ORIGINAL ARTICLE

Effect of Smoking on Macular Perfusion Using Optical Coherence Tomography Angiography

Ahmed A. Abdelghany, Osama M. Elnahrawy, Khaled A. Zaky, Mohammed F. A. Zidan *

Department of Ophthalmology, Faculty of Medicine for Boys, Suez Canal University, Ismailia, Egypt

Abstract

Background: ***Worldwide, smoking causes premature death among the elderly and impacts nearly every organ in the body. Additionally, it significantly increases the likelihood of developing cognitive decline, Alzheimer's disease, and dementia.***

Aim and objectives: ***To evaluate the effect of smoking on macular perfusion using optical coherence tomography angiography (OCTA).***

Subjects and methods: ***This case-control study was conducted on 96 eyes of patients at the ophthalmology outpatient clinic, Suez Canal University Hospital, Ismailia, Egypt, from January 2023 to January 2024.***

Results: ***When comparing smokers' eyes to those of healthy people who do not smoke, we see that the former have a larger FAZ and smaller foveal VD of the superior ciliary plane and inferior ciliary plane, respectively. The control group had a mean whole superficial layer density of 49.51±2.96, while the smoker's group had 47.30±3.29, with a statistically significant P-value<0.001. With a statistically significant P-value<0.001, the control group had a mean entire deep layer density of 51.15±5.29 while the smoker's group had 45.69±4.62. The control group had a mean FAZ area (mm2) of 0.24±0.08 while the smoker's group had a mean of 0.32±0.09, with a statistically significant P-value<0.001.***

Conclusion: ***Smoking has obvious consequences on the eyes, particularly on the macular perfusion. A notable decline in VD, particularly in deep layer density, and an expansion of FAZ area were noted.***

Keywords: Smoking ;Macular perfusion; Optical coherence tomography angiography

1. Introduction

Worldwide, smoking causes premature death among the elderly and impacts nearly every organ in the body. Additionally, it significantly increases the likelihood of developing cognitive decline, Alzheimer's disease, and dementia.[1]

Cancers (particularly lung cancer), respiratory diseases (most commonly chronic obstructive pulmonary disease), and cardiovascular diseases (most commonly coronary heart disease) account for the vast majority of smoking-related fatalities.[2]

It was shown that smoking is associated with several common eye illnesses, including cataracts, age-related macular degeneration (AMD), primary open-angle glaucoma, thyroid ophthalmopathy, and anterior ischemic optic neuropathy (AION). Direct toxic injury to the optic nerve, known as tobacco optic neuropathy (TON), can develop in those who smoke heavily.[3]

Several well-documented OBF assessment methods are available, including color duplex imaging, laser Doppler velocimetry, flowmetry, and laser speckle flowgraph. These methods offer a good evaluation of various segments of eye blood flow.[4]

The microvasculature of the retina and choroidal regions can now be seen more clearly thanks to optical coherence tomography (OCT) methods. 1 In 2015, Savastano et al. Optical coherence tomography angiography is the name of this cutting-edge technique. The choroidal and retinal vascular structures can be quickly and easily seen without invasiveness. Making it easier to diagnose and monitor chorioretinal vascular diseases, including vascular occlusion, diabetic retinopathy, and age-related macular degeneration.[5]

Accepted 19 January 2025.
Available online 31 March 2025

* Corresponding author at: Ophthalmology, Faculty of Medicine for Boys, Suez Canal University, Ismailia, Egypt.
E-mail address: dr.zezo92@gmail.com (M. F. A. Zidan).

https://doi.org/10.21608/aimj.2025.446489

Cigarette smoke affects microcirculation in a number of ways, including by reducing endothelium-dependent vaso relaxation, causing platelets to aggregate, malfunctioning endothelial cells, and activating circulating leukocytes. Tobacco use causes leukocyte and platelet aggregation and adherence to microvascular endothelium in venules and arterioles via these pathways.[6]

The aim of this study was to evaluate the effect of smoking on macular perfusion using OCTA.

