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Original article

Effect of Smoking on Macular Perfusion Using Optical Coherence Tomography Angiography

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Abstract:

Background: Chronic smoking's impact on ocular health remains an area of concern, particularly its effect on macular perfusion. This study aimed to evaluate the influence of long-term smoking on macular perfusion using Optical Coherence Tomography Angiography (OCTA). **Methods**: A prospective, randomized clinical trial was conducted at Benha University Hospital's ophthalmology division from January 2020 to December 2021. Forty participants were divided into smoking (Group 1) and control (Group 2) groups. Exclusion criteria included systemic and ocular diseases, refractive errors, retinal vasculopathies, ocular surgeries, or media opacity. OCTA assessed macular perfusion, while other ophthalmic parameters were measured. **Results:** The smoking group exhibited a higher smoking index (490.00±325.64) and duration (17.30±7.37 years) compared to controls. Despite comparable visual acuity and intraocular pressure between groups, smokers demonstrated significantly lower superficial and deep layer densities across various macular regions ($p < 0.001$). The foveal avascular zone (FAZ) area was notably larger in smokers ($p < 0.001$), indicating compromised perfusion. **Conclusions:** DCP's is more vulnerable to oxidative damage and poor perfusion brought by cigarette smoking, which led to a considerable drop in VD of DCP compared to SCP. In addition, bigger research examining the long-term effect of smoking on retinal microcirculation in the macula may help clarify the significance of smoking as a risk factor for systemic vascular diseases.

Keywords: Cigarette smoking; retinal blood flow; Optical coherence tomography Angiography.

Introduction

Smoking is the leading preventable cause of mortality among people worldwide who are 65 years old and older (1). It is a major contributor to the development of dementia, and Alzheimer's disease (2). Tobacco use has been linked to a variety of eye diseases, namely those caused by ischemia or oxidative causes. Tobacco includes oxidising chemicals that generate free radicals, which may harm cells or trigger their programmed death pathway, apoptosis (3).

Cigarette smoking has been linked to many common eye illnesses, including age-related macular degeneration (AMD), anterior ischemic optic neuropathy (AION), cataract, thyroid ophthalmopathy, and primary open angle glaucoma. Direct toxic injury to the optic nerve, particularly in frequent smokers, may cause tobacco optic neuropathy (TON) (4). There has been research on the short-term and long-term effects of smoking on eye circulation and its effect on retinal circulation by peripheral effect of nicotine (5). Cigarette smoking negatively affects the microcirculation via a number of processes, such as impaired endothelium-dependent vaso-relaxation, platelet aggregation, endothelial cell dysfunction, and activated circulating leukocytes. Cigarette smoking causes leukocyte and/or platelet aggregation and adherence to the micro vascular endothelium in arterioles and venules through these mechanisms (6). Despite research into the methods by which cigarette smoking activates the sympathetic nervous system in humans, the full extent to which smoking affects hemodynamics of ocular blood flow (OBF) is yet unknown (7). Older methods in OBF assessment, such as laser speckle flowgraphy, colour duplex imaging, laser Doppler velocimetry, and flowmetry, are well documented and provide good assessment of different segments of the eye's blood flow (8). Current methods in optical coherence tomography (OCT) have allowed for clearer visualisation of retinal and choroidal microvasculature (9). This new technology is optical coherence tomography angiography (OCTA) which provides a cutting-edge imaging method for examining the blood vessels in the eye that is painless, quick, and does not need any preparation of the eye. Macular perfusion and Chorio-retinal vascular diseases, including diabetic retinopathy, age-related macular degeneration, and vascular occlusion, may be easily diagnosed and monitored (10).

Therefore, optical coherence tomography angiography was used to assess the impact of smoking on macular perfusion in this investigation (OCTA).

Patients and Methods

Benha University Hospital's ophthalmology division played host to this prospective, randomised clinical trial. Before beginning data collection, approval and informed permission were received from the IRB (Institutional Review Board) at Benha University and the Human Research Ethics Committee of the Benha Faculty of Medicine, respectively. The time frame of the research was from January 2020 to December 2021.

