ORIGINAL ARTICLE

Evaluation of Optic Nerve Head Perfusion in Unilateral Full-Thickness Idiopathic Macular Hole: An Optical Coherence Tomography Angiography Study

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ABSTRACT

Purpose: To investigate the perfusion status of the optic nerve head using optical coherence tomography angiography (OCTA) in patients who had an operation for idiopathic macular hole (IMH) and to compare the differences in the blood flow status of the optic nerve head in both eyes of the patients with unilateral IMH with healthy control eyes.

Materials and Methods: The study included patients that underwent surgery with the diagnosis of full-thickness unilateral IMH, with the affected eyes being evaluated as Group 1 and the unaffected eye of the same patients being evaluated as Group 2. A control group (Group 3) was formed with age-matched healthy individuals. In addition to a general ophthalmologic examination, OCTA imaging was performed. Optic disc density and retinal nerve fiber layer (RNFL) measurements were compared between the three groups.

Results: The peripapillary and inferior RNFL measurements were lower in Group 1 compared to Group 3 ($p<0.05$ for both). The optic disc density measurements were lower in Group 1 compared to Group 3 in all areas. However, there was no statistically significant difference between Group 2 and Group 3.

Conclusions: The optic nerve head blood flow density is reduced in IMH, and a decrease in the optic disc vessel density revealed by OCTA can be an early indicator of the development of IMH.

Keywords: Optical coherence tomography angiography, Idiopathic macular hole, Optic disc, Optic nerve.

INTRODUCTION

A macular hole is the localized loss of retinal tissue holding the fovea as a result of tangential vitreoretinal shrinkage.[1] In a full-thickness macular hole, there is loss of retinal tissue in the foveal region from the internal limiting membrane to the retinal pigment epithelium.[2] It has been shown that approximately 87% of full-thickness macular holes are idiopathic macular holes.[3] Reported risk factors for IMH include vitreofoveal traction, axial length, aging, and some hormonal changes.[4-6] However, epidemiological studies have shown that in 11.7% of patients, IMH is seen in both eyes, and in unilateral cases, the estimated risk of IMH formation in the other eye is 12% at five years and 16.9% at 10 years.[7]

Optical coherence tomography angiography (OCTA) is an imaging method that can be applied in ophthalmology to offer detailed visualization of the perfusion of vascular networks in the eye. OCTA presents high-resolution images in a non-invasive manner and in three dimensions based on motion-control contrast-enhanced imaging using the split-spectrum amplitude-decoration angiography algorithm.[8] The major advantage of OCTA is that unlike fundus fluorescein angiography, it separately evaluates capillary plexuses (superficial and deep capillary plexus, and choriocapillaris) and provides quantitative data on capillary non-perfusion areas and density of vascular structures.[9] As a non-invasive technology, OCTA can easily visualize all layers of the retina and vasculature of the optic disc without dye injection.

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In a recent study, Ahn et al.[10] found that the vascular density of the choriocapillaris was lower in surgically closed macular holes than in healthy controls and suggested that variation in choriocapillaris blood flow played a role in the pathogenesis of macular holes. Liu et al.[2] evaluated the relationship between optic nerve head perfusion and macular blood perfusion in patients with a unilateral IMH and revealed that these patients had a decreased optic nerve head vascular density in both eyes and their optic nerve head vascular densities in the parafoveal region had a positive correlation with both hem retinal capillaries and choriocapillaris. A decreased vascular density may be an indicator of hypoperfusion in eyes with IMH. However, the only study in the literature evaluating optic nerve blood supply using OCTA in patients with IMH belongs to Liu et al., who, based on the association of IMH development with hypoxia, emphasized the need to conduct prospective studies on this subject.

In this study, we aimed to investigate the perfusion status of the optic nerve head in patients with full-thickness IMH using OCTA and to compare the differences in the blood flow status of the optic nerve head in both eyes of the patients with unilateral IMH with healthy control eyes.

MATERIALS AND METHODS

Study design

This prospective case-control study was carried out between November 2019 and September 2020 in the ophthalmology clinic of ……... During this period, patients who were those diagnosed with unilateral full-thickness IMH and underwent surgical operation and healthy volunteers were asked to participate in the study. Informed consent was obtained from each participant before commencing the study. After receiving approval from the Ethics Committee, the study was carried out in accordance with the principles of the Declaration of Helsinki. Visual acuity measurement, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, slit lamp biomicroscopic examination, fundoscopy, color fundus photography, optical coherence tomography, and OCTA were performed in all participants in the given order. OCTA scans of eyes operated with IMH were performed 3 months after the ILM peel operation.