2. Patients and methods

Between January 2023 and January 2024, 96 eyes of patients undergoing ophthalmology outpatient treatments at Suez Canal University Hospital in Ismailia, Egypt, were the subjects of this case-control study.

Inclusion criteria:

Individuals of either sex who are 40 or older and who have smoked continuously for at least 10 years and who smoke 20 cigarettes daily or more.

Exclusion criteria:

Subjects with systemic diseases (eg. Diabetes mellitus, kidney diseases, etc.); subjects with ocular diseases (eg. glaucoma, uveitis, etc.); individuals who have undergone prior ocular surgery or sustained eye injuries, and individuals whose refractive defects exceed 8 diopters of myopia or 6 diopters of hyperopia; subjects with retinal vasculopathy (eg. Diabetic retinopathy, hypertensive retinopathy, CRVO, etc.); subjects with ocular media opacity.

Sampling:

We took the right eye of all patients who matched the criteria that came to our clinic and divided them into two groups: The first group: 48 normal eyes with no ocular or systemic related pathology; The second group: 48 eyes of smokers (for over a decade, smoking twenty cigarettes daily or more). We matched the same age group in smokers and non-smokers.

Sample size:

The sample size was calculated using the G-power program version 3.1.9.7. The effect size: The Superficial Parafoveal VD (%) in the control group (n=80)=54.75±2.30. The Superficial Parafoveal VD (%) in the smoker's group (n=80)=52.09±4.56. The effect size=0.7365.[7]

The power of the test=80% so, the minimum sample size needed for this study was 48 subjects (96 eyes).

Methods:

What each and every patient had to go through: information gathering: name, age, sex, residency, address, profession, and phone number; special habits, particularly smoking; a first-degree relative's history of glaucoma; a history of prior ocular trauma or surgery; a history of ocular medications; a history of systemic diseases or chronic illnesses, such as diabetes or hypertension; previous drug use, such as steroids.

Ophthalmic Examination:

Assessment of unaided visual acuity using Landolt C chart was done; external eye examination by slitlamb; examination of ocular motility; Refraction using auto ref/keratometer ARK-1 (NIDEK Co, Aichi, Japan 2013); assessment of best corrected visual acuity refraction by Landolt C chart; slit lamp (SL-D7 slit-lamp Topcon Co, Tokyo, Japan, with Galilean magnification changer with converging binocular tubes) examination was done to exclude any anterior media opacity and examine the anterior segment; intraocular pressure measurement using Haag Astrid Applanation was taken after the installation of topical anesthetic eye drops; benoxinate hydrochloride 0.4% solution (Benox, property of EIPICO 2005. Egypt); fundus examination using a binocular indirect ophthalmoscope (Model AAIO-7 Appasamy associates 2014, India) and Volk double aspheric +20.00D lens (Volk Optical, Ohio 1988) after instillation of cyclopentolate 1.0%, two times with 10 minutes interval, 30 minutes before examination.

Specific Examinations:

Optical coherence tomography angiography (OCT-A) is done by Topcon® DRI Triton Plus (Topcon Co, Tokyo, Japan), which is a swept-source OCT device. When dilated, the pupil is dilated 20 minutes before retinal imaging using Mydriacyl® eye drops (Alcon, Texas, USA), 1-2 drops repeated after five minutes. The patient is asked to fixate on the device target and maintain his head and chin resting upon the device head frame, thus minimizing ocular or head movement. The patient was alerted that the 6 mm x 6 mm scan, taking about 20-30 seconds, was started to attain gaze fixation.

Measurements are taken by the OCT-A device:

Macular vessel density by centering the OCT scan on the macula using the same OCTA system. Macular vascular density was measured & and represented as a computer-generated map with quantitative percentage measures. Two maps of superficial layer density and deep layer density were selected. Each map is divided into four regions (temporal, superior, nasal, and inferior). FAZ area with mm map compared between the two groups.