Approval code: MS.16.6.2021

Forty participants from Benha University Hospital were split into two groups for the research. Those in Group 1 smoked for at

least 10 years on average whereas those in Group 2 non-smoker individuals comparable in age and sex (control group).

Criteria for include cases in the study:

The age of the participants was varied, from 40 to 65.

Criteria for exclude cases in the study:

Subjects with systemic diseases (such as hypertension or diabetes) or ocular diseases (such as glaucoma or uveitis) or a history of ocular surgery or trauma, refractive errors greater than 8 diopters of myopia or 6 diopters of hyperopia, retinal vasculopathies (such as diabetic or hypertensive retinopathy or central retinal vein occlusion), or ocular media opacity were not included.

In group 1, the smoking index was determined by multiplying the daily cigarette count by the number of years the patient had been a smoker. Visual acuity measured using Decimal Notation, autorefractometer (Topcon type), slit-lamp anterior segment examination, intraocular pressure measured using Goldmann applanation tonometry, dilated fundus examination using 20D lens, and OCTA (Optovue type) assessment of superficial layer density and deep layer density in macula and with scan size of 6 mm 6 mm and measurement of size of FAZ.

Statistical analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test (11). For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5 (11). P-values less than 0.05 were deemed significant.

Results

The our respondents' ages varied from 40 to 65, with a mean of 54.40±7.83 years in the smoking group and a mean of 53.80±6.71 years in the control group (p = 0.327). There were 18 men and 2 females in the sample of smokers. With a p-value of 0.235, the analysed control group consisted of 14 men and 6 females. Smokers (at least one pack per day for more than ten years) had a mean smoking index of 490.00±325.64 and a mean smoking duration of 17.30±7.37 years. A 0.000 P-value was obtained. **Table 1**

The mean the smokers' group had a BCVA of 0.85±0.16, whereas the controls had a BCVA of 0.89±0.10 (P = 0.171). Mean intraocular pressure (IOP) in the smoking group was 16.20±3.09 mmHg, whereas the IOP in the control group was 15.43±1.81 mmHg (P = 0.176).

With a p-value of 0.187, the spherical equivalent was -1.52±2.54 for the smoking group and -0.77±2.49 for the control group. **Table 2**

The mean whole (Superficial layer density), hemi superior density, and hemi inferior density were significant lower in the smokers group than in the control group. with P-value <0.001 which is statistically significant. Parafovea (Superficial layer density), temporal Parafovea superior Parafovea, nasal Parafovea and inferior Parafovea were significant lower in the smokers group than in the control group with P-value <0.001. **Table 3**

Smokers had a considerably reduced density of regions in both the superficial layer (Peri fovea 3-5 mm from the centre) and the deep layer than nonsmokers. Table 4

When comparing the smokers and nonsmokers, the average para fovea and Perifoveal (deep layer density) was significantly lower in the smokers group (P0.001), as was the mean para fovea and Perifoveal (deep layer density) in the temporal region, superior region, nasal region, and inferior region. **Table 5**

The mean FAZ area (mm2) was significant higher in the smokers group than in the control group with P-value <0.001. **Table 6**

Case presentations:

Case 1 were illustrated in **Figure 1**.

Case 2 were illustrated in **Figure 2**.

Table 1: Distribution according the age groups, sex and smoking index

	Smokers		Non smokers		P value
	No	%	No	%	
Sex:					
Male	18	90.0	14	70.0	0.235
Female	2	10.0	6	30.0	
Age:(year)					
Mean ±SD	54.40±7.83		53.80±6.71		0.321
Smoking Index					
Mean ±SD	490±325.64		----		----

Table 2: The ophthalmologic examination

	Smokers	Non smoker	P-value
	Mean±SD	Mean±SD	
BCVA	0.85±0.16	0.89±0.10	0.171
IOP	16.20±3.09	15.43±1.81	0.176
SE	-1.52±2.54	-0.77±2.49	0.187

