Microvascular changes in amblyopic eyes detected by optical coherence tomography angiography

Mujdat Karabulut, MD, Sinem Karabulut, MD, Sabahattin Sül, MD, and Aylin Karalezli, MD

PURPOSE To investigate retinal microvascular findings detected by optical coherence tomography angiography (OCT-A) in amblyopic eyes compared with normal eyes.

METHODS A total of 23 amblyopic (strabismic, ametropic, anisometropic, and meridional amblyopia) and 22 normal eyes were included in this prospective observational, comparative study. All patients underwent complete ophthalmological examination and OCT-A imaging. Vessel density (VD) percentage in the superficial and deep retinal vessel plexus, foveal avascular zone (FAZ) area, flow area in the outer retina and choriocapillaris, and retinal thickness in μm in a 6.00 × 6.00 mm scan size were measured and compared between groups.

RESULTS There were no statistically significant differences between groups in terms of age ($P = 0.584$) and sex ($P = 0.661$). Mean FAZ area was smaller in the amblyopic group; however, the difference was not statistically significant ($P = 0.145$). The outer retina flow area was significantly wider in the amblyopic group ($P = 0.03$). The fovea was thicker in the amblyopic group ($P = 0.02$). In addition, VD in both the superficial and deep retinal plexus was significantly lower in amblyopic eyes in all quadrants except the fovea. In amblyopic subgroups, VD of anisometropic amblyopic eyes was significantly higher than other subgroups in both superficial and deep retinal plexuses at all regions except the fovea. Other measures were similar in between groups.

CONCLUSIONS Microvascular retinal structural anomalies detectable on OCT-A could shed further light on the causes of amblyopia. (J AAPOS 2019;23:155.e1-4)

Amblyopia is associated with strabismus (strabismic amblyopia) and unilateral or bilateral blurred retinal image secondary to refractive error or media opacity (anisometropic, ametropic, meridional, and stimulus-deprivation amblyopia). Although it has been reported that amblyopia primarily causes cerebral anatomical alterations in lateral geniculate bodies and the visual cortex, it can also affect retinal layers and vascular structures.[1,2] Optical coherence tomography angiography (OCT-A) is a noninvasive technique that uses motion contrast imaging to obtain high-resolution volumetric blood flow information to generate angiographic images in a matter of seconds. It provides structural and functional information and images both retinal and choroidal microvasculature. Vessel density (VD) in the superficial and deep retinal plexus (Figures 1 and 2), the foveal avascular zone (FAZ; Figure 3), the flow area in the outer retina, and choriocapillaris and retinal thickness can be measured using different scan sizes. The aim of the current study was to examine amblyopic eyes using OCT-A and compare retinal microvascular measurements with healthy, age- and sex-matched control eyes.

Author affiliations: Department of Ophthalmology, Sıtkı Kocman University, Mugla, Turkey

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Correspondence: Mujdat Karabulut, MD, Mğla Sıtkı Koçman Universitesi Tip Fakultesi Hastanesi, Goz Hast, AD 04800 Muğla, Turkey (email: mujdatkarabulut@gmail.com).

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Subjects and Methods

Ethical approval for this prospective study was obtained from the Muğla Sıtkı Koçman University Clinical Research Ethics Committee. Informed consent was obtained from all patients and parents of children <18 years of age. This study included 23 amblyopic eyes of 17 patients 8-26 years of age (4 strabismic, 4 ametropic, 6 anisometropic, and 9 meridional amblyopia) and 22 normal healthy eyes of 11 age- and sex-matched controls. Patients with stimulus deprivation amblyopia, nystagmus, neurological diseases, glaucoma, and diseases such as retinal vascular diseases that can alter OCT-A measurements or individuals who had undergone previous ocular surgery were excluded. The mean age of the amblyopic cohort was 18.78 years; of the controls, 19.73 years.

Subjects received a full ocular examination, including visual acuity, cycloplegic refraction, ocular motility testing, and anterior segment and fundus examination. OCT-A was performed using the Optovue (Optovue, Inc; Fremont, CA) on a 6.00 × 6.00 mm macular region centered on the fovea. The VD (%) in the superficial and deep retinal vessel plexus, FAZ area (mm^2), flow area (mm^2) in the outer retina and choriocapillaris, and retinal thickness (μm) in a 6.00 × 6.00 mm scan size were measured.

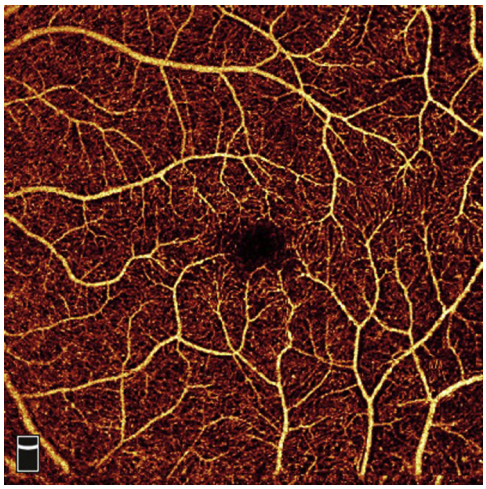

FIG 1. Angio-superficial scan in a 6.00 × 6.00 mm macular scan size.

