https://doi.org/10.34883/PI.2025.15.1.015

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Studying the Effects of High Myopia with Maculopathy in Chronic Smokers Versus Non-Smokers Using Optical Coherence Tomography Angiography

Conflict of interest: nothing to declare.
Authors' contribution: all authors are involved in this research. We certify that we have participated sufficiently in the intellectual content, conception and design of this work or the analysis and interpretation of the data, as well as the writing of the manuscript.
Funding: not applicable as no fund was obtained for the research.
Data availability statement: data of all patients will be available at any time for review. Please contact the corresponding author for any data.
Ethics statement: this study approved by Local ethics committee and Beni-Suef University Institutional Review Board (FM-BSU REC). FM-BSU REC is organized and operated according to guidelines of the declaration of Helsinki and international conference of harmonization ICH, and united states codes of federal regulations and registered in under the federal wide assurance (FWA) for the protection of human subjects.

Submitted: 16.12.2024
Accepted: 24.02.2025
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Abstract

Purpose. To detect changes in high myopic eyes with maculopathy by optical coherence tomography angiography (OCTA) in non-smokers and smokers and compare these results to high myopic eyes without maculopathy.
Materials and methods. This comparative study was applied to 120 eyes of 60 high myopic subjects (40 high myopic eyes without maculopathy, 40 with maculopathy in non-smoker subjects, 40 with maculopathy in chronic smokers). All patients were subjected to OCTA scanning Key measurements included thickness across all macular subfields, macular ganglion cell complex (GCC) thickness, peripapillary retinal nerve fiber layer (RNFL) thickness, foveal avascular zone (FAZ) area, and superficial and deep macular vessel density (VD), as well as optic disc VD and choroidal thickness.
Results. The FAZ area was 0.215±0.09 in smokers, 0.210±0.07 in non-smokers, and 0.180±0.04 in the control group (p=0.038). Thickness across all macular subfields, along with choroidal, GCC, and RNFL thicknesses were lower in the smokers compared to the other 2 groups. The whole disc VD was 35.45±7.62% in smokers, 42.49±9.27% in non-smokers, and 48.26±5.2% in the control group (p<0.004). The superficial and deep foveal VD were17.3±7.6%, 26.6±4.2% respectively in smokers, 24.3±9.1%, 37.5±5.1% respectively in non-smokers, and 40.5±4.9%, 43.8±7.3% respectively in control group (p<0.001). The superficial and deep parafoveal VD were recorded at 21.0±6.2% and 27.1±1.6% for smokers, 33.1±7.9% and 37.4±1.3% for non-smokers, and 45.6±5.8% and 47.4±1.4% in controls (p<0.001).
Conclusions. High myopia with maculopathy impacted the structure of the macula, optic nerve, and choroid. It enlarged the FAZ area and decreased macular and Optic disc (except inside the disc) VDs. Chronic smoking causes more significant effects.
Keywords: high myopia, myopic maculopathy, chronic smoking, OCTA

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Изучение эффектов миопии высокой степени с макулопатией у хронических курильщиков по сравнению с некурящими с использованием оптической когерентной томографической ангиографии

Конфликт интересов: не заявлен.
Вклад авторов: все авторы приняли участие в этом исследовании (интеллектуальное содержание, концепция и дизайн работы, анализ и интерпретация данных), а также в написании рукописи.
Финансирование: для исследования не было получено финансирования.
Заявление о доступности данных: данные всех пациентов будут доступны для просмотра в любое время. Пожалуйста, свяжитесь с соответствующим автором для получения любых данных.
Этическое заявление: это исследование одобрено местным этическим комитетом и институциональным наблюдательным советом университета Бени-Суэф (FM-BSU REC).
FM-BSU REC организован и работает в соответствии с руководящими принципами Хельсинкской декларации и международной конференции по гармонизации ICH, а также кодексами федеральных правил США и зарегистрирован в соответствии с федеральной широкой гарантией (FWA) для защиты прав субъектов.

Подана: 16.12.2024
Принята: 24.02.2025
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Резюме

Цель. Выявить изменения в глазах с миопией высокой степени и макулопатией с помощью оптической когерентной томографической ангиографии (ОКТА) у некурящих и курильщиков и сравнить эти результаты с глазами с миопией высокой степени без макулопатии.

Материалы и методы. Это сравнительное исследование было применено к 120 глазам 60 пациентов с миопией высокой степени (40 глаз с миопией высокой степени без макулопатии, 40 с макулопатией у некурящих пациентов, 40 с макулопатией у хронических курильщиков). Все пациенты прошли ОКТА-сканирование. Ключевые измерения включали толщину во всех полях макулы, толщину комплекса ганглиозных клеток макулы (GCC), толщину перипапиллярного слоя нервных волокон сетчатки (RNFL), площадь фовеолярной аваскулярной зоны (FAZ), поверхностную и глубокую плотность макулярных сосудов (VD), а также VD диска зрительного нерва и толщину хориоидеи.

