

Disc–fovea distance and choroidal thickness: is there a relationship?

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Abstract

Background: The distance between the optic disc center and the fovea is a biometric parameter; however, it is unclear whether DFD (disc–fovea distance) affects the choroidal thickness.

Objective: The aim of this study is to investigate the association between DFD and choroidal thickness.

Design: This is a prospective, and cross-sectional study.

Methods: Two hundred fifty eyes of 250 healthy participants were examined in terms of DFD, age, axial length, spherical equivalent, and choroidal thickness. Inclusion criteria included aged between 20–40 years, no posterior segment disorders, and participants with best-corrected visual acuity (10/10 according to Snellen's chart). Participants with high hypermetropia (>4 diopter) or myopia (>6 diopter) or any systemic disease likely to affect choroidal thickness were excluded. Choroidal thickness measurements were performed at subfoveal, 1.0 mm temporal, and 1.0 mm nasal using the enhanced-depth imaging optical coherence tomography.

Results: The mean age of all the participants was 26.21 ± 5.73 years, mean DFD was 4634.29 ± 274.70 μm , mean axial length was 23.62 ± 0.83 mm, and mean spherical equivalent was -0.61 ± 1.06 diopter. The mean subfoveal, nasal, and temporal choroidal thicknesses were 388.73 ± 90.15 μm , 351.26 ± 88.09 μm , and 366.50 ± 79.56 μm , respectively. A negative correlation was found between subfoveal, nasal, and temporal choroidal thicknesses and axial length ($r = -0.157$, $p = 0.013$; $r = -0.168$, $p = 0.008$; $r = -0.174$, $p = 0.006$, respectively). Insignificant correlation was found between choroidal thicknesses and spherical equivalent ($p > 0.05$). There was not a statistically significant correlation between DFD and subfoveal, nasal, and temporal choroidal thicknesses ($r = -0.028$, $p = 0.655$; $r = 0.030$, $p = 0.641$; $r = -0.025$, $p = 0.699$, respectively). In addition, there was not a statistically significant correlation between age and choroidal thickness.

Conclusion: This study shows that DFD and spherical equivalent do not affect choroidal thickness; axial length negatively affects choroidal thickness. In addition, age does not affect choroidal thickness between 20 and 40 years.

Keywords: choroidal thickness, disc–fovea distance, enhanced-depth imaging optical coherence tomography, healthy participants

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Introduction

The choroid is the tissue between the retina and the sclera. This tissue has a high vascular structure and takes part in important missions, regulating the temperature of the retina and supplying nutrients and oxygen to the outer

retinal layers especially for the photoreceptors and optic disc.

The number of studies investigating choroidal thickness (CT) has been increased in recent years with the development of optical coherence

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tomography (OCT) technologies. Enhanced-depth imaging with spectral-domain optical coherence tomography (EDI-OCT) allows the physician to measure the CT and gives information about the choroidal structure.¹ Changing in the choroidal vascularity affects the CT directly. When choroidal vessels dilate, vascular permeability and hydrostatic pressure increase, and these changes result in increased CT.² Thinning of the choroidal tissue causes dysfunction of the retinal pigment epithelium (RPE) and photoreceptor cell loss with inadequate nutrition of the retina.³ Central serous chorioretinopathy and Vogt-Koyanagi-Harada disease are an example of diseases that cause an increase in CT.^{2,4} On the contrary, high myopia and age-related macular degeneration are an example of diseases that cause a decrease in CT.^{5,6} Thus, understanding of normal choroidal structure/thickness and its variability is essential for choroidal diseases and macular diseases.

The thickness of the choroid is affected by some factors such as age, axial length (AL), refractive error, sex, and circadian rhythm.^{7,8} Another factor that may affect the CT may be the distance between the optic disc center and the fovea. The disc-fovea distance (DFD) is an important landmark of the posterior fundus.⁹ DFD can be measured with fundus photography or OCT. Using OCT to detect the fovea is superior to fundus photography because the fovea can be pinpointed at the OCT. Qiu *et al.*¹⁰ hypothesized that an increase in DFD may cause stretching of the posterior fundus, which may result in a change of the CT, and they reported that DFD was significantly associated with macular thickness. Furthermore, Jonas *et al.*¹¹ reported that DFD was associated with AL. Hence, it is crucial to determine the effect of DFD on measurements of CT.

