EJO European Journal of Ophthalmology

Original research article

European Journal of Ophthalmology
2021, Vol. 31(6) 3124–3132

DOI: 10.1177/1120672121990562
journals.sagepub.com/home/ejo
SAGE

Optical coherence tomography angiography findings of diabetic patients with and without retinopathy

Emine Temel[1] and Figen Batıoğlu[2]

Abstract

Purpose: To emphasize the importance of optical coherence tomography angiography (OCTA) in the diagnosis and follow-up of diabetic individuals with and without retinopathy.

Methods: Retrospective, cross-sectional, observational study of healthy persons and diabetic individuals with and without retinopathy. Area of the foveal avascular zone (FAZ) (mm^2), non-perfused areas in the superficial capillary plexus (SCP), mean vessel density (VD) in the SCP, and deep capillary plexus (DCP) were calculated. In eyes with diabetic retinopathy (DR), measurements at baseline, 3rd, 6th, 9th, and 12th months were evaluated.

Results: This study conducted on 39 eyes of 23 patients with DR (group 1), 59 eyes of 30 diabetic individuals without DR (group 2), and 51 eyes of 27 healthy persons (group 3). When the mean area of the FAZ at baseline was compared between groups, the difference among groups 1 and 3 ($p < 0.001$) and the difference among groups 2 and 3 ($p = 0.001$) were statistically significant. There was no significant difference among the measurements of mean area of the FAZ, mean non-perfused area in the SCP, mean VD in SCP, and DCP at baseline, 3rd, 6th, 9th, and 12th months in group 1.

Conclusion: OCTA is a developing technology that can detect early microvascular changes in diabetic patients.

Keywords

Diabetic retinopathy, optical coherence tomography angiography, foveal avascular zone

Date received: 19 August 2020; accepted: 30 December 2020

Introduction

Diabetes mellitus (DM) is characterized by hyperglycemia caused by defects in insulin secretion, action, or both. In recent years, it has become an increasingly important health problem all over the world. According to the data published by the World Health Organization in 2016, there are almost 422 million DM patients worldwide; this number is expected to reach 750 million in 2030.[1]

One of the most significant causes of vision loss between the ages of 20 and 75 is diabetic retinopathy (DR).[2] The most important factor in the occurrence of DR is the duration of the disease. While the DR rate is 20% in 10-year-old diabetic patients, this rate rises to 85% in 25-year-old diabetic patients.[3,4] As the number of diabetic patients with retinopathy is expected to increase, more research is needed on diagnostic methods that allow early detection of microvascular changes and evaluate the effectiveness of treatment.

A standard screening test for DR is a biomicroscopic dilated fundus examination. While performing an eye examination is recommended 5 years after the onset of diabetes in type 1 DM, retinopathy may have already developed when the diagnosis is made in type 2 DM. Therefore, a detailed eye examination is recommended as soon as type 2 DM is diagnosed. Methods like optical coherence tomography (OCT), fluorescein angiography (FA) are significant in categorizing DR severity in the

[1]Department of Opthalmology, Kırşehir Ahi Evran Training and Research Hospital, Kırşehir, Turkey
[2]Department of Ophthalmology, Ankara University Faculty of Medicine, Ankara, Turkey

Corresponding author:
Emine Temel, Department of Ophthalmology, Kırşehir Ahi Evran Training and Research Hospital, Kırşehir, Turkey.
Email: emine912@hotmail.com

clinic; however, these are subjective methods and may be inadequate to display some clinically important minimal microvascular changes in capillaries. FA is a gold standard imaging method for showing retinal vascular pathologies such as microaneurysms, retinal edema, impaired macular perfusion, venous beading, and intraretinal microvascular abnormalities. However, since it is an invasive method that requires intravenous contrast agent use, there are some side effects that limit the use of FA in patients with DR. Optical coherence tomography (OCT) is a non-invasive tool that provides micrometer-level axial resolution in cross-sectional imaging of the retina and has been clinically adopted as the standard to observe structural changes of diabetic retinopathy.[5] OCT provides an assessment of both qualitative (diabetic macular edema pattern, presence of cysts, localization of fluid, integrity, and reflectivity of the retinal outer layers) and quantitatively (macular volume, central retinal thickness (CRT)). The inability to distinguish DR-related changes in the retinal vascular structure (especially peripheral ischemia) is the limitation of OCT.