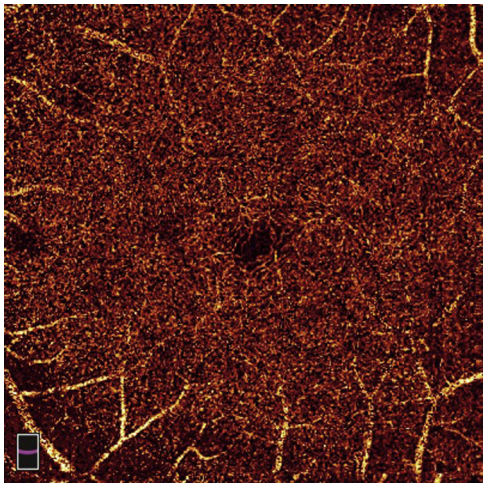

FIG 2. Angio-deep scan in a 6.00 × 6.00 mm macular scan size.

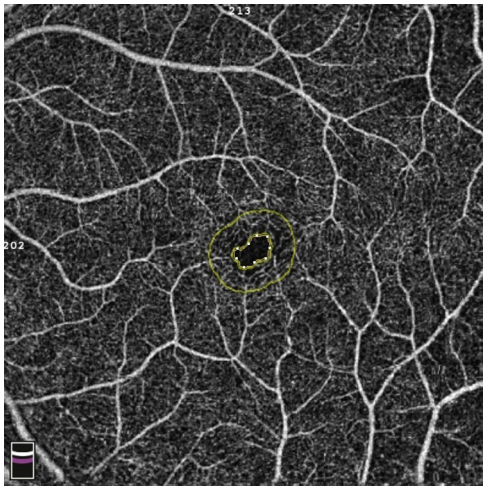

FIG 3. Foveal avascular zone in a 6.00 × 6.00 mm macular scan size.

Table 1. Demographic characteristics and mean best-corrected visual acuity (BCVA)

Characteristic	Amblyopic group (n = 17)	Control group (n = 11)	*P* value
Mean age, years	18.7	19.7	0.58
Sex			0.66
Male	8	5	
Female	9	6	
BCVA, logMAR	0.5	1.0	

BCVA, best-corrected visual acuity.

Table 2. Optical coherence tomography angiography findings and comparison of eyes on a macular 6.00 × 6.00 mm scan

Macular trait	Amblyopic eyes (n = 23)	Control eyes (n = 22)	*P* value
FAZ area, mm^2	0.250	0.300	0.14
Outer retina flow area, mm^2	0.986	0.613	0.03
Foveal thickness, μm	248	236	0.02

FAZ, foveal avascular zone.

Table 3. Vessel density on a macular 6.00 × 6.00 mm scan

	Density (%)		
Retinal plexus	Amblyopic eyes (n = 23)	Control eyes (n = 22)	*P* value
Superficial			
Whole image	48.2	60.9	<0.05
Parafovea	50.5	78.3	<0.05
Perifovea	48.7	53.2	<0.05
Fovea	22.1	20.9	0.65
Deep			
Whole image	49.7	59.4	<0.05
Parafovea	56.2	61.8	<0.05
Perifovea	50.5	60.9	<0.05
Fovea	39.1	38.7	0.89

All of the data were analyzed using SPSS version 21.0.0.0 software (IBM Corp Armonk, NY, 2012). Comparisons between amblyopic and normal healthy eyes were performed using an independent-samples *t* test, comparisons of amblyopic subgroups were performed using Kruskall Wallis test. A *P* value of <0.05 was considered statistically significant.

Results

There were no statistically significant differences in terms of age ($P = 0.584$) or sex ($P = 0.661$) between the two groups. The mean best-corrected visual acuity was 0.5 logMAR in the amblyopic eyes and 1.0 logMAR in the control eyes (Table 1). The mean FAZ area was 0.250 mm^2 and 0.300 mm^2 in the amblyopic and control eyes, respectively ($P = 0.145$). The outer retina flow area was 0.986 mm^2 and 0.613 mm^2 in the amblyopic and control eyes, respectively ($P = 0.03$). Despite these differences in the outer retina, there were no statistically significant differences in the choriocapillaris flow area. The foveal thickness was 248 μm

Table 4. The mean VD, FAZ area, foveal thickness, and outer retina flow area in the amblyopic subgroups