We hypothesized that DFD may be another biometric parameter that may influence the CT. However, to the best of our knowledge, the relationship between DFD and CT has not been investigated yet. The main goal of this study was to evaluate the relationship between DFD and CT using EDI-OCT in normal participants.

Methods

This prospective and cross-sectional study was performed in the Department of Ophthalmology of the Hitit University (Çorum, Turkey). All participants agreed to participate in the present

study, and a written informed consent form was obtained from each participant. Approval for the study was obtained from Ethical Committee of Hitit University Faculty of Medicine (25/11/2020-352). The study conformed to the tenets of the Declaration of Helsinki.

The study was performed between November 2020 and March 2021. During this period, 250 right eyes of 250 healthy participants were enrolled. The first patient was enrolled on 30 November 2020.

The inclusion criteria were the following: (1) age between 20 and 40 years, (2) best-corrected visual acuity (BCVA) was 20/20 according to Snellen's chart, and (3) intraocular pressure (IOP) between 10 and 21 mmHg.

The exclusion criteria were the following: (1) any situation which affects the measurement results such as poor OCT images due to cataract or unstable fixation; (2) refractive errors over +4.0 diopter (D) or under -6.0 D; (3) IOP greater than 21 mmHg; (4) cup/disc ratio greater than 0.3; (5) history of significant ocular disease such as corneal disease, retinal disease, uveitis, glaucoma, tumor/trauma, ocular surgery, and systemic and/or topical drug-using; (6) previous retinal treatment (laser photocoagulation or intravitreal injection); (7) smoking; (8) history of refractive surgery; and (9) systemic disorders such as cardiovascular disease, autoimmune disease, hypertension or diabetes mellitus, and respiratory disease.

All participants underwent a complete ophthalmic examination. This examination includes refraction measurements (TOPCON KR-8900; Topcon Corporation, Tokyo, Japan), BCVA according to Snellen's chart, anterior segment examination with slit-lamp biomicroscopy, IOP measured using Goldmann applanation tonometry (Haag-Streit, Bern, Switzerland), fundus examination, and OCT measurements including CT and central macular thickness (CMT). AL measurements were performed with Nidek AL-Scan (Nidek Co., Aichi, Japan) optical biometer with three consecutive measurements. The mean of these three measurements was used as the AL measurement for each eye. During the examination, if unilateral amblyopia was detected, the eye with amblyopia was excluded and the other healthy eye was included in the study.

Choroidal and macular thickness measurements

All participants were imaged with enhanced-depth imaging (EDI) mode, a 6-mm horizontal single line scan, through the fovea between 10.00 and 12.00 in the morning (to avoid the diurnal variation of the CT) by a Heidelberg Spectralis® OCT (Heidelberg Engineering) with an excitation wavelength of 870 nm and a scanning speed of 40,000 A-scans per second. CT was measured using the caliper that is present from the hyper-reflective line corresponding to the Bruch's membrane under the RPE to the interface of the choroid and sclera, in the central horizontal B-scan passing directly through the foveal center. Choroidal thickness was measured at the fovea, and 1000 μm nasal and temporal to the fovea (Figure 1). If eye movements during image acquisition were seen, measurements were excluded and reperfomed. The average number of EDI-OCT was 1.1 for each participant.

CMT measurements were also performed using a macular thickness map, which is divided into three concentric circles centered on the fovea. The diameters are as follows: 1 mm (CMT), 3 mm (parafoveal ring), and 6 mm (perifoveal ring).¹²

Measurements of optic DFD

DFD measurements were performed in the OCT images. The center of the fovea was detected using macular sections in OCT. Afterward, the optic disc center was determined in the same OCT image; two diagonal lines (height and width) were drawn, and their crossing was considered as the center of the optic disc. DFD was measured based on the coordinates of the center of the fovea and the center of the optic disc by using the OCT caliper system manually (Figure 2).

The measurements were performed by the same ophthalmologist at two different times (S.C.). When the difference between the measurements was more than 10%, they were excluded from the study. The arithmetic means of the two measurements were calculated.