Statistical analysis:

Software developed and maintained by IBM Corp. in Armonk, New York, USA, known as SPSS, version 28, was used for data coding and entry. For quantitative variables, we used the mean and standard deviation; for categorical variables, we used the frequencies (case count) and relative frequencies (%) to describe the data.

We used unpaired t-tests to compare the

groups. A Chi-square (2) test was run to compare categorical data. Instead, an exact test was utilized in cases where the anticipated frequency was below 5. Statistical significance was defined as a p-value below 0.05.

Ethical considerations:

An ethical committee from Suez Canal University's School of Medicine examined the research. Before recruiting anyone for the study, we made sure to get their written, informed consent.

3. Results

The participants' ages varied from 40 to 65. Group 1 had an average age of 50.46±6.68 years, whereas group 2 had an average age of 50.81±6.69 years, and the p-value for group 2 was 0.796, meaning it was not statistically significant. There were 44 men and 4 females in the group of smokers that were studied. With a p-value of 0.217, the control group that was investigated consisted of 40 males and 8 females, (table 1).

Table 1. Demographic data of the studied subjects.

		SMOKERS		NON-SMOKERS		P-VALUE
		Mean	SD	Mean	SD	
AGE (YEAR)		50.46	6.68	50.81	6.69	0.796
SEX		Count	%	Count	%	
	Male	44	91.7%	40	83.3%	0.217
	Female	4	8.3%	8	16.7%	

A measure of long-term cigarette consumption, the smoking index is determined by multiplying CPD by years of tobacco usage. There were four groups based on the smoking index: nonsmokers, mild (<400), moderate (400–799), and heavy (≥800).[8]

The average duration of smoking for the smokers' group (more than 10 years at least 20 cigarettes per day) was 17.30±7.37, the average number of cigarettes per day was 27.25±9.05, and the average smoking index was 480.00±72.43, (table 2).

Table 2. Distribution according to the smoking index.

	SMOKERS	
	Mean	SD
SMOKING INDEX	480.00	72.43

With a p-value of 0.862, the control group had a mean best corrected visual acuity (BCVA) of 0.84±0.18 while the smoker's group had 0.83±0.17.

With a p-value of 0.816, the control group had an average intraocular pressure (IOP) of 15.88±3.06 mmHg, whereas the smoker's group had an average of 15.75±2.09 mmHg.

With a p-value of 0.866, the spherical equivalent was -0.64±2.31 in the group of smokers and -0.53±2.41 in the group of control subjects, (table 3).

Table 3. Distribution according to the ophthalmologic examination.

	SMOKERS		NON-SMOKERS		P-VALUE
	Mean	SD	Mean	SD	
BCVA	0.83	0.17	0.84	0.18	0.862
IOP	15.75	2.09	15.88	3.06	0.816
SE	-0.64	2.31	-0.53	2.14	0.866

With a statistically significant P-value of 0.001, the control group had a mean entire (Superficial layer density) of 49.51±2.96 while the smoker's group had 47.30±3.29. With a statistically significant P-value<0.001, the control group had a mean superior density of 54.23±3.64 and the smoker's group 47.23±4.46. In the smoker's group, the average inferior density was 47.58±4.37, while in the control group, it was 52.98±4.19, and the difference was statistically significant (P<0.001).

The control group had a mean temporal density of 52.11±4.67 while the smoker's group had 47.82±7.5, with a statistically significant P-value of 0.001. With a statistically significant P-value of 0.014, the smoker's group had an average nasal density of 46.93±4.55 while the control group had 48.83±2.56. A statistically significant P-value of 0.181 indicates that the control group had a mean foveal density of 22.41±5.4 whereas the smoker's group had a mean foveal density of 20.42±8.66, (table 4; figure 1).

Table 4. Distribution according to the superficial layer area density.