Результаты. Площадь FAZ составила 0,215±0,09 у курильщиков, 0,210±0,07 у некурящих и 0,180±0,04 в контрольной группе (p=0,038). Толщина во всех полях макулы, а также толщина хориоидеи, GCC и RNFL были ниже у курильщиков по сравнению с двумя другими группами. Общий VD диска составил 35,45±7,62% у курильщиков, 42,49±9,27% у некурящих и 48,26±5,2% в контрольной группе (p<0,004). Поверхностный и глубокий фовеолярный VD составили 17,3±7,6% и 26,6±4,2% у курильщиков, 24,3±9,1% и 37,5±5,1% у некурящих и 40,5±4,9% и 43,8±7,3% в контрольной группе (p<0,001) соответственно. Поверхностный и глубокий парафовеолярный VD зарегистрированы на уровне 21,0±6,2% и 27,1±1,6% у курильщиков, 33,1±7,9% и 37,4±1,3% у некурящих и 45,6±5,8% и 47,4±1,4% в контрольной группе (p<0,001) соответственно.

Выводы. Миопия высокой степени с макулопатией повлияла на структуру макулы, зрительного нерва и сосудистой оболочки. Она увеличила площадь FAZ и уменьшила макулярный и зрительный диск (за исключением внутренней части диска) VD. Хроническое курение вызывает более значимые эффекты.
Ключевые слова: миопия высокой степени, миопическая макулопатия, хроническое курение, ОКТА

■ INTRODUCTION

Globally, over two billion individuals, representing 28.3% of the population, suffer from myopia, with 277 million, or 4.0%, having very high myopia. This makes myopia a major and increasingly pressing issue in public health around the world. A refractive error of squared plus or minus 6.00 diopters is considered high myopia. Pathologic myopia is characterized by high myopia that presents with myopic lesions in the posterior segment of the eye. Examples include myopic maculopathy, which may result in reduced or complete loss of vision [1].

One of the most serious consequences of high myopia in middle-aged and elderly individuals is myopic maculopathy, which can lead to severe vision loss. Myopia is becoming more common among people all over the world, which means that myopic maculopathy is likely to become more common as well. As a result, lowering the global burden of myopic maculopathy requires a focus on prevention and early treatment [2].

Smoking is a major problem in public health around the world, responsible for over 7 million fatalities annually. The human circulatory system is particularly vulnerable to the many harmful and poisonous substances included in cigarette smoke. Multiple epidemiological studies have found a high correlation between smoking and ocular vascular disorders, including anterior ischemic optic neuropathy and retinal ischemia [3].

Noninvasive optical coherence tomography (OCT) devices use in vivo imaging techniques to detect and assess retinal layer thickness [4]. New OCT technologies have recently allowed for clearer imaging of the choroidal and retinal veins and arteries. The new technology known as optical coherence tomography angiography (OCTA) enables the imaging of the superficial and deep capillary plexus, as well as the quick visualization of the vasculature of the optic disc, choroidal, and retina. As a result, it facilitates the identification of choroidal and retinal vascular diseases [5].

■ PURPOSE

The purpose of our study was to detect the changes in high myopic eyes with maculopathy by using OCTA in non-smokers and chronic smokers.

■ MATERIALS AND METHODS

This research was an observational case-control study conducted on 120 eyes from 60 healthy adults with high myopia (≥18 years old), characterized by a refractive error of –6 D or more and/or an axial globe more than 26 mm in length. The study took place in the ophthalmology department from June 2019 to May 2022. The Participants were categorized into three distinct groups: Group 1 (control) included 40 high myopic eyes without any presence of myopic maculopathy; Group 2 (non-smokers) comprised 40 high

myopic eyes displaying myopic maculopathy in non-smokers; and Group 3 (smokers) consisted of 40 high myopic eyes displaying myopic maculopathy in chronic smokers (who have been smoking for a minimum of 10 years and consume at least one pack daily). The types of myopic maculopathy were distributed equally between Groups 2 and 3. They included inactive myopic CNV (either early or treated CNV, totaling 30 eyes), myopic scar (30 eyes), and myopic chorioretinal atrophy (20 eyes). All participants provided written informed consent, and the study protocol received approval from the ophthalmology ethical committee for scientific research (FM-BSU-REC (FWA00015574)) at Beni-Suef University.

The study excluded individuals with a history of ocular surgeries, trauma, other ocular or systemic diseases, or active CNV. Each participant underwent a thorough history review, including details on smoking habits (daily cigarette intake, length of smoking) and medical history to rule out any systemic or ocular conditions or extended drug use. Clinical evaluations also included random blood glucose measurement vital signs at the outpatient clinic.

Ophthalmic exams were conducted on both eyes of all participants, including measurements of best corrected visual acuity (BCVA), refraction assessment via an automatic refractometer (with spherical equivalent calculations), intraocular pressure (IOP) using a Goldman applanation tonometer as well as slit-lamp biomicroscopy and a fundus exam using a 90 D Volk lens under slit-lamp biomicroscopy.