Statistical analysis

SPSS (Version 22.0, SPSS, Inc., Chicago, IL, USA) package program was used for the statistical analysis. Descriptive statistics were presented as mean $\pm$ standard deviation (SD) or median

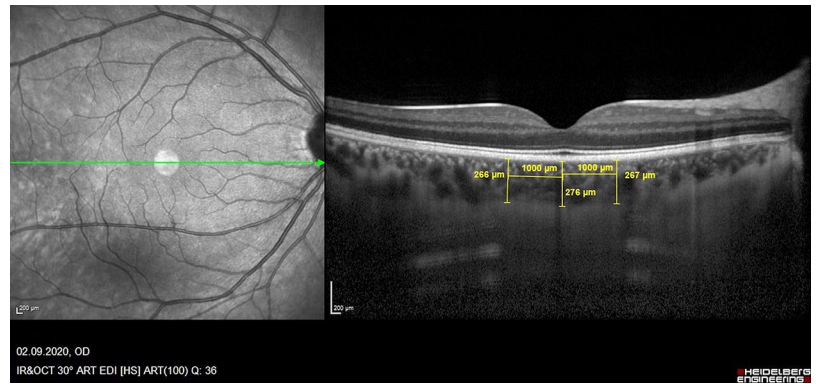


Figure 1. Enhanced-depth imaging optical coherence tomography shows choroidal thicknesses.

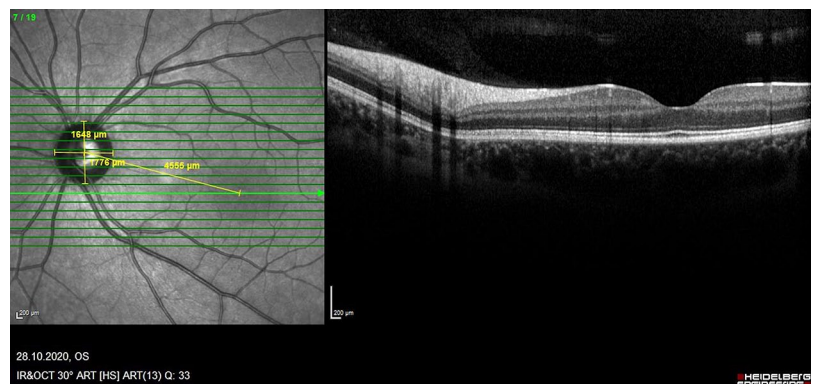


Figure 2. Optical coherence tomography image shows the optic disc-fovea distance (yellow line).

(minimum–maximum), number, and percentage (%) for categorical data in accordance with the data distribution. The distribution of normality was analyzed using the Kolmogorov–Smirnov and the Shapiro–Wilk tests. In the comparison of numerical variables between two independent groups, the independent-sample *t*-test was used for normally distributed data and the Mann–Whitney *U* test was used for data that did not show normal distribution. In the comparison of numerical variables between more than two independent groups, one-way analysis of variance (ANOVA) was used for normally distributed data and the Kruskal–Wallis test was used for data that did not show normal distribution. The relationship between numerical variables was examined with the correlation coefficient in accordance with the data distribution. G*Power 3.1.9.4 software was used for the sample size calculation. In order to reach 90% power with $\alpha = 0.05$ error

Table 1. Characteristics of the study population.

Parameters	N	Mean	SD	Minimum	Maximum
Age (years)	250	26.21	5.73	20	40
SE (diopter)	250	-0.61	1.06	-4.50	3.75
AL (mm)	250	23.62	0.83	21.68	26.27
CMT (μm)	250	267.33	18.43	214	316
DFD (mm)	250	4634.29	274.70	3706	5643
CT subfoveal (μm)	250	388.73	90.15	145	620
CT nasal (μm)	250	351.26	88.09	139	598
CT temporal (μm)	250	366.50	79.56	165	566
AL, axial length; CMT, central macular thickness; CT, choroidal thickness; DFD, disc-fovea distance; SD, standard deviation; SE, spherical equivalent.					

(double-sided hypothesis), it was decided to include a minimum of 243 patients in the study as a result of the power analysis calculated using $\rho = 0.3$ (medium effect) effect size to reveal a correlation of 0.3 by using expert opinion. For the statistical significance level, $p < 0.05$ was considered.