*: significant P value, BCVA: corrected visual acuity, IOP: intra ocular pressure, SE: spherical equivalent

Table 3: Distribution according the superficial layer areas density and the superficial layer areas density (Parafoveal 1-3 mm from centre)

	Smokers	Non smokers	
	Mean±SD	Mean±SD	P value
whole (Superficial layer density)	47.33±3.40	50.37±2.63	< 0.001*
Hemi superior (Superficial layer density)	47.20±3.57	50.24±2.86	< 0.001*
Hemi-inferior (Superficial layer density)	47.36±3.81	50.49±2.51	< 0.001*
Fovea (Superficial layer density)	22.13±8.62	23.49±4.84	0.387
Superficial layer areas density (Parafoveal 1-3 mm from center)			
Parafovea (Superficial layer density)	49.78±4.83	53.90±2.71	< 0.001*
Temporal Parafoveal (Superficial layer density)	50.87±4.19	53.81±2.49	< 0.001*
Superior Parafoveal (Superficial layer density)	50.63±4.91	54.97±3.56	< 0.001*
Nasal Parafoveal (Superficial layer density)	47.82±7.63	52.86±3.10	< 0.001*
Inferior Parafoveal (Superficial layer density)	50.08±5.31	54.11±3.31	< 0.001*

*: significant P value

Table 4: Distribution according the superficial layer areas density (Peri fovea 3-5 mm from the centre) and the deep layer areas density

	Smokers	Non smokers	
	Mean±SD	**Mean±SD**	**P value**
Peri fovea (Superficial layer density)	47.93±3.57	51.11±2.96	< 0.001*
Temporal (Superficial layer density)	45.79±4.54	48.07±2.58	0.008*
Superior (Superficial layer density)	47.29±4.36	50.99±3.27	< 0.001*
Nasal (Superficial layer density)	50.76±4.18	53.82±4.79	0.003*
Inferior (Superficial layer density)	47.79±4.50	51.13±2.98	< 0.001*
Deep layer areas density			
Whole (Deep layer density)	44.00±4.59	53.53±4.81	< 0.001*
Hemisuperior (Deep layer density)	44.46±5.17	53.33±4.79	< 0.001*
Hemi-inferior (Deep layer density)	44.05±5.00	53.72±4.97	< 0.001*
Fovea (Deep layer density)	32.86±10.12	42.25±5.03	< 0.001*

*: significant as P-value

Table 5: Distribution according the deep layer areas density between two groups (Parafoveal and Perifoveal))

	Smokers	Non smokers	
	Mean±SD	**Mean±SD**	**P value**
Parafovea (Deep layer density)	48.21±4.12	56.40±3.90	< 0.001*
Temporal Parafoveal (Deep layer density)	49.42±4.20	56.85±4.22	< 0.001*
Superior Parafoveal (Deep layer density)	47.84±4.29	55.72±4.69	< 0.001*
Nasal Parafoveal (Deep layer density)	48.05±5.62	57.22±3.35	< 0.001*
Inferior Parafoveal (Deep layer density)	47.23±4.75	54.79±4.52	< 0.001*
Perifoveal			
Perifovea (Deep layer density)	44.59±5.60	55.06±5.48	< 0.001*
Temporal (Deep layer density)	46.45±5.00	57.02±4.45	< 0.001*
Superior (Deep layer density)	43.21±6.49	54.50±5.57	< 0.001*
Nasal (Deep layer density)	43.71±6.44	54.49±5.92	< 0.001*
Inferior (Deep layer density)	43.04±6.08	54.35±5.99	< 0.001*

*: significant as P-value

Table 6: Distribution according to FAZ area (mm2) between two groups

	Smokers	Non smokers	
	Mean±SD	**Mean±SD**	**P value**
FAZ area (mm^2)	0.32±0.08	0.22±0.07	< 0.001*