Optical coherence tomography angiography (OCTA) is a non-invasive technology that has revolutionized the imaging of the retinal and choroidal microvasculature.[6,7] This technology is based on the detection of the movement of red cells in sequential OCT scans. This technique is oversensitive to minor eye movements and requires patient cooperation to maintain fixation. The introduction of eye trackers and improved software protocols have significantly improved these problems.[8,9]

In eyes with DR, the high-resolution microvascular detail provided by OCTA allows the foveal avascular zone (FAZ) to be more easily identified and capillary changes can be detected even in the early stages.[10,11] With OCTA, capillary non-perfuse areas, intraretinal microvascular abnormalities (IRMA), retinal neovascularization (NVE), and disc neovascularization (NVD) can be displayed in higher resolution and in greater detail than FA.[12,13] OCTA also provides 3D images of the retinal and choroidal microvascular structure and vascular mapping of macular perfusion.[13,14] Moreover, while OCTA allows superficial capillary plexus (SCP) and deep capillary plexus (DCP) to be viewed separately, DCP cannot be imaged with FA.[15]

DM-related pathologic changes on OCTA have been extensively described.[16–18] The main feature of our study was not only evaluating the OCTA parameters in diabetic patients with and without retinopathy and the control healthy persons but also evaluating the DR stage and HbA1c levels at 3-month intervals for 1 year and comparing all data between the groups.

Methods

We retrospectively reviewed 39 eyes of 23 patients with non-proliferative DR (NPDR) (group 1), 59 eyes of 30 diabetic patients without DR (group 2). 51 eyes of 27 healthy persons (group 3) were included in the study as a control group. Information about demographic characteristics of patients, type of diabetes, duration of diabetes, and HbA1c values was obtained from clinical records. The criteria for exclusion from the study were determined as additional retinal diseases like retinal vascular occlusive disease, hypertensive retinopathy, central serous chorioretinopathy, age-related degeneration of the macula, presence of diabetic macular edema, previous intraocular surgery or retinal laser photocoagulation, previous intravitreal injection, glaucoma, and optic neuropathy.

Best-corrected visual acuity (BCVA), biomicroscopic anterior segment examination, and dilated fundus examination records were evaluated. Patients with DR findings were classified as mild NPDR, moderate NPDR, and severe NPDR according to the classification made by the "Early Treatment Diabetic Retinopathy Study Group" based on the Modified Airlie House classification. Our study was performed in adherence to the tenets of the Declaration of Helsinki and was approved retrospectively by our institutional review board.

In the AngioVue OCTA software used in our clinic, the split spectrum amplitude-decorrelation angiography (Split Spectrum Amplitude Decorrelation Angiography-SSADA) is used together with Spectral domain-OCT, the wavelength in this system is 70 kHz 840 nm. This system detects movement in the vascular lumen by measuring changes in the OCT signal amplitude between consecutive sectional scans. This algorithm performs consecutive OCT scans and compares each OCT scan to the next one. For this reason, OCTA provides information on both structural and vascular changes. Thanks to the SSADA algorithm, high-quality vascular images can be obtained in a short time with the AngioVue imaging system. The highest quality OCTA images available today are obtained with this algorithm. In addition, automatic segmentation of SCP and DCP, outer retina, and choriocapillaris can be performed with an automated software option of OCTA.

CRT measurements were performed with Spectral domain-OCT. 6×6 mm OCTA images using AngioVue OCTA software (RTVue XR Avanti, Optovue, Inc., Fremont, CA) were evaluated, and the mean area of the FAZ (mm^2) (Figure 1), non-perfused areas in the SCP (mm^2) (Figure 2), mean vessel density (VD) in the superior, inferior, temporal and nasal quadrants in SCP and DCP in the parafoveal and perifoveal region (%) were calculated (Figures 3 and 4). In patients with DR, BCVA, fundus examination, Spectral domain-OCT, and OCTA images were evaluated at the baseline, 3rd, 6th, 9th, and 12th months. OCTA imaging was performed only once in groups 2 and 3.

The evaluated parameters were compared statistically among all groups. The analysis of the data was done in IBM SPSS 11.5 (SPSS Inc., Chicago, IL, USA) program.

