Macular Thickness and Volume by Spectral-Domain Optical Coherence Tomography and their Related Factors in the Elderly Population

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Abstract

Purpose: To determine the distribution of macular thickness and macular volume in an elderly healthy population 60 years of age and above and their determinants.

Methods: The sampling was performed using a multistage stratified random cluster sampling method on the geriatric population 60 years of age and above in Tehran, Iran. All participants underwent optometric examinations, slit-lamp examination, and optical biometry. Retinal imaging was performed by spectral-domain optical coherence tomography.

Results: The means ± standard deviation and 95% confidence interval of central macular thickness (CMT), average macular thickness (AMT), and macular volume were 221 ± 33 (218–223) μ m, 267 ± 29 (265–269) μ m, and 8.36 ± 0.44 (8.33–8.39) mm³, respectively. The CMT was significantly lower in females than males (β : –5.77; P=0.002). The AMT was significantly lower in females than males (β : –10.32; P<0.001) and was significantly directly related to intraocular pressure (β = 0.63; P = 0.038). The macular volume was significantly lower in females than males (β = –0.01; P<0.001). In addition, the macular volume had a significant inverse and direct relationship with axial length (β = –0.04; P = 0.011) and keratometry (β = 0.03; P<0.001).

Conclusions: Macular thickness in the Iranian geriatric population was slightly less than the populations studied in other countries. The role of sex should also be taken into account in the interpretation of macular thickness findings.

Keywords: Elderly, Macular thickness, Macular volume, Population-based study, Spectral-domain optical coherence tomography

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INTRODUCTION

Assessing the morphology and structure of the macula is helpful in diagnosing, monitoring, and classifying many ocular and systemic diseases, and macular thickness is a reliable and valuable marker in assessing the efficacy of treatments for diseases causing macular structural changes.^{1,2}

The structure of the retina is affected by many ocular and systemic diseases, including multiple sclerosis,³



Parkinson's disease,⁴ Alzheimer's disease,⁵ diabetes mellitus,⁶ hypertension,⁷ and even cardiovascular disease,⁸ all of which are more prevalent in the geriatric population. Due to the reported early changes in choroidal thickness and/or retinal thickness in many of these diseases, some researchers have tried to use these parameters as a new marker for the early diagnosis of diseases. For example, in a study by Aydin *et al.*, choroidal thickness was proposed as a new marker for early

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detection of cardiovascular disease, and choroidal thinning was reported as a risk factor for coronary heart disease.⁹

The availability of normal databases in different age, sex, and racial groups is important to compare quantitative parameters and report their differences compared to the normal range.¹⁰ The central macular thickness (CMT) in adults has been reported from 176.40 to 255.40 µm in previous studies.¹¹⁻¹⁵ Optical coherence tomography (OCT) technology enables fast, noninvasive, accurate, and quantitative *in vivo* evaluation of retinal structure with high resolution and reliability.¹⁶ Spectral-domain (SD) OCT is the advanced modification that can easily measure the thickness of different retinal layers in a few seconds with high reproducibility and high resolution.¹⁷

Various studies have examined the distribution of macular thickness and its associated factors.^{5,9,11,12,14,18,19} However, most of these studies had a wide age range, and no study has specifically examined macular thickness in the elderly population above 60 years of age. The present population-based study aimed to evaluate the distribution of macular thickness and its related factors using SD-OCT in an Iranian geriatric population over 60 years of age.

Methods

The present population-based, cross-sectional study was conducted on the geriatric population of 60 years of age and above in Tehran, Iran, in 2019. The sampling was performed using a multistage stratified random cluster sampling method. A total of 160 clusters were randomly selected proportionally to size from 22 strata of Tehran city (municipality districts were considered as strata). After the study participants presented to the examination site, complete demographic and case history information were collected through a face-to-face interview. The anthropometric indices including height and weight were measured, and blood pressure was measured in standard conditions by a trained person. Blood samples were taken from all participants to determine fasting blood sugar (FBS) and glycated hemoglobin (HbA1c).

The uncorrected distance visual acuity was measured by an LED visual acuity chart (Smart LC 13, Medizs Inc., Korea) at a distance of 6 m. The objective refraction was performed using an autorefractometer (ARK-510A, Nidek Co, Aichi, Japan). The subjective refraction was performed to determine the optimal distance vision correction, and the best-corrected distance visual acuity (BCVA) was recorded. A complete anterior and posterior segment ocular health examination was undertaken by an ophthalmologist using a slit-lamp biomicroscope (Haag-Streit AG, Bern, Switzerland). A +90 lens was used to examine the posterior segment. In the next step, optical biometry was performed using the IOL Master 500 (Carl Zeiss Meditec, Jena, Germany). Finally, all participants underwent retinal imaging under cycloplegic conditions (using tropicamide 1% drops) by SD-OCT (Heidelberg Engineering, Heidelberg, Germany). The mean retinal thicknesses of the four areas in the inner and outer rings are defined as the average inner and outer macular thicknesses, respectively.