*: significant as P-value

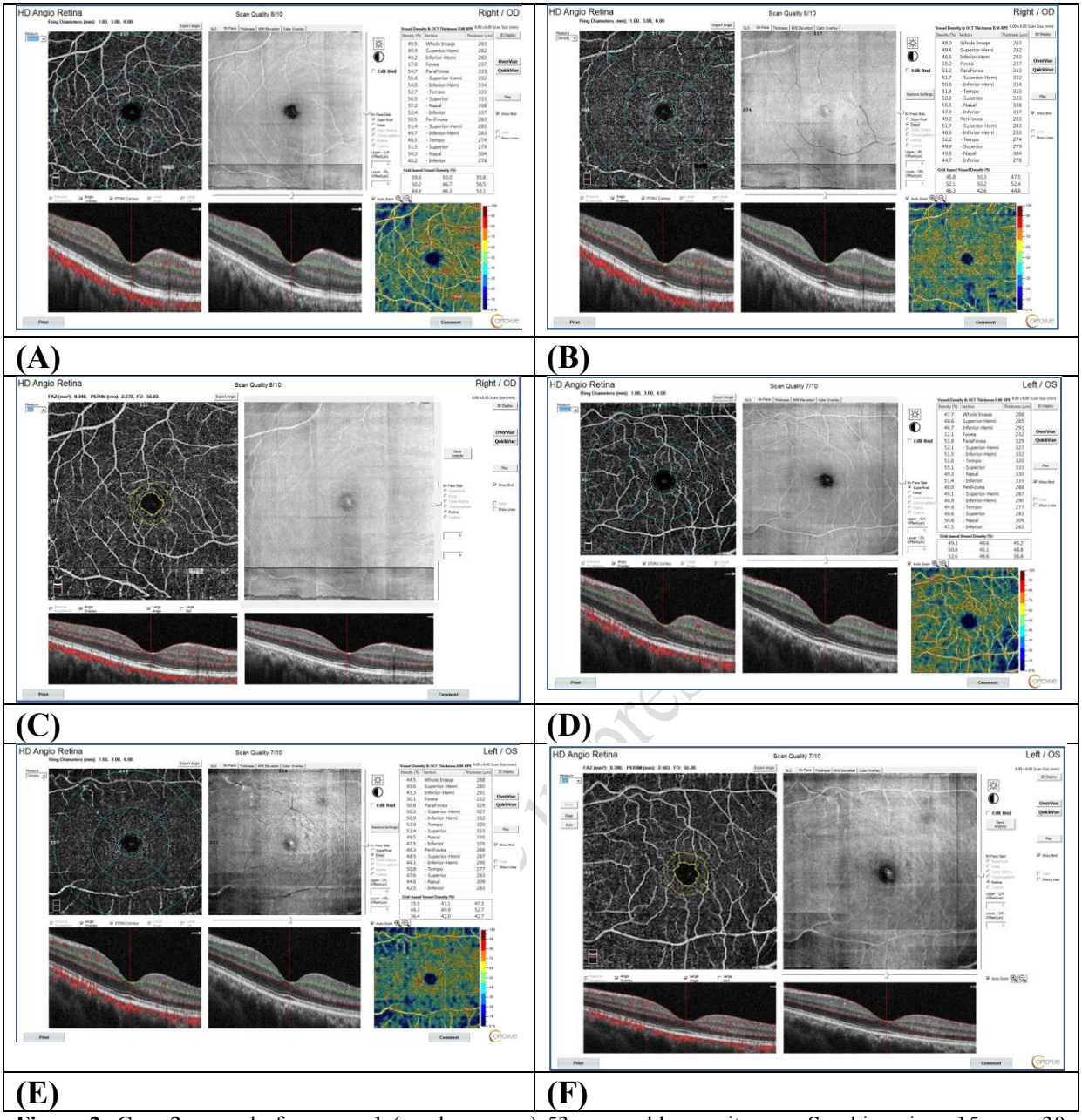

Figure 2: Case 2:example for group 1 (smoker group) 53 years old, security man Smoking since 15 years,30 cigarettes per day , Smoking index 450, (A) Superficial layer density OD, (B) Deep layer density OD, (C) FAZ area OD, (D) Superficial layer density OS, (E) Deep layer density OS, and (F) FAZ area OS

