56,45	5,77	2,778	0,006
	Hasta	60	53,14	6,44		

Bölge	Grup	N	Ort.	ss.	t	p
İnf.Hemi	Kontrol	48	56,81	6,10	2,673	0,009
	Hasta	60	53,53	6,54		
Fovea	Kontrol	48	38,45	7,73	1,487	0,140
	Hasta	60	36,29	7,32		
Para.Fovea	Kontrol	48	59,30	3,74	2,868	0,005
	Hasta	60	57,15	3,97		
Para.Sup.Hemi	Kontrol	48	59,62	3,75	3,058	0,003
	Hasta	60	57,24	4,22		
Para.İnf.Hemi	Kontrol	48	58,98	3,93	2,270	0,025
	Hasta	60	57,25	3,94		
Para.Temporal	Kontrol	48	60,22	3,67	2,756	0,007
	Hasta	60	58,18	3,93		
Para.Sup.	Kontrol	48	59,07	4,02	2,961	0,004
	Hasta	60	56,59	4,56		
Para.Nasal	Kontrol	48	60,16	4,03	2,623	0,010
	Hasta	60	58,14	3,96		
Para.İnf.	Kontrol	48	57,83	4,57	2,120	0,036
	Hasta	60	55,92	4,74		
Peri.Fovea	Kontrol	48	58,17	6,33	2,659	0,009
	Hasta	60	54,67	7,14		
Peri.Sup.Hemi	Kontrol	48	58,00	6,23	2,842	0,005
	Hasta	60	54,32	7,04		
Peri.İnf.Hemi	Kontrol	48	58,33	6,65	2,623	0,010
	Hasta	60	54,73	7,43		
Peri Temporal	Kontrol	48	58,68	5,63	1,913	0,058
	Hasta	60	56,49	6,09		
Peri.Sup.	Kontrol	48	57,53	6,79	2,503	0,014
	Hasta	60	53,97	7,76		
Peri.Nasal	Kontrol	48	58,23	6,44	2,927	0,004
	Hasta	60	54,07	7,99		
Peri.İnf.	Kontrol	48	58,60	7,22	2,506	0,014
	Hasta	60	54,81	8,26		

Table 7. *Retina Derin Katmanının Kalınlık (Thickness) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sağ Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Fovea	Kontrol	48	203,25	11,89	-0,592	0,555
	Hasta	60	204,77	14,20		
Para.Temporal	Kontrol	48	210,96	8,20	0,421	0,674
	Hasta	60	210,10	12,06		
Para.Sup	Kontrol	48	212,65	8,56	-0,193	0,847
	Hasta	60	213,02	10,87		
Para.Nasal	Kontrol	48	214,81	7,80	0,762	0,448
	Hasta	60	213,23	13,48		
Para.İnf	Kontrol	48	209,40	8,44	1,298	0,197
	Hasta	60	206,83	11,40		

Bölge	Grup	N	Ort.	ss.	t	p
Peri.Temporal	Kontrol	48	184,65	8,17	0,317	0,751
	Hasta	60	184,02	11,62		
Peri.Sup	Kontrol	48	187,48	7,87	-0,720	0,473
	Hasta	60	188,78	10,39		
Peri.Nasal	Kontrol	48	185,96	8,86	0,235	0,815
	Hasta	60	185,50	10,97		
Peri.İnf	Kontrol	48	178,04	8,10	0,698	0,487
	Hasta	60	176,77	10,37		

Table 8. *Retina Derin Katmanının Kalınlık (Thickness) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Fovea	Kontrol	48	202,92	11,70	-1,214	0,228
	Hasta	60	206,50	17,57		
Para.Temporal	Kontrol	48	209,96	8,35	0,177	0,859
	Hasta	60	209,58	12,59		
Para.Sup	Kontrol	48	212,96	8,25	-0,692	0,490
	Hasta	60	214,57	14,29		
Para.Nasal	Kontrol	48	214,65	7,79	-0,160	0,874
	Hasta	60	215,05	17,58		
Para.İnf	Kontrol	48	208,54	7,65	0,204	0,839
	Hasta	60	208,03	15,85		
Peri.Temporal	Kontrol	48	183,42	7,70	-0,089	0,930
	Hasta	60	183,58	11,06		
Peri.Sup	Kontrol	48	187,79	7,77	-1,013	0,314
	Hasta	60	189,67	11,41		
Peri.Nasal	Kontrol	48	185,77	8,94	0,254	0,800
	Hasta	60	185,27	11,21		
Peri.İnf	Kontrol	48	176,98	7,64	-0,693	0,490
	Hasta	60	178,37	12,95		