Results

There were a total of 250 right eyes of 250 healthy participants in the study; 95 (38%) participants were female, and 155 (62%) participants were male. The mean age of female participants was 26.47 ± 5.11 years, and the mean age of male participants was 26.43 ± 6.24 years. The mean age of all participants was 26.21 ± 5.73 years.

The mean CTs were $388.73 \pm 90.15 \mu\text{m}$ at the subfoveal region, $351.26 \pm 88.09 \mu\text{m}$ at the nasal region, and $366.50 \pm 79.56 \mu\text{m}$ at the temporal region. The mean DFD was 4634.29 ± 274.70 mm (range = 3706–5643 mm). Demographics of the study population were shown in Table 1.

Males have lower spherical equivalent (SE) values than females ($p < 0.001$). Males have a longer AL ($p = 0.003$), thicker CMT ($p < 0.001$), thicker CT at subfoveal ($p = 0.043$), and nasal ($p = 0.014$) regions than females. These informations were shown in Table 2.

There was not any correlation between age and CT. There was a negative correlation between AL and CT. There was no positive or negative

correlation between SE and CT. There was no positive or negative significant correlation between DFD and CT (Table 3).

Figures 3–5 show us the association between DFD and CTs, the association between AL and CTs, and the association between AL and DFD, respectively. Pearson's correlation and Spearman's correlation methods were used.

Discussion

The tissue, between the sclera and the retina that has rich blood flow, is the choroid. This special vascularized and pigmented tissue supplies nutrients to the RPE and outer retina and plays in role metabolic exchange. More importantly, the metabolic requirements of the avascular fovea are provided by the choroid. Furthermore, the choroid regulates the temperature of the retina and IOP by modulating the ocular blood flow.¹³

In order to accurately measure the thickness of the tissue, it is first necessary to know the parameters and factors that affect the thickness of this tissue. Factors that are known to affect CT are age, AL, refractive error, sex, and circadian rhythm.^{7,8}

In literature, some authors found that CT decreases with aging. Ikuno *et al.*¹⁴ detected that CT decreases by $14 \mu\text{m}$ with every decade. Similarly, Margolis *et al.*¹⁵ reported a $15.6\text{-}\mu\text{m}$ decrease, and Chhablani *et al.*¹⁶ reported an $11.8\text{-}\mu\text{m}$ decrease in CT every decade. On the contrary, Bhayana *et al.*¹⁷ found a negative correlation

Table 2. Comparison of the parameters between males and females.

Parameters	Sex	n	Mean	SD	Median	Minimum	Maximum	p value
SE (diopter)	Male	155	-0.43	1.01	0	-4.00	3.75	<0.001 ^{a*}
	Female	95	-0.90	1.09	-0.50	-3.75	1	
	Total	250	-0.61	1.06	-0.25	-4.00	3.75	
AL (mm)	Male	155	23.74	0.81	23.70	21.68	26.27	0.003 ^{b*}
	Female	95	23.42	0.83	23.40	21.73	25.39	
	Total	250	23.62	0.83	23.59	21.68	26.27	
CMT (µm)	Male	155	272.90	16.23	273	236	316	<0.001 ^{b*}
	Female	95	258.24	18.27	259	214	304	
	Total	250	267.33	18.43	269.5	214	316	
DFD (µm)	Male	154	4614	245.28	4625.5	3976	5239	0.162 ^b
	Female	95	4667.2	315.26	4665	3706	5643	
	Total	250	4634.29	274.70	4635	3706	5643	
CT, subfoveal (µm)	Male	155	396.28	89.39	397	145	591	0.043 ^{a*}
	Female	95	376.42	90.50	354	232	620	
	Total	250	388.73	90.15	380	145	620	
CT, nasal (µm)	Male	155	361.91	89.77	364	139	582	0.014 ^{b*}
	Female	95	333.89	82.84	325	169	598	
	Total	250	351.26	88.09	348	139	598	
CT, temporal (µm)	Male	155	371.20	82.33	370	165	566	0.234 ^b
	Female	95	358.84	74.62	351	214	564	
	Total	250	366.50	79.56	367.5	165	566	

AL, axial length; CMT, central macular thickness; CT, choroidal thickness; DFD, disc-fovea distance; SD, standard deviation; SE, spherical equivalent.

^aMann-Whitney *U* test.