Macular trait	Strabismic (n = 4)	Anisometropic (n = 6)	Meridional (n = 9)	Ametropic (n = 4)	*P* value
Density (%)					
Superficial					
Whole image	50.9	52.5	45.1	46.4	0.011
Parafovea	53.7	55.1	46.7	48.9	0.048
Perifovea	51.5	52.7	45.4	47.2	0.021
Fovea	21.7	25.1	18.5	26.4	0.649
Deep					
Whole image	52.5	56.4	47.0	42.8	0.007
Parafovea	59.2	60.2	54.8	50.4	0.021
Perifovea	54.4	57.9	47.2	43.1	0.007
Fovea	44.0	40.6	37.1	35.9	0.055
FAZ area, mm^2	0.195	0.248	0.270	0.261	0.284
Foveal thickness, μm	255	246	249	234	0.185
Outer retinal flow area, mm^2	1.129	0.629	0.986	1.364	0.064

FAZ, foveal avascular zone; *VD*, vessel density.

and 236 μm in the in the amblyopic and control eyes, respectively ($P = 0.02$; Table 2). The VD in both superficial and deep retinal plexus was significantly lower in the amblyopic eyes in all quadrants except the fovea (Table 3). The mean FAZ and outer retinal flow area and foveal thicknesses were similar in amblyopic subgroups (Table 4). The mean VD of anisometropic amblyopic eyes was significantly higher than other subgroups in both superficial and deep retinal plexuses at all regions except fovea (Table 4).

Discussion

Amblyopia is caused by the abnormal development of the visual cortex arising from several factors, including strabismus, blurred vision from refractive error, or visual deprivation.[3] Although visual deprivation can result in a decrease in cell size in the lateral geniculate body in human and animals models,[4-6] evidence of direct retinal changes in amblyopic eyes is inconclusive. Some investigators have reported increased peripapillary retinal nerve fiber layer (cpRNFL) and macular thickness[7-9] using OCT in amblyopic eyes compared with healthy eyes; others have found no significant differences.[10,11]

Some investigators have reported retinal microvascular changes in amblyopic eyes detected on OCT-A. Lonngi and colleagues[12] reported that OCT-A revealed subnormal results in both superficial and deep retinal capillary density in the macula of patients with amblyopia. The macular VD of both the superficial and deep capillary plexus were significantly lower in the amblyopic group than in the control group as shown on 6.00 × 6.00 mm scans.

Yılmaz and colleagues[13] designed a study to quantify the VD of the superficial capillary plexus (SCP), deep capillary plexus (DCP), and FAZ of amblyopic eyes in children and to compare the measurements with those of healthy eyes and age-matched controls. Although there was no significant difference in FAZ among groups, the VD of the SCP and DCP of eyes with amblyopia was significantly lower than those of control eyes.

The present study found a mean FAZ of 0.250 mm^2 and 0.300 mm^2 in amblyopic and control eyes, respectively. Although the mean FAZ area was smaller in the amblyopic group, the difference was not statistically significant. The VD in both the SCP and DCP were significantly lower in amblyopic eyes in all quadrants except the fovea, which is avascular.

Macular thickness measured with OCT in different types of amblyopia has been reported with inconsistent results. Most recent studies have shown that amblyopic eyes have anomalous maculae.[9] Increased macular thickness and decreased foveal depression have been reported in amblyopic patients assessed using OCT.[14,15] This finding may be related to the lack of some cells on the macula flava, such as rods, short-wavelength-sensitive cones, blue-cone bipolar cells, astrocytes, and microglial cells, which normally occur shortly after birth in healthy infants.[15,16] Dickmann and colleagues[17] reported that macular thickness in amblyopic eyes was greater than in normal companion eyes on OCT.

On the other hand, some studies have failed to find a significant relationship between macular thickness and amblyopia. Kee and colleagues[15] found no significant difference between foveal thickness in amblyopic and nonamblyopic eyes. Wang and Taranath[18] reported no significant differences in central macular thickness or macular volume between amblyopic and companion eyes in 14 subjects with hyperopic anisometropic amblyopia. In our study, the mean foveal thickness was 248 μm and 236 μm in amblyopic and control eyes, respectively. Thus, the mean fovea in amblyopic eyes was significantly thicker than in the controls ($P = 0.02$).

Flow area measurements quantify an area of vascularization in a user-defined region of interest. OCT-A reveals flow in the vascular structures of the segmented volume. Flow is important for the study and follow-up of vessel progression and regression in neovascular membranes and

proliferative retinopathies. In our study, the mean outer retina flow area was significantly larger in amblyopic eyes than in control eyes (0.986 mm^2 vs 0.613 mm^2 [$P = 0.03$]). On the other hand, the choriocapillary flow area was almost equal in both groups.

We also compared the amblyopic subgroups. We did not find any significant difference between subgroups in terms of FAZ, outer retinal flow area, and foveal thickness. However, the anisometropic subgroup showed higher VD rates than other subgoups in all regions except the fovea. Due to the smaller number of patients in subgroups, we are unable to comment on the significance.

This study has several limitations. The number of subjects was small, and subgroup comparisons are sometimes inaccurate. We also cannot exclude the possibility that changes in the FAZ were due to different-sized eyes (eg, as in anisometropic amblyopia, wherein one eye is hyperopic and therefore smaller). Further studies should help to clarify the validity of our findings.

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