Each eye was imaged with OCTA using the AngioVue system (Optovue RTVue XR Avanti; Optovue Inc., Fremont, California, Software version 2016.0.0.52). This device employs an 840 nm diode laser source. The device offers an axial resolution of 5 μm and a 45 nm bandwidth, to create a 3D OCTA image centered on the fovea (3×3 mm scan). Using the AngioVue software, the vascular region was automatically segmented into four distinct layers: superficial, deep, outer retina, and choroidal layers. The SVP, or superficial vascular plexus, ranged from the inner limiting membrane to a point 10 μm above the inner plexiform layer. In comparison, the deep vascular plexus (DVP) spanned from 10 μm above the inner plexiform layer to 10 μm below the outer plexiform layer. Vascular density was determined by calculating the percentage of the area within a region occupied by vessels, including terminal arterioles, venules, and capillaries. The foveal region was identified as a circular area with a 1 mm diameter centered on the fovea, while the parafoveal region extended from 1 to 3 mm around the foveal center and divided into four quadrants (superior, inferior, nasal and temporal). The software performed automated VD calculations for both DVP and SVP.

With the image scale set to 3×3 mm, the software enabled automated FAZ (foveal avascular zone) border detection, visible under the "FAZ" measurement display on the screen. The peripapillary retinal nerve fiber layer (RNFL) thickness was evaluated through optical coherence tomography (OCT), targeting an elliptical annulus surrounding the optic disc. Additionally, the macular ganglion cell complex (GCC) was analyzed for average thickness and measurements like superior, inferior, global loss volume (GLV), and focal loss volume (FLV), using a 3×3 mm scan of the macula centered on the fovea. Choroidal thickness (CT) was manually measured with a caliper system from the outer boundary of the hyperreflective retinal pigment epithelium to the hyperreflective inner scleral boundary at three locations: subfoveal, 0.5 mm temporal, and 0.5 mm nasal.

Using the optic disc angiography feature, the software automatically identified the optic disc›s elliptical annulus shape (4.5×4.5 mm enface image), and flow density was evaluated in six regions: nasal, inferior-nasal, inferior-temporal, superior-temporal, superior-nasal, and temporal. Each region extended from the inner annulus to 0.75 mm beyond the outer edge. Additionally, the software provided vascular density measurements for the entire enface image, peripapillary, and inner disc regions. To maintain consistency, all OCTA and OCT scans were performed by the same trained investigator at the same time each day (between 8:00 a.m. and 12:00 p.m.) under standardized conditions. Three scans were captured for each eye, with the highest-quality scan selected for statistical analysis.

Statistical analysis

We used SPSS for Mac, V.22, from IBM/SPSS in Chicago, Illinois, USA, to do the statistical study. One-way analysis of variance (ANOVA) was used to compare the differences in our groups regarding the normally distributed variables. The Kruskal Wallis test (KW) was used for comparing the differences between our groups regarding not normally distributed variables. P-value <0.05 is considered statistically. Also, p1 represents the difference between myopic patients without maculopathy and non-smoker myopic with maculopathy, p2 represents the difference between myopic patients with maculopathy and smoker myopic with maculopathy and p3 difference between non-smokers and smoker myopic with maculopathy. Tukey Honest Significant test was also used in our data analysis to compare each of the two groups.

■ RESULTS

A total of 120 eyes of 60 healthy high myopic subjects were included in our study (40 eyes for each group). The age ranged from 30–50 years. It included 54 males and 6 females. All groups were age and sex-matched. In the smoker's group, the number of cigarettes/days ranged from 20–30, and the mean was 22±3. Duration of smoking (years) ranged between 10–12 years with an average of 11.2±0.5 years. The type of myopic maculopathy included in our study varied from inactive myopic CNV (30 eyes), myopic scar (30 eyes), and myopic chorioretinal atrophy (20 eyes).

The FAZ area differed significantly among the groups under study, which was the largest in smokers followed by non-smokers but smallest in control group ($p<0.001$). Regarding choroidal thickness, there was a significant difference between the studied groups, with the lowest thickness in the smokers group followed by non-smokers and the highest in the control group in all areas, nasal ($P<0.001$), sub-foveal ($P<0.001$) or temporal ($P=0.002$), except the temporal area between smokers and non-smokers where there was no significant difference ($p=0.07$) (Table 1).

Significant variations in macular thickness, specifically in the superior, inferior, central, nasal, and temporal regions, were noted between the groups analyzed ($P<0.001$). Also, on comparing the two groups, there was a significant difference, where the control group had significantly higher macular thickness in all these aspects ($P<0.001$). However, the central macular thickness didn't differ significantly Comparing the smoker group with the non-smoker group (Table 2).