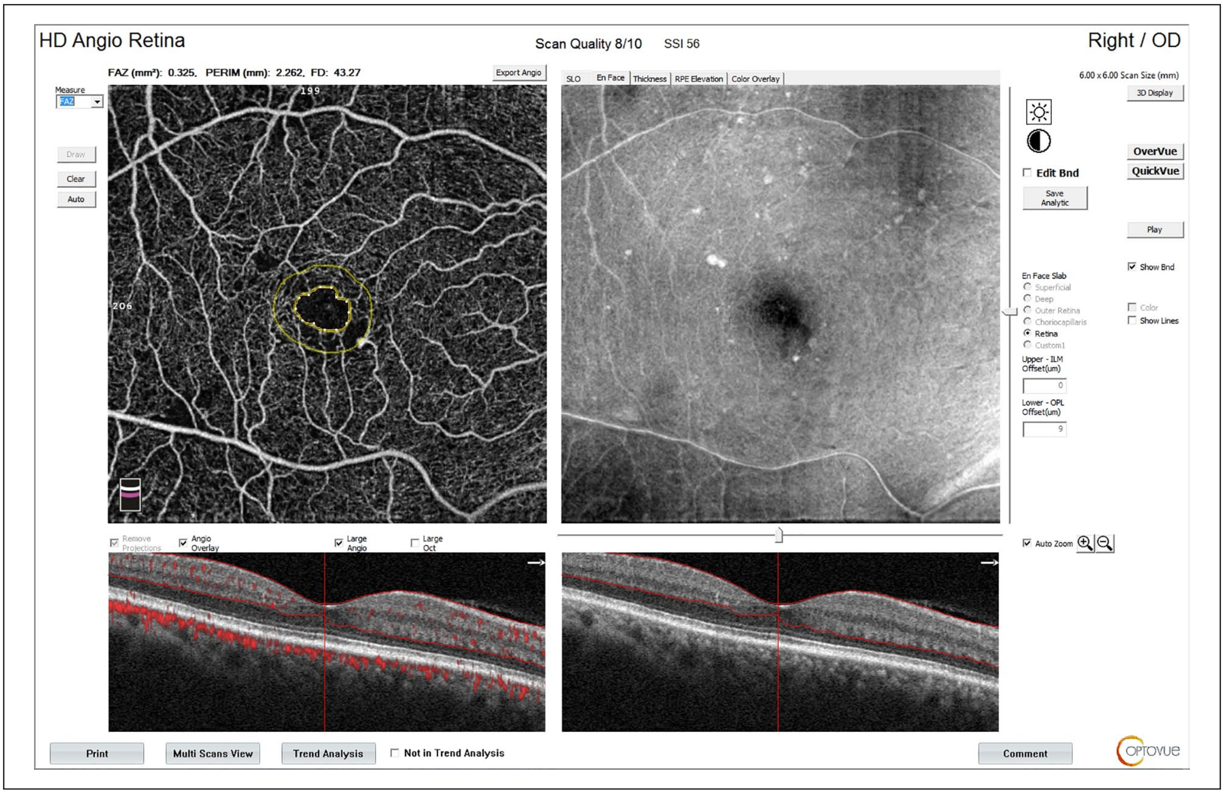

Figure 1. FAZ area measurement of the retina using 6 × 6-mm OCTA scan.

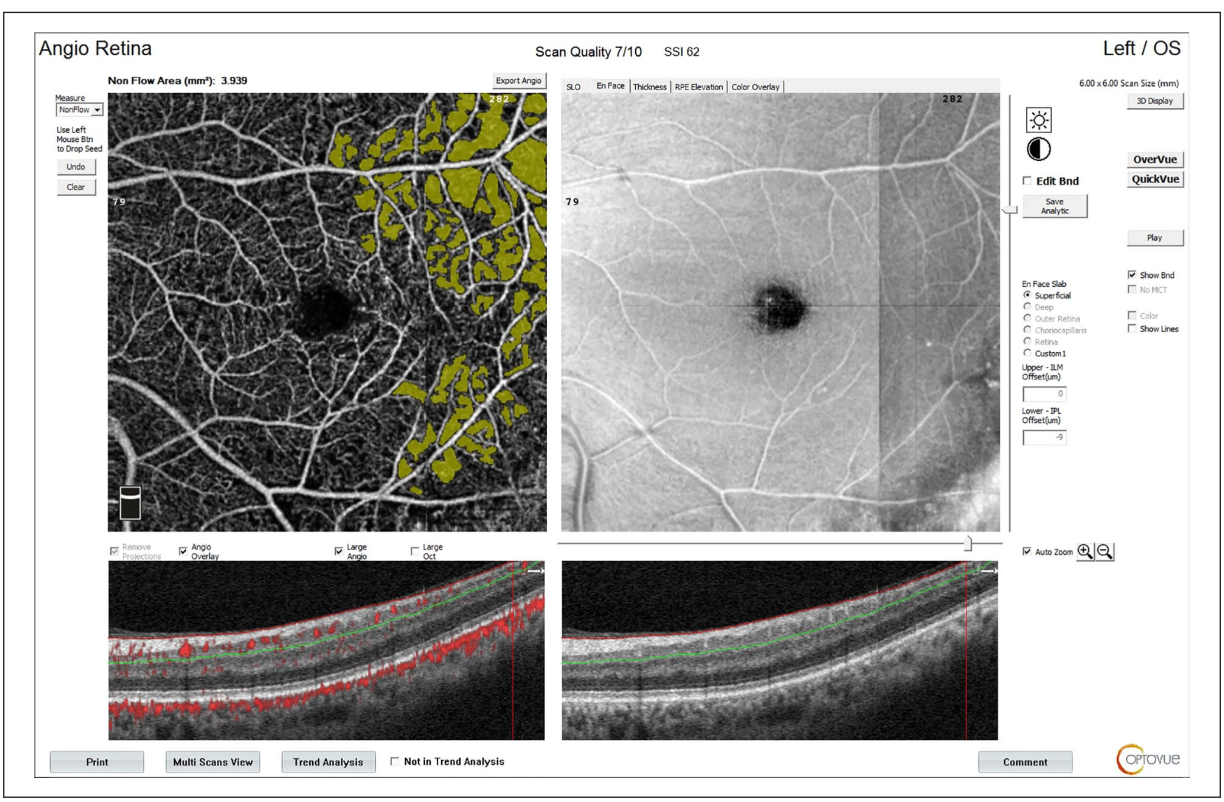

Figure 2. Quantitative measurement of non-perfused areas in SCP using 6 × 6-mm OCTA scan.

