Impact of the Morphologic Characteristics of Optic Disc on Choroidal Thickness in Young Myopic Patients

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Submitted: December 8, 2018
Accepted: June 5, 2019

Citation: Chen Q, He J, Yin Y, et al. Impact of the morphologic characteristics of optic disc on choroidal thickness in young myopic patients. *Invest Ophthalmol Vis Sci*. 2019;60:2958–2967. https://doi.org/10.1167/iovs.18-26393

Purpose. To explore the characteristics of tilted optic disc and peripapillary atrophy (PPA), and their associations with choroidal thickness (ChT) in young myopic patients.

Methods. A total of 821 patients were enrolled in this cross-sectional study. Optic disc tilt ratio, PPA area, macular ChT (mChT), and peripapillary ChT (pChT) were measured. Subjects were divided into four groups purely on the basis of the axial length (AL). Relationships between ChT and the morphologic characteristics of optic disc were analyzed using logistic regression.

Results. The prevalence of tilted optic disc and PPA increased as myopia severity increased. Every 0.1-mm^2 increase in PPA area was associated with a 14.93-µm decrease in mChT and a 9.54-µm decrease in pChT; and every 0.1 increase in tilt ratio was correlated with a 5.38-µm increase in mChT and a 6.21 decrease in pChT. After stratifying by myopia severity, these trends were still observed in the high myopia group. A larger PPA area (odds ratio [OR] = 2.33; $P < 0.01$), a longer AL (OR = 1.34; $P < 0.01$), an increased pChT (OR = 1.11; $P < 0.01$), and a decreased mChT (OR = 0.93; $P < 0.01$) were associated with higher odds of having tilted optic disc.

Conclusions. In young myopic patients, mChT was negatively associated with PPA area and positively associated with tilt ratio, while pChT was negatively associated with PPA area and tilt ratio. In this population, larger PPA area, longer AL, and thinner mChT were associated with higher odds of tilted optic disc.

Keywords: tilted optic disc, PPA area, choroidal thickness, young highly myopia

Myopia is one of the major causes of correctable visual impairment, even in children, adolescents, and younger adults around the world.[1] Five billion and 1 billion people are estimated to be affected by myopia and high myopia, respectively, by 2050.[2] The continuously increasing prevalence of myopia as well as high myopia, especially in Asian populations,[3–5] highlights the importance of taking action to prevent the progression of myopia and the ocular complications and vision loss that may result from high myopia.

A tilted optic disc, which is characterized by the oblique insertion of the optic nerve into the globe,[6] is a relatively common condition in myopic eyes. Previous studies have reported that the degree of optic disc tilt is strongly associated with severe myopia and longer axial length (AL).[7–10] A tilted optic disc is also associated with reduced sensitivity on visual field tests and may lead to severe macular complications.[11] Some authors have reported the progression of optic disc tilt and formation of optic nerve crescents (peripapillary atrophy, PPA) over time in some patients with mild myopia.[12,13] In such cases, optic disc tilt and PPA were observed initially, followed by the formation of posterior staphyloma and lacquer cracks; ultimately, the authors observed the onset of chorioretinal atrophy.[12–14]

To date, most published studies have focused on glaucomatous features and have reported associations between macular and peripapillary retinal nerve fiber layer (RNFL) thickness profiles and tilted optic discs in myopic eyes.[15–18] However, the impact of tilted optic discs on choroidal thickness (ChT) in these patients remains unclear. Previous studies also reported reduced ChT in subjects with high myopia, and reduced macular ChT (mChT) is associated with myopic chorioretinal features,[19–21] including myopic macular degeneration and myopic choroidal neovascularization, either of which may result in severe visual impairment. In a cohort aged from 14 to 65 years, subfoveal choroidal thickness correlated positively and significantly with visual acuity and negatively with axial elongation, but the visual prognosis was benign.[22] The thinning of the choroid is noted early in myopic progression, and increases in AL and choroidal thinning are associated independently with myopic shift.[23] A study that evaluated the progression pattern of disc and retinal lesions in highly myopic adolescents found that progressive worsening of myopia and early-onset fundus tessellation were associated with thinner choroid.[24] Therefore, it is important to explore the associations between tilted optic discs and ChT in young myopic patients.

The purpose of the present study was to evaluate the associations between tilted optic discs, PPA area, and these parameters in different degrees of myopia among young myopic patients.

Methods

Setting and Participants

The protocol for this cross-sectional study was approved by the Ethics Committee of Shanghai General Hospital, Shanghai Jiao Tong University, Shanghai, China, and followed the tenets of the Declaration of Helsinki. All participants understood the study protocol and provided signed informed consent.

The study subjects were students attending Shanghai University in October 2016 who volunteered to participate after reading our description of the study and an open invitation to become a participant. Each students' systolic (SBP) and diastolic (DBP) blood pressure was measured. The mean arterial pressure (MAP) was calculated using the following formula: (SBP + 2 × DBP) / 3. A detailed medical history was recorded for each student. All participants underwent comprehensive ophthalmic examinations, including refractive error assessment using an autorefractor instrument (model KR-8900; Topcon, Tokyo, Japan), measurement of best-corrected visual acuity (BCVA) and IOP (Full Auto Tonometer TX-F; Topcon), slit-lamp biomicroscopy, color fundus examination, and measurement of the thickness of choroid, retina, and nerve fiber layer using swept-source optical coherence tomography (SS-OCT; model DRI OCT-1 Atlantis; Topcon). The central corneal thickness (CCT), lens thickness (LT), anterior chamber depth (ACD), and AL were measured using optical low-coherence reflectometry (Lenstar; Haag-Streit AG, Koeniz, Switzerland). Subjective refraction was performed for all subjects by a trained optometrist. The spherical equivalent refraction (SER) was calculated as the sphere plus half a cylinder. BCVA was converted into logMAR.