The exclusion criteria were poor-quality OCT images (signal strength <6),²⁰ BCVA worse than 20/30, a history of cataract and glaucoma surgery, a history of any retinal therapeutic intervention, ophthalmoscopic signs of retinal disease, missing macular thickness data, and outlier data.

Myopia and hyperopia were defined as a spherical equivalent worse than -0.50 diopter (D) and +0.5 D, respectively. Individuals with Hb1Ac >6.4% or FBS >200 mg/dl, or who were taking diabetes medication were defined as diabetics.

Statistical analysis

To provide a complete database in this report, we reported most of the descriptive indices for macular thickness. Mean, standard deviation (SD), 95% confidence interval (CI), and different percentiles (25^{th} , 75^{th} , 90^{th} , and 95^{th}) were presented separately by age, sex, and refractive errors. The normal range was also reported to show the normal distribution of macular thickness values. The normal range was calculated as the mean ± 2 SD. To calculate the standard error, the cluster sampling method was taken into account, and the results were age and sex standardized based on the population of Tehran in 2019. The relationship between macular thickness and demographic, laboratory, blood pressure, and ocular variables was investigated using simple and multiple linear regression models, and regression coefficients (with 95% CI) were reported. P < 0.05 was considered statistically significant.

Informed consent was obtained from all participants. The principles of the Declaration of Helsinki were followed in all stages of this study. The protocol of the study was approved by the Ethics Committee of the National Institute for Medical Research Development under the auspices of the Iranian Ministry of Health (ethics code: IR.NIMAD.REC.1397.292).

RESULTS

Of the 3791 invitees, 3310 participated in this study (response rate: 87.3%). After applying the exclusion criteria, 2275 eyes of 1191 individuals were analyzed. Of these, 693 (58.2%) individuals were females, and the mean age of the study participants was 67.3 ± 5.9 years (60–94 years). Table 1 shows the mean \pm SD, and 95% CI of central subfield thickness, the average inner macular thickness, the average outer macular thickness, the inner and outer macular thicknesses in different quadrants, and average overall macular thickness in the whole sample and by gender and refractive groups. The mean \pm SD and 95% CI of macular thickness values in different age groups are shown in Table 2. The mean central subfield thickness was $221 \pm 33 \ \mu m$ (95% CI: 218–223) in the whole sample. The mean central subfield thickness was significantly higher in males than females (P < 0.001). This index was marginally higher, showing a significant increase only in the age group of 80 years and older compared to the age group of 60-64 years (P = 0.052).

	Total (<i>n</i> =2275), mean±SD (95% Cl)	Male (<i>n</i> =1332), mean±SD (95% Cl)	Female (<i>n</i> =943), mean±SD (95% Cl)
Central subfield thickness	221±33 (218–223)	223±27 (221–226)	218±39 (214–221)
Average of macular thickness	267±29 (265–269)	273±26 (270–275)	261±31 (259–264)
Superior inner macular thickness	334±21 (333–335)	336±20 (334–338)	332±20 (330–333)
Inferior inner macular thickness	331±20 (330–333)	334±18 (332–336)	329±23 (327-330)
Nasal inner macular thickness	336±20 (335–337)	339±19 (337–340)	333±21 (331–335)
Temporal inner macular thickness	323±19 (322–324)	326±18 (324–328)	320±19 (319-322)
Average inner	331±19 (330–332)	334±17 (332–335)	329±19 (327-330)
Superior outer macular thickness	287±16 (286–288)	288±15 (286–289)	287±17 (286–288)
Inferior outer macular thickness	278±17 (277–279)	279±15 (277-280)	277±18 (276-279)
Nasal outer macular thickness	304±18 (302-305)	304±16 (303-306)	303±20 (301-304)
Temporal outer macular thickness	276±16 (275–277)	278±15 (277–280)	274±16 (273–275)
Average outer	286±15 (285–287)	287±14 (286–289)	285±16 (284–286)
Macular volume	8.36±0.44 (8.33-8.39)	8.4±0.4 (8.36-8.44)	8.32±0.46 (8.29-8.35)

Table 1: The mean, standard deviation, and 95% confidence interval of macular thickness (μ) and macular volume (mm³) in elderly by gender