Table 1
Comparison between the studied groups regarding FAZ area

Parameter, mean±SD	Groups			p-value
	Myopic group without maculopathy, N=40	Non-smoker group with maculopathy, N=40	Smoker group with maculopathy, N=40	
FAZ (mm^3)	0.180±0.04	0.210±0.07	0.230±0.09	<0.001*
	P1<0.001*	0.021*	0.029*	
Choroidal thickness				
Nasal	229.75±47.45	200.56±30.68	180.42±30.2	<0.001*
	P1<0.001*	P2=0.004*	P3=0.045*	
Sub-foveal	240.1±34.41	203.0±25	182.2±30.4	<0.001*
	P1<0.001*	P2=0.002*	0.025*	
Temporal	249.25±52.96	205.39±35.36	182.56±42.4	0.002*
	P1=0.003*	P2<0.001*	0.070	

Note: one Way ANOVA test P1 (control vs non-smoker), P2 (control vs smoker), P3 (non-smoker vs smoker).

There were substantial differences between the groups studied concerning average, superior, and inferior GCC thickness. The lowest GCL thickness occurred in the smoker's group (P<0.001). In the pairwise comparison concerning average and inferior GCC, A significant difference was observed between the two groups. As regards superior GCC thickness, A significant difference was observed between the control group and both non-smokers or smokers' groups (P<0.001). Still, no significant difference between smokers and non-smokers groups (p=0.054) was found. Significant variations in global and focal loss volume were found between the groups under study (P<0.001), where smokers had significantly the highest GVL and FVL. There was a significant difference between the studied groups regarding average peripapillary RNFL thickness (P<0.001) (Table 3).

Table 2
Comparison between the studied groups regarding macular thickness

Parameter	Groups			P-value
	Myopic group without maculopathy, N=40 (%)	Non-smoker group with maculopathy, N=40 (%)	Smoker group with maculopathy, N=40 (%)	
	mean±SD	mean±SD	mean±SD	
Superior parafoveal	285±9.5	268±8.4	237±5.9	<0.001*
	P1<0.001**	P2<0.001*	P3<0.001*	
Inferior parafoveal	275±5	260±7	247±4	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Central	250±9	188±8	186±8.5	<0.001*
	P1<0.001*	P2<0.001*	P3=0.133	
Nasal parafoveal	305±10	267±9	242±7	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Temporal parafoveal	270.5±5	261±3	253±4.1	<0.001*
	P1=0.001**	P2<0.001*	P3<0.001*	

Notes: * p<0.05 is statistically significant, P1 (control vs non-smoker), P2 (control vs smoker), P3 (non-smoker vs smoker).

Table 3
Comparison between the studied groups regarding ganglion cell layer analysis

Parameter median (range)	Groups			p-value (KW)
	Myopic group without maculopathy, N=40	Non-smoker group with maculopathy, N=40	Smoker group with maculopathy, N=40	
Average (mm)	93 (88–120)	73 (53 – 101)	45 (39–91)	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Superior (mm)	97±5.5	78±15	71±17	<0.001*
	P1<0.001*	P2<0.001*	P3 =0.054	
Inferior (mm)	91±7.2	78±5.1	46±6.02	<0.001*
	P1<0.001*	P2<0.001*	P3 <0.001*	
Flv (%)	1.435±0.3	16.87±2.3	34.63±5.5	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Glv (%)	7.46 (0.05–12.27)	20.86 (4.27–47.05)	53.97 (7.58–61.08)	<0.001*
	P1=0.004*	P2=0.001*	P3=0.002*	
RNFL thickness	106±7	96±3	86±4	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	

Notes: KW – Kruskal Wallis, P1 (control vs non-smoker), P2 (control vs smoker), P3 (non-smoker vs smoker).

Significant variations in superficial and deep VD were found between the groups across all macular regions (P<0.001), where smokers had the lowest superficial and deep VD in each aspect (Tables 4, 5).

Table 4
Comparison between the studied groups regarding superficial vessel density in macular angiogram

Parameter	Groups			p-value
	Myopic group without maculopathy	Non-smoker group with maculopathy	Smoker group with maculopathy	
	Mean±SD	Mean±SD	Mean±SD	
Whole	46.1±3.3	36.6±6.4	31.2±4.7	<0.001*
	P1<0.001*	P2<0.001*	P3=0.003*	
Superior-hemi	44.6±5.2	36.7±6.8	26.4±7.4	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Inferior-hemi	43.3±5.4	34.7±8.9	26.4±6.8	<0.001*
	P1=0.001*	P2<0.001*	P3=0.002*	
Fovea	40.5±4.9	24.3±9.1	17.3±7.6	<0.001*
	P1<0.001*	P1<0.001*	P3=0.012*	
Parafoveal	45.6±5.8	33.1±7.9	21.0±6.2	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Parafoveal				
Superior hemi	46.0±5.6	37.6±4.9	23.4±8.4	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Inferior hemi	44.9±6.4	37.3±5.9	24.7±7.2	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Temporal	42.9±5.0	33.5±6.2	24.3±6.9	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	

End of table 4

Superior	46.3±6.2	31.6±8.6	21.9±6.4	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Nasal	45.2±6.5	33.9±6.9	19.3±7.8	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Inferior	46.1±6.4	36.4±8.2	21.6±7.1	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	

Notes: one Way ANOVA, P1 (myopic vs non-smoker), P2 (myopic vs smoker), P3 (non-smoker vs smoker).