The inclusion criteria were as follows: age between 16 and 40 years; SER less than 0.5 D; IOP 21 mm Hg or less; normal anterior chamber angles; normal optic nerve head without glaucomatous changes, such as neuroretinal rim narrowing and peripapillary hemorrhage; and no RNFL abnormalities. Subjects older than 40 years were excluded from the study, as the incidence of glaucoma is associated with age, and the lenticular changes might affect the myopic refractive error. Participants with a history of ocular or systemic diseases, including congenital cataract and glaucoma, hypertension, and diabetes, previous intraocular or refractive surgery, and other evidence of retinal pathology, were also excluded. In general, except for the optic disc and peripapillary changes associated with myopia, each patient had no other ocular abnormalities. Only the right eye of each patient was selected for statistical analyses.

SS-OCT Imaging

The average thicknesses of macular retinal and choroidal layers, as well as peripapillary RNFL and choroidal layers, were measured using SS-OCT, which had a lateral resolution of 10 μm and a depth resolution of 8 μm. The machine also provided a fast scanning speed of 100,000 A-scans per second with a 1050-nm wavelength light source. Before OCT image collection, spherical power diopter, cylindrical power diopter, cornea curvature radius, and AL were input into the system to adjust the magnification factors associated with AL. The scan protocol used the 12-line radial scan pattern with a resolution of 1024 × 12 centered on the fovea and optic disc. The segmentation of each layer was automatically obtained with the built-in software, and manual segmentation was performed when the software misjudged the borderline of each layer.

The tomography maps were overlapped to an Early Treatment Diabetic Retinopathy Study (ETDRS) grid (6 × 6 mm) that was focused on the macular or optic disc. Thus, each scan was divided into three concentric circles with nine regions as follows: the central circle with 1-mm diameter, inner circle with 3-mm diameter, and outer circle with 6-mm diameter. The average thickness in each region of the grid was automatically acquired by built-in software. In the macular area, the thickness was an average from the nine regions of the ETDRS grid. While in the optic disc area, only four regions of the outer circle were used to analyze the average thickness, because there was no choroidal tissue in the central and inner circle, and the topographic maps were not reliable in these regions.[25] The circle placement was manually adjusted if necessary.

All measurements were conducted by a single technician who was experienced in taking OCT images. Images with signal strength index 60 or less were excluded for statistical analysis. The SS-OCT was performed twice for the first 30 participants to assess measurement reproducibility.

Tilt Ratio and Peripapillary Atrophy Area Measurements

Retinal photographs centered on the macular and optic disc were acquired from the same SS-OCT, which was fitted with a digital, nonmydriatic retinal camera. The optic disc tilt and the PPA area were calculated from these photographs using ImageJ version 1.60 software (http://imagej.nih.gov/ij/; provided in the public domain by the National Institutes of Health, Bethesda, MD, USA). The averaged data were used for the final analysis.

The definition of optic disc tilt was considered as the tilt ratio of the minimum-to-maximum disc diameter, and a tilted optic disc had a tilt ratio 0.80 or less, as described previously.[7,26] The PPA area was measured carefully by two independent, experienced observers who were masked to the other ocular characteristics of the participants, as described previously.[27] In order to determine the intraobserver repeatability, the measurements were performed twice in the first 20 images by the same examiner (QYC). Another examiner (YY) independently repeated the measurements in the same 20 images to determine the interobserver repeatability. The results revealed that the intraobserver (intraclass correlation coefficient [ICC] 0.994; 0.985–0.998) and interobserver (ICC 0.988; 0.971–0.995) reproducibility was good to excellent for all measurements.

Briefly, the PPA area (an inner crescent of chorioretinal atrophy with good visibility of the large choroidal vessels and the sclera) was determined as the total number of pixels using ImageJ software in a circumferential pattern (Fig. 1). The magnification by the fundus camera was 1.4×, and the total magnification was calculated after taking into account the magnification factor of the ImageJ platform. The area of PPA was converted from pixels into square millimeters. The magnification was corrected for each AL by applying Littmann's formula.[28]

All participants were divided into four groups by the length of ocular axis as follows: the AL1 group had an AL 24 mm or less, the AL2 group had an AL between 24 and 25 mm, the AL3

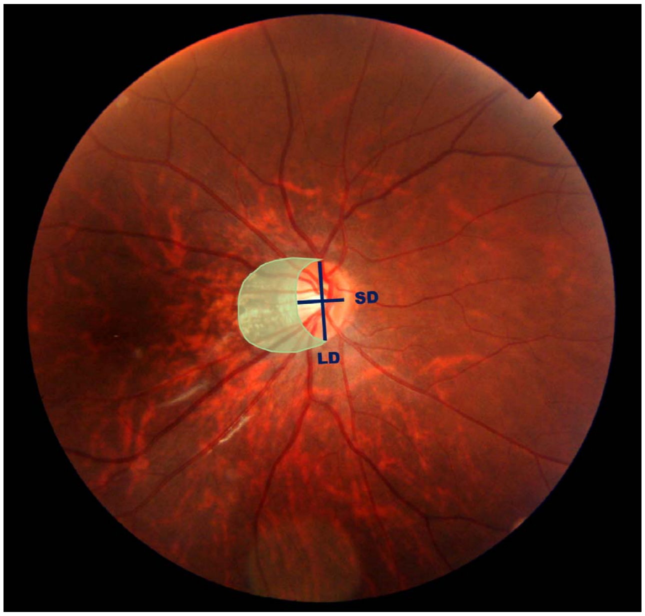

FIGURE 1. Measurement of tilt ratio and area of peripapillary atrophy by ImageJ software. The *dark blue lines* indicate the shortest diameter (SD) and the longest diameter (LD) of the optic disc. The tilt ratio was defined as the ratio between the SD and the LD. The area of peripapillary atrophy was outlined manually (*green shade area*) and the pixel area was calculated automatically using the software.

group had an AL between 25 and 26 mm, and the AL4 group had an AL 26 mm or more. Each group was further subdivided into subjects with and without tilted optic discs.