Table 9. *Retina Derin Katmanının Kalınlık (Thickness) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sağ Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Peripapille	Kontrol	48	114,31	9,37	-1,315	0,191
	Hasta	60	117,63	15,35		
Suphemi	Kontrol	48	112,92	9,31	-1,526	0,130
	Hasta	60	117,33	18,23		
İnfhemi	Kontrol	48	116,04	11,17	-1,297	0,197
	Hasta	60	121,10	25,08		
Superior	Kontrol	48	131,75	11,98	-1,228	0,222
	Hasta	60	135,50	18,24		
İnferior	Kontrol	48	146,77	17,10	-0,667	0,506
	Hasta	60	150,03	30,24		

Bölge	Grup	N	Ort.	ss.	t	p
Nasal	Kontrol	48	104,69	12,13	-0,747	0,456
	Hasta	60	106,82	16,48		
Temporal	Kontrol	48	76,17	8,85	-0,691	0,491
	Hasta	60	78,35	22,37		

Table 10. *Retina Sinir Lifi Dansitesi (RNFL) Ortalamalarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Bölge	Grup	N	Ort.	ss.	t	p
Peripapille	Kontrol	48	114,77	10,83	-0,749	0,456
	Hasta	60	116,55	13,31		
Suphemi	Kontrol	48	114,75	11,43	-0,875	0,384
	Hasta	60	116,75	12,10		
İnfhemi	Kontrol	48	114,85	11,84	-0,801	0,425
	Hasta	60	117,17	16,97		
Superior	Kontrol	48	135,94	17,21	-0,084	0,933
	Hasta	60	136,20	15,09		
İnferior	Kontrol	48	145,10	17,67	-0,064	0,949
	Hasta	60	145,37	23,40		
Nasal	Kontrol	48	102,56	11,11	-1,742	0,084
	Hasta	60	108,20	20,08		
Temporal	Kontrol	48	76,21	8,23	-0,739	0,462
	Hasta	60	78,00	16,38		

Table 11. *Optik Diskte Cup Disk Oranlarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sağ Göz)*

Parametre	Grup	N	Ort.	ss.	t	p
Verticalc/d	Kontrol	48	0,35	0,20	2,715	0,008
	Hasta	60	0,24	0,24		
Horizontalc/d	Kontrol	48	0,30	0,17	2,513	0,013
	Hasta	60	0,21	0,20		

Table 12. *Optik Diskte Cup Disk Oranlarının Hasta ve Kontrol Grubuna Göre Karşılaştırılmasına İlişkin t Testi Sonuçları (Sol Göz)*

Parametre	Grup	N	Ort.	ss.	t	p
Verticalc/d	Kontrol	48	0,31	0,22	1,218	0,226
	Hasta	60	0,26	0,22		
Horizontalc/d	Kontrol	48	0,26	0,19	0,678	0,499
	Hasta	60	0,24	0,19		

temporal, peri. sup. peri. inf.) sub-regionsin the deep layer of the left eye's retina were significantly lower in the experimental 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 ofthe 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-regionsof the deep layer ofthe 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 RNFLvalues in the left eye ($p>0.05$) (Table 10).

It wasfound that the mean vertical cup-disc ratio of the right eye's optic disc in the patient 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 yet, it is considered as 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 disorders.

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 revealed 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 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. [13] 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. [14] reported thinner retinal nerve fiber layer thickness (RSLT) and wider FAZ area in migraine patients. Lower superficial and deeper foveal VDs were found using OCTA but there was no statistically significant difference in parafoveal VDs.

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. [15] 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. [16] reported a thinner RSLT in migraine patients in comparison to the control group. Acer et al. [17] found no significant difference between patients and controls in terms of GCL and macular thickness. Salman et al. [18] also determined thatthere 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 to ischemia [19,20].

Karaca et al. [21] 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 wasdetermined 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 experimental groups during headache-free periods might be because ofthe vasoconstriction originating from the autonomic nervous system dysfunction.

Aoet al. [22] 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 [23] revealed thatthe incidence of low-tension glaucoma in migraine patients was higher and it was attributed to the

narrowing of retrobulbar arteries. Grosberget al. [24] 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. These studies suggest that migraine is not a central but a systemic disease.

Conclusion

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

Ethical approval

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

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