Journal of Advances in Medicine and Medical Research

33(21): 46-55, 2021; Article no.JAMMR.74710
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

The Influence of Smoking on Choroidal, Macular and Retinal Nerve Fiber Layer Thickness

Mona Ahmed El Rokh[1*], Raouf Ahmed Gaber[1], Elsaed Ebrahem Eldesoky[1] and Hamouda Hamdy Ghoraba[1]

[1]Ophthalmology Department, Faculty of Medicine, Tanta University, Tanta, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i2131133
Editor(s):
(1) Prof. Arun Singh, Bareilly International University, India.
(2) Dr. Ashish Anand, GV Montgomery Veteran Affairs Medical Center, University of Mississippi Medical Center and William Carey School of Osteopathic Medicine, USA.
Reviewers:
(1) J. Sivakumar, Guru Nanak College, India.
(2) En C. Guillermo Yanowsky Reyes, Universidad de Guadalajara, México.
Complete Peer review History: https://www.sdiarticle4.com/review-history/74710

Original Research Article

Received 11 August 2021
Accepted 21 October 2021
Published 26 October 2021

ABSTRACT

Background: Smoking is one of the most serious health hazards because it affects every organ in our bodies. Cigarette smoking increases the chance of developing systemic and ocular vascular diseases significantly. Although the exact mechanism behind the association between ocular vascular disorders and smoking are unknown, the peripheral vasoconstriction action of nicotine is believed to lead to an increase in peripheral blood flow resistance. This study was designed to examine the impact of smoking with Spectral Domain Optical Coherence Tomography (SD-OCT) on the peripapillary retinal nerve fibre (RNFL), macular, and choroidal thickness.
Methods: This prospective study was done on 50. It included 25 healthy cigarette smokers with no systemic or ocular illness and another 25 age- and gender-matched healthy non-smokers.
Results: The smoking group had a substantial reduction in central macular and choroidal thickness as compared to the nonsmoker group. The RNFL peripapillary thickness across groups was not significantly altered, with the exception of the temporal (T) quadrant which was significantly thinner in the smoking group. This study discovered a substantial negative correlation between peripapillary RNFL, central macular thickness, and smoking exposure.
Conclusions: Smoking reduces the mean thickness of the peripapillary retinal nerve fibre layer (particularly in the temporal quadrant), the choroidal layer, and the central macular layer statistically significantly.

**Corresponding author: E-mail: paradiserose91@gmail.com;*

Keywords: Smoking; choroidal; macular; retinal nerve fiber; layer thickness.

1. INTRODUCTION

Nicotine use is one of the most serious and avoidable public health concerns of our day. According to the World Health Organization, smoking kills up to 50% of its users. Each year, tobacco kills approximately 8 million people. Over 7 million of these fatalities are directly attributable to tobacco use, whereas around 1.2 million are attributable to non-smokers who are exposed to passive smoking [1].

Cigarette smoke contains over 4000 compounds that have been shown to have a detrimental effect on the respiratory and cardiovascular systems. Smoking is recognized to change the macrovasculature and microvasculature anatomically, making it the major cause of atherosclerotic cardiovascular disease [2].

Smoking has an effect on the endothelium of the blood vessels by raising oxidative stress, reducing antioxidant vitamin C, and causing aberrant nitric oxide activity. These alterations cause increase in arterial wall thickness, atherosclerosis and thromboembolic events, besides to direct vasoconstrictive effect of nicotine [3].

The high vascular structure of the eye makes smoking a fascinating subject for the retina and choroid in addition to being a risk factor for ocular vascular disease such as hypertensive retinopathy, age-related macular degeneration, anterior ischemic optic neuropathy, cataract, glaucoma, thyroid eye disease, and keratoconjunctivitis sicca [4].

Although the exact mechanism behind the association between ocular vascular disorders and smoking are unknown, Nicotine's peripheral vasoconstriction effect is thought to result in an increase in peripheral resistance to blood flow. The pathophysiology of choroidal disorders and chorioretinal diseases must be understood by the quantitative study of choroidal vasculature [5]. Choroidal thickness measurement was utilized in this investigation since it has been established that choroidal blood flow alters choroidal thickness [6].

