Choroidal Thickness and Its Association With Age, Axial Length, and Refractive Error in Chinese Adults

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Purpose. To identify the association between the choroidal thickness (ChT) with age and axial length (AL) under different refractive errors (REs) in Chinese adults.

Methods. Swept-source optical coherence tomography was used to measure ChT in 2126 right eyes of 2126 participants. The participants were classified as having pathologic myopia (PM), high myopia without PM (HM), low myopia (LM), and nonmyopia (non-M) according to their REs and META-PM (the Meta-Analysis of Pathologic Myopia) classification criteria.

Results. The mean age was 52.49 ± 20.39 years (range, 18–93 years), and the mean RE was −5.27 ± 5.37 diopters (D; range, −25.5 to +7.75 D). The mean average ChT was 159.25 ± 80.75 µm and decreased in a linear relationship from non-M to PM (190.04 ± 72.64 µm to 60.99 ± 37.58 µm, $P < 0.001$). A significant decline in ChT was noted between 50 and 70 years ($r = -0.302$, $P < 0.001$) and less rapidly after the age of 70 years ($r = -0.105$, $P = 0.024$). No correlation was noted between age and ChT under 50 years ($P = 0.260$). A significantly higher association with AL was noted in the central fovea ($\beta^{HM} = -23.92$, $\beta^{LM} = -23.88$, $\beta^{Non\text{-}M} = -18.80$, all $P < 0.001$) and parafoveal ChT ($\beta^{HM} = -22.87$, $\beta^{LM} = -22.31$, $\beta^{Non\text{-}M} = -18.61$, all $P < 0.001$) when compared with the perifoveal region ($\beta^{HM} = -19.80$, $\beta^{LM} = -18.29$, $\beta^{Non\text{-}M} = -13.95$, all $P < 0.001$). Within each group of PM, HM, LM, and non-M, regression analysis showed that the coefficients of age and AL with different macular regions of ChT varied significantly.

Conclusions. ChT was negatively correlated with age after 50 years. The thinning of the choroid was more prominent in the center and parafoveal regions as AL increased. Varied distributions of ChT decrease associated with AL and age were noted among different refractive groups.

Keywords: choroidal thickness, myopia, high myopia, pathologic myopia

Myopia is a global health problem that affected nearly 30% of the world's population in 2020.[1] Fifty percent of the global population is expected to be affected by myopia by 2050, of whom 10% will have high myopia.[1] The rising prevalence of myopia with a disproportionately greater increase in high myopia forecasts a future increase in vision loss due to uncorrected myopia and myopia-related complications such as myopic macular degeneration.[2] The precise mechanism underlying myopia progression is still not clear. Although both genetic[3] and environmental factors[4] may affect the development of myopia, growing evidence indicates that the choroid plays a critical role in the pathophysiology of myopia. The choroid is a highly vascularized structure that regulates the scleral extracellular matrix remodeling, leading to changes in eye size and refraction, by relaying retina-derived signals to the sclera and influencing the oxygen levels and nutrient supply of the sclera.[5–7]

Numerous studies have employed optical coherence tomography (OCT) to assess the choroidal thickness (ChT) in vivo, whereby a reduction in the ChT was noted with increasing age, elongation of the axial length (AL), and decrease in the refractive diopter.[8–27] The reduction of subfoveal ChT with age and AL has been reported to vary in eyes with high myopia (age: −1.25 to −3.03 µm/y; AL: −9.88 to −30.87 µm/mm),[10,15,18,23,26] in normal eyes (age: −1.56 to −5.4 µm/y),[8,16,19] and in eyes with a full range of refractive errors (REs) (age: −1.8 to −4.14 µm/y; AL: −21.93 to −58.2 µm/mm).[9,11,12,17,23–25] Although some earlier studies compared different parts of the ChT in the macular region among different refractive groups,[12,14,20,22,23,28] only one study[25] analyzed the association between different regions of ChT with AL and REs in a relatively smaller age range. Thus, due to the relatively small study sample size and selection bias in age or RE so far, there is no direct evidence indicating whether the changes of ChT from various

macular regions were associated with age and AL uniformly or unevenly under different REs.[15] Therefore, we conducted a large-scale population study whereby a wide range of ages and REs were included to make a full perspective view of ChT changes with its associations. Our objectives were to elucidate and compare the ChT in different regions of the posterior pole and its association with age and AL under different REs in Chinese adults.

Methods

Study Population

The Shanghai High Myopia Study for Adults (SHMSA) is an ongoing highly myopic cohort study (NCT03446300), which was started in 2016 at the Shanghai Eye Diseases Prevention and Treatment Center in Shanghai, China. Individuals aged ≥18 years, with spherical power ≤−6.00 diopters (D) or AL ≥26 mm in either eye were invited to register for the study. Simultaneously, from August 2016 to October 2016, we conducted another cross-sectional study named the Shanghai General Hospital Myopia Study (SGHMS), whereby Chinese adults (≥18 years) who were referred to the physical examination center in Shanghai General Hospital volunteered to participate after reading our description of the study and accepting an open invitation to become participants. Both study protocols were approved by the Medical Ethics Committee of Shanghai General Hospital, Shanghai Jiao Tong University, School of Medicine, according to the Declaration of Helsinki. Written informed consent was obtained from all study participants.

Inclusion and Exclusion Criteria

The inclusion criteria of the present study from SHMSA and SGHMS were mentioned above. The exclusion criteria included coexisting or history of ocular disorders, such as corneal opacity, secondary myopia, glaucoma, age-related macular degeneration, diabetic retinopathy, retinal vein occlusion, central serous chorioretinopathy, retinitis pigmentosa, amblyopia, and uveitis. Patients with a history of undergoing eye surgeries, including refractive surgeries, cataract surgeries, vitreoretinal surgeries, photodynamic therapy, and those who made use of systemic corticosteroids, were excluded. Eyes with advanced cataract and insufficiently clear OCT images, including poor-quality images for measuring ChT and any images missing due to the eye movements or blinks, were excluded as well. Only the right eye of each patient was selected for statistical analyses.

Definitions and Classifications

Pathological myopia (PM) was defined according to the META-PM (the Meta-Analysis of Pathologic Myopia) classification system as myopic maculopathy equal to or more serious than diffuse choroidal atrophy (category 2) or the presence of plus lesions such as myopic choroidal neovascularization or lacquer cracks, reported previously.[26] According to the International Myopia Institute,[29] high myopia (HM) was defined as an RE ≤−6.0 D without PM changes, low myopia (LM) was defined as an RE >−6.0 D and ≤−0.5D without PM changes, and nonmyopia (non-M) was defined as an RE >−0.5 D. The Lens Opacity Classification System II was used to grade patients' cataracts.[30] A nuclear, cortical, and posterior subcapsular lens opacity was considered advanced if the grade of the opacity was greater than grades NII, CII, or PSCII, respectively.[31,32]

Ophthalmic Examinations

All participants underwent a standardized clinical interview and a comprehensive ophthalmic examination, including intraocular pressure (IOP), AL, RE, slit-lamp biomicroscopy, color fundus photography, and measurement of ChT using swept-source optical coherence tomography (SS-OCT; model DRI OCT-1 Atlantis; Topcon, Tokyo, Japan). The IOP was measured with a Full Auto Tonometer (TX-F; Topcon, Tokyo, Japan), and AL measurements were performed using Lenstar (Haag-Streit AG, Koeniz, Switzerland). Additional measurements were performed using the IOL Master (Carl Zeiss, Tubingen, Germany) when the AL exceeded the maximum 32-mm range of the Lenstar. The AL was measured five times, and the mean values were used for statistical analysis. The RE assessment was performed using an autorefractor machine (model KR-8900; Topcon, Tokyo, Japan) without cycloplegia and was calculated as the sphere value plus half a cylinder value. Height and weight were measured as well, and the body mass index (BMI) was calculated using the following formula: weight (kg) / [height (m)]^2.