Statistical Analyses

SAS (version 8.0; SAS Institute, Cary, NC, USA) was used for all statistical analyses. All data were double entered independently by two research associates and all discrepancies were adjudicated. Baseline characteristics were shown as counts or proportions for categoric data and as means ± standard deviation for continuous data. The distribution of all variables was examined for normality using the Kolmogorov-Smirnov test. One-way ANOVA and the X^2 test were used to compare differences among the four groups, and the Bonferroni method was used for post hoc tests. The Student's *t*-test and X^2 test were performed to detect differences in biometry parameters as well as each layer's thickness between the subjects with and without tilted optic discs in the four groups, as appropriate. Partial correlation analysis was used to investigate the relationship between pChT or mChT and ocular parameters adjusted for sex. Multivariate linear regression analyses adjusted for age and sex were performed to determine the effects of tilted optic disc, PPA, and AL on pChT and mChT. Multivariate logistic regression models were constructed with a tilted optic disc as the independent variable to assess associations with ocular parameters. Statistical significance was set as $P < 0.05$ (two-sided).

RESULTS

General Characteristics

Among the 914 students enrolled in the study, 12 were excluded because of an IOP higher than 21 mm Hg, 47 for SER 0.5 or more diopters (D), 6 for losing fundus examinations, and another 28 owing to poor SS-OCT images. Finally, the data of 821 (89.8%) students were included in the analysis. The thickness measurements with SS-OCT were highly reproducible in each layer, with a test–retest correlation coefficient of 0.97 to 0.99 ($n = 30$).

Among the 821 participants, 108 belonged to the AL1 group (13.2%), 227 belonged to the AL2 group (27.7%), 264 belonged to the AL3 group (32.2%), and 222 belonged to the AL4 group (27.0%). Additionally, 465 had tilted optic discs (56.6%), whereas 356 did not have tilted optic discs (43.4%). The AL4 group had significantly higher frequency of tilted optic discs and PPA compared with the other three groups (Table 1). This is further illustrated in the results in Figure 2, which were stratified by myopia severity; they show the relative proportions of participants with tilted optic discs and PPA.

The baseline characteristics of the subjects with and without tilted optic discs in different myopia groups are presented in Table 2. In all four groups, more females had tilted optic discs than males. In the AL4 group, AL was longer in subjects with tilted optic discs than in those without tilted optic discs, whereas in the other three groups, AL was similar between the groups. Compared with subjects without tilted optic discs, those with tilted optic discs had a larger PPA area (all $P < 0.01$) in all four groups. The mReT ($P = 0.03$, $P < 0.01$, respectively) and the mChT (both $P < 0.01$) were significantly thinner in subjects with tilted optic discs than in those without tilted optic discs in the AL3 and AL4 groups. No significant differences were observed between subjects with and without tilted optic discs in the pRNFLT and pChT in all four groups.

Correlations Between the Morphologic Characteristics of Optic Disc and mChT

Partial correlation coefficients between mChT and ocular parameters after adjusting for sex are summarized in Table 3. The mChT was negatively associated with PPA area ($r = -0.44$, $P < 0.01$), followed by AL ($r = -0.42$, $P < 0.01$) and BCVA ($r = -0.15$, $P < 0.01$), and it was positively associated with SER ($r = 0.36$, $P < 0.01$) and tilt ratio ($r = 0.31$, $P < 0.01$).

Further, we constructed a multivariate linear regression model to explore the independent factors associated with mChT. The multivariate model showed that sex, AL, tilt ratio, and PPA area were independently associated with mChT ($P = 0.01$, $P < 0.01$, $P = 0.03$, and $P < 0.01$, respectively). According to the model, every 1-mm increase in AL was associated with a 15.42-µm decrease in mChT; every 0.1-mm^2 increase in PPA area was associated with a 14.93-µm decrease in mChT (Fig. 3C); and every 0.1 increase in tilt ratio was associated with a 5.38-µm increase in mChT (Fig. 3A). The combination of these factors yielded an adjusted R^2 of 0.279 (Table 4).

After stratifying by myopia severity, the multiple regression model showed that the PPA area correlated negatively with mChT in all four groups (Fig. 3D), whereas the tilt ratio correlated positively with mChT only in the AL4 group (Fig. 3B). AL was also shown to be negatively associated with mChT in the AL1, AL2, and AL4 groups. The overall R^2 values derived from the multiple regression model for mChT were 0.133, 0.112, 0.162, and 0.272 in the AL1, AL2, AL3, and AL4 groups, respectively (Table 4).

Correlations Between the Morphologic Characteristics of Optic Disc and pChT

Partial correlation coefficients between pChT and ocular parameters after adjusting for sex are shown in Table 3. Similar to mChT, the pChT was also negatively associated with AL ($r = -0.33$, $P < 0.01$), followed by PPA area ($r = -0.29$, $P < 0.01$) and BCVA ($r = -0.11$, $P = 0.02$), and it was positively associated with SER ($r = 0.26$, $P < 0.01$) and tilt ratio ($r = 0.08$, $P = 0.02$).