The studied groups showed notable differences concerning VD of the whole optic disc, inside disc, peripapillary, superior hemisphere optic disc, and inferior hemisphere optic disc (P=0.004, P=0.002, P<0.002, P<0.001, P=0.002 respectively). There was a significant difference between every 2 groups, where smokers had the lowest optic disc VD in all aspects except the inside disc, where it had the highest inside disc VD (Table 6).

Table 5
Comparison between the studied groups regarding deep vessel density (macula angiogram)

Parameter	Groups			p
	Myopic group without maculopathy	Non-smoker group with maculopathy	Smoker group with maculopathy	
	N=20 (%)	N=20 (%)	N=20 (%)	
Whole	54.6±3.3	41.4±11.9	34.6±6.8	<0.001*
	P1<0.001*	P2<0.001*	P3=0.029*	
Superior-hemi	55.1±3.4	41.3±10.9	34.1±3.1	<0.001*
	P1<0.001*	P2<0.001*	P3=0.004*	
Inferior-hemi	54.1±3.3	42.7±12.5	39.6±10.6	<0.001*
	P1=0.001*	P2<0.001*	P3=0.578	
Fovea	43.8±7.3	37.5±5.1	26.6±4.2	<0.001*
	P1=0.003*	P2<0.001*	P3<0.001*	
Parafoveal	47.4±1.4	37.4±1.3	27.1±1.6	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Parafoveal				
Superior-hemi	46.9±1.1	37.5±1.5	27.3±1.6	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Inferior-hemi	47.5±1.5	38.0±1.4	27.2±1.3	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Temporal	55.3±4.6	40.9±12.3	36.6±9.1	<0.001*
	P1<0.001*	P2<0.001*	P3<0.001*	
Superior	47.4±1.6	37.7±1.4	27.1±1.2	<0.001**
	P1<0.001*	P2<0.001*	P3<0.001*	
Nasal	47.5±1.4	37.3±1.2	27.4±1.5	0.029*
	P1<0.001*	P2<0.001*	P3<0.001*	
Inferior	47.5±1.8	38.1±1.6	27.3±1.5	<0.001**
	P1<0.001*	P2<0.001*	P3<0.001*	

Notes: P1 (myopic vs non-smoker), P2 (myopic vs smoker), P3 (non-smoker vs smoker).

Table 6
Comparison between the studied groups regarding optic disc vessels density (optic disc angiography)

Parameters	Groups			P
	Myopic group without maculopathy	Non-smoker group with maculopathy	Smoker group with maculopathy	
	Mean±SD	Mean±SD	Mean±SD	
Whole	48.26±5.2	42.49±9.27	35.45±7.62	0.004*
	P1=0.019*	P3<0.001*	P3=0.014*	
Inside disc	55.08±3.59	60.56±8.69	64.05±2.08	0.002*
	P1<0.001*	P2<0.001*	P3<0.001*	
Peripapillary	46.38±4.12	38.94±10.01	26.8±7.74	0.002*
	P1=0.003*	P2<0.001*	P3=0.001*	
Superior	45.94±3.81	38.2±10.62	22.85±12.41	<0.001*
	P1=0.002*	P2<0.001*	P3<0.001*	
Inferior	49.8±5.9	41.05±9.78	33.5±6.99	0.002*
	P1=0.001*	P2<0.001*	P3=0.007*	

Note: one Way ANOVA test *p<0.05 is statistically significant.

■ DISCUSSION

Myopic maculopathy, which is a major alteration in the retinal histology, is a known complication of high myopia. It continues to be a major cause of blindness in many industrialized nations [6].

A total of 120 eyes from 60 healthy subjects with high myopia were included in our study and categorized into 3 groups: control group without myopic maculopathy, non-smokers group with myopic maculopathy, and smokers with myopic maculopathy. We investigated the effects of high myopia and chronic smoking on the FAZ area, macula thickness and vasculature, choroidal thickness, GCC thickness, RNFL thickness, and optic disc vasculature.

We found that the presence of maculopathy in high myopic subjects caused a marked increase in the size of the FAZ area. Also, the FAZ area was found to be notably larger in smokers than in non-smokers. Thoughts on what causes the FAZ to enlarge in myopic eyes are few. One theory is that as myopia progresses, the retinal vascular trunk drags, which reduces retinal blood flow and can lead to different FAZ sizes in different eyes. Another theory is that macular thinning is due to axial elongation in the eyes which reduces the amount of oxygen consumed, which in turn reduces blood flow to the retina and causes larger FAZs [7]. Smoking could be associated with microinfarcts, capillary non-perfusion, impairment, and decrease of blood flow, thus causing expansion of the FAZ [8].