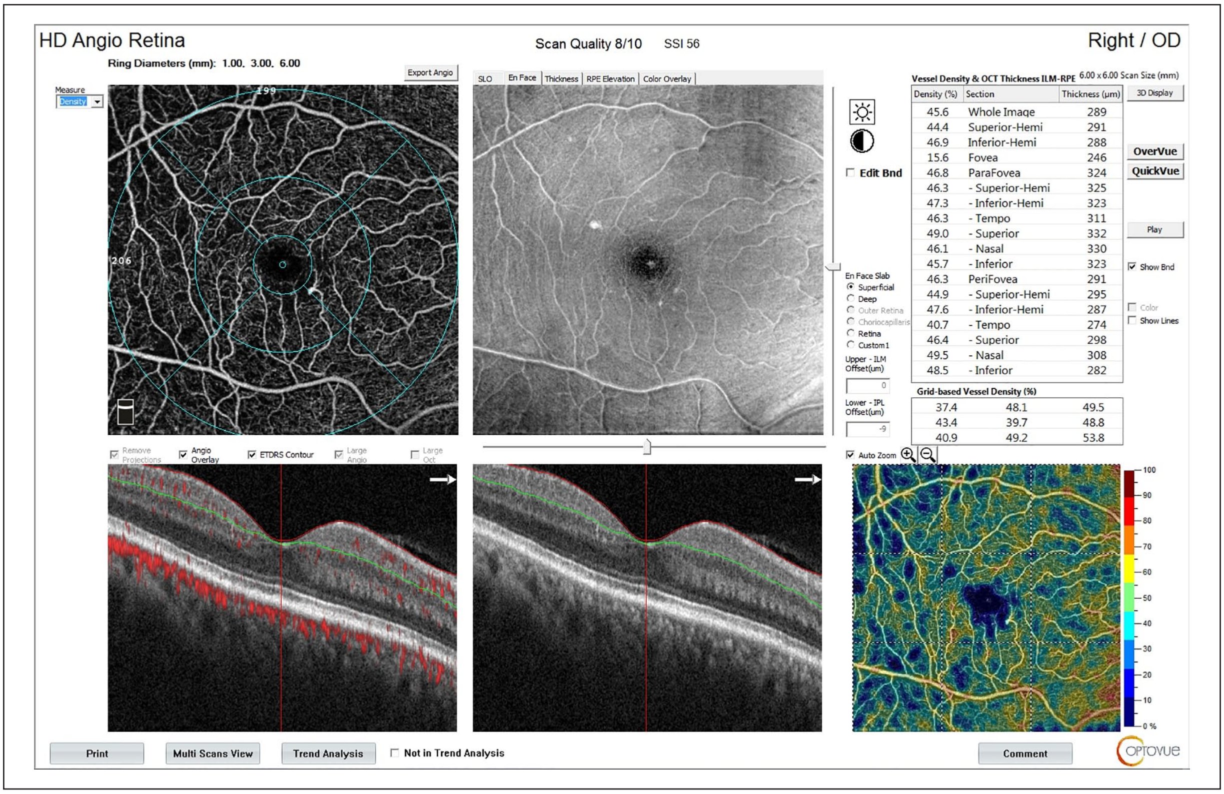

Figure 3. Parafoveal and perifoveal mean VD measurement in SCP using 6 × 6-mm OCTA scan.