Table 1. Demographic and Ocular Characteristics of Study Population

Variable	Total (*n* = 821)	AL1 (*n* = 108)	AL2 (*n* = 227)	AL3 (*n* = 264)	AL4 (*n* = 222)	*P* Value	Post Hoc‡
Age, y	19.83 ± 2.618	19.94 ± 2.51	19.74 ± 2.85	19.65 ± 2.36	20.08 ± 2.72	0.29†	/
Sex, frequency of female (%)	451 (54.9)	74 (68.5)	142 (62.6)	140 (53.0)	95 (42.8)	**<0.01‡**	AL1/AL2>AL3>AL4
MAP, mm Hg	88.49 ± 11.16	89.44 ± 11.43	87.33 ± 12.00	88.19 ± 10.85	89.58 ± 10.40	0.14†	/
SER, D	−4.24 ± 2.45	−1.79 ± 1.43	−2.96 ± 1.75	−4.60 ± 1.75	−6.31 ± 2.32	**<0.01†**	AL1>AL2>AL3>AL4
BCVA, logMAR	0.03 ± 0.07	0.01 ± 0.03	0.02±0.04	0.03 ± 0.08	0.04 ± 0.09	**<0.01†**	AL1<AL3/AL4; AL2<AL4
IOP, mm Hg	14.01 ± 2.79	14.09 ± 2.82	14.03 ± 2.82	13.94 ± 2.78	14.01 ± 2.76	0.97*	/
ACD, mm	3.72 ± 0.24	3.58 ± 0.25	3.66 ± 0.22	3.75 ± 0.20	3.81 ± 0.24	**<0.01†**	AL1<AL2<AL3<AL4
CCT, μm	536 ± 35	540 ± 37	538 ± 36	536 ± 34	532 ± 37	0.20†	/
LT, mm	3.51 ± 0.21	3.56 ± 0.24	3.53 ± 0.24	3.50 ± 0.19	3.49 ± 0.20	**<0.01†**	AL1>AL3/AL4; AL2>AL4
AL, mm	25.29 ± 1.13	23.53 ± 0.42	24.56 ± 0.28	25.46 ± 0.27	26.70 ± 0.64	**<0.01†**	AL1<AL2<AL3<AL4
Number (%) with tilted optic disc	465 (56.6)	40 (37.0)	116 (51.1)	152 (57.6)	157 (70.7)	**<0.01‡**	AL1<AL2<AL3<AL4
Tilt ratio	0.79 ± 0.09	0.83 ± 0.08	0.79 ± 0.09	0.78 ± 0.09	0.77 ± 0.08	**<0.01†**	AL1>AL2>AL3>AL4
Number (%) with PPA	656 (79.9)	67 (62.0)	165 (72.7)	222 (84.1)	202 (91.0)	**<0.01‡**	AL1/AL2<AL3<AL4
PPA area, mm^2	0.16 ± 0.12	0.10 ± 0.09	0.14 ± 0.11	0.16 ± 0.11	0.21 ± 0.12	**<0.01†**	AL1<AL2<AL3<AL4
pRNFLT, μm	89.52 ± 8.23	88.23 ± 8.53	88.57 ± 7.97	89.49 ± 7.24	91.17 ± 9.16	**<0.01†**	AL1/AL2/AL3<AL4
pChT, μm	147.99 ± 44.31	167.90 ± 47.59	155.78 ± 43.75	147.47 ± 42.81	130.97 ± 38.78	**<0.01†**	AL1>AL2>AL3>AL4
mReT, μm	276.69 ± 12.12	281.25 ± 12.65	277.82 ± 11.80	275.87 ± 11.11	274.30 ± 12.65	**<0.01†**	AL1>AL2>AL4; AL1>AL3
mChT, μm	215.62 ± 59.31	249.45 ± 57.73	231.29 ± 55.13	211.56 ± 58.25	187.98 ± 51.89	**<0.01†**	AL1>AL2>AL3>AL4

Factors with statistical significance are shown in boldface.
* Multiple comparisons among the four axial length groups.
† One-way ANOVA test.
‡ X^2 test.

The multivariate model showed that sex, AL, PPA area, and tilt ratio were independently associated with pChT (all $P < 0.05$). Every 1-mm increase in AL was correlated with a 10.94-μm decrease in pChT; every 0.1-mm^2 increase in PPA area was correlated with a 9.54-μm decrease in pChT (Fig. 4C); and every 0.1 increase in tilt ratio was correlated with a 6.21-μm decrease in pChT (Fig. 4A). The combination of these factors yielded an adjusted R^2 of 0.158 (Table 5).

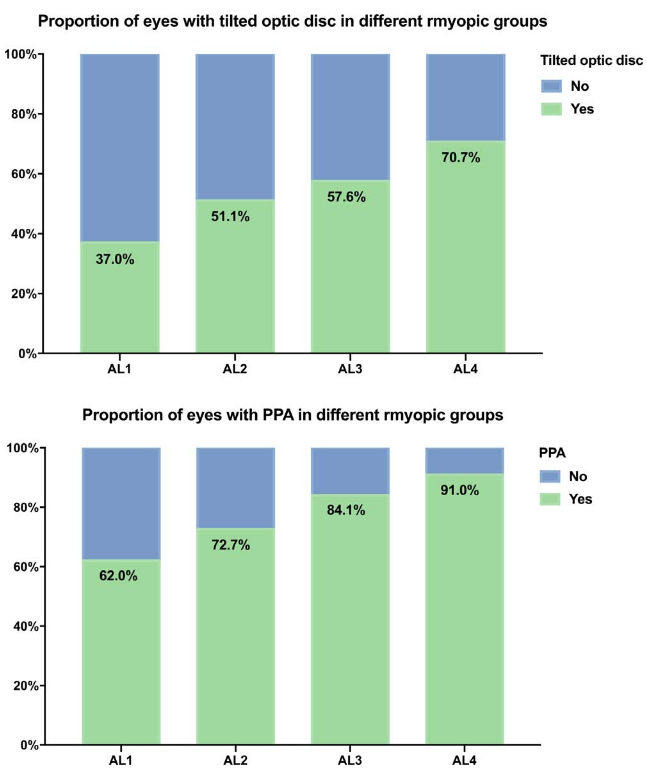

Figure 2. Comparison of the proportions of subjects with a tilted optic disc and PPA in different myopic groups.

After stratifying by myopia severity, the multiple regression model showed that the PPA area correlated negatively with pChT in all four groups (Fig. 4D), whereas the tilt ratio correlated negatively with pChT only in the AL4 group (Fig. 4B). We also observed that AL was negatively associated with pChT in the AL1 and AL4 groups. The overall R^2 values for pChT derived from the multiple regression model were 0.122, 0.153, 0.063, and 0.133 in the AL1, AL2, AL3, and AL4 groups, respectively (Table 5).