SD: Standard deviation, CI: Confidence interval

Table 2: The mean, standard deviation, and 95% confidence interval of macular thickness (μ) and macular volume (mm³) in elderly by age

Age (year)	60–64 (<i>n</i> =926), mean±SD (95% CI)	65–69 (<i>n</i> =673), mean±SD (95% CI)	70–74 (<i>n</i> =418), mean±SD (95% CI)	75–79 (<i>n</i> =163), mean±SD (95% CI)	≥80 (<i>n</i> =95), mean±SD (95% CI)
Central subfield thickness	220±23 (218-222)	220±30 (217-222)	222±34 (218-226)	217±29 (210-223)	227±53 (207-247)
Average of macular thickness	266±24 (264–268)	266±29 (264–269)	269±33 (265–274)	268±24 (263-274)	270±35 (258–281)
Superior inner macular thickness	337±22 (335-339)	334±19 (332–336)	333±21 (330-335)	331±16 (327–335)	322±17 (316-329)
Inferior inner macular thickness	334±18 (332–335)	331±20 (329–333)	331±22 (328-333)	331±18 (326-336)	324±23 (317-331)
Nasal inner macular thickness	338±18 (336-340)	336±21 (334–338)	335±23 (332-338)	335±18 (330-339)	329±19 (320-337)
Temporal inner macular thickness	326±17 (324–327)	323±20 (321-325)	323±22 (320-325)	322±17 (318-326)	314±18 (307-321)
Average inner	334±17 (332–335)	331±19 (329–333)	330±20 (327-333)	330±16 (325-334)	322±18 (315-329)
Superior outer macular thickness	290±15 (289-292)	288±16 (286–289)	286±17 (284–289)	284±15 (281-288)	277±15 (271-284)
Inferior outer macular thickness	280±15 (279-282)	278±18 (276-280)	277±19 (275-279)	277±15 (273-280)	270±15 (264-276)
Nasal outer macular thickness	306±16 (305-308)	304±19 (302-306)	302±20 (300-305)	301±16 (297-305)	293±16 (287–299)
Temporal outer macular thickness	278±14 (277-279)	276±16 (275-278)	275±18 (273-278)	274±14 (271-277)	269±13 (264-275)
Average outer	289±14 (287-290)	287±16 (285-288)	285±17 (283-287)	284±14 (281-287)	278±14 (272-283)
Macular volume	8.43±0.39 (8.39-8.47)	8.36±0.45 (8.32-8.41)	8.34±0.47 (8.28-8.4)	8.3±0.39 (8.21-8.4)	8.12±0.41 (7.96-8.28)

SD: Standard deviation, CI: Confidence interval

The distribution of the average macular thickness (AMT) values in different types of refractive errors is shown in Table 3. The relationship between macular thickness and macular volume with the severity of refractive errors showed that the central subfield thickness significantly increased with increasing the intensity of refractive errors; this relationship is shown in Figure 1.

The relationship between central subfield thickness and each of the studied variables was investigated by a simple linear regression model [Table 4]. The relationship between central subfield thickness and the studied variables was also investigated in a multiple regression model. The results of this model showed that only central subfield thickness was significantly lower in females than males ($\beta = -5.77$; 95% CI: -9.42 to -2.13; P = 0.002).

The mean average overall macular thickness was $267 \pm 29 \ \mu m \ (95\% \ CI: 265-269)$, which was significantly





Refractive errors	Emmetropia (n=863), mean±SD (95% Cl)	Myopia (n=468), mean±SD (95% Cl)	Hyperopia (<i>n</i> =944), mean±SD (95% CI)
Central subfield thickness	220±29 (217–222)	226±45 (217–234)	219±28 (216-221)
Average of macular thickness	267±29 (265–270)	272±32 (266–278)	264±27 (262–266)
Superior inner macular thickness	335±24 (333–337)	333±20 (330–336)	333±17 (332–335)
Inferior inner macular thickness	331±21 (329–333)	331±22 (328–335)	332±19 (330–333)
Nasal inner macular thickness	337±20 (335–339)	336±21 (333–339)	335±19 (333–337)
Temporal inner macular thickness	324±19 (322–325)	323±21 (320-326)	323±18 (321-324)
Average inner	332±19 (330–333)	331±20 (328–334)	331±17 (329-332)
Superior outer macular thickness	288±17 (287–290)	287±18 (284–289)	287±14 (286–288)
Inferior outer macular thickness	278±17 (277-280)	277±19 (275-280)	278±15 (277-280)
Nasal outer macular thickness	304±18 (302–306)	303±19 (300–305)	304±17 (302-305)
Temporal outer macular thickness	277±16 (275-278)	275±17 (273–278)	276±14 (275–277)
Average outer	287±16 (285–288)	286±17 (283–288)	286±14 (285–288)
Macular volume	8.38±0.44 (8.33-8.42)	8.35±0.48 (8.28-8.41)	8.35±0.4 (8.32-8.39)