Measurements of ChT

The average thickness of the macular choroidal layer was measured using SS-OCT. The OCT scanning protocols included a length of 9 mm with 12 equal radial meridian scans centered on the fovea. Individuals whose OCT image signal strength was larger than 60 were included in the final analyses. The measurement was conducted from 10 AM to 3 PM to reduce the impact of diurnal variation.[33] The segmentation of each layer was obtained automatically, and manual segmentation was performed while the automatic segmentation was inaccurate or led to measurement artifacts. To determine the reproducibility of manual correction, 20 images that needed manual segmentation were randomly selected and corrected twice by a specific technician. A Bland–Altman plot showed high reproducibility of the ChT segmentation (Fig. 1). The mean difference between two corrections was

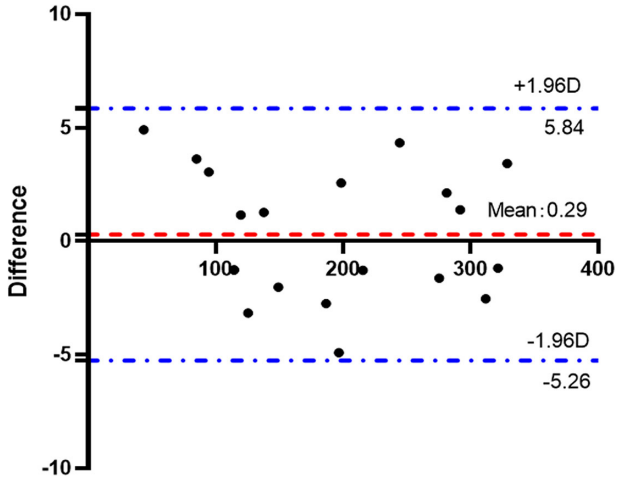

Figure 1. Bland–Altman plot illustrating the reproducibility of the average ChT measured from the two repeated scans by one technician.

0.3 µm, and the 95% limits of agreement ranged from −5 to 6 µm. The ChT was defined as the vertical distance between Bruch's membrane and the choroid–sclera interface. The tomographic maps were overlapped to an Early Treatment Diabetic Retinopathy Study (ETDRS) grid (6 × 6 mm) that was focused on the macular. Thus, each scan was divided into three concentric circles with nine regions as follows: the central circle with a 1-mm diameter (central foveal circle), the inner circle with a 3-mm diameter (parafoveal circle), and the outer circle with a 6-mm diameter (perifoveal circle). The inner parafoveal circle and the outer perifoveal circle were further divided into four quadrants, including temporal (T), superior (S), nasal (N), and inferior (I) quadrants. The average thickness in each sector of the grid was automatically calculated using a built-in software. In the macular region, all nine sectors of the grid were applied to analyze the average thickness.

Statistical Analysis

The data are presented as means ± standard deviations for continuous variables and as counts for the categorical data. The one-way analysis of variance with Bonferroni adjustment and univariate linear regression were employed to explore the relationship among age, RE, AL, IOP, BMI, and ChT values at different locations for PM, HM, LM, and non-M. The ChT at different regions was compared using repeated-measures analysis of variance by testing for sphericity. When the sphericity assumption was violated, the Greenhouse–Geisser test was used. The Bonferroni method was used to adjust for comparisons across these post hoc tests. The Pearson's correlation coefficient was calculated to assess the correlation of ChT with age and AL. Multivariate linear regression analysis was undertaken on age, gender, AL, IOP, and BMI as independent variables to predict ChT. The SPSS 22.0 software (IBM Corp., Armonk, NY, USA) was used to conduct statistical analysis. A P value <0.05 was considered statistically significant.

Results

Participants' Demographic and Clinical Characteristics at Baseline

A total of 2569 right eyes of 2569 participants were initially screened. Among them, 42 eyes had a history of undergoing eye surgeries for various pathologies other than cataract; 168 eyes had received cataract surgery; 102 eyes had advanced cataract; 46 eyes had ocular disorders other than myopia, such as glaucoma, age-related macular degeneration, diabetic retinopathy, retinal vein occlusion, central serous chorioretinopathy, and amblyopia; and 85 eyes had low-quality OCT images. Finally, 2126 right eyes of 2126 participants (940 men and 1186 women) were included in this study.

The participants' mean age was 52.49 ± 20.39 years (range, 18–93 years), the mean RE was −5.27 ± 5.37 D (range, −25.5 to +7.75 D), and the mean AL was 25.90 ± 2.34 mm (range, 21.05–33.68 mm). When participants were categorized according to RE and fundus photographs, those with PM were significantly older than those with HM, LM, and non-M (P < 0.001, Table 1). Univariate linear regression analysis showed that AL had a linear relationship from PM to non-M (P < 0.001). The comparison of demographic characteristics between SHMSA and SGHMS studies is presented in Supplementary Table S1.

Comparing ChT Between Groups With Different Refractive Statuses

For all participants, the mean ChT in the central foveal was 164.46 ± 91.51 µm, and the mean average ChT was 159.25 ± 80.75 µm. ChT had a positive relationship from PM to non-M in all nine macular sectors of the ETDRS grid (P < 0.001, Table 1). Figure 2 shows the topographic variation of ChT among four RE groups.

In the horizontal section, the choroid in the outer-T sector was the thickest among the outer-N, inner-N, central foveal, and inner-T sectors in PM (all P < 0.001). For participants with HM and LM, the choroid in the central foveal sector

Table 1. Comparison of General Characteristics and ChTs in Groups With Different Refractive Statuses in the Macular Region