Study groups

Patients with full-thickness IMH in one eye and an unaffected other eye were included in the study. The control group was formed with age-matched healthy individuals. The diagnosis of full-thickness IMH was confirmed using the spectral-domain optical coherence tomography (SD-OCT) system (Cirrus, Carl Zeiss Meditec AG, Jena, Germany) and intraoperative observation.

Sixty-seven eyes of 46 participants were included in the study. 21 participants had full-thickness IMH in one eye and constituted the patient group. The control group consisted of 25 healthy volunteers. The eyes with full thickness IMH were evaluated as Group 1, the unaffected eyes of the IMH patients as Group 2, and one eye of the controls as Group 3.

The inclusion criteria for the healthy eyes were as follows: 1) best-corrected visual acuity (BCVA) better than 0.9, 2) IOP ≤ 21 mmHg, 3) axial length ≤ 26 mm, 4) no history of ocular disease, and 5) no history of systemic disease.

The exclusion criteria for all eyes included in the study were as follows: 1) Glaucoma, uveitis, history of retinal disease, retinal surgery or laser treatment, ocular trauma or tumor, poor image quality due to media opacity, or other eye diseases, including unstable eye fixation; 2) age below 40 or over 80 years; 3) a refractive error of greater than -6.00 or +4 diopters; 4) IOP > 22 mmHg; and 5) axial length > 26 mm.

Measurement devices

The Diabetic Retinopathy Early Treatment Trial (ETDRS) scheme was used to test visual acuity and all participants were placed in the same position at the same distance under the same illumination. IOP was measured with the Goldmann applanation tonometer.

The OCTA imaging of all cases was performed with the RTVue-XR Avanti (Optovue, Inc., software V.2015.100.0.33) device equipped with a spectral field system at 840 nm wavelength and 45 nm bandwidth and 70.000 A scanning/sec scanning speed. Using this device, a scanning area of 4.5 mm × 4.5 mm centered on the optical disc was evaluated. The peripapillary region was defined as a 700 μm-wide elliptical ring extending from the optic disc border and divided into six parts: nasal, inferior nasal, inferior temporal, superior nasal, superior temporal, and temporal (Figure 1). All images were measured by the same ophthalmologist, and those with poor quality or a signal strength index below 60 were excluded from the study.

Statistical analysis

All statistical analyses were undertaken using SPSS v. 23.0 (SPSS Inc., IL, United States). Data were expressed as mean ± standard deviation for continuous variables and as percentages for categorical variables. The Shapiro-Wilk test was used to determine the normality. Continuous variables were compared using one-way analysis of variance. Categorical variables and frequencies were compared using the $\chi 2$ test.

RESULTS

Twenty-one IMH patients and 25 healthy controls were included in the study. The mean age of the patient group was 62 ± 5.1 (range 52-75) years, and that of the control group was 60 ± 4.52 (range 51-77) years (p = 0.542). There was no statistically significant difference between Group 1 and Group 3 in terms of gender, age, or axial length (Table 1).

Table 1: *Demographic characteristics of the participants.*

	Group 1	Group 3	P value
Gender (female/male)	11/10	13/12	0.691
Mean age (years)	62.2±5.1	60.4±4.52	0.542
Axial length	23.4±0.94	23.2±0.89	0.754
BCVA LogMAR	0.85±0.26	0.1±0.02	**<0.001**

BCVA: Best-corrected visual acuity; p: independent-samples t-test

The mean IOP was 13.8 ± 2.1 mmHg in Group 1, 14.3 ± 2.2 mmHg in Group 2, and 13.5 ± 2.2 mmHg in Group 3. The mean image quality indices of Groups 1, 2 and 3 were 8.3 ± 0.5, 8.6 ± 0.6 and 8.4 ± 0.7, respectively. There was no statistically significant difference in the mean IOP and image quality index between the three groups (p = 0.625 and p = 0.565, respectively).