^bStudent's *t*-test.

* Correlation is significant at the 0.05 level (2-tailed).

between subfoveal CT and age without statistical significance. The mean age of the study of Bhayana *et al.* was 28.70 ± 11.28 years, ranging from 19 to 60 years. In the present study, it was detected that age has no effect on CT. The mean age of the healthy participants in our study was 26.44 ± 5.93 years and ranged from 20 to 40 years. The age range of our study is narrow, and SE values were between +4 and -6 D. Our study shows that age does not affect the CT in healthy participants, aged between 20 and 40 years. Age

is likely to affect the CT at an older age. Ding *et al.*¹⁸ reported that this age-related thinning occurs only in age older than 60 years of age. This study supports our study's results.

The relationship between AL and CT is well known. A negative correlation was reported by many authors.^{6,19} The degree of this negative correlation was prominent in participants with AL >25 mm. Some authors reported that AL less than 25 mm did not affect the CT.^{16,20} In the

Table 3. Associations between DFD, AL, age, and SE and subfoveal, nasal, and temporal CT ($n = 250$; bivariate correlation analysis).

Parameters		CT, subfoveal	CT, nasal	CT, temporal
AL	r	-0.157*	-0.168**	-0.174**
	p	0.013^a	0.008^b	0.006^b
DFD	r	-0.028	0.030	-0.025
	p	0.655 ^a	0.641 ^b	0.699 ^b
SE	r	0.031	0.064	0.008
	p	0.623 ^a	0.311 ^a	0.901 ^a
Age	r	-0.018	0.011	-0.029
	p	0.782 ^a	0.864 ^a	0.658 ^a
AL, axial length; CT, choroidal thickness; DFD, disc-fovea distance; SE, spherical equivalent. Bold-faced values: Statistically significant. ^a Spearman's rho. ^b Pearson's correlation. *Correlation is significant at the 0.05 level (two-tailed). **Correlation is significant at the 0.01 level (two-tailed).				

present study, we detected a negatively significant relationship between CT with AL. In the present study, the mean AL was 23.62 mm (range = 21.68–26.27 mm). Similar to previous studies, eyes with long AL had thinner choroid, while eyes with short AL had thicker choroid in our study. AL and CT were highly significantly correlated ($p < 0.001$) in our study.

In literature, there were many studies that investigated the relationship between CT and refractive error. Wei *et al.*⁷ have reported a negative correlation between CT and refractive error. They found that for the SE range of -1 toward hyperopia, the relationship between CT and SE was not statistically significant, whereas for the myopic refractive error range of more than -1 D, it was significantly correlated. Flores-Moreno *et al.*²¹ stated that SE was significantly correlated with CT in patients with high myopes. In contrast, Ozdogan *et al.*²² reported that there were not any effects of SE on CT. On the contrary, Bhayana *et al.* studied the CT in Indian participants, aged between 19 and 60 years; they found a positive correlation between SE and CT. Similarly to the study of Ozdogan *et al.*, we found insignificant correlation between CT and SE.

The relationship between CT and sex has been evaluated by many authors. Gupta *et al.*²³ reported thicker CT in males than females. Study from Denmark, Li *et al.*²⁴ reported that CT was 18%

higher in men than in women. Similarly, Pongsachareonnont *et al.*²⁵ found the CT thicker in males than females. In our study, we found similar results with the literature; males have thicker CT than females. Females have a higher basal sympathetic tone than males which can cause vasoconstriction.²⁶ This may explain the difference.

It is very difficult to evaluate CT in both the pediatric population and the elder population. Participants with age more than 60 years have ocular or systemic pathologies such as cataract, age-related macular degeneration, diabetes mellitus, and hypertension. These problems both decrease the quality of the choroidal image and affect the choroidal structure. In the pediatric population, compliance with the measurement of the tomography device is low and the CT is variable since the eye is at the development stage. Therefore, we chose the study population, healthy participants with aged between 20 and 40 years.