Characteristic	Total (N = 2126)	PM (n = 338)	HM (n = 662)	LM (n = 610)	Non-M (n = 516)	P-Diff	P-Trend
Age, y	52.49 ± 20.39	66.77 ± 9.39	41.68 ± 19.28	47.65 ± 19.88	62.75 ± 17.23	<0.001	<0.001
Gender, female, %	55.79	63.91	54.68	50.33	58.33	<0.001	/
SE, D	−5.27 ± 5.37	−10.90 ± 6.15	−8.96 ± 2.68	−3.33 ± 1.76	0.85 ± 0.99	<0.001	<0.001
AL, mm	25.90 ± 2.34	29.02 ± 1.74	27.33 ± 1.05	25.22 ± 1.43	23.19 ± 0.79	<0.001	<0.001
IOP, mm Hg	14.06 ± 3.17	14.27 ± 3.19	14.75 ± 2.98	14.09 ± 3.17	13.03 ± 3.12	<0.001	<0.001
BMI, kg/m^2	23.63 ± 3.67	24.23 ± 4.06	22.94 ± 3.43	23.66 ± 3.81	24.12 ± 3.36	<0.001	<0.001
Inner-T, µm	171.66 ± 89.95	58.92 ± 43.40	171.14 ± 73.69	203.65 ± 83.27	208.35 ± 78.01	<0.001	<0.001
Inner-S, µm	172.00 ± 91.97	58.63 ± 39.97	169.53 ± 75.23	201.38 ± 86.20	214.71 ± 80.71	<0.001	<0.001
Inner-N, µm	150.10 ± 85.84	52.14 ± 38.55	141.09 ± 65.28	176.88 ± 81.13	194.16 ± 83.53	<0.001	<0.001
Inner-I, µm	163.27 ± 91.04	58.04 ± 41.36	160.37 ± 72.25	194.26 ± 87.88	199.29 ± 86.77	<0.001	<0.001
Outer-T, µm	173.70 ± 85.51	69.21 ± 44.32	180.66 ± 72.65	207.05 ± 80.72	193.81 ± 73.8	<0.001	<0.001
Outer-S, µm	177.80 ± 88.83	68.59 ± 41.38	181.52 ± 76.28	206.69 ± 83.48	210.41 ± 76.36	<0.001	<0.001
Outer-N, µm	119.58 ± 70.51	50.48 ± 37.77	111.19 ± 53.69	140.22 ± 69.29	151.21 ± 73.98	<0.001	<0.001
Outer-I, µm	158.16 ± 84.72	63.18 ± 41.53	160.86 ± 70.04	189.32 ± 82.82	180.09 ± 80.74	<0.001	<0.001
Central foveal ChT, µm	164.46 ± 91.51	53.68 ± 39.89	158.35 ± 72.70	193.69 ± 85.81	210.32 ± 82.45	<0.001	<0.001
Parafoveal ChT, µm	164.33 ± 87.80	57.05 ± 38.41	160.54 ± 69.96	194.04 ± 82.31	204.13 ± 79.70	<0.001	<0.001
Perifoveal ChT, µm	157.37 ± 78.53	62.97 ± 37.31	158.56 ± 64.66	185.82 ± 74.56	183.88 ± 71.34	<0.001	<0.001
Average ChT, µm	159.25 ± 80.75	60.99 ± 37.58	158.90 ± 65.85	187.87 ± 76.35	190.04 ± 72.64	<0.001	<0.001

Values are presented as mean ± SD unless otherwise indicated. P-diff, ANOVA; P-trend, linear trend from PM to non-M.
SE, spherical equivalent.

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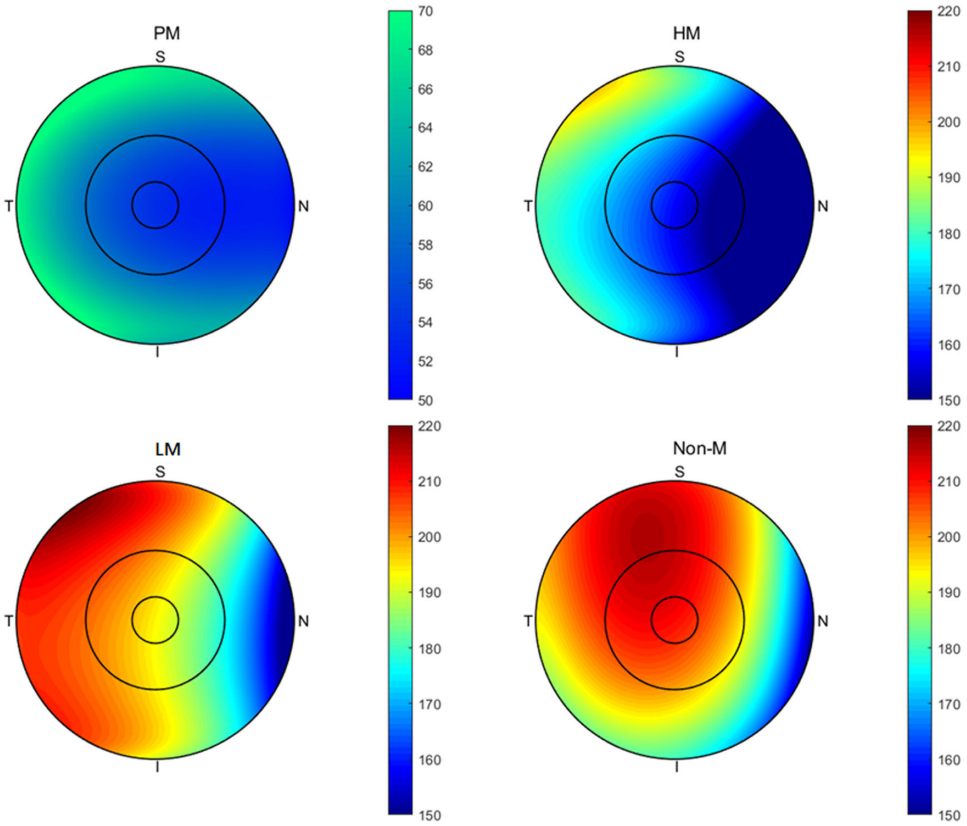

Figure 2. The topographic variation of ChT in the macular area among PM, HM, LM, and non-M.

was thicker than that in outer-N and inner-N sectors (all $P <$ 0.001) and thinner than that in inner-T and outer-T sectors (all $P < 0.001$). In non-M participants, the ChT in the central foveal sector was thicker in the outer-N, inner-N, and outer-T sectors (all $P < 0.001$). In the vertical section, the choroid in the central foveal sector was significantly thinner than that in the outer-S, inner-S, inner-I, and outer-I sectors (all $P <$ 0.001) for PM. For HM and LM, ChT of the outer-S sector was significantly thicker than that of the central foveal, inner-I, inner-S, and outer-I sectors (all $P < 0.001$). For non-M, the choroid in the outer-I sector was significantly thinner than that of the central foveal, inner-S, inner-I, and outer-S sectors (all $P < 0.001$). Across the three myopic groups, the choroid was thicker in the outer-T and outer-S sectors and thinner in the outer-N sector (all $P < 0.001$). In contrast, in eyes of non-M, the choroid was thickest in the inner-S sector, followed by the central foveal region, outer-S sector, and outer-N sector ($P < 0.001$).

The ChT values in the central foveal, parafoveal, and perifoveal regions were significantly different in the four RE groups (all $P < 0.01$). In PM, ChT was the thinnest in the central foveal region, followed by the parafoveal region, and was the thickest in the perifoveal region ($P < 0.001$). In HM, the choroid in the parafoveal region was thicker when compared with the central foveal and perifoveal regions ($P < 0.001$). In LM, ChT in the perifoveal region was thinner than those in parafoveal and central foveal regions ($P < 0.001$). In non-M, the choroid was the thinnest in the perifoveal region, followed by the parafoveal region, and was the thickest in the central foveal region (both $P < 0.001$).

Correlation Between ChT and Age

All patients were assigned into seven groups (A–G) according to age at 10-year intervals. As shown in Figure 3, the ChT in the perifoveal region started to decrease after age 40 years, while there was no significant difference between age-based groups of B and C. However, ChT in the center foveal,

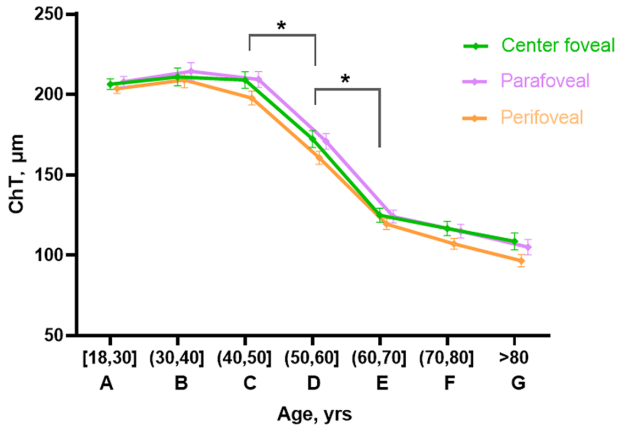

Figure 3. The variations of mean ChT in the central foveal, parafoveal, and perifoveal regions with age. There is a significant difference in ChT between groups C and D and between groups D and E at the center foveal, parafoveal, and perifoveal regions (all $P < 0.001$). The ChT decreased dramatically after age 50 years and less rapidly after age 70 years.