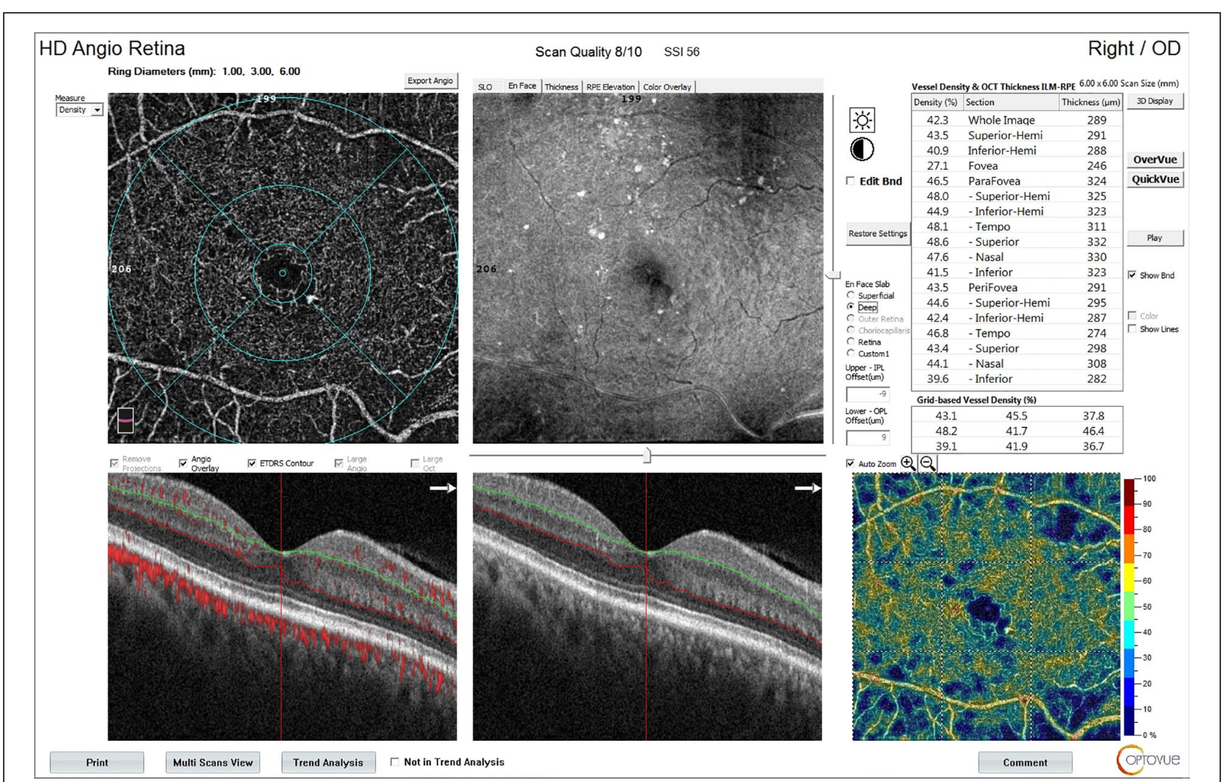

Figure 4. Parafoveal and perifoveal mean VD measurement in DCP using 6 × 6-mm OCTA scan.

Table 1. Demographic and clinical data of the cases included in the study.

	Group 1	Group 2	Group 3	*p* values Anova/Kruskal–Wallis
Number of patients	23	30	27	
Number of eyes	39	59	51	
Mean age	54.2 ± 10.2	52.6 ± 14.4	47.8 ± 12.0	0.062
Male/Female	13/10	14/16	14/13	0.077
Diabetes mellitus type (Type 1/Type 2)	3/20	4/26		1.000
Average DM duration (years)	13.51 ± 4.4	12.5 ± 13.3		0.053
Average HbA1c	9.6% ± 1.5%	8.4% ± 1.8%	4.2% ± 0.3%	0.005*

DM: diabetes mellitus.
*Statistically significant *p* value.

Descriptive statistics were defined as mean ± standard deviation for variables with normal distribution, median (min-max) for non-distributed variables, and the number of cases (%) for nominal variables. When the number of groups was three, the significance of the difference among the groups was investigated by the One Way Variance Analysis/Kruskal Wallis test. In groups with differences, binary comparisons were made to evaluate which groups the difference originated from. Measurements applied to patients at different times were evaluated with Variance Analysis by Repetitive Measurements. When the difference was found, it was evaluated from which time points the difference originated with binary comparisons. Results for $p < 0.05$ were considered statistically significant.

Results

The study included 39 eyes of 23 patients with DR (group 1), 59 eyes of 30 diabetic patients without DR (group 2), and 51 eyes of 27 healthy persons (group 3). There were 10 (43.5%) female and 13 (56.5%) male in group 1; 16 (53.3%) female and 14 (46.7%) male in group 2. Of the control group, 13 (48.1%) were female and 14 (51.9%) were male. Mean age was 54.2 ± 10.2 years in group 1, 52.6 ± 14.4 years in group 2, and 47.8 ± 12.0 years in group 3.

In group 1, 3 cases had type 1 and 20 cases had type 2 DM; in group 2, 4 cases had type 1, 26 cases had type 2 DM. The mean duration of DM was 13.51 ± 4.4 years in group 1, and 12.5 ± 13.3 years in group 2. Mean HbA1c was 9.6% ± 1.5 in group 1, 8.4% ± 1.8 in group 2, and 4.2% ± 0.3 in group 3. The demographic and clinical data of the patients and statistical comparisons can be seen in Table 1.

Of the 39 eyes in group 1, 18 had mild NPDR, 19 had moderate NPDR and 2 had severe NPDR. Since the distribution among groups was not homogeneous in DR classification, comparisons between HbA1c levels and DR stage were made between mild and moderate NPDR groups. HbA1c levels were higher in the moderate NPDR group than the mild NPDR group, however, it was not statistically significant ($p = 0.492$).