Table 3: The mean,	, standard deviation,	and 95%	confidence	interval	of macular	thickness	(μ) a	and m	nacular	volume
(mm ³) in elderly by	refractive errors									

SD: Standard deviation, CI: Confidence interval

Table 4: Association of macular thickness (μ), macular volume (mm³), and average macular thickness with other variables in simple regression models

Variables	Central subfield thic	kness	Average of macular th	ickness	Macular volume		
	Coefficient (95% CI)	Р	Coefficient (95% CI)	Р	Coefficient (95% CI)	Р	
Age (year)	0.19 (0.79–-0.41)	0.535	0.19 (0.570.2)	0.333	-0.01 (-0.010.02)	< 0.001	
Gender (male/female)	-5.77 (-2.139.42)	0.002	-11.17 (-8.0614.29)	< 0.001	-0.09 (-0.040.14)	< 0.001	
Education (year)	-0.18 (0.240.59)	0.401	-0.02 (0.260.31)	0.869	0 (0.01–0)	0.124	
Smoking (yes/no)	0.8 (6.09–-4.48)	0.764	3.6 (8.561.36)	0.153	0.05 (0.120.03)	0.212	
HbA1c (%)	1.53 (3.460.4)	0.119	0.61 (2.571.35)	0.538	0.01 (0.040.03)	0.731	
Blood sugar (mmol/L)	0.01 (0.050.03)	0.594	0.01 (0.040.03)	0.709	0 (0–0)	0.993	
Diabetes (yes/no)	2.29 (6.551.97)	0.290	0.14 (3.983.71)	0.945	-0.02 (0.050.08)	0.597	
Systolic blood pressure (mm/Hg)	0.1 (0.220.03)	0.132	0.08 (0.17-0)	0.061	0 (0–0)	0.313	
Diastolic blood pressure (mm/Hg)	0.01 (0.170.15)	0.902	0.1 (0.250.05)	0.205	0 (0–0)	0.845	
BMI	-0.3 (0.050.65)	0.090	-0.47 (-0.170.77)	0.002	0 (0.010.01)	0.538	
Axial length (mm)	0.33 (1.71.04)	0.634	1.21 (2.750.33)	0.122	-0.05 (-0.020.07)	0.001	
Mean keratometry (diopter)	0.64 (2.150.86)	0.401	0.49 (1.570.58)	0.367	0.03 (0.04-0.02)	< 0.001	
White-to-white (mm)	-1.87 (3.317.05)	0.476	-0.26 (3.794.31)	0.898	0.01 (0.070.05)	0.703	
Intraocular pressure (mm/Hg)	0.28 (0.940.37)	0.394	0.8 (1.4-0.2)	0.010	0.01 (0.02-0)	0.071	
Refractive errors							
Emmetropia	0		0		0		
Муоріа	5.96 (15.423.51)	0.216	4.48 (11.522.56)	0.210	-0.04 (0.040.11)	0.330	
Hyperopia	-1.08 (2.384.54)	0.539	-2.92 (0.296.12)	0.074	-0.02 (0.030.07)	0.399	

BMI: Body mass index, SD: Standard deviation, CI: Confidence interval, HbA1c: Glycated hemoglobin

lower in females than males (P < 0.001) and increased significantly with age (P = 0.003). The relationship between the average overall macular thickness and other variables is shown in Table 4. As seen, the average overall macular thickness was significantly directly related to systolic and diastolic blood pressures and inversely related to body mass index. The results of the multiple regression model showed that this index had a statistically significant relationship with sex ($\beta = -10.32$; 95% CI: -13.57 to -7.07; P < 0.001). In addition, the average overall macular thickness was significantly directly related to intraocular pressure ($\beta = 0.63$; 95% CI: 0.04-1.22; P = 0.038). The mean average inner macular thickness was 331 ± 19 (95% CI: 330-332) µm. The maximum and minimum macular thicknesses in the inner part were related to the nasal and temporal quadrants, respectively. The repeated measures analysis of variance showed a statistically significant difference between the 4 quadrants in the inner part (P < 0.001). The mean average outer macular thickness was 286 ± 15 (95% CI: 285-287) µm. The maximum and minimum macular thicknesses in the outer part were related to the nasal and temporal quadrants, respectively (P < 0.001).