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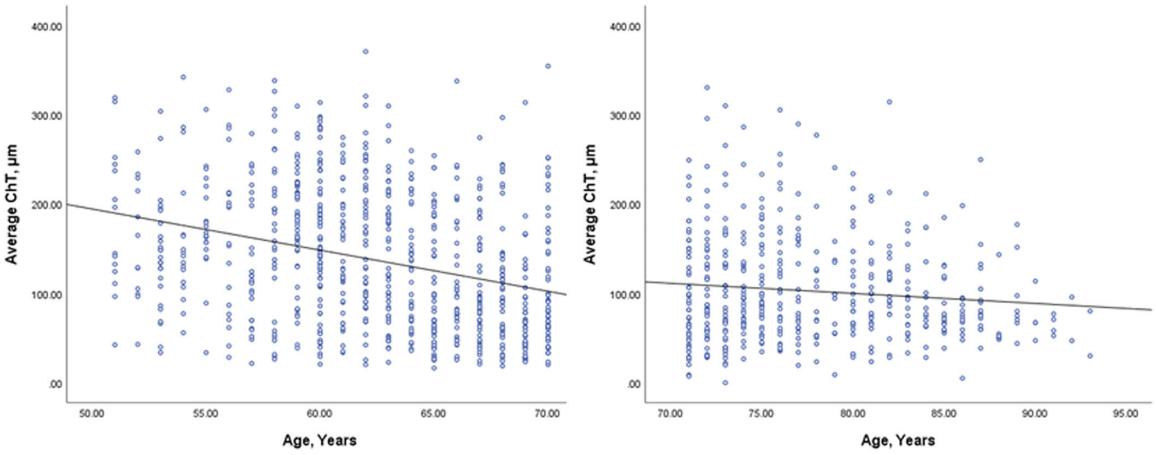

Figure 4. The correlation of average ChT with age. (*Left*) The correlation between average ChT and age in patients aged >50 to ≤70 years ($r = -0.302$, $P < 0.001$). (*Right*) The correlation between average ChT and age in patients aged >70 years ($r = -0.105$, $P = 0.024$).

parafoveal, and perifoveal regions remarkably decreased after age 50 years (all $P < 0.001$). The rate of decrease in the ChT slowed down after age 70 years (all $P > 0.1$).

On the basis of these findings, we combined the A, B, and C groups, D and E groups, and F and G groups into three age subgroups: ≤50 years old (Age 1), >50 to ≤70 years old (Age 2), and ≥70 years old (Age 3). Age was found to be negatively correlated with average ChT in the Age 2 ($r = -0.302$, $P < 0.001$) and Age 3 ($r = -0.105$, $P = 0.024$) subgroups (Fig. 4), while no correlation was noted between age and the average ChT in the Age 1 subgroup ($P = 0.260$). The distributions of the ChT in the four different RE groups for each age-based group are shown in Figure 5. In the three groups of myopia, especially LM and HM, ChT decreased significantly in the Age 2 subgroup when compared with the Age 1 subgroup and slowly declined in the Age 3 subgroup. However, in non-M, ChT decreased gradually with age in all three age groups.

Univariate Linear Regression of ChT With Age and Axial Length

AL was negatively associated with average ChT ($r = -0.456$, $P < 0.001$) and RE ($r = -0.804$, $P < 0.001$). The univariate linear regression model showed that ChT was not associated with age in the center foveal, parafoveal, or perifoveal region in the Age 1 subgroup (all $P > 0.05$, Table 2). However, AL was associated with center foveal, parafoveal, and perifoveal ChT in all three age-based groups (all $P < 0.001$). The correlation coefficient between ChT and AL was highest for the center foveal region ($\beta^{\text{Age 1}} = -27.15$, $\beta^{\text{Age 2}} = -24.89$, $\beta^{\text{Age 3}} = -16.34$), followed by the parafoveal region ($\beta^{\text{Age 1}} = -26.67$, $\beta^{\text{Age 2}} = -23.36$, $\beta^{\text{Age 3}} = -14.75$), and was the lowest in the perifoveal region ($\beta^{\text{Age 1}} = -22.54$, $\beta^{\text{Age 2}} = -19.15$, $\beta^{\text{Age 3}} = -11.40$) in the Age 1, Age 2, and Age 3 subgroups, respectively. However, the correlation coefficient between ChT and age was similar among the center foveal ChT ($\beta^{\text{Age 2}} = -5.56$, $\beta^{\text{Age 3}} = -1.26$), parafoveal ChT ($\beta^{\text{Age 2}} = -5.51$, $\beta^{\text{Age 3}} = -1.28$), and perifoveal ChT ($\beta^{\text{Age 2}} = -4.83$, $\beta^{\text{Age 3}} = -1.31$) in the Age 1, Age 2, and Age 3 subgroups, respectively. Furthermore, the correlation coefficient between ChT and age in the Age 2 subgroup was higher when compared with the Age 3 subgroup among all ChT regions.

Multivariate Linear Regression Analysis

The associations between average ChT and age, AL, gender, IOP, and BMI were analyzed using multivariate linear regression analysis. As shown in Figure 3 and the univariate linear regression analysis, the correlation between ChT and age was not linear under the age of 50 years. Therefore, for this analysis, we converted age into categorical variables as explained earlier. The results revealed that older age, longer AL, and the female gender were significantly associated with a lower ChT average (Age 2: $\beta = -60.80$; Age 3: $\beta = -114.54$; AL: $\beta = -18.67$; female: $\beta = -21.64$; all $P < 0.001$). Multivariate linear regression analyses were further performed for each of the four RE groups (Table 3). The coefficients of AL and age were greater in HM, LM, and non-M (AL: $\beta^{\text{HM}} = -20.61$, $\beta^{\text{LM}} = -19.38$, $\beta^{\text{Non-M}} = -12.50$; Age 3: $\beta^{\text{HM}} = -91.3$, $\beta^{\text{LM}} = -126.42$, $\beta^{\text{Non-M}} = -137.79$; all $P < 0.001$) than that in PM (AL: $\beta = -4.24$; Age 3: $\beta = -27.81$; both $P < 0.001$). Gender was not generally associated with the average ChT in PM ($P = 0.377$), whereas female participants had a relatively thinner ChT than male participants in the HM, LM, and non-M groups (all $P < 0.001$).