Numerous studies have been conducted in the past to measure ocular blood flow in smokers and nonsmokers using color duplex imaging, laser speckle technique, and laser Doppler flowmetry. Recently, optical coherence tomography (OCT) has been shown to be effective at determining choroidal thickness when combined with specialized software programs such as enhanced depth imaging. This enables the capture of high-resolution pictures, which enables the assessment of ocular tissues deeper than the retina [7].

The purpose of this study was to assess the influence of smoking on the peripapillary retinal nerve fibre layer (RNFL), macular, and choroidal thicknesses using Spectral Domain Optical Coherence Tomography (SD-OCT).

2. PATIENTS AND METHODS

This is prospective descriptive cross-sectional research utilizing Spectral Domain Optical Coherence Tomography (SD-OCT) to determine the effect of smoking on the thickness of the macula, choroid, and peripapillary retinal nerve fibre layer (RNFL). It was carried out at Tanta university hospital's department of ophthalmology. The research lasted from August 2019 through January 2021. The current study enrolled 50 participants, who were split into two groups: 25 were healthy cigarette smokers with no systemic or ocular illness (smoker group). While the remaining 25 participants were age- and gender-matched and had never smoked cigarettes (nonsmoker group). We included patients above 18 years, males & females with smoking index ≥ 200 cigarette-years. “Cigarettes-years" is a unit of measurement for the quantity of cigarettes smoked over an extended period of time. It is calculated by this equation:

Cigarettes-years = number of cigarettes smoked/ day × number of years smoked.

Systemic disease like diabetes mellitus, hypertension, Ocular disease affecting choroidal, macular and peripapillary retinal nerve fiber layer (RNFL) thickness like glaucoma., Previous ocular operations affecting choroidal, macular and peripapillary retinal nerve fiber layer (RNFL) thickness, Smoking material like hashish, bango and marijuana were excluded.

All participants were subjected to the following:

History taking: Smoking index, past ocular history (disease, surgery and laser), other associated

systemic diseases (HTN, diabetes) and any other medication.

Best corrected and uncorrected visual acuity was determined using a Snellen eye chart. A slit lamp examination of the anterior section was conducted. Posterior segment examination was performed using slit lamp biomicroscopy with a +90 diopter Volk lens after approximately 30 minutes of pupillary dilatation with three drops of Cyclopentolate HCL. All OCT scans were done the morning following the examination (between 9:00 and 12:00 am to avoid diurnal fluctuations). The macula and peripapillary RNFL were measured using the Heidelberg Spectralis (software version 5.7.5; Heidelberg Engineering, Heidelberg, Germany). The images of the choroid were acquired in enhanced depth imaging (EDI) mode. The Heidelberg Spectralis was used to determine the central foveal and choroidal thicknesses from a horizontal section passing directly through the fovea's center. The Central foveal thickness was measured as the distance between the inner border of the hyper-reflective line representing the internal limiting membrane and the inner border of the hyper-reflective line representing the retinal pigment epithelium (Fig.1).

Choroidal thickness was measured manually from the outer border of the hyper-reflective line corresponding to the retinal pigment epithelium to the hyper-reflective line of the inner sclera border. seven measurements; one subfoveal, three temporal to fovea, and three nasal to fovea were taken at 500 µm intervals up to 1500 µm via the software caliper (Fig.2).

Peripapillary RNFL thickness was measured (G: global, T: temporal, Ts: temporal superior, Ti: temporal inferior, N: nasal, Ns: nasal superior, Ni: nasal inferior Fig. 3).