The mean macular volume was $8.36 \pm 0.44 \text{ mm}^3$ (95% CI: 8.33–8.39). This index was significantly lower in females than

males (P < 0.001) and decreased significantly with age from 8.43 mm³ in the age group of 60–64 years to 8.12 mm³ in the age group of ≥80 years. Investigation of the relationship between the variables in the multiple model showed that the macular volume was significantly lower in females than males ($\beta = -0.13$; 95% CI: -0.17 to -0.08; P < 0.001) and decreased with age ($\beta = -0.01$; 95% CI: -0.02 to -0.01; P < 0.001). In addition, macular volume had a significant inverse relationship with the axial length ($\beta = -0.04$; 95% CI: -0.07 to -0.01; P = 0.011) and a significant direct relationship with mean keratometry ($\beta = 0.03$; 95% CI: 0.01-0.05; P < 0.001).

DISCUSSION

The present population-based study examined the distribution of macular thickness and macular volume and their related factors specifically in a geriatric population of 60 years of age and above using SD-OCT for the first time. Various studies have investigated the distribution of these parameters worldwide.^{9,11-14,19} In addition to the small sample size as well as demographic and sampling differences, the type of OCT instrument used was also different among previous studies. A point to consider is the difference between the time-domain OCT (TD-OCT) and SD-OCT results.¹⁷ According to the findings of the previous studies mentioned in Table 5, the values obtained by TD-OCT were less than SD-OCT types.

Huang *et al.*²² compared the results of two generations of OCT in healthy individuals and reported that SD-OCT has higher reproducibility compared to TD-OCT. Furthermore, the values obtained with the TD-OCT were lower than the SD-OCT values in all the Early Treatment Diabetic Retinopathy Study macular subfields. However, both devices displayed the same thickness pattern across the foveal, parafoveal, and perifoveal regions, so that the foveal thickness was the thinnest, while the inner macular thickness was greater than the outer macular thickness.²² This difference may be partly due to the fact that the borders of the retinal thickness defined in the two devices are different. However, studies have shown that differences in segmentation algorithms are not the only reason for discrepancies between devices, indicating that macular thickness measurements are not interchangeable with different OCT devices.^{17,23,24} In the present study, the mean average overall macular thickness and the mean CMT were 267 and 221 µm, respectively. The mean overall macular thickness reported in previous studies using SD-OCT varied from 262.8 µm in the Pakistani population¹¹ aged 16-80 years to 280.25 µm in the Chinese population²¹ aged 40-80 years. This difference was also evident in the CMT, which ranged from 176.40^{12} to 255.40^{13} µm. In addition to the age distribution and the type of OCT used, race is another important factor contributing to these discrepancies among previous studies.^{1,13} In a study conducted by Wong et al., there was a statistically significant difference in the macular thickness between individuals of three races (Chinese, Malay, and Indian) after adjusting for other confounding variables, especially age.¹ In another study conducted by Hashemi et al.¹³ in northern Iran (Shahroud), the mean overall macular thickness and the mean CMT were 278.6 and 255.40 µm, respectively, which were slightly higher than the average values found in the present study.¹³ The age range was 45-69 years in the study of Hashemi et al.13 which was younger than the age range of the present study. Despite the considerable differences in the overall macular thickness and the CMT among studies, the higher inner macular thickness compared to the outer macular thickness (also found in the present study) is a finding which is consistent between most studies. In addition, in both the inner and outer parts of the macula, the nasal and temporal quadrants were the thickest and thinnest parts, respectively, and the thickness of the superior quadrant was higher than the inferior quadrant. This finding is probably due to the normal convergence of retinal fibers toward the optic nerve.^{11-15,21,22}

The mean macular volume was 8.36 mm³ in the present study. As for macular thickness, the reported macular volume means with TD-OCT was lower than SD-OCT. However, the values reported with SD-OCT devices were also very different. As shown in Table 5, the average macular volume measured by SD-OCT instruments has been reported in a wide range from 7.19 to 10.10 mm³ in the previous studies. Differences in age and sex distribution as well as race are the possible causes of discrepancies in the reported values.^{12,13,15,21,22}

The results of the present study in line with the previous studies showed that the macular thickness and volume were higher