We then analyzed the associations of ChT in different regions with age and AL. We found that the coefficients of AL in center foveal and parafoveal ChT (center foveal: $\beta^{\text{HM}} = -23.92$, $\beta^{\text{LM}} = -23.88$, $\beta^{\text{Non-M}} = -18.80$; parafoveal: $\beta^{\text{HM}} = -22.87$, $\beta^{\text{LM}} = -22.31$, $\beta^{\text{Non-M}} = -18.61$, all $P < 0.001$) were also greater than those in perifoveal regions ($\beta^{\text{HM}} = -19.80$, $\beta^{\text{LM}} = -18.29$, $\beta^{\text{Non-M}} = -13.95$, all $P < 0.001$) in HM, LM, and non-M (Supplementary Table S2). However, in PM, the coefficients of AL in center foveal ($\beta = -3.57$, $P = 0.004$), parafoveal ($\beta = -4.40$, $P < 0.001$), and perifoveal ($\beta = -4.23$, $P < 0.001$) ChT were similar. After analyzing the nine ChT regions using the ETDRS grid (Table 4), the coefficient of AL with ChT was highest in the outer-T sector ($\beta = -6.81$, $P < 0.001$) and lowest in the inner-N sector ($\beta = -3.12$, $P = 0.011$) in PM. However, in HM, the coefficient of AL with ChT was highest in the inner-T sector ($\beta = -24.27$, $P < 0.001$) and lowest in the outer-N sector ($\beta = -14.64$, $P < 0.001$). In LM, the coefficient of AL with ChT was highest in the center foveal region ($\beta = -23.88$, $P < 0.001$) and lowest

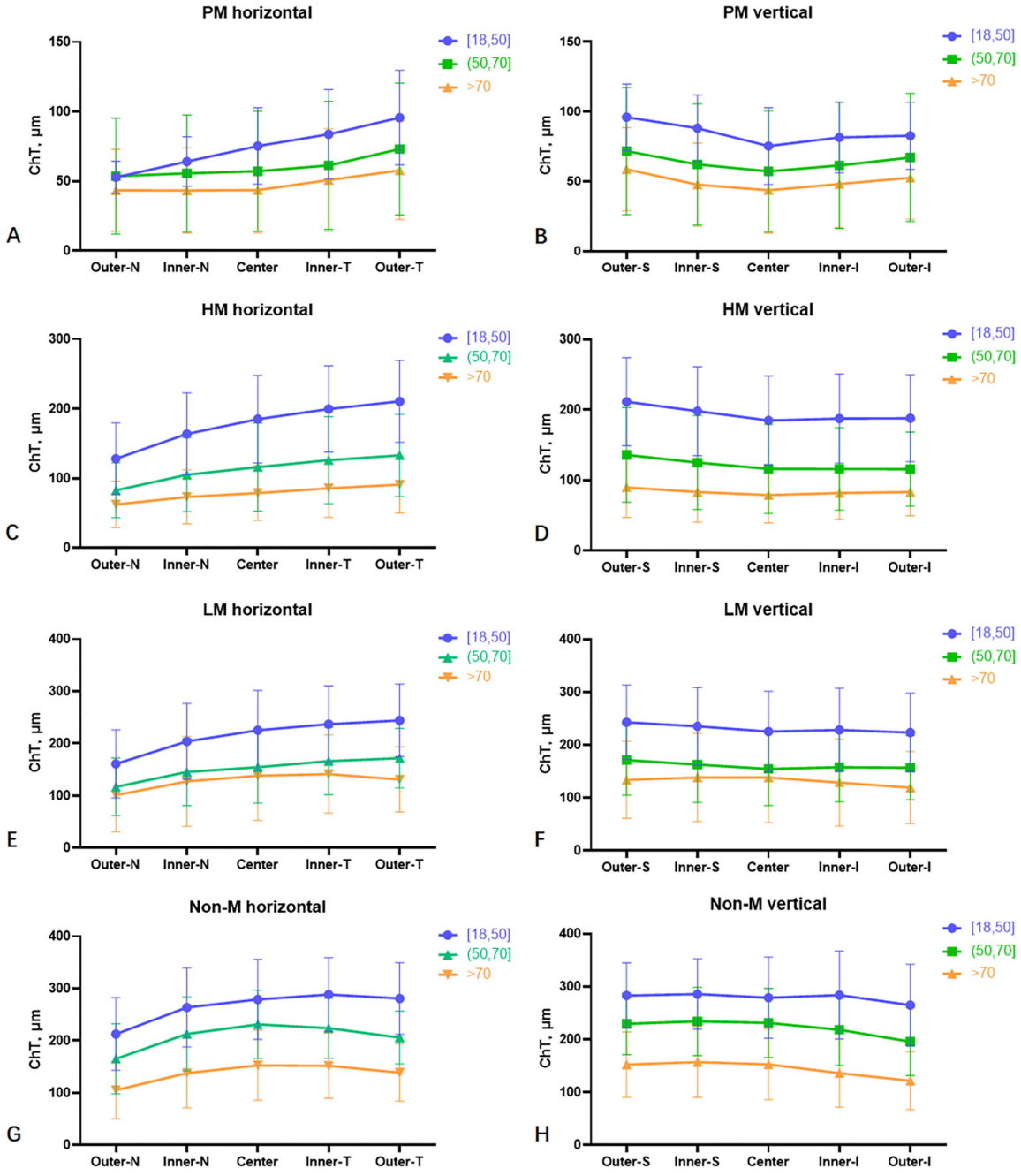

Figure 5. Graph showing the distribution of choroidal thickness for four different RE groups for each age group: PM (**A**, **B**), HM (**C**, **D**), LM (**E**, **F**), and non-M (**G**, **H**).

Table 2. Correlation Between Choroidal Thickness and Age and Axial Length

		Center Foveal ChT		Parafoveal ChT		Perifoveal ChT	
Age Group	**Parameters**	**Coefficient (95% CI)**	***P* Value**	**Coefficient (95% CI)**	***P* Value**	**Coefficient (95% CI)**	***P* Value**
Age 1	Age	0.026 (−0.48 to 0.53)	0.921	0.004 (−0.48 to 0.49)	0.988	−0.27 (−0.70 to 0.16)	0.211
	AL	−27.15 (−30.09 to −24.21)	<0.001	−26.67 (−29.44 to −23.90)	<0.001	−22.54 (−25.05 to −20.03)	<0.001
Age 2	Age	−5.56 (−6.84 to −4.28)	<0.001	−5.51 (−6.70 to −4.32)	<0.001	−4.83 (−5.84 to −3.82)	<0.001
	AL	−24.89 (−26.49 to −23.29)	<0.001	−23.36 (−24.85 to −21.87)	<0.001	−19.15 (−20.48 to −17.82)	<0.001
Age 3	Age	−1.26 (−2.47 to −0.05)	0.041	−1.28(−2.40 to −0.16)	0.025	−1.31 (−2.22 to −0.40)	0.005
	AL	−16.34 (−18.38 to −14.30)	<0.001	−14.75 (−16.67 to −12.83)	<0.001	−11.40 (−13.00 to −9.81)	<0.001

Age 1, age ≤50 years.
Age 2, age >50 to ≤70 years.
Age 3, age ≥70 years.