Comparison of Optic Nerve Head Values

The same is valid for the next paragraph.statistically significant difference (p = 0.005). The mean disc area was 1.98 ± 0.25 in Group 1 and 2.20 ± 0.32 in Group 3, with a statistically significant difference (p = 0.016). There was no statistically significant difference between Group 2 and Group 3. The mean RNFL-peripapillary thickness was 109 ± 18.87 in Group 1 and 117 ± 11.04 in Group 3, and the difference was significant (p < 0.05). The mean inferior thickness was 132 ± 32.95 in Group 1 and 152 ± 15.76 in Group 3, indicating a significant difference (p < 0.05) (Table 2).

Comparison of Radial Peripapillary Capillary (RPC) Density Values

In Group 1, the mean values of the whole density, intrapapillary density, peripapillary density, peripapillary superior hemisphere density and peripapillary inferior hemisphere density of the superficial vessels of RPC were significantly lower compared to Group 3 (p < 0.01, <0.01, <0.01, <0.05, and <0.01, respectively). There was no statistically significant difference between Group 2 and Group 3. When all RPC segments were evaluated, the mean values for the whole density, intrapapillary density, peripapillary density and peripapillary superior hemisphere density were also significantly lower in Group 1 compared to Group 3 (p < 0.01 for all). Lastly, the temporal and nasal density values were significantly lower in Group 1 than in Group 3 (p < 0.01 and p < 0.05, respectively) (Table 3).

DISCUSSION

In this study, we reported the use of OCTA to evaluate optic nerve head blood supply in unilateral full-thickness IMH. We found that optic disc area and rim area decreased after surgery compared to the healthy eyes. In addition,

Table 2: *Comparison of the RNFL measurements between the groups.*

	Group 1	Group 2	Group 3	P1	P2	P3
C/D area	0.14±0.20	0.15±0.15	0.09±0.09	0.831	0.216	0.190
C/D vertical	0.31±0.29	0.35±0.25	0.26±0.22	0.683	0.432	0.253
C/D horizontal	0.27±0.25	0.28±0.19	0.22±0.19	0.930	0.346	0.311
Rim area	1.70±0.38	1.74±0.36	1.99±0.36	0.712	**0.005**	0.070
Disc area	1.98±0.25	2.06±0.23	2.20±0.32	0.557	**0.016**	**0.250**
Cup volume	0.04±0.10	0.05±0.09	0.02±0.03	0.943	0.173	0.189
RNFL						
-Peripapillary thickness	109.14±18.87	114.24±15.06	117.16±11.04	0.354	**<0.05**	0.490
-Superior thickness	133.34±27.77	134.05±18.64	137.22±7.74	0.853	0.367	0.519
-Temporal thickness	75.26±21.89	80.36±8.39	74.30±11.57	0.295	0.907	0.111
-Inferior thickness	132.04±32.95	140.72±33.19	152.09±15.76	0.376	**<0.05**	0.169
-Nasal thickness	98.21±19.53	102.54±16.17	107.66±18.91	0.683	0.213	0.529

C/D: Cup Disk Ratio; RNFL: Retinal nerve fiber layer; **P1:** Group 1 versus Group 2; **P2:** Group 1 versus Group 3; **P3:** Group 2 versus Group 3

Table 3: *Comparison of optic disc density measurements using OCTA.*

	Group 1	Group 2	Group 3	P1	P2	P3
RPC SV WholeDen	45.14±4.00	48.07±3.39	49.03±2.71	**<0.01**	**<0.01**	0.741
RPC SV intrapapillary Dens	44.32±6.91	47.67±6.97	49.21±5.07	0.146	**<0.01**	0.216
RPC SV peripapillary Dens	48.36±4.75	51.41±4.24	52.16±3.16	**<0.05**	**<0.01**	0.908
RPC SV peripapillary superiorhemiDen	49.23±5.29	52.16±3.14	52.09±3.27	**<0.01**	**<0.05**	0.555
RPC SV peripapillary inferiorhemiDen	48.39±4.36	51.53±5.66	52.26±3.26	0.089	**<0.01**	0.486
RPC All WholeDen	52.74±4.20	54.82±3.88	55.70±2.74	**<0.01**	**<0.01**	0.246
RPC All intrapapillary Den	54.66±6.22	57.67±6.88	59.39±4.27	0.115	**<0.01**	0.161
RPC All peripapillary Dens	54.17±5.02	57.33±4.52	58.43±3.04	**<0.05**	**<0.01**	0.545
RPC All peripapillary superiorhemiDens	55.49±5.72	58.54±3.52	58.60±3.20	**<0.01**	**<0.01**	0.841
RPC All peripapillary inferiorhemiDens	54.73±5.62	56.46±5.97	56.40±9.64	0.088	0.112	0.829
Superior density	51.32±5.98	52.41±4.25	53.37±3.94	0.613	0.202	0.569
Temporal density	48.72±3.72	53.60±1.95	52.83±3.70	**<0.01**	**<0.01**	0.786
Inferior density	50.16±7.13	53.24±8.75	54.34±4.92	0.249	**<0.05**	0.431
Nasal density	46.09±6.87	49.19±6.16	49.27±3.50	0.071	0.075	0.863