Independent Factors Associated With Tilted Optic Disc

Using a logistic regression model, associations between various parameters and the presence of tilted optic discs were also analyzed. Our results showed that the odds of having tilted optic discs increased by 2.33 times for each 0.1-mm^2 increase in PPA area ($P < 0.01$) and by 1.34 times for each 1-mm increase in AL ($P < 0.01$). Reduced mChT and increased pChT (with every 10-μm change) were also significantly associated with higher odds of tilted optic discs (odds ratio [OR] [95% CI] = 0.93 [0.89, 0.97], $P < 0.01$ and OR [95% CI] = 1.11 [1.05, 1.17], $P < 0.01$). After stratifying by myopia severity, larger PPA areas remained independently associated with higher odds of having tilted optic discs in each group (OR = 2.45, 2.90, 2.14, and 2.20 in the AL1, AL2, AL3, and AL4 groups, respectively, all $P < 0.01$). Reduced mChT was significantly correlated with higher odds of having tilted optic discs in the AL3 and AL4 groups (OR = 0.92, $P = 0.02$ and OR = 0.88, $P = 0.01$), whereas increased pChT was associated with higher odds of having tilted optic discs in the AL2 and AL3 groups (OR = 1.14, $P = 0.02$ and OR = 1.14, $P < 0.01$) (Table 6).

Table 2. General Characteristics of the Participants With Different Degrees of Myopia and Comparison Among Groups With and Without a Tilted Optic Disc

	AL1 (n = 108)			AL2 (n = 227)			AL3 (n = 264)			AL4 (n = 222)		
	Subjects With a Tilted Optic Disc (n = 40)	**Subjects Without a Tilted Optic Disc (n = 68)**	***P***	**Subjects With a Tilted Optic Disc (n = 116)**	**Subjects Without a Tilted Optic Disc (n = 111)**	***P***	**Subjects With a Tilted Optic Disc (n = 152)**	**Subjects Without a Tilted Optic Disc (n = 112)**	***P***	**Subjects With a Tilted Optic Disc (n = 157)**	**Subjects Without a Tilted Optic Disc (n = 65)**	***P***
Age, y	19.38 ± 2.39	20.26 ± 2.53	0.08*	19.89 ± 2.89	19.58 ± 2.81	0.41*	19.51 ± 2.31	19.84 ± 2.42	0.26*	20.03 ± 2.84	20.18 ± 2.40	0.70*
Sex, frequency of female (%)	32 (80.0)	42 (61.8)	0.05†	85 (73.3)	57 (51.4)	**<0.01**†	94 (61.8)	46 (41.1)	**<0.01**†	77 (49.0)	18 (27.7)	**0.03**†
MAP, mm Hg	88.03 ± 10.14	90.27 ± 12.12	0.31*	87.07 ± 13.38	87.61 ± 10.42	0.74*	88.50 ± 11.16	87.78 ± 10.46	0.60*	89.60 ± 10.37	89.53 ± 10.55	0.96*
SER, D	−2.14 ± 1.45	−1.59 ± 1.39	0.06*	−3.06 ± 1.68	−2.86 ± 1.82	0.39*	−4.81 ± 1.80	−4.31 ± 1.66	**0.02***	−6.79 ± 2.20	−5.18 ± 2.23	**<0.01***
BCVA, logMAR	0.12 ± 0.04	0.01 ± 0.03	0.47*	0.01 ± 0.03	0.02 ± 0.04	0.25*	0.03 ± 0.07	0.03 ± 0.09	0.58*	0.04 ± 0.10	0.03 ± 0.05	0.39*
IOP, mm Hg	14.46 ± 2.85	13.89 ± 2.80	0.31*	13.82 ± 2.96	14.26 ± 2.67	0.24*	14.00 ± 2.77	13.87 ± 2.81	0.70*	14.08 ± 2.55	13.86 ± 3.24	0.64*
ACD, mm	3.58 ± 0.22	3.59 ± 0.27	0.81*	3.63 ± 0.22	3.70 ± 0.21	0.02*	3.73 ± 0.19	3.77 ± 0.22	0.14*	3.81 ± 0.22	3.82 ± 0.27	0.73*
CCT, μm	535 ± 33	542 ± 39	0.36*	536 ± 39	540 ± 32	0.42*	536 ± 34	536 ± 33	0.96*	535 ± 36	525 ± 38	0.06*
LT, mm	3.53 ± 0.26	3.58 ± 0.22	0.31*	3.55 ± 0.28	3.50 ± 0.19	0.11*	3.50 ± 0.19	3.49 ± 0.18	0.50*	3.49 ± 0.20	3.46 ± 0.21	0.30*
AL, mm	23.56 ± 0.38	23.52 ± 0.44	0.63*	24.54 ± 0.26	24.57 ± 0.29	0.46*	25.47 ± 0.29	25.45 ± 0.26	0.66*	26.78 ± 0.69	26.51 ± 0.46	**0.01***
Tilt ratio	0.75 ± 0.05	0.88 ± 0.05	**<0.01***	0.73 ± 0.06	0.87 ± 0.05	**<0.01***	0.72 ± 0.06	0.87 ± 0.04	**<0.01***	0.73 ± 0.06	0.86 ± 0.05	**<0.01***
Number (%) with PPA	32 (80.0)	35 (51.5)	**<0.01**†	102 (87.9)	63 (56.8)	**<0.01**†	139 (91.5)	83 (74.1)	**<0.01**†	151 (96.2)	51 (78.5)	**<0.01**†
PPA area, mm^2	0.13 ± 0.09	0.07 ± 0.07	**<0.01***	0.18 ± 0.11	0.10 ± 0.08	**<0.01***	0.20 ± 0.12	0.12 ± 0.09	**<0.01***	0.23 ± 0.12	0.14 ± 0.09	**<0.01***
pRNFLT, μm	86.80 ± 8.38	89.08 ± 8.57	0.18*	88.09 ± 8.40	89.07 ± 7.50	0.36*	89.86 ± 6.71	88.99 ± 7.91	0.35*	91.43 ± 9.70	90.53 ± 7.76	0.51*
pChT, μm	157.23 ± 45.16	174.17 ± 48.19	0.07*	157.41 ± 42.96	154.08 ± 44.68	0.57*	146.65 ± 41.24	148.59 ± 45.01	0.72*	128.40 ± 39.62	137.17 ± 36.21	0.13*
mReT, μm	278.35 ± 13.41	282.96 ± 11.95	0.07*	275.38 ± 11.44	280.37 ± 11.67	**<0.01***	274.63 ± 10.45	277.56 ± 11.79	**0.03***	272.94 ± 12.89	277.58 ± 11.49	**0.01***
mChT, μm	235.17 ± 57.22	257.85 ± 56.77	0.05*	224.85 ± 53.75	238.02 ± 56.00	0.07*	201.55 ± 52.30	225.13 ± 63.21	**<0.01***	177.78 ± 50.27	212.63 ± 47.60	**<0.01***