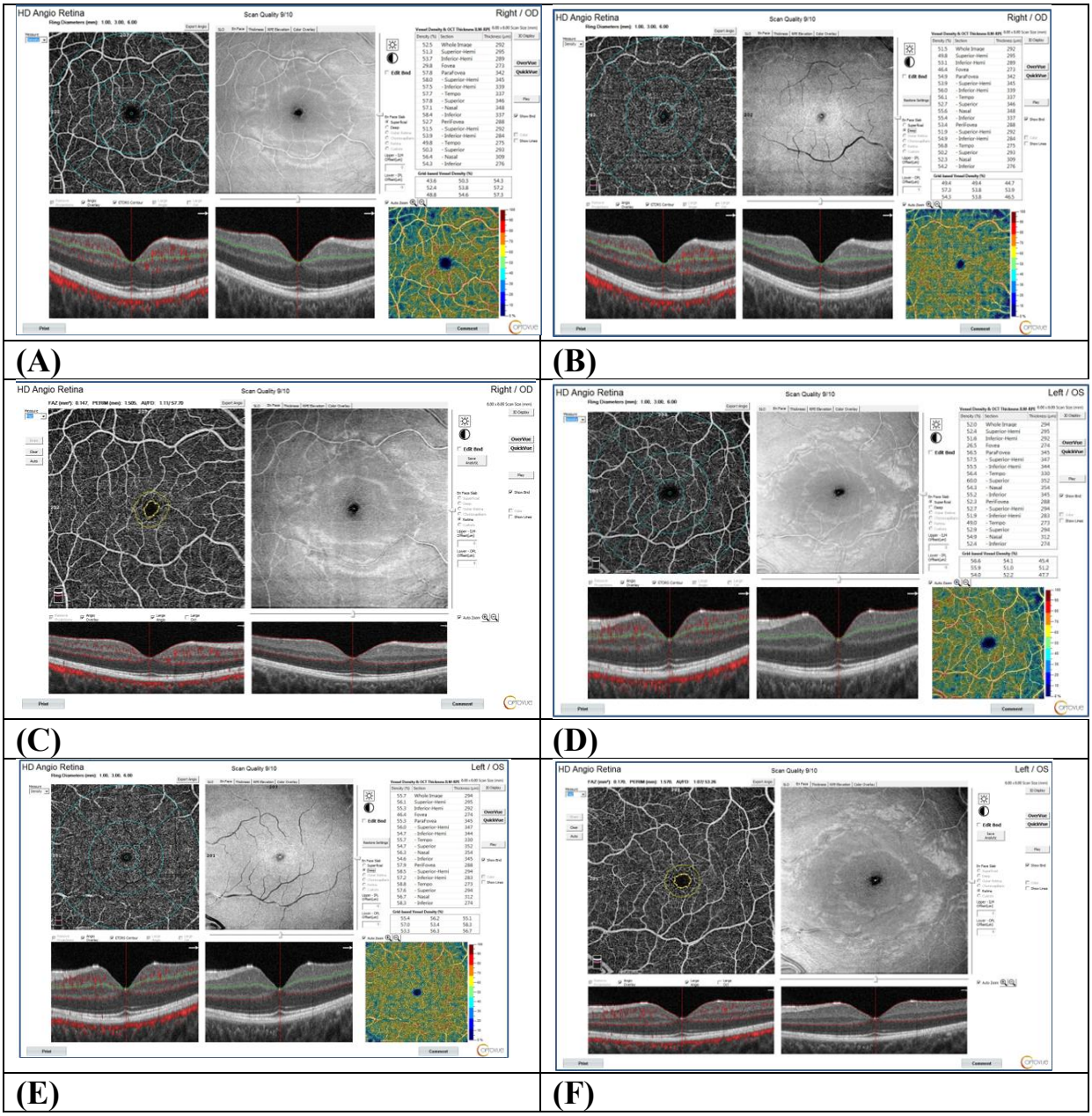

Figure 2: Case 2:example for group 2 (non-smoker group): 58 years old, security man, (A) Superficial layer density OD, (B) Deep layer density OD, (C) FAZ area OD, (D) Superficial layer density OS, (E) Deep layer density OS, and (F) FAZ area OS

Discussion

The Participants were split into a group of long-term smokers (those who had been smoking for at least ten years) and a group of non-smokers (the "control group").