Table 5: Summary of other studies on macular thickness (μ)														
Author (year)	п	Age	Country	Device	CMT	Inner			Outer				Macular	
						Superior	Nasal	Inferior	Temporal	Superior	Nasal	Inferior	Temporal	volume
Adhi et al.11	220	16-80	Pakistan	SD-OCT	229	290.3	292.6	287.1	275.2	247	268.5	243.2	232.5	-
Pradhan <i>et al</i> . ¹⁴	189	25-79	India	TD-OCT	186.7	264.72	263.26	263.31	252.34	232.96	255.11	231.58	216.67	-
Hashemi et al.13	3024	45–69	Iran	SD-OCT	255.4	319.8	321.4	316.7	307.9	275.7	294.1	267.4	263.8	10.1
Gupta et al.21	490	40-80	China	SD-OCT	250.38	323.11	325.14	319.09	310.00	279.62	299.38	266.19	261.48	10.09
Huang et al.22	32	20-60	China	SD-OCT	208.62	288.42	287.22	285.26	276.89	252.61	257.39	239.63	226.56	7.19
Huang et al.22	32	20-60	China	TD-OCT	193.73	274.57	269.06	271.54	263.80	244.33	261.79	232.67	238.72	6.98
Duan <i>et al</i> . ¹²	2230	30-85	China	TD-OCT	176.40	261.60	252.90	260.00	246.70	240.00	258.50	225.50	227.00	6.76
Song et al.15	198	17-83	Korea	SD-OCT	253.92	317.45	320.24	311.66	304.17	274.77	291.86	264.43	257.86	9.74
Current study	2275	≥60	Iran	SD-OCT	221	334	336	331	323	287	304	278	276	8.36

CMT: Central macular thickness, SD-OCT: Spectral-domain optical coherence tomography, TD-OCT: Time-domain optical coherence tomography

in all segments in males than females.^{11-15,22} It seemed that the higher macular thickness in males was due to the longer axial length; however, after adjusting for other factors in the multiple model, the confounding effect of other factors was rejected. Therefore, this sex-related difference can be attributed to anatomical differences in the retinal layers between males and females. In an animal model to study the role of sex in macular thickness, Salyer *et al.*²⁵ reported that males had a thicker retina due to the higher proportion of magnocellular ganglion cells (which are thicker and larger) than parvocellular cells.

Comparing the macular thickness and macular volume between different refractive errors, myopes showed a higher thickness than emmetropes and hyperopes only in the central 1-mm macular region [Table 1]. However, it is reported that central subfield thickness and average overall macular thickness increased at high degrees of refractive errors, especially myopia.¹⁵ Previous OCT studies have shown that myopes have higher foveal thickness but lower parafoveal and perifoveal thicknesses compared to nonmyopic individuals.^{15,26} This difference has been reported especially in individuals with high myopia and long axial length. It seems that axial elongation in high myopia leads to scleral stretching in the posterior pole with subsequent foveal stretching and thickening.²⁷

Chung et al. investigated the role of axial length in macular thickness and reported that the foveal thickness increased in axial lengths above 25.5 mm, but there was no significant association between axial length and macular thickness in individuals without high myopia.28 Hashemi et al. compared the thickness of different macular areas between individuals with different refractive errors and reported that the outer macular thickness was higher in hyperopes than myopes. However, no significant difference was observed in the central and inner macular thicknesses, which again confirms the results of the previous studies; myopes have higher foveal thickness but lower perifoveal and parafoveal thickness.13 In the present study, the general trend regarding changes in macular thickness in different areas in different refractive errors is similar to the previous studies.^{13,28} The significance or nonsignificance of differences in macular thickness among studies is due to the differences in refractive error and axial length ranges in the studied populations. The results of the multiple regression models in this study revealed a significant negative relationship between axial length and macular volume. According to the results, macular volume was lower in myopia exceeding 6 diopters compared to other degrees of myopia, while no significant relationship was observed between axial length and macular thickness. A negative correlation between axial length and macular volume has been reported in many previous studies.15,28

In the present study, no significant relationship was found between age and macular thickness in the multiple model, but macular volume showed a significant decrease with advancing age. Regarding the role of age in changes of the thickness in different parts of the retina, very conflicting results have been reported.^{1,11-13,15,21,22} In studies that included a wider age range from adolescence to older ages, the association between age and macular thickness was more evident. In the present study, due to the age distribution of the study population and the exclusion of all individuals with any retinal abnormalities from the analysis, despite the age dependence of many retinal diseases, no significant relationship was observed between age and macular thickness. Some studies in line with the present study did not show significant age-related changes in macular thickness.¹¹ Others such as the study by Hashemi et al. on a population aged 45-69 years reported an increase in the central foveal thickness and a decrease in the inner and outer macular thicknesses with advancing age.13 This trend was also observed in the present study but was not statistically significant. The age-related decrease in the thickness of the parafoveal and perifoveal regions has been attributed to the reduction of the density of ganglion cells, retinal nerve fiber layer, and photoreceptors.²⁹ The increase in central foveal thickness with age is probably due to inefficiency in the pumping function of the retinal pigment epithelium and a decrease in the choriocapillary circulation with subsequent central foveal edema.30