The mean BCVA was 0.9 (1.0–0.15) at baseline in group 1. The BCVA of all eyes in groups 2 and 3 was 1.0 at baseline. The mean CRT was 275.3 ± 25.7 ± µm in group 1, 221.1 ± 10.3 ± µm in group 2, and 220.3 ± 20.3 ± µm in group 3 ($p < 0.001$). The difference between group 1 and group 2 ($p < 0.001$) and group 1 and group 3 ($p < 0.001$) were statistically significant. The mean area of the FAZ was 0.326 ± 0.1 mm² in group 1, 0.297 ± 0.1 mm² in group 2, and 0.230 ± 0.1 mm² in group 3 ($p = 0.001$). The difference between group 1 and group 3 ($p < 0.001$) and group 2 and group 3 ($p = 0.001$) were statistically significant. The mean non-perfused area measurement in the SCP was 2.63 ± 0.1 mm² in group 1, 0.894 ± 0.5 mm² in group 2, and 0.158 ± 0.1 mm² in group 3 ($p = 0.001$). The difference between group 1 and group 3 ($p < 0.001$), group 2 and group 3 ($p = 0.001$), and group 1 and group 2 ($p = 0.001$) were statistically significant. Mean VD in the SCP in the parafoveal region was 49.6 ± 4.9 in group 1, 51.4 ± 3.9 in group 2, and 52.7 ± 2.3 in group 3 ($p < 0.001$). The difference between group 1 and group 3 ($p < 0.001$) and group 1 and group 2 ($p = 0.001$) were statistically significant. Mean VD in the DCP in the parafoveal region was 50.9 ± 4.0 in group 1, 52.28 ± 4.3 in group 2, and 54.27 ± 2.7 in group 3 ($p < 0.001$). The difference between group 1 and group 3 ($p < 0.001$), group 2 and group 3 ($p = 0.024$), and group 1 and group 2 ($p = 0.002$) were statistically significant. Mean VD in the SCP in the perifoveal region was 48.9 ± 3.1 in group 1, 49.39 ± 3.3 in group 2, and 50.74 ± 2.3 in group 3 ($p = 0.008$). The difference between group 1 and group 3 ($p = 0.006$) was statistically significant. Mean VD in the DCP in the perifoveal region was 48.10 ± 4.6 in group 1, 48.73 ± 7.8 in group 2, and 51.58 ± 4.07 in group 3 ($p = 0.001$). The difference between group 1 and group 3 ($p = 0.001$) was statistically significant. Baseline measurements of the patients and statistical comparisons are shown in Table 2.

In group 1, there was no change in the DR stage during the 1-year follow-up. In these eyes, measurements at baseline,

Table 2. Mean values at initial examination.

	Group 1	Group 2	Group 3	*p* values: ANOVA/Kruskal–Wallis	Comparisons between groups: Group 1 versus Group 3	Group 2 versus Group 3	Group 1 versus Group 2
BCVA (ETDRS)	0.9	1.0	1.0	1.000	=1.000	=1.000	=1.000
CRT (μm) Mean ± SD	275.3 ± 25.7	221.1 ± 10.3	220.3 ± 20.3	<.001*	<.001*	=.106	<.001*
FAZ area (mm^2) Mean ± SD	0.326 ± 0.1	0.297 ± 0.1	0.230 ± 0.1	=.001*	<.001*	=.001*	.727
Non-perfused area (mm^2) (SCP) Mean ± SD	2.63 ± 0.1	0.894 ± 0.5	0.158 ± 0.1	=.001*	<.001*	=.001*	=.001*
Parafoveal mean VD (%) (SCP) Mean ± SD	49.6 ± 4.9	51.41 ± 3.9	52.72 ± 2.3	<.001*	<.001*	.226	=.001*
Parafoveal mean VD (%) (DCP) Mean ± SD	50.9 ± 4.0	52.28 ± 4.3	54.27 ± 2.7	<.001*	<.001*	=.024*	=.002*
Perifoveal mean VD (%) (SCP) Mean ± SD	48.9 ± 3.1	49.39 ± 3.3	50.74 ± 2.3	=.008*	=.006*	.312	.318
Perifoveal mean VD (%) (DCP) Mean ± SD	48.10 ± 4.6	48.73 ± 7.8	51.58 ± 4.1	.001*	=.001*	.076	.324

BCVA: best corrected visual acuity; SD: standart deviation; FAZ: foveal avascular zone; SCP: superficial capillary plexus; DCP: deep capillary plexus; VD: vessel density.
*Statistically significant *p* value.