Could DFD be a parameter affecting the CT? The DFD can be of importance as an anatomical parameter of the posterior fundus. In literature, there were studies that investigated the relationship between DFD and ocular parameters. In the Beijing Eye Study 2011, Jonas *et al.*¹¹ reported that DFD was significantly associated with smaller optic disc-fovea angle, larger parapapillary alpha zone, larger parapapillary beta/gamma zone, larger optic disc area, longer AL, shallower anterior chamber depth, and thinner lens thickness. The study of Hong *et al.*²⁷ showed that the DFD is associated with the peripapillary retinal nerve fiber layer (RNFL) distribution in healthy participants. They reported that temporally deviated RNFL thickness profiles correlate with increased DFD.

Qiu *et al.*¹⁰ studied the influence of DFD on macular thickness measurements with OCT in healthy myopic eyes, and they found a negative correlation between DFD and macular thickness independent of AL and gender. In 2019, the same author studied the effect of DFD on the normative classifications of macular inner retinal layers in healthy participants, and they reported that DFD affects the thickness assessment of the macular inner retinal layers.²⁸ They recommended that macular inner layer thicknesses should always be interpreted in the context of DFD. In the present study, it was found that DFD did not affect the CT in healthy participants, aged between 20 and 40 years.

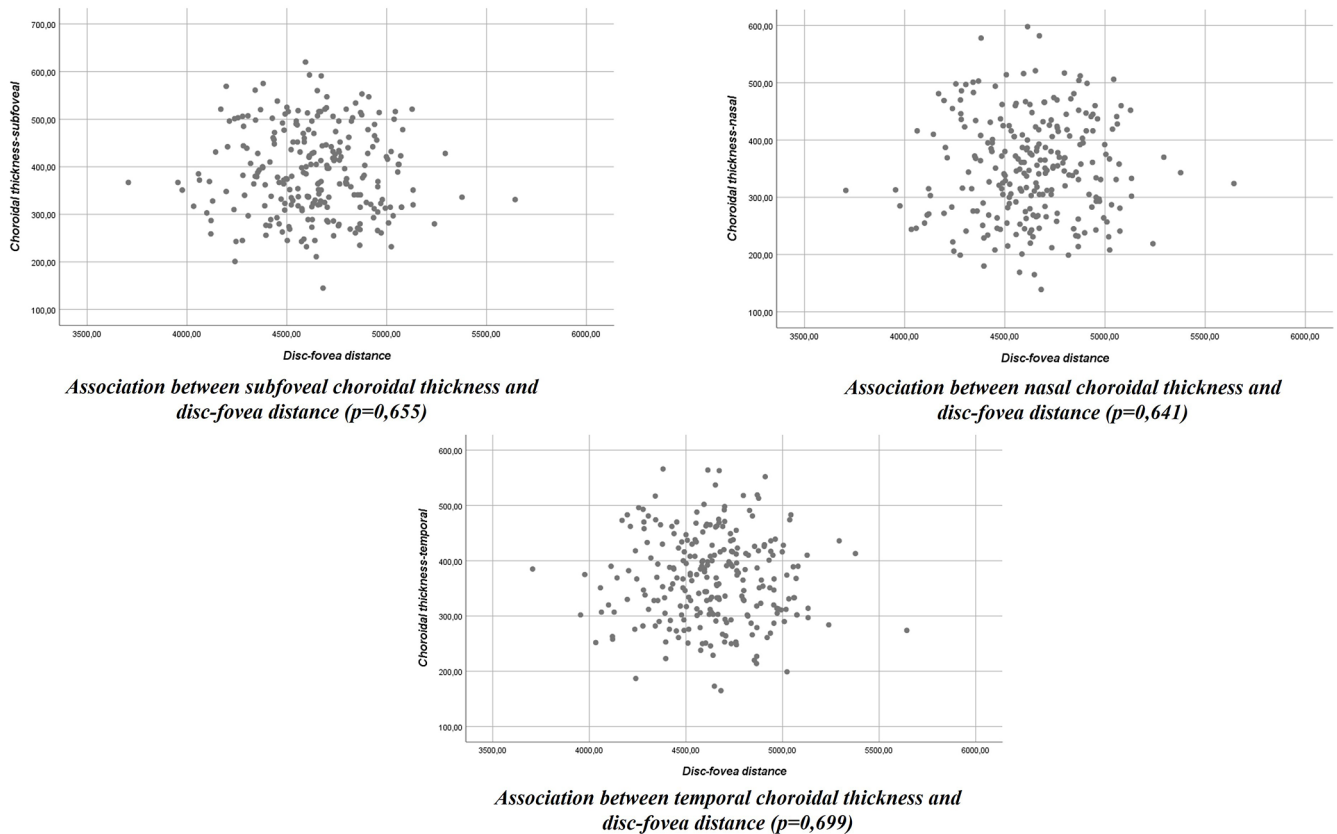


Figure 3. Association between disc-fovea thickness and choroidal thicknesses.