In coordination with our finding, a study conducted by Sung et al., who used OCTA to examine myopic eyes, found that extremely myopic eyes had bigger superficial and deep FAZ zones as well as reduced peripapillary VD [9]. Additionally, in cases of severe myopia, he and colleagues found that the FAZ region was larger. Still, the radial peripapillary and deep parafoveal VD were reduced [10]. Axial elongation was also associated with less VD in the deep and superficial layers and an increase in FAZ area, according to Cheng et al. [11]. FAZ size indirectly indicates differences in retinal perfusion, as all these investigations found that an enlarged FAZ was accompanied by a reduced density of retinal vessels

in the macular area. Piao et al. reported that individuals with high myopia had notably larger superficial and deep FAZ areas than those in the control group [7]. In contrast to our finding, Wong et al. found that the superficial FAZ region was smaller in the high myopes compared to the control group [12] and Kocer et al. found that pathological myopia (myopic maculopathy) patients had a smaller FAZ area than emmetropes [13]. This difference may be due to their different study design from our study.

Concerning the effects of smoking, Aboud et al. used OCTA to study healthy smokers. They found that smokers had a significantly larger FAZ area than non-smokers [8].

Our study found a significant decrease in the choroidal thickness in patients with maculopathy compared to high myopic patients without maculopathy. Alterations to choroidal vascular architecture may play a role, but the precise mechanism remains unknown. Subjects with myopic maculopathy had fewer choroidal veins and arterioles in their chorioretinal atrophic lesions, according to multiple clinical investigations that used indocyanine green angiograms [2]. Also, smoking was found to significantly decrease the choroidal thickness compared to non-smokers.

In a study comparing various stages of myopic maculopathy, Zhao et al. discovered that subfoveal choroidal thickness grew noticeably thinner as the severity of maculopathy increased. Maculopathy severity was linearly related to temporal, nasal, superior, and inferior Choroidal thickness. The choroid of 37 eyes with 4-grade maculopathy was abnormally thin [14]. Ueda et al. examined how choroidal thickness relates to the progression of myopic maculopathy, concluding that a thinner choroid was strongly associated with myopic maculopathy [2]. Similarly, Virgayanti & Faisal observed a marked reduction in choroidal thickness in smokers compared to non-smokers. He mentioned that several factors related to smoking affect the choroidal thickness, including the presence of a filter, number of packs per day, and duration of smoking [15].

In our study, all macular subfield thickness decreased significantly in patients with maculopathy compared to the control group. The theory behind this discovery is that the mechanical stretching and thinning of the retina occurs in myopic eyes as a result of the elongation of the globe. The thickness of the retina determines how much the eye stretches. Less resistance to traction and stretch is seen in the peripheral retina due to the absence of major blood arteries and optic fibers. The central retinal thickness can be preserved by compensating for the stretching over the entire retina, which results in a decrease in peripheral retinal thickness. Still, with the progression of myopia and the occurrence of myopic maculopathy, the central retina also became affected [16]. Also, smokers showed a significantly lower macular thickness compared to non-smokers except in central macular thickness, where there was no significant difference. This was due to the fact that tobacco has an oxidizing effect that can harm or kill cells in the macular, RNFL, and GCC areas [8].

Various studies have evaluated OCT changes in individuals with high myopia and observed a notable reduction in macular thickness compared to healthy controls. Our findings were consistent with Choudhary et al.'s study, which examined the effect of high myopia on macular thickness and reported similar values to ours [16]. Also, Meng et al. assessed the whole and regional macular retinal thickness parameters between the myopic severity groups. They found that as myopia progressed, the retina became thinner in the whole image, temporal, superior, nasal, and inferior parts of the macula [17].

According to Aboud et al., smokers had noticeably thinner macular subfields than non-smokers, with the exception of central macular thickness and temporal parafoveal subfield thickness, where the two groups did not differ significantly [8].

Significant differences were found among the studied groups regarding average, superior, and inferior GCC thickness. The smokers exhibited the lowest GCL thickness, though no significant difference was detected between smokers and non-smokers. Furthermore, global and focal loss volume differed significantly between the groups.

Similar values were obtained in the study of Ucak et al., who found that the average superior GCC thickness was 94.90±13.94. The inferior GCC was 91.55±14.53 and compared them to normal control patients, revealing that the thickness was significantly reduced in patients with high myopia [18]. Also, the study of Shukla et al. assessed the thickness of GCC in different degrees of myopia and reported that the mean average GCL thickness was 79.55±7.38 μm in low-grade myopic eyes, 73.77±12.26 μm in moderate-grade myopic eyes, and 60.00±15.67 μm in high-grade myopic eyes [19].

Our study found a significant difference between the studied groups regarding average peripapillary RNFL thickness. Research has shown that when myopia severity and axial length increase, RNFL thickness decreases significantly [20, 21].

In terms of smoking's effects, Aboud et al. observed similar outcomes. The results showed that the smokers' group had noticeably thinner inferior GCCs. Slightly thinner RNFLs, on average, in the upper and lower halves, were also found in the cigarette group [8]. Yang et al. conducted a meta-analysis study and found a significant decrease of RNFL and GCL in smokers [22].

There was a significant difference between the studied groups regarding superficial and deep VD in all macular regions. On comparing the two groups, there was a significant difference between each 2 group where the smoker's group had significantly lower superficial and deep VD in each aspect.