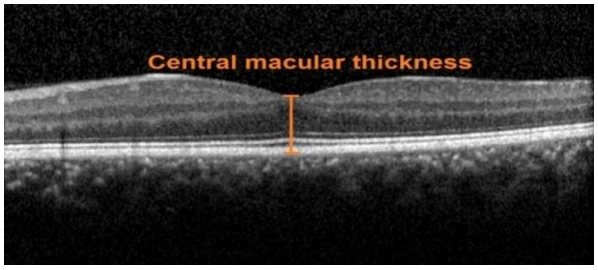

Fig. 1. Measurement of central macular thickness

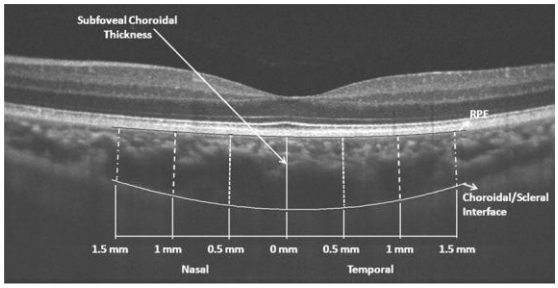

Fig. 2. Measurement of choroidal thickness

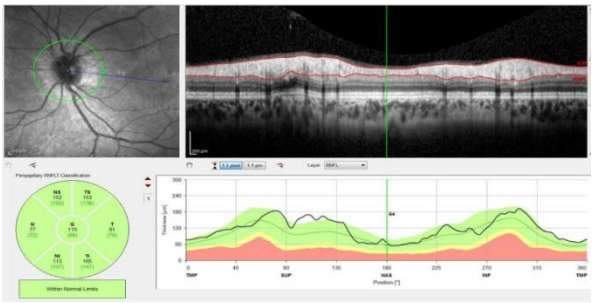

Fig. 3. Measurement of peripapillary retinal nerve fiber layer thickness

All participants completed the study, which included a comparison of the macula, choroidal, and peripapillary retinal nerve fibre layer thickness in both groups to determine the effect of smoking.

2.1 Statistical Analysis

The mean, standard deviation, student t-test, and Chi-square test were used to present and analyze the data in this study. The mean, standard deviation, student t-test, and Chi-square test (The hypothesis that the row and column variables are independent, without specifying the strength or direction of the association) were used to present and analyze the data. SPSS V20 was used to determine the connection between two quantitative variables in one group using Pearson chi-square and likelihood-ratio chi-square) and Linear Correlation coefficients.

3. RESULTS

There was no significant statistical difference between the two groups; all the studied participants were males (100%) The mean value of age among the two groups; it was 32.2 ± 4.5 years for smokers' group (range, 20-38 years), and for the nonsmoker's group, it was 31.6 ± 5.47 (range, 22-42 years), this didn't constitute a statistically significant difference as P- value was 0.67 (P > 0.05), Table 1.

Table 1. Comparison between smoker group and nonsmoker group according to age

		Group		T-Test	
		Smoker	**Non-Smoker**	**t**	**P-value**
Age	Range	20 - 38	22 - 42	0.423	0.674
	Mean ± SD	32.20 ± 4.51	31.60 ± 5.47		

Table 2. Comparison between the peripapillary RNFL thicknesses measured by SD-OCT in smoker and nonsmoker groups

Peripapillary Retinal quadrants		**Peripapillary RNFL thickness in (µm)**		**T-Test**	
		Smokers group	**Non-Smokers group**	**t**	**P-value**
Temporal (T)	Range	50 - 94	57 - 92	-2.501	0.014*
	Mean ± SD	69.36 ± 9.14	74.14 ± 9.95		
Superotemporal (ST)	Range	112 - 167	114 - 182	-1.165	0.247
	Mean ± SD	139.90 ± 16.61	144.14 ± 19.66		
Inferotemporal (IT)	Range	104 - 166	115 - 180	-1.741	0.085
	Mean ± SD	142.60 ± 12.09	148.62 ± 21.25		
Nasal (N)	Range	50 - 122	53 - 109	0.756	0.452
	Mean ± SD	85.68 ± 15.54	83.44 ± 14.06		
Superonasal (SN)	Range	70 - 166	93 - 156	-1.306	0.195
	Mean ± SD	124.28 ± 24.72	129.88 ± 17.55		
Inferonasal (IN)	Range	70 - 156	66 - 156	-1.592	0.115
	Mean ± SD	110.18 ± 20.41	116.78 ± 21.04		
Global (G)	Range	86	88 - 122	-2.009	0.047*
	Mean ± SD	103.52 ± 6.73	106.68 ± 8.86		