Factors with statistical significance are shown in boldface.
* Student's *t*-test.
† X^2 test.

Table 3. Partial Correlation Analysis Between Choroidal Thickness and Ocular Parameters Adjusted for Sex

	Macular Choroidal Thickness, μm		Peripapillary Choroidal Thickness, μm	
Variable	***r***	***P* Value**	***r***	***P* Value**
PPA area, mm^2	−0.44	<0.01	−0.29	<0.01
AL, mm	−0.42	<0.01	−0.33	<0.01
Tilt ratio	0.31	<0.01	0.08	0.02
SER, D	0.36	<0.01	0.26	<0.01
BCVA, logMAR	−0.15	<0.01	−0.11	0.02
MAP, mm Hg	0.08	0.03	0.10	<0.01
Age, y	0.00	0.99	−0.01	0.97
IOP, mm Hg	0.07	0.05	0.07	0.04
ACD, mm	−0.02	0.51	−0.01	0.70
CCT, μm	0.05	0.18	0.01	0.87
LT, mm	0.05	0.13	0.09	0.01

Discussion

In this basic cross-sectional study, we found that the prevalence of tilted optic discs and PPA were significantly higher in the more advanced myopia, or the AL4 group, than in the other three groups with different degrees of myopia. In the AL3 and AL4 groups, subjects with tilted optic discs were found to have significantly lower mChT and mReT than those without tilted optic discs. After adjusting for other parameters, the PPA area was found to be negatively associated with mChT and pChT, and the tilt ratio was found to be positively correlated with mChT and negatively correlated with pChT. And after stratifying by myopia severity, the same trends were still observed in the AL4 group. This is a clinically significant observation given that the ChT in high myopia may continue to thin with age and may lead to severe myopic chorioretinal pathology, suggesting that it is of vital importance to pay more attention to young myopic patients with tilted optic discs and PPA at an early stage.

To our knowledge, this is the first study to explore the correlation between the mChT and the morphologic characteristics of myopic optic disc. Our results have demonstrated a positive correlation between tilt ratio and mChT, even in the highly myopic group. The results of our study also suggest that reduced mChT and increased pChT are significantly associated with higher odds of having tilted optic discs, especially in highly myopic patients. A previous study has suggested that the degree of optic disc tilt may increase with the elongation of AL and the temporal side of the optic disc might be stretched; this deformation may happen in eyes with or without a posterior staphyloma.[29] Many other studies have reported a significant