Analysis of the optic disc VD in our study showed a significant difference between all groups regarding the whole, peripapillary, superior-inferior, and inside disc VD. The VD was significantly lower in patients with maculopathy compared to patients without maculopathy and lower in smokers than non-smokers. A decrease in the retinal vascular network may occur as a result of mechanical stretching of the retinal tissue caused by high myopia, which also causes choroidal and retinal thinning [23]. A potential contributor to the depletion of the capillary network could be the loss of the retinal pigment epithelium and the retinal vascular endothelium cells, which secrete vascular endothelial growth factor (VEGF). Also, VEGF has been observed to have an inverse relationship with axial length [24]. Low vessel density in high myopia with maculopathy may be due to reduced oxygen consumption in the atrophic areas relative to healthy eyes. This, in turn, may explain why there is less blood flow to the retina in these cases [13]. Microvascular and macrovascular atherosclerosis, vascular wall damage, and capillary loss are all consequences of smoking [8]. Our study found increased VD inside the optic disc in both non-smokers and smokers groups compared to control. The significance of retinal vascular regulation increases due to an automated adjustment process, which explains this conclusion. As regional oxygen demand might be impacted by lower peripapillary vascular perfusion, an appropriate function of retinal tissue can be ensured by increasing blood flow inside the disc, which can alleviate the decreased blood flow around the optic disc [25].

According to Jiang et al., high myopic eyes have much reduced VD in the macular superficial and deep layers compared to non-high myopic eyes. However, this difference is only seen in the inferior hemi aspect [6]. Wang et al. studied patients with different severe myopic refractive errors. They found that those with high myopia had the lowest levels of superficial, deep macular, and peripapillary VDs as compared to those with mild or moderate myopia. Compared to the other groups, those with severe myopia had a larger density within the optic disc [25]. Except for the fovea and inside disc VDs, which were identical in all groups, Yaprak & Yaprak discovered that the high myopia group had significantly lower superficial, deep macular, peripapillary, and whole disc VDs when compared to the healthy control group in all zones ($p < 0.005$) [26]. According to Mo et al., the pathological myopia group had fewer VDs overall, with the exception of the fovea and the inside disc, as compared to the emmetropia and high myopia groups. Because the foveal region was mostly devoid of blood arteries, it is less susceptible to differences between groups. Another possible explanation is that the intricate network of major vessels within the disc also makes it less sensitive to differences between groups [27]. In their study, Kocer et al. found that the groups with pathological myopia had lower macular and disc VDs compared to the high myopia and emmetropia groups. They also found that there were significant differences between the two groups, with the HM group showing lower vessel densities across the board, with the exception of the fovea and the interior of the disc [13]. In all previous studies, Patients with only myopic maculopathy weren't included, which explains the sparing of the foveal VD, unlike their being involved in our study.

Deep foveal, superficial, and deep parafoveal VDs were all significantly lower in the smoking group, according to Aboud et al. [8]. Takashi et al.'s earlier research, which showed that higher smoking intensity is linked to quicker vascular density loss over an average of four years, may help to explain this. Additionally, they clarified that the restricted capillary blood flow was caused by microinfarctions and capillary non-perfusion. Even in tissues that were not directly exposed to smoke, autopsy data from smokers have shown fibrous thickening of the blood vessel walls. Overall, smoking has a variety of acute and long-term consequences on the circulatory system and tissue [24].

■ CONCLUSIONS

The ocular effects of high myopia and smoking are mainly vascular. The degenerative vascular effect of myopic maculopathy with the vasoconstrictive effect of smoking impairs the vascular flow to the retina and choroid. A decrease in macular and optic disc vessel densities in high myopic smokers compared to non-smokers with maculopathy was detected. Also, macular, choroidal, GCCL, and RNFL thickness decreased and FAZ area enlarged in both non-smokers and smokers with myopic maculopathy.

■ REFERENCES

1. Li Y, Zheng F, Foo LL, et al. Advances in OCT imaging in myopia and pathologic myopia. *Diagnostics*. 2022 Jun 8;12(6):1418.
2. Ueda E, Yasuda M, Fujiwara K, et al. Association Between Choroidal Thickness and Myopic Maculopathy in a Japanese Population: The Hisayama Study. *Ophthalmology Science*. 2023 Dec 1;3(4):100350.
3. Xu H, Zong Y, Yu J, et al. Retinal microvascular reactivity in chronic cigarette smokers and non-smokers: an observational cross-sectional study. *Frontiers in Medicine*. 2021 Dec 20;8:782010.