**: significant as P value < 0.05*

Table 3. Comparison between smoker group and nonsmoker group according to central macular thickness

	Central macular thickness in (µm)		**T-Test**	
	Smokers group	**Non-Smokers group**	**t**	**P-value**
Range	224 - 296	218 - 301	-2.628	**0.010***
Mean ± SD	255.20 ± 18.91	264.82 ± 17.67		

**: significant as P value < 0.05*

Table 4. Comparison between smoker group and nonsmoker group according to choroidal thickness

Choroidal sections		Choroidal thickness in (µm)		T-Test	
		Smokers group	Non-Smokers group	t	P-value
Sub-foveal	Range	227 - 537	119 - 542	-3.708	<0.001*
	Mean ± SD	358.26 ± 84.56	426.56 ± 99.06		
Nasal 500µm	Range	201 - 535	217 - 537	-4.251	<0.001*
	Mean ± SD	334.60 ± 95.59	414.44 ± 92.20		
Nasal 1000µm	Range	193 - 523	220 - 540	-5.349	<0.001*
	Mean ± SD	328.48 ± 90.03	421.12 ± 83.02		
Nasal 1500µm	Range	143 - 508	207 - 546	-4.863	<0.001*
	Mean ± SD	314.28 ± 92.53	402.52 ± 88.89		
Temporal 500µm	Range	178 - 524	235 - 534	-4.378	<0.001*
	Mean ± SD	338.82 ± 91.927	417.40 ± 87.51		
Temporal 1000µm	Range	174 - 505	252 - 506	-4.433	<0.001*
	Mean ± SD	330.10 ± 82.26	404.22 ± 84.90		
Temporal 1500µm	Range	163 - 523	201 - 501	-5.161	<0.001*
	Mean ± SD	296.28 ± 89.79	386.50 ± 84.94		

**: significant as P value < 0.05*

Table 5. Correlation between peripapillary RNFL, central macular and choroidal thicknesses and smoking index

Correlations		
	Smoking index	
	r	P-value
Peripapillary RNFL thickness T	0.319	0.024*
Peripapillary RNFL thickness ST	-0.112	0.437
Peripapillary RNFL thickness IT	-0.153	0.289
Peripapillary RNFL thickness N	-0.379	0.007*
Peripapillary RNFL thickness SN	-0.450	0.001*
Peripapillary RNFL thickness IN	-0.290	0.041*
Peripapillary RNFL thickness G	-0.503	<0.001*
Central macular thickness	-0.274	0.054*
Choroidal thickness SF	-0.057	0.693
Choroidal thickness N 500µm	-0.023	0.875
Choroidal thickness N 1000µm	0.046	0.753
Choroidal thickness N 1500µm	-0.005	0.973
Choroidal thickness T 500µm	-0.069	0.634
Choroidal thickness T 1000µm	-0.165	0.252
Choroidal thickness T 1500µm	-0.211	0.142