According to the result of our study, DFD does not need to be taken into account when evaluating CT. However, DFD might probably affect the CT in a population other than young healthy controls. Terao *et al.*²⁹ investigated the risk factor of central serous chorioretinopathy; they found that short AL and hyperopia are risk factors. They stated that eyes with a short AL have a short distance from the macula to the ampulla of the vortex vein, and a steep inclination may be associated with choroidal vasodilation. Maltsev *et al.*³⁰ investigated the central serous chorioretinopathy patients and found that number of leaks, rate of bilateral involvement, and recurrence rate had a negative linear association with AL. If distance from macula to ampulla of the vortex vein can affect the choroidal vasodilation and if number of leaks had negative correlation with AL, another anatomic parameter, DFD, can affect the choroidal structure. Our insignificant correlation may be associated with properties of our study population. Our participants were young population, and we excluded high hyperopia and high myopia. It is possible that the DFD values of participants with higher or lower refractive errors

will be much different, and studies are needed to investigate whether DFD affects the choroid in these participants.

The strengths of this study are as follows. First, we included participants with a quite narrow range of SE (-6 to $+4$ D) and ALs (21.68 and -26.27 mm); the number of people with these values is higher in society. Second, this study includes healthy participants who have normal choroid to understand the affecting parameters of the choroid. Third, we think that using OCT to detect the center of the fovea is superior to using fundus photography.

This study has some limitations. First, the study population was relatively small. Second, CTs were conducted manually because the Heidelberg Spectralis OCT equipment does not provide automatic segmentation of the choroid. Third, the study population consisted of healthy individuals, aged between 20 and 40 years, and our results did not reflect those of a population other than healthy participants.