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Table 3. Multiple Linear Regression Model for Average Choroidal Thickness

	Total (N = 2126)			PM (n = 338)			HM (n = 662)			LM (n = 610)			Non-M (n = 516)		
Characteristic	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**
Constant	721.787	17.02	<0.001	197.162	35.885	<0.001	773.743	49.975	<0.001	763.894	62.417	<0.001	614.351	86.535	<0.001
Gender	−21.638	2.486	<0.001	−3.628	4.098	0.377	−21.85	4.099	<0.001	−23.984	5.489	<0.001	−23.529	5.277	<0.001
Axial length	−18.671	0.525	<0.001	−4.243	1.144	<0.001	−20.612	1.697	<0.001	−19.38	2.171	<0.001	−12.497	3.41	<0.001
Age 1	1.00 (reference)			1.00 (reference)			1.00 (reference)			1.00 (reference)			1.00 (reference)		
Age 2	−60.799	2.833	<0.001	−12.352	10.152	0.225	−58.068	4.868	<0.001	−59.366	6.527	<0.001	−60.892	7.997	<0.001
Age 3	−114.542	3.322	<0.001	−27.81	10.42	0.008	−91.3	6.201	<0.001	−126.415	8.106	<0.001	−137.793	8.533	<0.001
IOP	0.447	0.4	0.264	0.39	0.61	0.523	0.877	0.656	0.182	−0.22	0.874	0.801	−0.198	0.835	0.812
BMI	−0.219	0.342	0.523	0.139	0.482	0.772	−0.595	0.604	0.325	−0.527	0.708	0.457	−0.687	0.747	0.359

Age 1, age ≤50 years. Age 2, age >50 to ≤70 years. Age 3, age >70 years.

in the outer-T sector ($\beta = -15.76$, $P < 0.001$). Finally, in non-M, the coefficient of AL with ChT was highest in the inner-N sector ($\beta = -22.29$, $P < 0.001$) and lowest in the outer-S sector ($\beta = -11.78$, $P < 0.001$). Regarding the association between age and ChT, the coefficient of age was lowest in the outer-N sector in HM, LM, and non-M (Age 2: $\beta^{HM} = -38.33$, $\beta^{LM} = -39.48$, $\beta^{Non\text{-}M} = -50.49$, all $P < 0.001$; Age 3: $\beta^{HM} = -56.52$, $\beta^{LM} = -93.05$, $\beta^{Non\text{-}M} = -118.08$, all $P < 0.001$) and highest in the outer-S sector in HM and LM (Age 2: $\beta^{HM} = -66.67$, $\beta^{LM} = -66.76$, all $P < 0.001$; Age 3: $\beta^{HM} = -107.58$, $\beta^{LM} = -139.21$, all $P < 0.001$) and in the inferior sector in non-M (Age 2: $\beta^{outer\text{-}I} = -73.98$; Age 3: $\beta^{inner\text{-}I} = -159.21$, both $P < 0.001$).

Discussion

In the current study, we evaluated the association of age and AL with ChT in different macular regions among the Chinese population. To our knowledge, this is the first study to include a wide range of age (18−93 years) and REs (−25.5 to +7.75 D) to assess the associations for varied macular regions in patients with PM, HM, LM, and non-M. Age was not correlated with ChT under 50 years old. However, the ChT decreased rapidly in the 50- to 70-year age group and decreased at a slower rate after the age of 70 years. The association between AL and ChT was higher in the center foveal and parafoveal regions than in the perifoveal region in HM, LM, and non-M, indicating a more prominent ChT reduction in the center region in non-PM. Moreover, there are regional differences in the association of ChT with age and AL in each group of PM, HM, LM, and non-M by using the ETDRS grid, which indicate varied distribution patterns of ChT decrease among different refractive status.

Several clinical studies had assessed subfoveal ChT in adults without myopia (range, 242–375 µm)[8,9,11–13,16,17,19,21,23–25] and in adults with high myopia (range, 73–226 µm).[10,12,15,18,23,26] However, measurement of a few sampling points tended to be influenced by focal thickening or thinning of the choroid or, more often, by irregularity of the inner choroid−scleral border.[14] Therefore, it is more appropriate to evaluate the ChT in all sectors of the ETDRS grid and to discuss its variations with ocular parameters. The mean central foveal ChT and mean average ChT observed in our study was 164.46 ± 91.51 µm and 159.25 ± 80.75 µm, respectively, lower than those reported in previous studies (range, 203–332 µm).[14,20,22,25,27] This inconsistency may be related to the participants' higher mean age and myopia severity in our study. Previous studies have shown that ChT gradually decreases with increasing of age and the progression of myopia in adults.[8,19,24,25]

We explored different distribution patterns of ChT in PM, HM, LM, and non-M, with the thickest ChT in the central foveal region of non-M and the thinnest ChT in the central foveal region in PM. Moreover, consistent with previous studies,[25] ChT decreased at a slower rate with increasing AL in the perifoveal region compared to the parafoveal and central foveal regions in HM, LM, and non-M. The above-mentioned results indicated a more prominent decrease of ChT in the central region than that in the outer-macular region as the severity of myopia increased in eyes without PM, which was in agreement with previously reported outcomes.[9,12,13,22] This could likely be related to an irregular growth of the posterior eyeball, along with other factors, such as regional differences in the metabolic demands of the retina.[10,13,28] Several studies have demonstrated a nega-

Table 4. Multiple Linear Regression for Nine Regions of Choroidal Thickness by Using the ETDRS Grid in Each Refractive Status Group