**: significant as P value < 0.05*

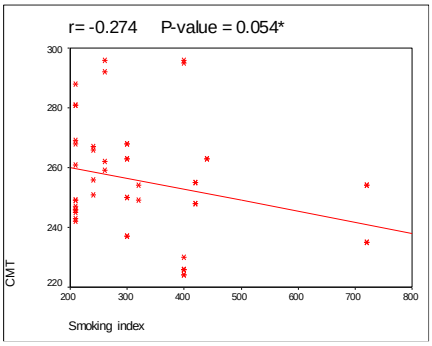

Fig. 4. Correlation between central macular thickness and smoking

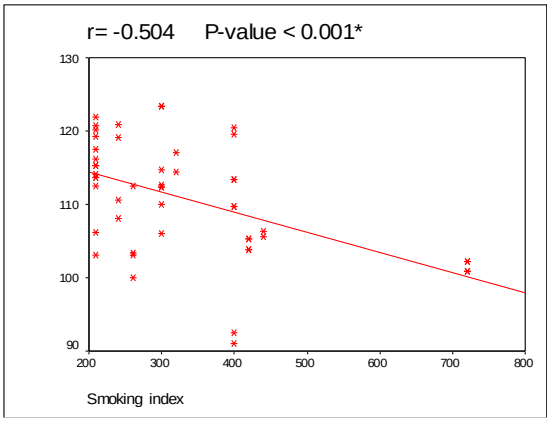

Fig. 5. Correlation between peripapillary RNFL thickness and smoking index

In the smoker group, the peripapillary RNFL thickness was 69.36±9.14 µm in the temporal quadrant, 74.14±9.95 µm in the nonsmoker group. Intergroup difference was statistically significant (p=0.014). In the remaining quadrants, there were no significant variations in peripapillary RNFL thickness between the two groups, Table 2.

Mean central macular thickness (CMT) was 255.2±18.91 µm in the smokers' group, in comparison to 264.82±17.67 µm in the nonsmokers' group, In the smoking group, there was a statistically significant reduction. in CMT as P- value was 0.010 (P < 0.05) Table 3**.**

Choroidal thickness in smoker group; was measured sub-foveal (358.26±84.56), 500µm nasal to the fovea (334.6±95.59), 1000µm nasal to the fovea (328.48±90.03), 1500µm nasal to the fovea (314.28±92.53) and 500µm temporal to the fovea (338.82±91.93), 1000µm temporal to the fovea (330.1±82.27) and 1500µm temporal to the fovea (296.28±89.79). While in nonsmokers' group were (426.56±99.06), (414.44±92.20), (421.12±83.02), (402.52±88.98), (417.4±87.51), (404.22±84.90) and (386.5±84.94), respectively. Between the two groups, all measures indicated a substantial decrease in choroidal thickness in the smoked group (p0.001). Table 4.

In a correlation between smoking index and peripapillary RNFL, central macular and choroidal thickness (Table 5), it showed a negative significant correlation between smoking index and peripapillary RNFL and central macular thickness, so the higher the smoking index was, the thinner the peripapillary RNFL and central muscular thicknesses were. The smoking index had a negative association with choroidal thickness, although it was not statistically significant (Figs. 4, 5).

4. DISCUSSION

The smoking group had a substantial reduction in central macular and choroidal thickness as compared to the nonsmoker group. There were no significant changes in peripapillary RNFL thickness across the groups, except that the Temporal (T) quadrant was considerably thinner in the smoking group. The connection between peripapillary RNFL, central macular thickness, and smoking index was shown to be negative and significant. There are a few studies that used OCT to determine the thickness of certain retinal layers in smokers. In our study there is a significant decrease in the temporal quadrant of the peripapillary RNFL in smoker group compared to nonsmoker group (p=0.014) with a negative significant correlation between peripapillary RNFL and smoking index, while other quadrants did not show significant.

Dervisoğulları et al. (2015) conducted research on the effects of smoking on the retinal layers, particularly the retinal nerve fibre layer (RNFL) and the ganglion cell-inner plexiform layer complex (GCIPL). The study found that smokers' Although the inferior and superior quadrants of RNFL were significantly thinner (p=0.001 and p=0.03, respectively), their nasal and temporal quadrants were not significantly thinner (p=0.07 and p=0.96, respectively) [8]. Similarly, El-Shazly et al. (2017) studied the effect of smoking, both active and passive, on RNFL. The inferior and superior quadrants of RNFL were significantly thinner in the active smoker group (p0.0001 and p0.0001, respectively), but not the nasal or

temporal quadrants (p=0.82 and p=0.18, respectively) [9].

Ahuja et al. (2016) studied the effects of chronic alcohol and/or tobacco use on the retinal nerve fibre layer RNFL (thickness and identified a substantial correlation between addiction severity and RNFL thinning, with RNFL thinning increasing as tobacco use severity increased [10].