Apart from sex, intraocular pressure was the only parameter that showed a significant relationship with the AMT in the multiple model, so that increasing intraocular pressure was associated with the increased AMT. Lee *et al.* examined the factors influencing the retinal thickness of healthy young individuals and reported that intraocular pressure was not effective in any of the retinal thickness variables.¹⁸ Some studies have reported retinal thinning, especially in the parafoveal and perifoveal regions, and no significant change in the central foveal thickness with increased intraocular pressure. The reason for the lack of change in the central foveal thickness is the absence of ganglion cells in that area.³¹ Due to the contradictory results among different studies, further studies in this field are recommended.

The strengths of the present study included its population-based design and a large sample of over 60 years of age population. However, the results of the study in a single population cannot be extrapolated to other populations, and attention should be paid to demographic and genetic characteristics and ethnicity of the populations before generalizing the results. On the other hand, it would be beneficial to present the thickness of different retinal layers separately. However, since this was not the objective of the current study, it was not addressed. It is suggested that future studies consider this aspect.

The results of the present population-based study can be used as a database to interpret OCT results in the elderly population. Due to lower central foveal thickness as well as parafoveal and perifoveal thicknesses in females than males, the role of sex should also be taken into account in the interpretation of the study findings. Our results showed that the macular thickness in the Iranian geriatric population is slightly less than the populations studied in other countries, which should be considered in diagnostic and clinical settings.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Wong KH, Tham YC, Nguyen DQ, Dai W, Tan NY, Mathijia S, *et al.* Racial differences and determinants of macular thickness profiles in multiethnic Asian population: The Singapore Epidemiology of Eye Diseases Study. Br J Ophthalmol 2019;103:894-9.
- Dai W, Tham YC, Cheung N, Yasuda M, Tan NY, Cheung CY, et al. Macular thickness profile and diabetic retinopathy: The Singapore Epidemiology of Eye Diseases Study. Br J Ophthalmol 2018;102:1072-6.
- Hu H, Jiang H, Gameiro GR, Hernandez J, Delgado S, Wang J. Focal thickness reduction of the ganglion cell-inner plexiform layer best discriminates prior optic neuritis in patients with multiple sclerosis. Invest Ophthalmol Vis Sci 2019;60:4257-69.
- Alves JN, Westner BU, Højlund A, Weil RS, Dalal SS. Structural and functional changes in the retina in Parkinson's disease. J Neurol Neurosurg Psychiatry 2023;94:448-56.
- Sánchez D, Castilla-Marti M, Marquié M, Valero S, Moreno-Grau S, Rodríguez-Gómez O, *et al.* Evaluation of macular thickness and volume tested by optical coherence tomography as biomarkers for Alzheimer's disease in a memory clinic. Sci Rep 2020;10:1580.
- Vujosevic S, Toma C, Villani E, Nucci P, Brambilla M, Torti E, *et al.* Longitudinal microvascular and neuronal retinal evaluation in patients with diabetes mellitus types 1 and 2 and good glycemic control. Retina 2023;43:1723-31.
- Güven YZ, Akay F, Akmaz B, Akmaz EN, Özen Ç. Evaluation of subclinical changes in recently diagnosed pediatric hypertension patients without hypertensive retinopathy: An OCT study. Int Ophthalmol 2023;43:2265-72.
- von Hanno T, Hareide LL, Småbrekke L, Morseth B, Sneve M, Erke MG, *et al.* Macular layer thickness and effect of BMI, body fat, and traditional cardiovascular risk factors: The tromsø study. Invest Ophthalmol Vis Sci 2022;63:16.
- Aydin E, Kazanci L, Balikoglu Yilmaz M, Akyildiz Akcay F, Bayata S. Analysis of central macular thickness and choroidal thickness changes in patients with cardiovascular risk factors. Eye (Lond) 2020;34:2068-75.
- 10. Simpson SH. Creating a data analysis plan: What to consider when choosing statistics for a study. Can J Hosp Pharm 2015;68:311-7.
- Adhi M, Aziz S, Muhammad K, Adhi MI. Macular thickness by age and gender in healthy eyes using spectral domain optical coherence tomography. PLoS One 2012;7:e37638.
- Duan XR, Liang YB, Friedman DS, Sun LP, Wong TY, Tao QS, *et al.* Normal macular thickness measurements using optical coherence tomography in healthy eyes of adult Chinese persons: The Handan eye study. Ophthalmology 2010;117:1585-94.
- Hashemi H, Khabazkhoob M, Yekta A, Emamian MH, Nabovati P, Fotouhi A. The distribution of macular thickness and its determinants in a healthy population. Ophthalmic Epidemiol 2017;24:323-31.
- 14. Pradhan ZS, Braganza A, Abraham LM. Determinants of macular thickness in normal Indian eyes. J Clin Ophthalmol Res 2013;1:11.