	SMOKERS		NON-SMOKERS		P-VALUE
	Mean	SD	Mean	SD	
WHOLE AVERAGE SUPERFICIAL MAC VD	47.3	3.29	49.51	2.96	0.001
SUPERIOR SUPERFICIAL MACULAR VD (%)	47.23	4.46	54.23	3.64	<0.001
INFERIOR SUPERFICIAL MACULAR VD (%)	47.58	4.37	52.98	4.19	<0.001
TEMPORAL SUPERFICIAL MACULAR VD (%)	47.82	7.5	52.11	4.67	0.001
NASAL SUPERFICIAL MACULAR VD (%)	46.93	4.55	48.83	2.56	0.014
FOVEA SUPERFICIAL MACULAR VD (%)	20.42	8.66	22.41	5.4	0.181

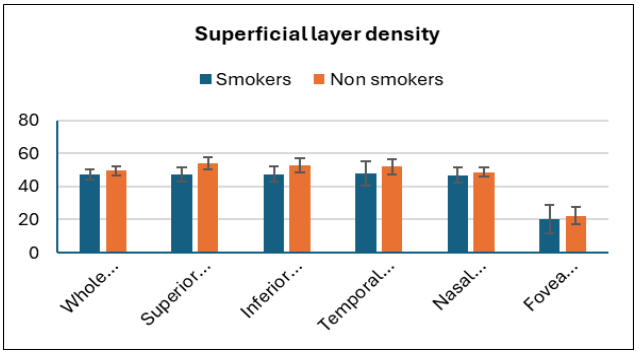

Figure 1. Distribution of superficial layer area density between the groups.

The control group had a mean deep layer density of 51.15±5.29 and the smoker's group had 45.69±4.62, a difference that was statistically significant with a P-value<0.001. The control group had a mean superior density of 54.73±5.82 and

the smoker's group 47.46±4.24, with a statistically significant P-value<0.001. The control group had an inferior density of 52.35±5.98 while the smoker's group had an average of 47.20±4.42, with a statistically significant P-value<0.001. The control group had a mean temporal density of 54.71±5.09 while the smoker's group had an average of 49.35±4.28, with a statistically significant P-value<0.001. With a statistically significant P-value<0.001, the control group had an average nasal density of 52.63±6.11 while the smoker's group had an average of 44.24±6.42. With a statistically significant P-value<0.001, the control group had a mean foveal density of 30.46±5.48 while the smoker's group had 24.62±6.32, (table 5; figure 2).

Table 5. Distribution according to the deep layer area density.

	SMOKERS		NON-SMOKERS		P-VALUE
	Mean	SD	Mean	SD	
WHOLE AVERAGE DEEP MAC VD	45.69	4.62	51.15	5.29	<0.001
SUPERIOR DEEP MACULAR VD (%)	47.46	4.24	54.73	5.82	<0.001
INFERIOR DEEP MACULAR VD (%)	47.2	4.42	52.35	5.98	<0.001
TEMPORAL DEEP MACULAR VD (%)	49.35	4.28	54.71	5.09	<0.001
NASAL DEEP MACULAR VD (%)	44.24	6.42	52.63	6.11	<0.001
FOVEA DEEP MACULAR VD (%)	24.62	6.32	30.46	5.48	<0.001

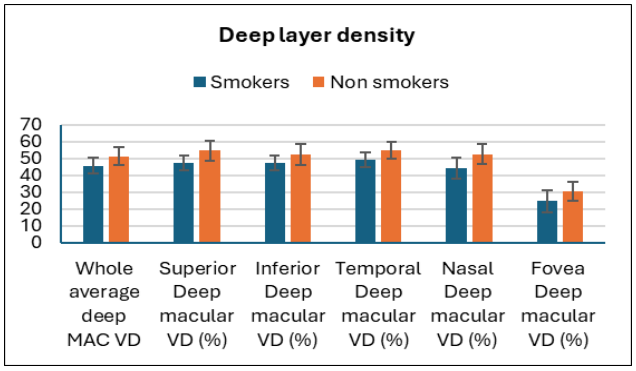

Figure 2. Distribution of deep layer area density between the groups.