Demirci et al. (2016) Ahmed examined the impact of cigarette smoking on the thickness of the peripapillary retinal nerve fibre layer (RNFL) in migraine sufferers. The study discovered that smokers with migraine had substantially lower average and inferior RNFL thicknesses than nonsmokers with migraine (p=0.011, p=0.045, respectively) [11].

Teberik (2019) demonstrated that smokers' temporal and inferonasal quadrants of peripapillary RNFL were substantially thinner than nonsmokers' (p=0.003 and p=0.005, respectively), but In the remaining quadrants, there were no significant variations in peripapillary RNFL thickness across the groups [12].

On the other hand, Duman et al. (2017) compared the thicknesses of the retinal layers in smokers and nonsmoking healthy participants utilizing (SD-OCT). Although the study focused on the thickness of all retinal layers inside the core Early Treatment Diabetic Retinopathy Study (ETDRS) zone of 1000, 3000, and 6000 m diameter, our study concentrated on peripapillary RNFL thickness. They found that there are not any significant differences in the RNFL thickness between smoker and nonsmoker group [13].

In our study, smokers had a substantially lower central macular thickness than nonsmokers (p=0.010), with a negative significant connection between central macular thickness and smoking index. In similar to our results, El-Shazly et al. (2018) recently published a cross-sectional clinical study in which he evaluated the influence of smoking on macular function and structure in 100 active smokers and 100 healthy passive smokers who were age- and sex-matched. It was discovered that the active smoker group's central foveal thickness reduced considerably (P = 0.0003) [9].

Opposing to our results, Teberik (2019) assessed the effect of smoking on central macular thickness and discovered no statistically significant difference between the two groups (p=0.99) [12].

The central macular thickness differences may be explained by the differences in race and gender percentage between the two studies, as in our study; males represent 100% of the smoker and nonsmoker group, while in Teberik's (2019) study; (males represent 67% of smoker group and 64% of nonsmoker group). CMT is influenced by gender, body mass index, and axial length. These criteria should be taken into account while evaluating retinal thickening as Wong et al. (2005) showed in his study [14]. CMT also affected by race as Kashani et al. (2010) reported that, African Americans have a considerably smaller mean foveal thickness than Caucasians (P 0.0001). [15].

The choroid is a dense network of blood vessels and pigmented stroma between the retinal pigment epithelium and the sclera. Its physiological function is to give nutrients to the retina's outer posterior layers, which means that choroidal thickness issues might impair vision. [16].

The choroidal thickness has a correlation with age and sex Lee et al. (2014. There were no significant variations in age between the two groups in our research (p=0.674). There are previous studies showed that choroid is thinner in females. 100% of the smokers and nonsmokers' group were males, as a result, there were no statistically significant gender-based differences across the two groups. [17].

To prevent diurnal variations, all OCT scans have been carried out in the morning following the assessment between 9:00 and 12:00 am in our research decreases after wakening from sleep Lee et al. (2014) [18].

Choroidal thickness was determined manually between the outer border of the hyper-reflective line corresponding to the retinal pigment epithelium and the inner sclera border hyper-reflective line. Seven measurements; sub-foveal, 500, 1000 and 1500μm nasal and temporal to fovea via the software caliper. All parameters were significantly decreased in the smoker group (p<0.001).

Similar to our result, Moschos et al. (2016) studied the effect of cigarette smoking on choroidal thickness on 31 smokers and 25 age-

and sex-matched nonsmokers in a cross-sectional randomized study. The choroidal thickness was determined in the sub-foveal region and at distances of 1500 and 3000m from the fovea's center in the superior, temporal, inferior, and nasal quadrants. The variations in choroidal thickness between the two groups were statistically significant (p0.001), with the smokers' group being thinner. [19]

Furthermore, Sızmaz et al. (2013) conducted a research that utilized Fourier domain OCT to determine the acute effect of cigarette smoking on choroidal thickness. The OCT measurements were taken eight hours before to smoking "baseline" cigarettes and one and three hours after smoking one standard cigarette (nicotine; 1.3 mg, tar; 15 mg). As a result of smoking one cigarette, choroidal thickness decreased significantly as compared to baseline. Additionally, the choroidal thickness decreased for at least three hours following smoking. [20].