3rd, 6th, 9th, and 12th months were evaluated and statistically analyzed (Table 3). The mean BCVA was 0.9 (1.0–0.15) at baseline, 3rd, 6th, 9th, and 12th months. The mean CRT was 275.3 ± 25.72 ± μm, 276.0 ± 26.4 ± μm, 274.8 ± 24.5 ± μm, 275.8 ± 25.5 ± μm, and 275.8 ± 25.8 ± μm at baseline, 3rd, 6th, 9th, and 12th months respectively. There was no statistically significant difference (p=0.894) between the groups in terms of mean BCVA. The mean area of the FAZ was 0.326 ± 0.1 mm^2, 0.325 ± 0.1 mm^2, 0.328 ± 0.1 mm^2, 0.327 ± 0.1 mm^2, and 0.326 ± 0.1 mm^2 at baseline, 3rd, 6th, 9th, and 12th months respectively. There was no statistically significant difference (p=1.000) between the groups at different visits. The mean non-perfused area in the SCP was 2.62 ± 0.08 mm^2, 2.81 ± 0.9 mm^2, 2.72 ± 1.2 mm^2, 2.72 ± 1.3 mm^2, and 2.72 ± 1.1 mm^2 at baseline, 3rd, 6th, 9th, and 12th months respectively. There was no statistically significant difference between the groups at different visits (p=0.621). Mean VD in the parafoveal region was 49.6 ± 4.9, 47.66 ± 4.1, 48.12 ± 3.9, 48.72 ± 3.0, and 49.12 ± 3.8 at SCP at baseline, 3rd, 6th, 9th, and 12th months, respectively; in DCP, it was 50.9 ± 4.0, 51.48 ± 4.4, 51.28 ± 4.5, 51.78 ± 3.5, and 51.08 ± 4.0. No statistically significant difference was found in the sequential comparison of SCP and DCP measurements (p=0.512 and p=0.618, respectively). Mean VD in the perifoveal region was 48.9 ± 3.1, 47.39 ± 3.1, 47.61 ± 3.1, 48.51 ± 3.0, and 48.91 ± 3.1 at SCP at baseline, 3rd, 6th, 9th and 12th months, respectively; In DCP, it was 48.10 ± 4.6, 48.35 ± 4.8, 49.01 ± 5.2, 49.20 ± 4.2, and 49.01 ± 4.2. No statistically significant difference was found in the sequential comparison of SCP and DCP measurements (p=0.521 and p=0.412, respectively).

Discussion

Diabetes Mellitus is a metabolic disorder that causes microvascular complications and is becoming more and more common. DR is known as one of the preventable causes of vision loss. The standard screening test for DR in clinical practice is the fundus examination performed with a 90D non-contact lens after pupil dilation. Methods such as OCT, FA are important in categorizing DR severity; however, these are subjective methods and may be inadequate to display some clinically important minimal microvascular changes in capillaries. FA, which is an invasive imaging method using intravenous contrast agent, is currently accepted as the gold standard imaging method in the evaluation of the diagnosis, follow-up and treatment response of DR. It is important that FA can demonstrate the blood-retinal barrier pathology, that both posterior pole and peripheral retina can be visualized during the procedure, and that there is little tendency for the artifacts. Its most obvious advantage is that it can dynamically show leakage from vascular structures. However, the images obtained are two-dimensional and DCP cannot be evaluated because of diffuse hyperfluorescence due to vascular

Table 3. Mean values at initial examination, 3rd, 6th, 9th, and 12th months in group 1.

	Initial examination	3rd months	6th months	9th months	12th months
HbA1c (%)	9.6 ± 1.5	9.1 ± 1.8	9.3 ± 1.5	9.4 ± 0.9	9.5 ± 1.2
BCVA (ETDRS)	0.9 (1.0–0.15)	0.9 (1.0–0.15)	0.9 (1.0–0.15)	0.9 (1.0–0.15)	0.9 (1.0–0.15)
CRT (μm) Mean ± SD	275.3 ± 25.72	276.0 ± 26.4	274.8 ± 24.5	275.8 ± 25.5	275.8 ± 25.8
FAZ area (mm²) Mean ± SD	0.326 ± 0.1	0.325 ± 0.1	0.328 ± 0.1	0.327 ± 0.1	0.326 ± 0.1
Non-perfused area (mm²) (SCP) Mean ± SD	2.62 ± 0.08	2.81 ± 0.9	2.72 ± 1.2	2.72 ± 1.3	2.72 ± 1.1
Parafoveal mean VD (%) (SCP) Mean ± SD	49.6 ± 4.9	47.66 ± 4.1	48.12 ± 3.9	48.72 ± 3.0	49.12 ± 3.8
Parafoveal mean VD (%) (DCP) Mean ± SD	50.9 ± 4.0	51.48 ± 4.4	51.28 ± 4.5	51.78 ± 3.5	51.08 ± 4. 0
Perifoveal mean VD (%) (SCP) Mean ± SD	48.9 ± 3.1	47.39 ± 3.1	47.61 ± 3.1	48.51 ± 3.0	48.91 ± 3.1
Perifoveal mean VD (%) (DCP) Mean ± SD	48.10 ± 4.6	48.35 ± 4.8	49.01 ± 5.2	49.20 ± 4.2	49.01 ± 4.2

BCVA: best corrected visual acuity; CRT: central retinal thickness; SD: standart deviation; FAZ: foveal avascular zone; SCP: superficial capillary plexus; DCP: deep capillary plexus; VD: vessel density.

leakage and staining. It is also a time-consuming method, and its mild side effects against intravenous contrast agents, as well as very serious side effects that can lead to anaphylactic shock and death, have brought some limitations to its clinical use.