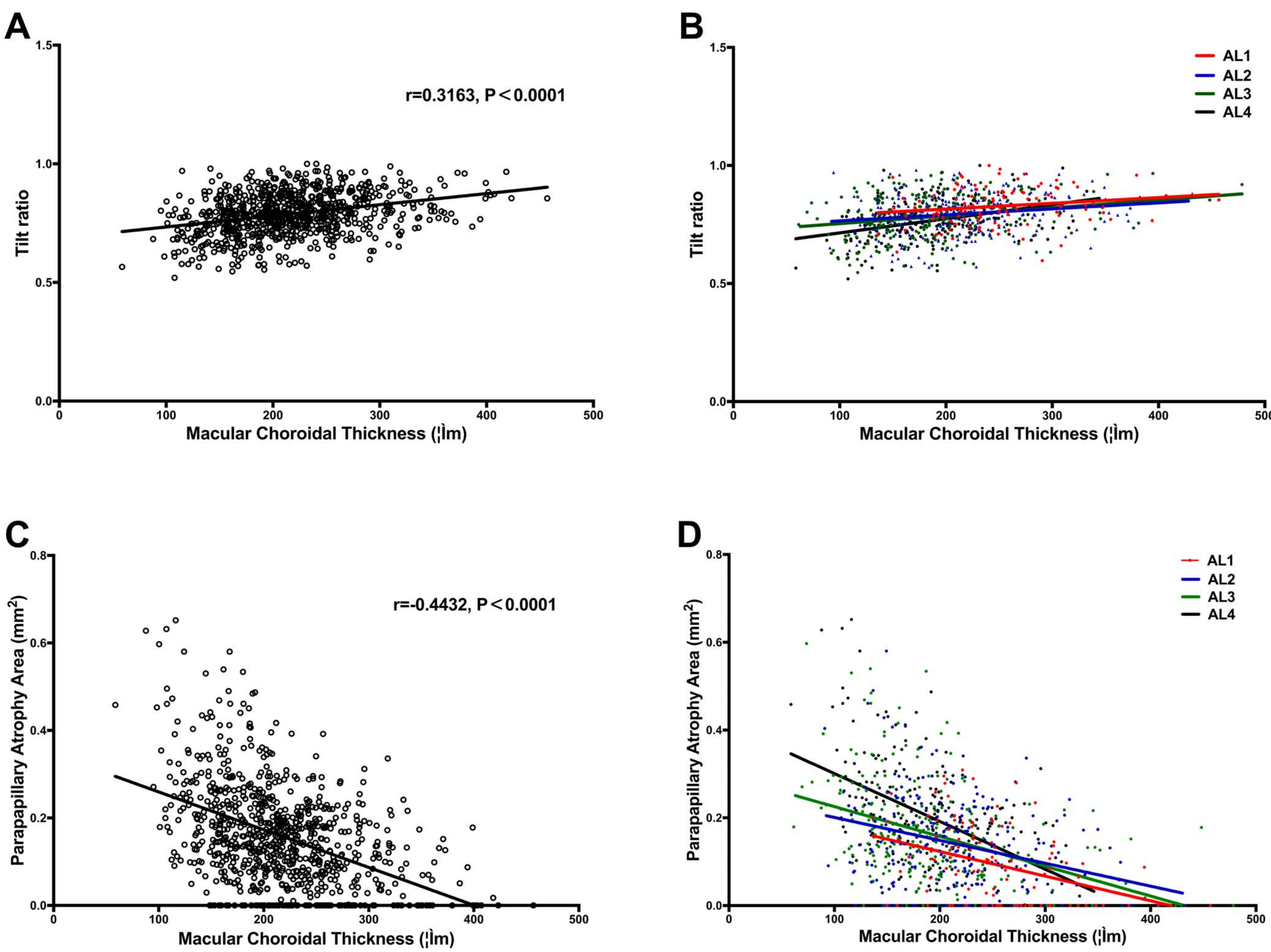

Figure 3. Linear correlation between the average macular choroidal thickness (mChT) and tilt ratio in all subjects (**A**) and groups with different degrees of myopia (**B**). Linear correlation between the average mChT and peripapillary atrophy area in all subjects (**C**) and groups with different degrees of myopia (**D**).

Table 4. Multivariate Regression Analysis of Associations With Macular Choroidal Thickness in All Subjects And Groups With Different Degrees of Myopia

	All Subjects			AL1			AL2			AL3			AL4		
Variables	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**
Sex (male:female)	−10.19	−0.09	**0.01**	−4.58	−0.04	0.73	−16.99	−0.15	**0.03**	−8.38	−0.07	0.25	−8.45	−0.08	0.21
Age, y	0.59	0.03	0.38	−1.67	−0.07	0.44	0.66	0.03	0.60	2.08	0.08	0.15	−0.15	−0.00	0.90
MAP, mm Hg	0.33	0.06	0.05	0.44	0.09	0.38	0.34	0.07	0.27	0.27	0.05	0.41	0.56	0.11	0.08
IOP, mm Hg	1.14	0.05	0.08	0.66	0.03	0.73	0.09	0.01	0.95	1.73	0.08	0.15	1.51	0.08	0.19
AL, mm	−15.42	−0.29	**<0.01**	−29.62	−0.21	**0.03**	−29.97	−0.15	**0.02**	−19.86	−0.09	0.11	−13.54	−0.17	**<0.01**
Tilt ratio	53.82	0.08	**0.03**	23.61	0.03	0.76	33.44	0.05	0.49	64.38	0.10	0.14	94.26	0.15	**0.03**
PPA area, mm^2	−149.26	−0.29	**<0.01**	−190.04	−0.28	**0.01**	−122.19	−0.23	**<0.01**	−164.90	−0.32	**<0.01**	−139.06	−0.32	**<0.01**

Adjusted for all variables listed. R^2 for all subjects: 0.279; R^2 for AL1: 0.133; R^2 for AL2: 0.112; R^2 for AL3: 0.162; R^2 for AL4: 0.272. Factors with statistical significance are shown in boldface.

Table 5. Multivariate Regression Analysis of Associations With Peripapillary Choroidal Thickness in All Subjects and Groups With Different Degrees of Myopia

	All Subjects			AL1			AL2			AL3			AL4		
Variables	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**	**B**	**β**	***P* Value**
Sex (male:female)	−6.74	−0.08	**0.04**	−7.11	−0.07	0.51	−9.83	−0.11	0.12	−1.15	−0.01	0.84	−10.48	−0.13	0.06
Age, y	0.44	0.03	0.43	−0.41	−0.02	0.82	0.99	0.07	0.33	0.71	0.04	0.52	−0.00	−0.00	0.99
MAP, mm Hg	0.34	0.08	**0.02**	0.71	0.17	0.09	0.03	0.01	0.92	0.32	0.08	0.21	0.63	0.17	**0.02**
IOP, mm Hg	0.86	0.05	0.10	0.11	0.01	0.94	1.33	0.09	0.20	0.12	0.01	0.90	1.64	0.12	0.08
AL, mm	−10.94	−0.28	**<0.01**	−29.43	−0.26	**0.01**	−20.16	−0.13	0.06	−18.89	−0.12	0.05	−12.14	−0.20	**<0.01**
Tilt ratio	−62.07	−0.12	**<0.01**	−45.32	−0.08	0.49	−71.74	−0.14	0.07	−49.45	−0.10	0.14	−68.74	−0.15	**0.04**
PPA area, mm^2	−95.39	−0.25	**<0.01**	−127.07	−0.23	**0.04**	−99.64	−0.24	**<0.01**	−108.08	−0.29	**<0.01**	−64.69	−0.20	**<0.01**

Adjusted for all variables listed. R^2 for all subjects: 0.158; R^2 for AL1: 0.122; R^2 for AL2: 0.053; R^2 for AL3: 0.063; R^2 for AL4: 0.133.Factors with statistical significance are shown in boldface.