The control group had a mean FAZ area (mm2) of 0.24±0.08 while the smoker's group had a mean of 0.32±0.09, with a statistically significant P-value<0.001, (table 6; figure 3).

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

	SMOKERS		NON-SMOKERS		P-VALUE
	Mean	SD	Mean	SD	
FAZ AREA (MM²)	0.32	0.09	0.24	0.08	<0.001

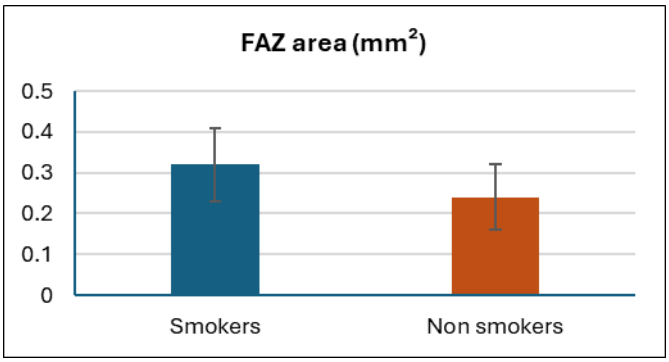

Figure 3. Measurements of FAZ area(mm2) between the two groups.

Case presentation:

Control group:

A 52-years old, farmer, UCVA 0.2 OD, 0.1 OS, error of refraction +3.25 sphere OD +2.75 sphere, -0.25-cylinder OS, BCVA 0.7 OD, 0.8 OS. He has a normal fundus and IOP is 13 OD, 13 OS.

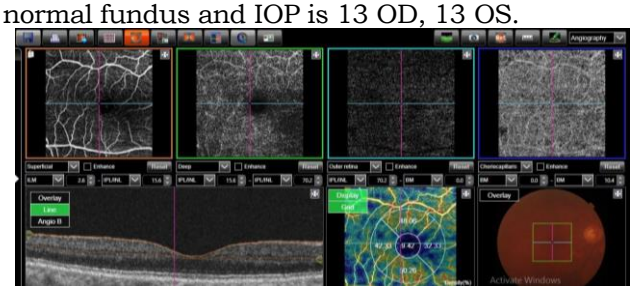

Figure 4. Macular OCT-A of non-smoking 52 y. man(Rt. eye).

Smoker group:

A 53-years old, security man, smoking for 15 years, 30 cigarettes per day, smoking index 450

UCVA 0.2 OD, 0.1 OS. The error of refraction +1.25 sphere, -0.25-cylinder OD, +1.75 sphere, -0.25-cylinder OS, BCVA 0.9 OD, 0.8 OS. He has a normal fundus, IOP is 13 OD, 15 OS.

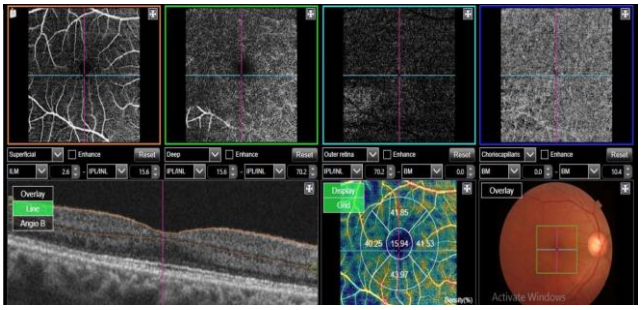

Figure 5. Macular OCT-A of smoker 53 y. man (Rt. eye).

4. Discussion

In comparison to the other imaging tools, OCTA is still a recent technique with continuously updated software that provides noninvasive, speed, and 3-dimensional scanning of choroidal, retinal, and ONH microvasculature, with depth encoded images of large and small caliber of retinal vasculature within the eye.[9]

It is noteworthy that this research aligns with the methodologies of other investigations

conducted by various authors. For instance, Ulaş et al.,[10] explored participants with a similar smoking profile, smoking for over 10 years with a daily consumption of at least 20 cigarettes. However, a divergence was noted in the age range, with one study encompassing individuals aged 23-35 years and another ranging between 25-35 years.