- Song WK, Lee SC, Lee ES, Kim CY, Kim SS. Macular thickness variations with sex, age, and axial length in healthy subjects: A spectral domain-optical coherence tomography study. Invest Ophthalmol Vis Sci 2010;51:3913-8.
- Pierro L, Giatsidis SM, Mantovani E, Gagliardi M. Macular thickness interoperator and intraoperator reproducibility in healthy eyes using 7 optical coherence tomography instruments. Am J Ophthalmol 2010;150:199-204.e1.
- Leung CK, Cheung CY, Weinreb RN, Lee G, Lin D, Pang CP, et al. Comparison of macular thickness measurements between time domain and spectral domain optical coherence tomography. Invest Ophthalmol Vis Sci 2008;49:4893-7.
- Lee SS, Lingham G, Alonso-Caneiro D, Charng J, Chen FK, Yazar S, et al. Macular thickness profile and its association with best-corrected visual acuity in healthy young adults. Transl Vis Sci Technol 2021;10:8.
- Söhnel T, Meigen C, Hiemisch A, Wahl S, Ziemssen F, Truckenbrod C, et al. Normative data for macular and retinal nerve fibre layer thickness in healthy German children and adolescents using optical coherence tomography. Ophthalmic Physiol Opt 2023;43:922-34.
- 20. Poh S, Tham YC, Chee ML, Dai W, Majithia S, Soh ZD, et al. Association between macular thickness profiles and visual function in healthy eyes: The Singapore Epidemiology of Eye Diseases (SEED) study. Sci Rep 2020;10:6142.
- 21. Gupta P, Sidhartha E, Tham YC, Chua DK, Liao J, Cheng CY, et al. Determinants of macular thickness using spectral domain optical coherence tomography in healthy eyes: The Singapore Chinese Eye Study. Invest Ophthalmol Vis Sci 2013;54:7968-76.
- Huang J, Liu X, Wu Z, Xiao H, Dustin L, Sadda S. Macular thickness measurements in normal eyes with time-domain and Fourier-domain optical coherence tomography. Retina 2009;29:980-7.
- Pierre-Kahn V, Tadayoni R, Haouchine B, Massin P, Gaudric A. Comparison of optical coherence tomography models OCT1 and stratus OCT for macular retinal thickness measurement. Br J Ophthalmol 2005;89:1581-5.
- 24. Sadda SR, Joeres S, Wu Z, Updike P, Romano P, Collins AT, et al. Error correction and quantitative subanalysis of optical coherence tomography data using computer-assisted grading. Invest Ophthalmol Vis Sci 2007;48:839-48.
- Salyer DL, Lund TD, Fleming DE, Lephart ED, Horvath TL. Sexual dimorphism and aromatase in the rat retina. Brain Res Dev Brain Res 2001;126:131-6.
- 26. Zereid FM, Osuagwu UL. Myopia and regional variations in retinal thickness in healthy eyes. J Ophthalmic Vis Res 2020;15:178-86.
- 27. McMonnies CW. An examination of the relation between intraocular pressure, fundal stretching and myopic pathology. Clin Exp Optom 2016;99:113-9.
- Chung YW, Choi MY, Kim JS, Kwon JW. The association between macular thickness and axial length in myopic eyes. Biomed Res Int 2019;2019:8913582.
- 29. Wang Q, Wei WB, Wang YX, Yan YN, Yang JY, Zhou WJ, *et al.* Thickness of individual layers at the macula and associated factors: The Beijing eye study 2011. BMC Ophthalmol 2020;20:49.
- Alvarez-Guzman C, Bustamante-Arias A, Colorado-Zavala MF, Rodriguez-Garcia A. The impact of central foveal thickness and integrity of the outer retinal layers in the visual outcome of uveitic macular edema. Int J Retina Vitreous 2021;7:36.
- Lee SY, Jeoung JW, Park KH, Kim DM. Macular ganglion cell imaging study: Interocular symmetry of ganglion cell-inner plexiform layer thickness in normal healthy eyes. Am J Ophthalmol 2015;159:315-23.e2.