	PM (n = 338)			HM (n = 662)			LM (n = 610)			Non-M (n = 516)		
Characteristic	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**	β	**Standard Error**	***P* Value**
Center foveal												
AL	−3.568	1.219	0.004	−23.921	1.958	<0.001	−23.878	2.54	<0.001	−17.795	4.1	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−14.711	10.839	0.176	−56.994	5.618	<0.001	−64.214	7.634	<0.001	−49.93	9.613	<0.001
Age 3	−29.755	11.12	0.008	−91.328	7.157	<0.001	−125.481	9.481	<0.001	−137.087	10.258	<0.001
Gender	−7.126	4.366	0.104	−24.615	4.731	<0.001	−28.874	6.42	<0.001	−23.663	6.344	<0.001
IOP	0.778	0.651	0.233	1.162	0.757	0.125	−0.246	1.022	0.81	−0.206	1.004	0.837
BMI	−0.005	0.514	0.993	−0.707	0.697	0.311	−0.684	0.828	0.409	−0.323	0.898	0.719
Inner-T												
AL	−5.736	1.339	<0.001	−24.272	1.923	<0.001	−21.636	2.406	<0.001	−16.471	3.737	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−16.347	11.908	0.171	−61.628	5.518	<0.001	−63.924	7.234	<0.001	−66.451	8.764	<0.001
Age 3	−29.941	12.216	0.015	−98.435	7.029	<0.001	−129.468	8.984	<0.001	−146.151	9.351	<0.001
Gender	−7.234	4.796	0.132	−23.763	4.646	<0.001	−27.812	6.083	<0.001	−19.308	5.783	0.001
IOP	0.205	0.715	0.775	1.06	0.744	0.155	−0.126	0.969	0.897	−0.423	0.915	0.644
BMI	0.207	0.565	0.714	−0.912	0.684	0.183	−0.959	0.784	0.222	−0.515	0.819	0.529
Inner-S												
AL	−5.197	1.184	<0.001	−24.204	1.992	<0.001	−21.309	2.547	<0.001	−16.118	4.007	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−21.062	10.531	0.046	−61.558	5.717	<0.001	−66.458	7.658	<0.001	−55.198	9.396	<0.001
Age 3	−37.435	10.804	0.001	−100.42	7.282	<0.001	−131.266	9.51	<0.001	−139.712	10.026	<0.001
Gender	−5.178	4.242	0.223	−23.475	4.813	<0.001	−24.002	6.439	<0.001	−24.552	6.201	<0.001
IOP	1.051	0.633	0.097	0.896	0.771	0.246	−0.368	1.025	0.72	−0.081	0.981	0.934
BMI	0.161	0.5	0.748	−0.459	0.709	0.518	−0.453	0.83	0.585	−0.585	0.878	0.506
Inner-N												
AL	−3.109	1.215	0.011	−20.367	1.827	<0.001	−22.609	2.481	<0.001	−22.288	4.17	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−5.423	10.8	0.616	−49.437	5.243	<0.001	−53.046	7.458	<0.001	−56.286	9.778	<0.001
Age 3	−19.402	11.079	0.081	−79.006	6.679	<0.001	−114.459	9.262	<0.001	−140.966	10.434	<0.001
Gender	−6.656	4.35	0.127	−19.009	4.415	<0.001	−25.214	6.271	<0.001	−30.353	6.453	<0.001
IOP	0.603	0.649	0.353	0.768	0.707	0.278	−0.37	0.999	0.711	0.04	1.021	0.969
BMI	0.122	0.512	0.811	−0.243	0.65	0.708	−0.407	0.809	0.615	−0.456	0.913	0.618
Inner-I												
AL	−3.642	1.262	0.004	−22.637	1.937	<0.001	−23.689	2.569	<0.001	−19.563	4.136	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−16.789	11.219	0.135	−61.216	5.558	<0.001	−63.887	7.723	<0.001	−68.298	9.699	<0.001
Age 3	−30.922	11.51	0.008	−92.962	7.08	<0.001	−137.652	9.591	<0.001	−159.21	10.35	<0.001
Gender	−2.757	4.519	0.542	−24.052	4.68	<0.001	−29.965	6.494	<0.001	−27.749	6.401	<0.001
IOP	0.525	0.674	0.436	1.387	0.749	0.065	−0.15	1.034	0.885	−0.007	1.013	0.994
BMI	−0.132	0.532	0.805	−0.402	0.689	0.56	−0.667	0.837	0.426	−0.104	0.906	0.908
Outer-T												
AL	−6.81	1.349	<0.001	−22.552	1.822	<0.001	−15.759	2.24	<0.001	−12.724	3.383	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−15.345	11.994	0.202	−64.509	5.227	<0.001	−66.171	6.733	<0.001	−70.324	7.934	<0.001
Age 3	−33.823	12.305	0.006	−105.241	6.659	<0.001	−135.812	8.362	<0.001	−147.721	8.466	<0.001
Gender	−2.946	4.831	0.542	−23.968	4.401	<0.001	−24.29	5.662	<0.001	−15.72	5.236	0.003
IOP	−0.031	0.72	0.966	1.125	0.705	0.111	0.012	0.902	0.989	−0.618	0.828	0.456
BMI	0.097	0.569	0.865	−1.048	0.648	0.106	−1.154	0.73	0.114	−1.242	0.741	0.095
Outer-S												
AL	−5.407	1.234	<0.001	−22.319	2.008	<0.001	−17.856	2.385	<0.001	−11.779	3.691	0.002
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−19.167	10.974	0.082	−66.674	5.76	<0.001	−66.756	7.169	<0.001	−54.77	8.655	<0.001
Age 3	−33.599	11.258	0.003	−107.575	7.338	<0.001	−139.207	8.903	<0.001	−137.856	9.235	<0.001
Gender	−3.166	4.42	0.474	−25.249	4.85	<0.001	−21.537	6.028	<0.001	−24.693	5.712	<0.001
IOP	1.082	0.659	0.102	0.659	0.776	0.397	−0.744	0.96	0.438	−0.39	0.904	0.666
BMI	−0.091	0.521	0.861	−0.69	0.714	0.335	−0.094	0.777	0.903	−1.667	0.809	0.054
Outer-N												
AL	−0.417	1.212	0.731	−14.637	1.585	<0.001	−19.726	2.166	<0.001	−16.101	3.789	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	0.459	10.778	0.966	−38.332	4.548	<0.001	−39.479	6.511	<0.001	−50.488	8.886	<0.001
Age 3	−9.602	11.057	0.386	−56.517	5.794	<0.001	−93.048	8.086	<0.001	−118.075	9.481	<0.001
Gender	−2.417	4.341	0.578	−14.426	3.83	<0.001	−21.243	5.475	<0.001	−26.681	5.864	<0.001
IOP	0.152	0.647	0.815	0.185	0.613	0.763	−0.125	0.872	0.886	0.079	0.928	0.932
BMI	0.338	0.511	0.51	−0.361	0.564	0.522	−0.065	0.706	0.927	−0.392	0.83	0.637
Outer-I												
AL	−4.35	1.249	0.001	−19.67	1.877	<0.001	−19.835	2.395	<0.001	−15.19	3.806	<0.001
Age 1		1.00 (reference)			1.00 (reference)			1.0 (reference)			1.00 (reference)	
Age 2	−11.631	11.106	0.296	−63.196	5.385	<0.001	−60.701	7.199	<0.001	−73.977	8.926	<0.001
Age 3	−27.675	11.394	0.016	−93.784	6.86	<0.001	−135.129	8.941	<0.001	−151.596	9.524	<0.001
Gender	−1.579	4.473	0.724	−23.005	4.534	<0.001	−24.37	6.054	<0.001	−24.776	5.891	<0.001
IOP	0.03	0.667	0.965	1.401	0.726	0.066	0.048	0.964	0.961	0.098	0.932	0.916
BMI	0.043	0.527	0.934	−0.302	0.668	0.652	−0.584	0.781	0.455	−0.436	0.834	0.602

Age 1, age ≤50 years. Age 2, age >50 to ≤70 years. Age 3, age >70 years.

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Table 5. Correlation Between Choroidal Thickness With Various Ocular and Demographic Factors