Some researchers have looked at how long people smoke for when researching the impacts on choroidal and retinal thickness; however, they have neglected to include age and daily cigarette use in their analyses.[11]

Age and sex were not factors in any of the aforementioned research. We did not control for sex in our study; nevertheless, all participants were of the same age. Forty men and 8 females were in the control group that was studied. There were 44 men and 4 females in the smoking group that was studied.

One of the exclusion criteria in all the previous studies was that the examined subjects in both groups must have no systemic or local disease to ensure that any ocular vascular or functional effect was only due to smoking. This was also excluded in our research.

In this study, 96 eyes were studied (48 smokers and 48 controls) as the effect of smoking is systemic, causing bilateral ocular effects, and provided a large number of studied subjects and a wider range of results.

In our study and Aboud et al.,[12] we take only the right eye for more sample screening, and because the effect of smoking is systemic, causing bilateral ocular effects.

With a p-value of 0.862, the control group had a mean best corrected visual acuity (BCVA) of 0.84±0.18 while the smoker's group had 0.83±0.17.

We looked at long-term, habitual smokers' effects on macular microvasculature for a minimum of ten years. Ciesielski et al.,[13] looked at the effects right after smoking and 30 minutes later and discovered none.

We used optical coherence tomography (OCTA) to measure the densities of vessels in the superficial and deep capillary plexuses in long-term smokers and non-smokers, namely in the foveal, superior, inferior, nasal, and temporal plexuses.

In comparison to non-smokers, we discovered that smokers' FAZ areas were significantly larger and their superficial and deep VDs were significantly smaller.

Given its proximity to the outer retina, high metabolic demand, and intricate vascular anatomy, the DCP may be more vulnerable to injury than the major arterioles.[14]

There was a statistically significant decrease in VD of DCP compared to the decrease in VD of SCP between the two groups we evaluated, with a p-value<0.001 in all locations, which is in agreement with the previous study's findings.

The vascularity of the SCP and DCP can be automatically evaluated with OCTA. The results of OCTA in chronic smokers have been shown in numerous studies to reveal alterations in vascular density, most notably a decrease in vascular density and an enlargement of the FAZ.[15]

Consistent with previous research, this study examined the effects of smoking on macular perfusion in both healthy individuals and control groups. According to Ayhan et al., who employed OCTA to measure the effects of nicotine on the choriocapillaris area's blood flow index, smoking significantly reduced this index.[16]

There is no immediate effect of smoking on vascular density characteristics evaluated by OCTA in healthy habitual smokers, according to other research that reviewed the literature on the effects of smoking on FAZ and VD.[13]

It is possible to identify FAZ enlargement with OCTA, a fast, dependable method that does not involve injecting dye. Microangiopathies caused by smoking can be objectively assessed with OCTA.[17]

In numerous vascular retinal disorders, the degree to which capillaries are not perfused can be connected to the FAZ dimension.[18]

According to a review of the literature on OCTA evaluations of retinal microcirculation in cigarette smokers, some writers found that smoking increases the FAZ area and decreases vascular densities.[19]

Our investigation concurred with our findings, demonstrating a statistically significant enlargement of the Foveal Avascular Zone (FAZ) in individuals who are habitual cigarette smokers in comparison to the control group (p-value<0.001). Moreover, our study revealed that both superficial and deep total vascular densities were markedly lower in the smoker group when contrasted with the control group (p=0.001, p=0.001, p=0.001, p=0.001, and p=0.001, respectively).

4. Conclusion

Smoking has obvious consequences on the eyes, particularly on the macular perfusion. A notable decline in VD, particularly in deep layer density, and an expansion of FAZ area were noted.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

Funding

No Funds : Yes

Conflicts of interest

There are no conflicts of interest.