Similarly, Zengin et al. (2014) used optical coherence tomography to examine the acute effect of nicotine oral consumption (nicotine gum) on choroidal thickness (OCT). After 1 hour of oral consumption, nicotine produces a substantial reduction in choroidal thickness. This immediate reduction might be a result of decreased ocular blood flow caused by nicotine's vasoconstrictive impact. [21]

On the other hand, Ulaş et al. (2014) investigated the acute and chronic effects of cigarette smoking on choroidal thickness in 40 nonsmokers (20 men and 20 women) and 30 chronic smokers (15 males and 15 females) aged 25–35 years. There was no statistically significant difference in choroidal thickness between smokers and nonsmokers, the researchers observed. They did discover, however, that in smokers, choroidal thickness rose considerably within the first 5 minutes after smoking but recovered to baseline levels after 1 hour. Carbon monoxide, rather than nicotine, increases choroidal thickness during the acute stage of smoking by boosting retinal and choroidal blood flow. [22]

Furthermore Kantarci et al. (2016) and Teberik (2019) no significant variations in macular and choroidal thickness existed between smokers and nonsmokers. The discrepancies in results across prior research might be ascribed to the use of different scanning technologies and algorithms for aligning and registering OCT images. [13, 23]

Another Meta-analysis of all available observational studies was done by Yang et al. (2019) investigated the effects of cigarette smoking on the retinal and choroidal thicknesses. They performed subgroup analyses to get more data from the included studies. The subgroup analyses by regions demonstrated that only the studies conducted in Africa showed significant decrease in central retinal thickness, and the average, inferior and superior quadrants of RNFL thickness in smokers. Regarding to the subgroup analyses of the effect of smoking on choroidal thickness, it found that in America and Africa but not Europe there was a significant decrease in choroidal thickness [24].

Finally, we know that cigarette smoking is considered a risk factor for the incidence of several chronic diseases and contains a lot of chemicals which can affect the ocular vascularity but the exact mechanism of the effect of smoking on blood vessels has not yet understood and still being investigated in several studies.