Study	No. of Eyes	OCT Device	Ethnicity	Subjects' Type	Age, Mean ± SD (Range), y	Mean RE, D	AL, Mean ± SD, mm	ChT, Mean ± SD, µm	Change of Variable per Year of Age	Change of Variable per mm of AL	Change of Variable per D of RE
Central ChT											
Ouyang et al.[20]	55	HD-OCT SD-OCT	Mixed	Not special to RE	32.85 ± 11.45 (20–68)	−0.5	23.83 ± 1.33	297.8 ± 82.2	−1.95	−31.96	
Tan and Cheong[25]	300	SD-OCT	Chinese	Not special to RE	23 ± 1.9 (21–33)	−4.0 ± 1.9	25.4 ± 1.4	324.9 ± 94.3	−3.01*	−36.1	20
Total ChT											
Ouyang et al.[20]	55	HD-OCT SD-OCT	Mixed	Not special to RE	32.85 ± 11.45 (20–68)	−0.5	23.83 ± 1.33	297.8 ± 82.2	−1.85	−28.44	
Hirata et al.[14]	31	SS-OCT	Japanese	Not special to RE	64.6 ± 17.3 (21–87)	−1.67 ± 5.1	24.6 ± 2.1	191.5 ± 74.2	−3.04	−24.95	
Wang et al.[27]	146	SS-OCT	Chinese	RE between ±6 D	47.9 ± 14 (20–86)		23.5 ± 1.1	264.1 ± 105.9	−2.29	−42.81	
Subfoveal ChT											
Li et al.[17]	93	SD-OCT	Danish	Not special to RE	24.9 ± 2.6 (19.6–33.4)	−1.43 ± 2.9	24	342 ± 118		−58.2	−25.4
Wei et al.[24]	3233	SD-OCT	Chinese	Not special to RE	64.3 ± 9.6 (50–93)	−0.18 ± 1.98	23.2	253.8 ± 107.4	−4.12	−44.7	15* (<−1 D)
Tan and Cheong[25]	300	SD-OCT	Chinese	Not special to RE	23 ± 1.9 (21–33)	−4.0 ± 1.9	25.4 ± 1.4	324.9 ± 94.3	−2.94*	−37	20.1
Gupta et al.[13]	540	SD-OCT	Singaporean malay	Not special to RE	62.7 ± 8.91 (45–85)	0.11 ± 1.74	23.59 ± 0.96	242.28 ± 97.58	−4.14	−32.11	10.77
Gupta et al.[12]	648	SD-OCT	Singaporean malay	HM: RE lower than −6 D EM: RE <0.5 D	HM: 21.59 ± 1.15 EM: 22.06 ± 0.97	HM: −8.68 ± 2.05 EM: 0.12 ± 0.24	HM: 27.32 ± 1.16 EM: 23.69 ± 0.62	EM:375.15 ± 6.58 HM: 225.87 ± 5.51		−24.23	13.11*
Margolis and Spaide[19]	54	SD-OCT		RE between ±6 D	50.4 (19–85)	−1.3 ± 2.1		287 ± 76	−1.56*		
Ikuno et al.[16]	86	HP-OCT	Japanese	RE lower than −6 D	39.4 ± 16 (23–88)	−1.9 ± 2.3	24.4 ± 1.24	354 ± 111	−4.32	NS	29.13
Ding et al.[8]	420	SD-OCT	Chinese	RE between ±6 D	49.73 ± 17.89 (20–85)	−0.87 ± 1.98		261.93 ± 88.42	−5.4 (>60 y)		10.87 (<60 y)
Fujiwara et al.[10]	55	SD-OCT		RE more than −6 D	59.7 ± 17.6 (24–90)	−11.9 ± 3.7		93.2 ± 62.5	−1.25		7.84
Flores-Moreno et al.[9]	120	3D-2000 OCT		RE more than −6 D or AL ≥26 mm	54.4 ± 18.2 (18–99)	−14.3 ± 5.4	29.17 ± 2.44	115.5 ± 85.3	−1.8	−25.17	9.39*
Ho et al.[15]	108	SD-OCT		RE more than −6 D	50.4 ± 2.03 (42–62)	−8.7		118 ± 68	−3.03		9.98
Wang et al.[23]	466	SD-OCT	Chinese	HM: RE more than −6 D EM: RE between ±3 D	HM: 22.23 ± 6.5 Normal: 23.36 ± 7.4	HM: −7.56 ± 1.99 Normal: −0.74 ± 1.47	26.56 ± 1.01 23.71 ± 0.89	HM: 200.54 ± 69.39 Normal:276.21 ± 64.67	NS	Total: −21.93 HM: −30.87	Total: 3.36
Liu et al.[18]	312	SD-OCT		RE more than −6 D	47.47 ± 14.11 (18–88)	−14.58 ± 5.52	29.45 ± 2.31	83.77 ± 54.64	−1.42	−16.8	−5.63
Fang et al.[26]	1487	SS-OCT		RE more than −8 D or AL ≥26.5 mm	58.4 ± 16.3 (3–91)	−13.2 ± 4.0	29.9 ± 2.0	72.7 ± 55.1	−1.75	−9.88	

EM, emmetropia; HD-OCT, high-definition optical coherence tomography; SD-OCT, spectral-domain optical coherence tomography; NS, not significant.
* Univariate values.

tive correlation between age and ChT,[9,10,15,18,19,26] while a number of studies did not find such correlation.[16,20,25] In the present study, ChT was not correlated with age under 50 years. However, a rapid decrease in the ChT was noted between 50 and 70 years. The decrease in ChT slowed down after the age of 70 years. The discrepancy may be caused by a relatively small study scale in previous studies,[10,19] selection bias from a particular group (e.g., high myopia or pathologic myopia),[18,26] and different scanning protocols and methods for measuring ChT.[9,15] Our findings align with the study of Ding et al.[8] and Wei et al.,[24] whereby age was a factor associated with subfoveal ChT in patients older than 60 years and older than 50 years, respectively. Furthermore, AL and age were more strongly correlated with ChT in non-PM eyes compared with PM eyes. This may be related to the fact that ChT was already extremely thin in PM eyes and could not decrease further with age and elongation of AL. Additionally, the formation of PM is very complicated, and other factors, such as rupture of the Bruch's membrane,[34,35] staphyloma,[36] and some molecular changes,[6,37] could be simultaneously involved in the development mechanism of PM and thinning of the choroid. Multivariate regression also showed that females tended to have a relatively thinner choroid when compared with males without PM, as also shown in previous studies.[11,17,24,27] This variation could be due to the larger eye size in men and hormonal differences.[27] As shown in previous studies, higher estrogen levels and the use of hormone replacement therapy in women could influence ocular blood flow and may further affect the ChT.[38,39] Similarly, due to the complexity of PM formation, other factors may have a stronger association with ChT rather than gender itself. Therefore, further studies are recommended to evaluate the effect of hormone levels and the distribution of estrogen receptors in the choroid on ChT.

Several previous studies identified AL and age as the two most critical factors associated with ChT. The variations of subfoveal ChT change ranged from –9.88 to –58.2 µm per millimeter of AL and from −1.25 to −5.4 µm per year[8–12,15–19,23–26] (Table 5). However, only one study[25] analyzed the locational differences of ChT changes with AL and RE. Therefore, to our knowledge, this is the first study to describe the association of ChT in different macular regions with age and AL under different refractive groups. Our results showed different distribution patterns of ChT decrease in the macular region among PM, HM, LM, and non-M. The association between AL and ChT may indicate a pathologic process in myopia progression. At the same time, the association between age and ChT may suggest a physiologic process under certain refractive status. The different patterns of ChT decrease among the four refractive groups could be attributed to either nonuniformed mechanical forces caused by the eye elongation or the difference in anatomic characteristics of varied macular regions. It has been hypothesized that the concentration of unevenly distributed nonvascular smooth muscle cells in the choroid may influence the extent of ChT decrease.[28,40] Future studies investigating the differences in the mechanical force and distribution density of cells or receptors in varied regions of the choroid under different refractive errors and age may help to clarify the physiologic mechanism.

This study is not without limitations. First, as this is a cross-sectional study, the causation of the association and the exact growth rate of ChT among different groups could not be determined. The RE might be confused with the development of nuclear cataracts, resulting in a further myopic shift. However, the introduction of this bias was reduced by excluding patients with advanced cataracts. Another potential limitation is that we did not perform cycloplegia refraction in our study, and this may have led to the overestimation of the LM and HM group. However, some studies demonstrated that the difference in RE with and without cycloplegia was small among adults.[41,42] Additionally, the presence and type of the staphyloma were not investigated in the current study due to the lack of wide-field SS-OCT.[36] Finally, we did not consider the role of peripapillary ChT in the progression of myopia.[20,43,44] Hence, further research on ChT in both macular and peripapillary areas is recommended to overcome the shortcomings mentioned above and confirm our findings.

In conclusion, we demonstrated that ChT was not correlated with age under 50 years, but it had an accelerated decline in the 50- to 70-year age group and decreased at a slower rate after age 70 years. A more prominent reduction of ChT in the center foveal and parafoveal regions compared to that in the perifoveal region was found as AL increased in patients without PM. Moreover, regional differences in the association between ChT with age and AL were noted in PM, HM, LM, and non-M by using the ETDRS grid, indicating varied distribution patterns of ChT decrease associated with age and AL under different refractive statuses.

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