RPC: Radial Peripapillary Capillary; SV: Superficial Vessel; WholeDen: Whole Density; Dens: Density P1: Group 1 versus Group 2; P2: Group 1 versus Group 3; P3: Group 2 versus Group 3.

we determined that the peripapillary and lower RNFL thicknesses were statistically significantly reduced in the operated eyes compared to the healthy eyes.

In terms of optic disc densities, when the operated eyes of the IMH patients and the eyes of the healthy subjects were compared, the density of all areas and the superficial and peripapillary densities were statistically significantly decreased in the operated group. Furthermore, these values were lower among the operated eyes of the IMH patients compared to their unaffected eyes at a statistically significant level. From this point of view, hypoperfusion in the optic nerve head may play a role in the development of IMH.

There are several possible causes of decreased blood perfusion in the optic nerve head of patients with IMH. One possible mechanism is decreased optic nerve head blood supply accompanying decreased chorioretinal blood flow in these patients. The rim and disc areas of the patients with IMH being lower compared to the healthy eyes may be due to the thinning of the optic nerve head tissues, leading to a decrease in oxygen demand and a consequent reduction in blood circulation. Another possible mechanism in the development of IMH is systemic hypoxia and/or hypovolemia, which may be effective in reducing the rim and disc areas in the unoperated eyes of IMH patients compared to the healthy controls. Previous studies have shown reduced optic nerve head blood flow in patients with myopia, glaucoma, multiple sclerosis, and central retinal artery occlusion.[11-14] However, the mechanisms of reduced blood flow in eyes with IMH still require further research.

Previous research has revealed that hypoxia may play a role in patients with IMH. Reibaldi et al.[15] evaluated the choroidal layer in patients with IMH using Enhanced depth imaging optical coherence tomography. The authors found that the choroidal thickness was decreased not only in the eyes with IMH but also in the unaffected eyes of these patients. Aras et al.[16] demonstrated that the mean blood flow and velocity were decreased in eyes with stage 4 and stage 1a IMH compared to normal eyes according to retinal flowmeter measurements. Liu et al.[2] found a statistically significant decrease in the RPC vessel density in patients with IMH compared to healthy eyes. In the same study, no statistically significant difference was observed between the affected and unaffected eyes of the patients with IMH in terms of the RPC vessel densities. Although our findings were consistent with those reported by Liu et al., the statistically significant difference we detected between the affected and unaffected eyes of the patients with IMH in relation to the RPC vessel density suggests that different mechanisms other than hypoxia may also be effective in the development of this condition. In these patients, secondary to increased hypoxia, local factors (e.g., hypovolemia) in systemic blood circulation may also have been involved. Consequently, the development of IMH may have been accelerated in affected eyes. Considering that in patients with unilateral IMH, the risk of developing this condition in the other eye within 10 years is 16.9%, there may be similar local factors that become effective in the other eye over time. A possible mechanism may be impaired autoregulation and

increased resistance in the optic nerve head vessels. One of our findings that supports this hypothesis is the decrease in the densities of the peripapillary regions and all RPC areas in the eyes with IMH. The decrease in these values can be used as an indicator for detecting the development of IMH in individuals at risk. However, studies on peripapillary perfusion in eyes with IMH are very limited; therefore, prospective studies on this subject are warranted.

This study was limited by its cross-sectional design since it led to a relatively small number of participants of the same racial background. Therefore, there is a need for longer-term studies with larger samples from a broader age spectrum to offer further insights into ocular changes in patients with IMH.

In conclusion, our study revealed that the optic nerve head blood flow density was decreased in IMH, which could be detected using OCTA. Our study also showed that the decrease in the RPC vessel densities may suggest the presence of hypoperfusion and hypovolemia in eyes with IMH.

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