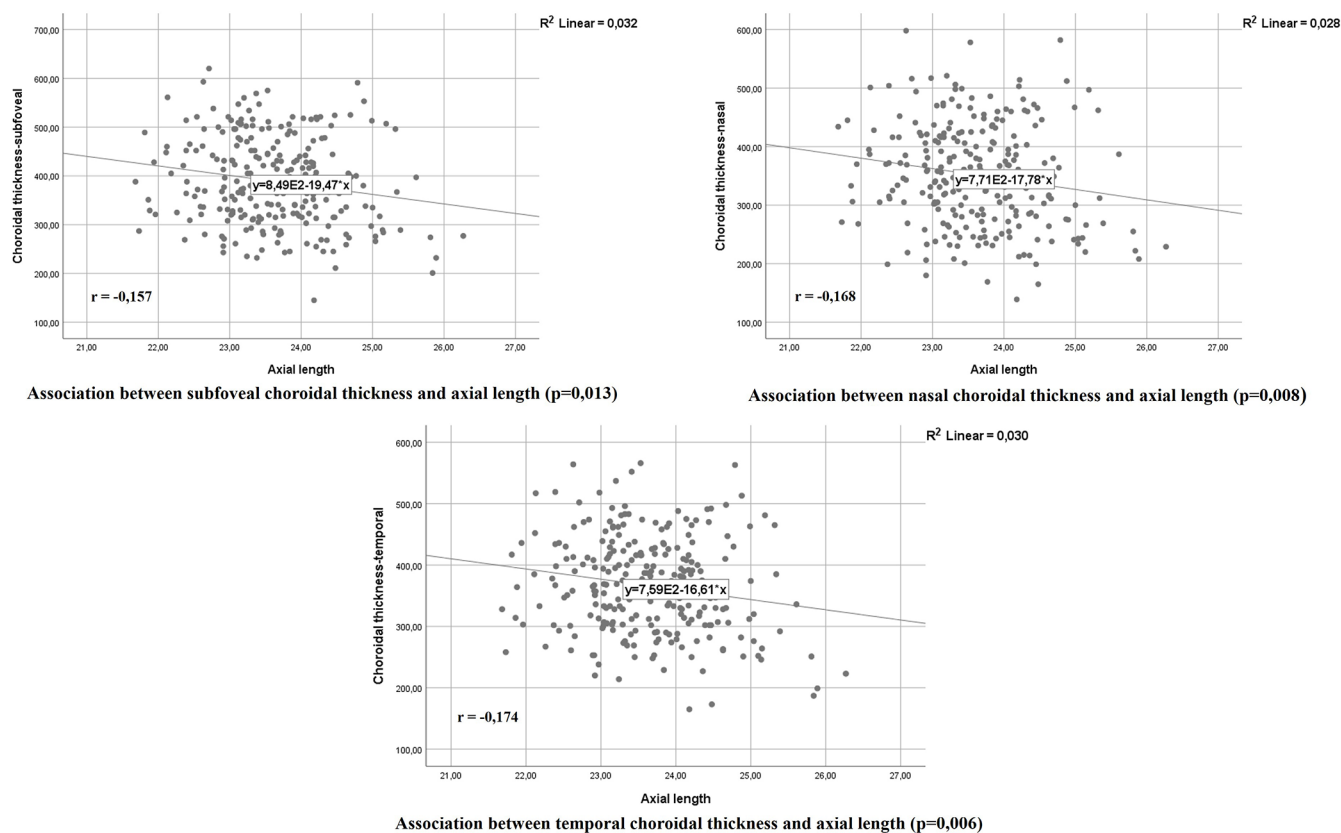


Figure 4. Association between axial length and choroidal thicknesses.

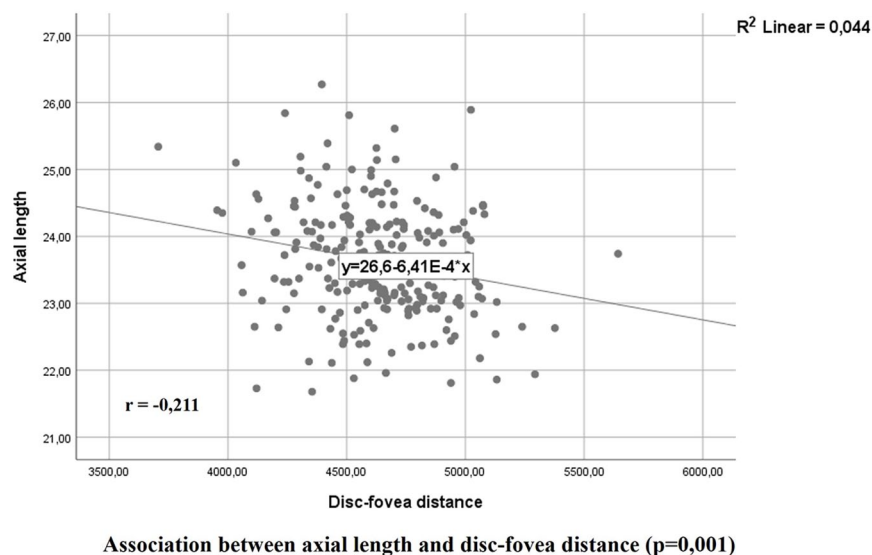


Figure 5. Association between axial length and disc-fovea distance.

Conclusion

In the present study, the factors that affect the thickness of the choroidal tissue were argued, and this study is the first study that investigated the relationship between DFD and CT. Our

study contributes to the literature by showing that there is no relationship between DFD and CT in healthy participants, aged between 20 and 40 years. In addition, the present study investigated the relationship between SE, AL,

and age with CT. This study reported that age does not affect the choroid in healthy individuals between the ages of 20 and 40 years; AL negatively affects the CT, and SE positively affects the CT.

Ethics approval and consent to participate

The study followed the tenets of the Declaration of Helsinki. Ethical board approval was obtained from the Ethical Committee of Hitit University Faculty of Medicine, Çorum, Turkey, with number 25/11/2020-352, before the study was initiated. Written informed consents were obtained from all participants.

Author contribution(s)

Selim Cevher: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Mehmet Barış Üçer: Data curation; Investigation; Methodology; Resources; Supervision; Visualization.

Tayfun Şahin: Data curation; Investigation; Methodology; Resources; Supervision.

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Conflict of interest statement

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