5. CONCLUSION

Our study concluded that smoking induces a statistically significant decrease in mean peripapillary retinal nerve fiber layer thickness "particularly temporal quadrant", choroidal and central macular thickness. This implies that cigarette smoking as a factor of systemic and ocular vascular disorder has an effect on posterior layers of eye decreasing its thickness.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. WH. O. Don't Let Tobacco Take Your Breath Away: Choose Health, not Tobacco; 2019. Available:https://www3.paho.org/hq/index.php?option=com_content&view=article&id=15121:world-no-tobacco-day-2019-tobacco-and-lung-health&Itemid=40273&lang=en#:~:text=Every%20year%2C%20on%2031%20May,of%20tobacco%20in%20any%20form.
2. Tousoulis D, Davies G, Stefanadis C, Toutouzas P, Ambrose JA. Inflammatory and thrombotic mechanisms in coronary atherosclerosis. Heart. 2003;89:993-7.
3. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. J Am Coll Cardiol. 2004;43:1731-7.
4. Lois N, Abdelkader E, Reglitz K, Garden C, Ayres JG. Environmental tobacco smoke exposure and eye disease. Br J Ophthalmol. 2008;92:1304-10.
5. Chhablani J, Wong IY, Kozak I. Choroidal imaging: A review. Saudi J Ophthalmol. 2014;28:123-8.
6. Maul EA, Friedman DS, Chang DS, Boland MV, Ramulu PY, Jampel HD, et al. Choroidal thickness measured by spectral domain optical coherence tomography: factors affecting thickness in glaucoma patients. Ophthalmology. 2011;118:1571-9.
7. Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. Am J Ophthalmol. 2009;147:811-5.
8. Dervişoğulları MS, Totan Y, Tenlik A, Yüce A, Güler E. Effect of smoking on retina nerve fiber layer and ganglion cell-inner plexiform layer complex. Cutan Ocul Toxicol. 2015;34:282-5.
9. El-Shazly AAE, Farweez YAT, Elewa LS, Elzankalony YA, Farweez BAT. Effect of Active and Passive Smoking on Retinal Nerve Fibre Layer and Ganglion Cell Complex. J Ophthalmol. 2017;2017:6354025.
10. Ahuja S, Kumar PS, Kumar VP, Kattimani S, Akkilagunta S. Effect of chronic alcohol and tobacco use on retinal nerve fibre layer thickness: a case-control study. BMJ open ophthalmology [Internet]. 2017 2017;1(1):[e000003 p.]. Available:http://europepmc.org/abstract/MED/29354691https://doi.org/10.1136/bmjophth-2016000003https://europepmc.org/articles/PMC5759398https://europepmc.org/articles/PMC5759398?pdf=render.
11. Demirci S, Gunes A, Demirci S, Kutluhan S, Tok L, Tok O. The effect of cigarette smoking on retinal nerve fiber layer thickness in patients with migraine. Cutan Ocul Toxicol. 2016;35:21-5.
12. eberik K. The Effect of Smoking on Macular, Choroidal, and Retina Nerve Fiber Layer Thickness. Turk J Ophthalmol. 2019;49:20-4.
13. Duman R, Duman R, Sabaner MC, Çetinkaya E. Effect of smoking on the thickness of retinal layers in healthy smokers. Cutan Ocul Toxicol. 2017;36:366-9.
14. Wong AC, Chan CW, Hui SP. Relationship of gender, body mass index, and axial length with central retinal thickness using optical coherence tomography. Eye (Lond). 2005;19:292-7.
15. Kashani AH, Zimmer-Galler IE, Shah SM, Dustin L, Do DV, Eliott D, et al. Retinal thickness analysis by race, gender, and age using Stratus OCT. Am J Ophthalmol. 2010;149:496-502.e1.
16. Linsenmeier RA, Padnick-Silver L. Metabolic dependence of photoreceptors on the choroid in the normal and detached retina. Invest Ophthalmol Vis Sci. 2000;41:3117-23.
17. Lee SW, Yu SY, Seo KH, Kim ES, Kwak HW. Diurnal variation in choroidal thickness in relation to sex, axial length, and baseline choroidal thickness in healthy Korean subjects. Retina. 2014;34:385-93.
18. Moschos MM, Nitoda E, Laios K, Ladas DS, Chatziralli IP. The Impact of Chronic Tobacco Smoking on Retinal and Choroidal Thickness in Greek Population. Oxid Med Cell Longev. 2016;2016:2905789.
19. Sizmaz S, Küçükerdönmez C, Pinarci EY, Karalezli A, Canan H, Yilmaz G. The effect of smoking on choroidal thickness measured by optical coherence tomography. Br J Ophthalmol. 2013;97:601-4.
20. Zengin MO, Cinar E, Kucukerdonmez C. The effect of nicotine on choroidal thickness. Br J Ophthalmol. 2014;98:233-7.
21. Ulaş F, Çelik F, Doğan Ü, Çelebi S. Effect of smoking on choroidal thickness in

healthy smokers. Curr Eye Res. 2014;39:504-11.
22. Kantarci FA, Tatar MG, Colak HN, Uslu H, Yildirim A, Goker H, et al. A Pilot Study of Choroidal Thickness in Long-Term Smokers. Retina. 2016;36:986-91.
23. Yang TK, Huang XG, Yao JY. Effects of Cigarette Smoking on Retinal and Choroidal Thickness: A Systematic Review and Meta-Analysis. J Ophthalmol. 2019;2019:8079127.
24. Steigerwalt RD, Jr., Laurora G, Incandela L, Cesarone MR, Belcaro GV, De Sanctis MT. Ocular and orbital blood flow in cigarette smokers. Retina. 2000;20: 394-7.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/74710