References

1. Jha P. The hazards of smoking and the benefits of cessation: a critical summation of the epidemiological evidence in high-income countries. Elife.2020;9:e49979.
2. West R. Tobacco smoking: Health impact, prevalence, correlates and interventions. Psychol Health.2017;32(8):1018-1036.
3. Baj J, Forma A, Kobak J, et al. Toxic and Nutritional Optic Neuropathies-An Updated Mini-Review. Int J Environ Res Public Health.2022;19(5):3092.
4. Kunikata H, Nakazawa T. Recent Clinical Applications of Laser Speckle Flowgraphy in Eyes with Retinal Disease. Asia Pac J Ophthalmol (Phila).2016;5(2):151-158.
5. Fang PP, Lindner M, Steinberg JS, et al. Klinische Anwendungen der OCT-Angiographie [Clinical applications of OCT angiography]. Ophthalmologe.2016;113(1):14-22.
6. Mahmoudinezhad G, Nishida T, Weinreb RN, et al. Impact of Smoking on Visual Field Progression in a Long-term Clinical Follow-up. Ophthalmology.2022;129(11):1235-1244.
7. Dawson B, Trapp RG. Research questions about relationships among variables. Basic and Clinical Biostatistics. 4th edn. Lange Medical Books/McGraw-Hill.2004;190-220.
8. Nagata N, Niikura R, Shimbo T, et al. Alcohol and smoking affect risk of uncomplicated colonic diverticulosis in Japan. PLoS One.2013;8(12):e81137.
9. Chalam KV, Sambhav K. Optical Coherence Tomography Angiography in Retinal Diseases. J Ophthalmic Vis Res.2016;11(1):84-92.
10. Ulaş F, Çelik F, Doğan Ü, et al. Effect of smoking on choroidal thickness in healthy smokers. Curr Eye Res.2014;39(5):504-511.
11. Gokmen O, Ozgur G. The Effects of chronic smoking on retinal vascular densities and choroidal thicknesses measured by optical coherence tomography angiography. Eur J Ophthalmol.2023;33(1):455-462.
12. Aboud SA, Hammouda LM, Saif MYS, et al. Effect of smoking on the macula and optic nerve integrity using optical coherence tomography angiography. Eur J Ophthalmol.2022;32(1):436-442.
13. Ciesielski M, Rakowicz P, Stopa M. Immediate effects of smoking on optic nerve and macular perfusion measured by optical coherence tomography angiography. Sci Rep.2019;9(1):10161.
14. Nakahara T, Hoshino M, Hoshino S, et al. Structural and functional changes in retinal vasculature induced by retinal ischemia-reperfusion in rats. Exp Eye Res.2015; 135:134-145.
15. Al-Sheikh M, Akil H, Pfau M, et al. Swept-Source OCT Angiography Imaging of the Foveal Avascular Zone and Macular Capillary Network Density in Diabetic Retinopathy. Invest Ophthalmol Vis Sci.2016; 57(8):3907-3913.
16. Ayhan Z, Kaya M, Ozturk T, et al. Evaluation of Macular Perfusion in Healthy Smokers by Using Optical Coherence Tomography Angiography. Ophthalmic Surg Lasers Imaging Retina.2017;48(8):617-622.
17. Ragkousis A, Kozobolis V, Kabanarou S, et al. Vessel Density around Foveal Avascular Zone as a Potential Imaging Biomarker for Detecting Preclinical Diabetic Retinopathy: An Optical Coherence Tomography Angiography Study. Semin Ophthalmol.2020;35(5-6):316-323.
18. Cavalleri M, Sacconi R, Parravano M, et al. Optical Coherence Tomography Angiography in Central Retinal Vein Occlusion: Macular Changes and Their Correlation with Peripheral Nonperfusion at Ultra-Widefield Fluorescein Angiography. Ophthalmologica. 2022; 245(3): 275-284.
19. Kalayci M, Cetinkaya E, Suren E, et al. The effect of electronic cigarette smoking on retinal microcirculation: Enlargement of the foveal avascular zone. Photodiagnosis Photodyn Ther.2020;32:102068.