Among order to attain the necessary period of smoking in smokers, participants' ages varied from 40 to 65 in both groups, researchers in two additional studies (12) and (13) looked at people who had smoked cigarettes for at least ten years and had smoked at least a pack a day, but the participants in those studies were much younger.

Smokers in our study group smoked at least one pack per day for at least ten years , the authors in other study did not specify how long they had been smokers (14).

All of the aforementioned research included participants of similar ages and sexes in both groups. All of the people in our research were of similar ages, although they were of different sexes. There were 14 men and 6 women in the analyzed control group. There were a total of 20 smokers analysed (18 men and 2 women) as most of smokers are men.

In order to ensure that any ocular vascular or functional impact was solely attributable to smoking, it has been a requirement of all prior research that the studied participants in both groups had no systemic or local illness. Our investigation also omitted this possibility.

Since the effects of smoking are systemic, resulting in a bilateral ocular impact. We looked at the impact of smoking over at least a decade on the microvasculature of the macula in heavy, habitual smokers.

Reduced blood flow to the eye and decreased macular perfusion has been linked to cigarette smoking (15).

To determine if long-term smokers differ from non-smokers in terms of FAZ, foveal, parafoveal, and perifoveal vascular density, we used optical coherence tomography angiography (OCTA).

When comparing smokers and nonsmokers, we discovered that the smokers had much larger FAZ areas and lower VD levels overall.

The deep capillary plexus may be particularly vulnerable to injury because to its location distant from the major arterioles, its high metabolic requirement as the outer retina, and its complicated vascular anatomical design (16).

Our findings corroborated those of the previous research; we discovered a statistically significant difference (p 0.001) between the two groups in terms of the decline in vessel density of DCP against the decline in vessel density of superficial capillary plexus.

OCTA allows for a mechanized assessment of the SCP and DCP's vascularity. Numerous investigations utilizing OCTA have shown that chronic smokers have changes in vascular density, with most showing a decrease in vascular density and enlargement of the FAZ (17).

OCTA is a reliable, fast method that does not need dye injection to identify FAZ enlargement. Microangiopathies brought on by smoking may be evaluated objectively using OCTA (18). In many cases of vascular retinal illness, the size of the FAZ is associated with the degree of capillary non-perfusion (19).

Some authors using OCTA to study retinal microcirculation in cigarette smokers have observed that smoking induces an increase of the FAZ region and a reduction in vascular density (2).

Our findings corroborated those of others who have shown that cigarette smokers had a significantly higher FAZ compared to nonsmokers (p 0.001). There was a statistically significant difference between the two groups (p 0.001) in the superficial para foveal, superficial total, deep foveal, deep para foveal, and deep total vascular densities, although the smokers had much lower densities across the board.

Our research does have certain caveats. It is still unclear if the amount of smoking one does has a linear effect on retinal blood flow. It may be difficult to investigate the dose-dependent influence of smoking on the retinal circulation parameters due to variations in nicotine concentration per cigarette and the actual quantity of smoke ingested by the smoker. The potential acute impact of smoking on result was not taken into account.

Conclusions

Foveal and macula retinal microcirculation are both impaired in smokers' eyes. FAZ enlargement and decreased foveal VD of the SCP and DCP in smokers' eyes compared to those of non-smokers. Due to its high metabolic activity and complicated vasculature, DCP is more vulnerable to oxidative damage and poor perfusion induced by cigarette smoking, and our results show that this makes DCP much less viable than SCP. In addition, bigger research examining the long-term effect of smoking on retinal microcirculation in the macula may help clarify the significance of smoking as a risk factor for systemic vascular diseases.

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