4. Savastano MC, Lumbroso B, Rispoli M. In vivo characterization of retinal vascularization morphology using optical coherence tomography angiography. *Retina.* 2015 Nov 1;35(11):2196–203.
5. Fang PP, Lindner M, Steinberg JS, et al. Clinical applications of OCT angiography. *Der Ophthalmologe.* 2016 Jan;113:14–22.
6. Jiang Y, Lou S, Li Y, et al. High myopia and macular vascular density: an optical coherence tomography angiography study. *BMC ophthalmology.* 2021 Dec;21:1–5.
7. Piao H, Guo Y, Zhang H, et al. Acircularity and circularity indexes of the foveal avascular zone in high myopia. *Scientific Reports.* 2021 Aug 19;11(1):16808.
8. Aboud SA, Hammouda LM, Saif MY, Ahmed SS. Effect of smoking on the macula and optic nerve integrity using optical coherence tomography angiography. *European journal of ophthalmology.* 2022 Jan;32(1):436–42.
9. Sung MS, Lee TH, Heo H, Park SW. Association between optic nerve head deformation and retinal microvasculature in high myopia. *American Journal of Ophthalmology.* 2018 Apr 1;188:81-90.
10. He J, Chen Q, Yin Y, et al. Association between retinal microvasculature and optic disc alterations in high myopia. *Eye.* 2019 Sep;33(9):1494–503.
11. Cheng D, Chen Q, Wu Y, et al. Deep perifoveal vessel density as an indicator of capillary loss in high myopia. *Eye.* 2019 Dec;33(12):1961–8.
12. Wong CW, Matsumura S, Htoon HM, et al. Assessment of the macular microvasculature in high myopes with swept source optical coherence tomographic angiography. *Frontiers in Medicine.* 2021 May 17;8:619767.
13. Kocer AM, Goker YS, Sogut FE. The Effect of Pathological Retinal Changes on Retinal Capillary Circulation in Myopic Patients. *Beyoglu Eye Journal.* 2022;7(4):282.
14. Zhao X, Ding X, Lyu C, et al. Morphological characteristics and visual acuity of highly myopic eyes with different severities of myopic maculopathy. *Retina.* 2020 Mar 1;40(3):461–7.
15. Virgayanti V, Faisal M. Comparison of Choroidal Thickness Between Smokers with Non-Smokers Using Optical Coherence Tomography. *International Journal of Research Publications*. 2021;67(1):7.
16. Choudhary A, Venkatesh RH, Jayashree MP, et al. Effect of high myopia on macular thickness: An optical coherence tomography study in a tertiary care hospital, Karnataka, India. *Journal of Clinical Ophthalmology and Research*. 2021 Jan 1;9(1):14–7.
17. Meng Y, Yi ZH, Xu YS, et al. Changes in macular vascular density and retinal thickness in young myopic adults without pathological changes: an OCTA study. *Eur Rev Med Pharmacol Sci.* 2022 Aug 1;26(16):5736–44.
18. Ucak T, Icel E, Yilmaz Het al. Alterations in optical coherence tomography angiography findings in patients with high myopia. *Eye.* 2020 Jun;34(6):1129–35.
19. Shukla B, Sinha VB, Sharma AK, Kumar P. Determination of the association of ganglion cell–inner plexiform layer and retinal nerve fiber layer thickness with different grades of myopia: A spectral domain OCT-based study. *EyeQuest.* 2022 Nov 1;47(2):45–51.
20. Sharawy AS, Aldghaimy AH, Soghair E, et al. Assessment of retinal nerve fiber layer thickness in myopic patients using optical coherence tomography. *SVU-International Journal of Medical Sciences.* 2019 Jan 1;2(1):55–9.
21. Porwal S, Nithyanandam S, Joseph M, Vasnaik AK. Correlation of axial length and peripapillary retinal nerve fiber layer thickness measured by Cirrus HD optical coherence tomography in myopes. *Indian Journal of Ophthalmology.* 2020 Aug 1;68(8):1584–6.
22. Yang TK, Huang XG, Yao JY. Effects of Cigarette Smoking on Retinal and Choroidal Thickness: A Systematic Review and Meta-Analysis. *Journal of Ophthalmology.* 2019;2019(1):8079127.
23. Grudzińska E, Modrzejewska M. Modern diagnostic techniques for the assessment of ocular blood flow in myopia: current state of knowledge. *Journal of ophthalmology.* 2018;2018(1):4694789.
24. Chen W, Song H, Xie S, et al. Correlation of macular choroidal thickness with concentrations of aqueous vascular endothelial growth factor in high myopia. *Current Eye Research.* 2015 Mar 4;40(3):307–13.
25. Wang T, Li H, Zhang R, et al. Evaluation of retinal vascular density and related factors in youth myopia without maculopathy using OCTA. *Scientific Reports.* 2021 Jul 28;11(1):15361.
26. Yaprak AC, Yaprak L. Retinal microvasculature and optic disc alterations in non-pathological high myopia with optical coherence tomography angiography. *Graefe's Archive for Clinical and Experimental Ophthalmology.* 2021 Nov;259(11):3221–7.
27. Mo J, Duan A, Chan S, et al. Vascular flow density in pathological myopia: an optical coherence tomography angiography study. *BMJ open.* 2017 Feb 1;7(2):e013571.
28. Nishida T, Weinreb RN, Tansuebchueasai N, et al. Smoking Intensity is Associated With Progressive Optic Nerve Head Vessel Density Loss in Glaucoma. *Journal of Glaucoma.* 2024 Jun 1;33(6):394–9.