OCTA has taken its place in clinical practice in recent years, and since it is not an invasive method, it does not cause side effects counted for FA in diabetic patients.[6] It also has advantages such as repeatability and completion of shooting in a short time. It is a non-invasive imaging method that creates three-dimensional, detailed images of blood flow using the intrinsic motion contrast of erythrocytes. With this technique, some early microvascular changes that cannot be seen in biomicroscopic dilated fundus examination can be detected in diabetic patients. In eyes with DR, the high-resolution details provided by OCTA allow microvascular changes to be detected in more detail. OCTA does not show patterns of vascular leakage, staining, and pooling. Although this feature can be interpreted as a disadvantage, microvascular structures can be displayed in higher quality and in detail because they cannot be masked by hyperfluorescence. With OCTA, microaneurysms, capillary non-perfused areas, dilatation of retinal capillaries, enlargement in the mean area of the FAZ, retinal neovascularization can be defined. Even if DR findings are not noticed in the clinical examination, early microvascular changes such as telangiectasia, capillary loop formation, broad and irregular area of the FAZ can be displayed in OCTA. In addition, OCTA can display SCP and DCP in separate layers owing to its segmentation feature different from FA.

We determined that the mean area of the FAZ in diabetic patients with and without retinopathy was significantly higher than the controls. In accordance with our findings, Hwang et al.[19] found that the area of the FAZ and total avascular zone area were significantly higher in eyes with DR than in the control group. In the study of Conrath et al.,[20] microvascular changes in FAZ in eyes with DR were evaluated and the results were compared with healthy persons. It was shown that the area of the FAZ in diabetic patients was increased compared with healthy persons and there was a correlation between DR stage and area of the FAZ. Bresnick et al.[21] showed that area of the FAZ was enlarged in the group with diabetes compared to the controls. In the study of Talisa et al.,[12] microvascular changes were examined with OCTA in individuals with diabetes and did not have DR findings. FAZ changes and capillary non-perfused areas were more common in diabetic patients without DR than in the healthy group. In addition, it was reported that the size of the area of the FAZ was larger in diabetic patients than in healthy persons. With the help of all these data obtained, it was emphasized that the early changes in foveal microvascularity could be detected with OCTA even without DR.

The values of the mean non-perfused area in the SCP in the DR + group were significantly higher than the group of diabetic individuals without DR and the control group. The amount of non-perfused area in the group of diabetic patients who had not yet developed DR findings was significantly higher than the control group. In a study by Krawitz et al.,[22] non-perfusion areas were measured in the parafoveal region in 30 eyes with DR and in 15 eyes without DR, a significant elevation was found in the group with DR findings compared with other groups. This result is compatible with our results. In contrast, they did not find any significant difference between diabetic patients without DR and the control group.

We found that mean VD in SCP and DCP in the parafoveal region was significantly lower in diabetic patients with retinopathy than the group of diabetic patients without retinopathy and the control group. Mean VD in the DCP was found to be significantly lower in diabetic patients without retinopathy compared to the controls. Hwang et al.[19] measured the mean VD in the parafoveal area using OCTA in 12 eyes. In accordance with our results, the mean parafoveal VD was statistically significantly lower in eyes with DR. Dimitrova et al.[23] found a significant difference in mean VD in SCP and DCP and area of the FAZ compared to the control group in 29 diabetic individuals without retinopathy.

In our study, OCTA images of eyes with DR findings, which were performed at a regular interval of 3-months during the 1-year follow-up period, were evaluated. In this group, there was no significant change in the DR stage and HbA1c levels during the 1-year follow-up. When the data obtained at baseline and during the 1-year follow-up period were compared, no significant alteration was observed in terms of BCVA, CRT, and area of the FAZ. It was determined that mean non-perfused area measured in SCP was larger at the end of the 1-year follow-up period, this difference was not statistically significant. When compared to the mean VD in SCP and DCP in the parafoveal region, there was no significant change during the 1-year follow-up. In our opinion, the longer follow-up period could reveal the significance of the changes in vascular structures in the long term.

We are aware that this study has a number of limitations. First, the sample size is relatively small, as eyes with DME were not included in the study and the distribution among groups was not homogeneous in DR classification. Second, OCTA image artifacts can interfere with an accurate evaluation of the actual status of the retinal microvasculature; for example, projection artifacts might interrupt the visualization of the deep layers. Third, this is a one-year follow-up study whereas the longer follow-up periods could reveal the significance of the changes in vascular structures in the long term.

In conclusion, OCTA is developing technology and it can show microvascular pathologies such as microaneurysms, FAZ changes, non-perfusion areas, decreased vascular density in SCP, and DCP separately which is impossible with FA. Early microvascular changes can be detected in the absence of DR. This technique will complement the traditional angiography methods that require intravenous contrast agents and add quantitative dimensions to the diagnosis of DR, with the development and sensitivity of new software for the removal of artifacts.

Authors' note

The manuscript has been read and approved by all the authors.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Emine Temel https://orcid.org/0000-0001-6302-9175

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