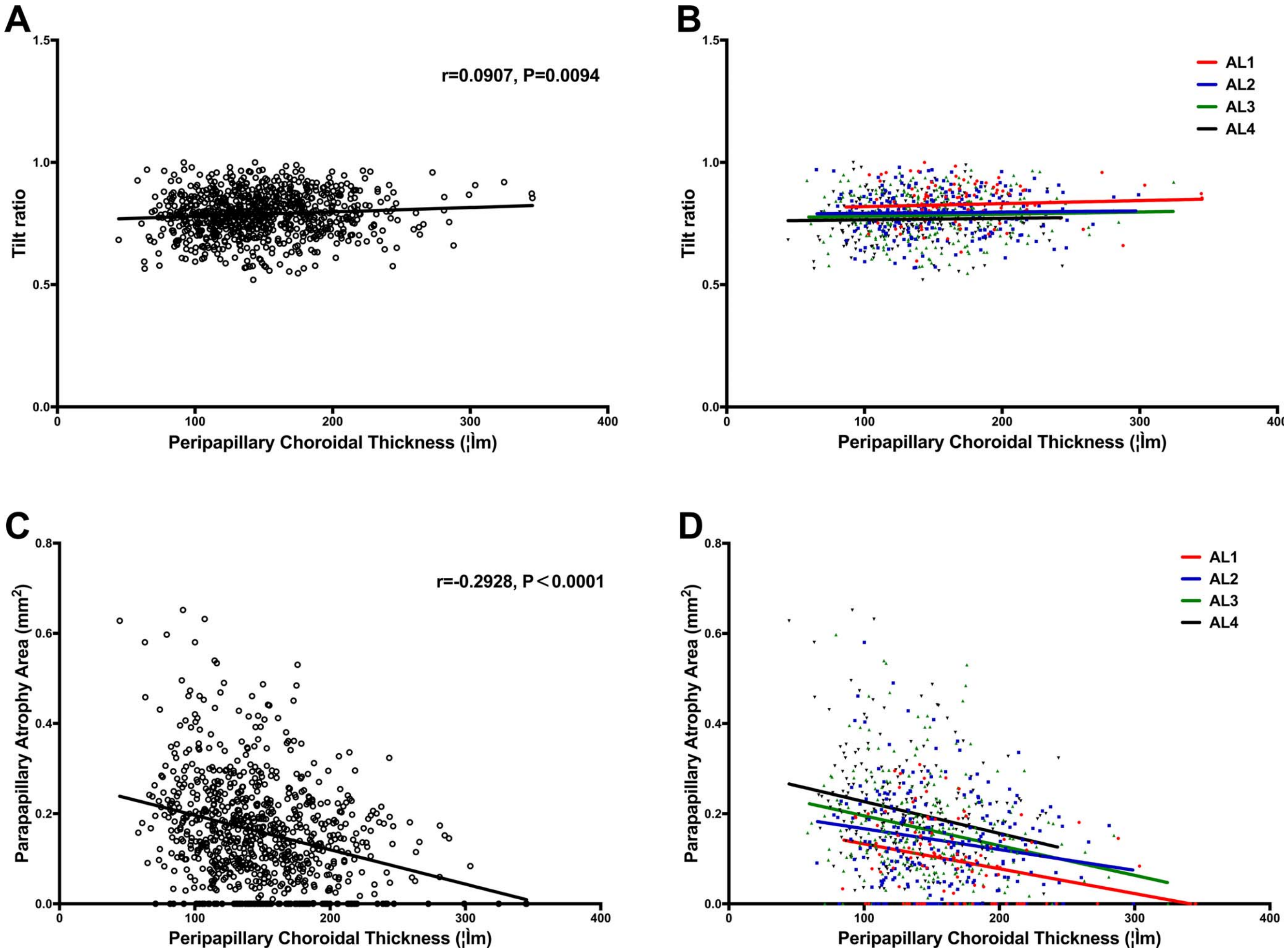

Figure 4. Linear correlation between the average peripapillary choroidal thickness (pChT) and tilt ratio in all subjects (**A**) and groups with different degrees of myopia (**B**). Linear correlation between the average pChT and peripapillary atrophy area in all subjects (**C**) and groups with different degrees of myopia (**D**).

association between the presence of posterior staphyloma and choroidal thinning in highly myopic patients.[30–32] Although no obvious posterior staphyloma was found in the young myopia patients in the present study, subclinical staphylomas are sometimes observed in this population. Furthermore, changes in mChT and pChT may suggest that the retina is stretched in these areas. Given that a posterior staphyloma was not yet evident in these young myopic patients, the presence and progression of a tilted optic disc may be a predictor of the asymmetric deformation of the eyeball at an early stage.

We further found that larger PPA area was associated with higher odds of having tilted optic discs, which was similar to the results of previous studies.[33–35] Consistent with the findings of Harb et al.,[36] our results suggested that the PPA area in young, highly myopic patients correlated significantly and negatively with pChT and mChT, even at the early myopic stage. Recently, several studies have reported that the development or enlargement of PPA was a risk factor for the progression of myopic maculopathy, as well as a risk factor for the progression from high myopia to pathologic myopia.[37,38] Although most young myopic patients in the present study did not yet have myopic maculopathy, choroid thinning has been observed, especially in those with larger PPA area. With the progression of myopia, especially severe myopia, the deformation of the eyeball is gradually aggravated, the ChT in subjects with a larger PPA area is more susceptible to further thinning and subsequent myopic chorioretinal changes may occur.[19,21,39–41] Hence, close monitoring is essential for myopic patients with large PPA areas.

This study had several limitations. First, the tilted optic disc was measured in two dimensions, which might not exactly reflect the shapes of the three-dimensional optic disc. Hence, a three-dimensional method to measure the tilt ratio needs to be developed in future studies. Second, the present study was a University-based study, and the subjects' age distribution was biased toward ages 16 to 40 years. Hence, the results might not be truly representative of the entire myopic population. Third, the probability of congenital tilted disc might not be completely ruled out, and given that the visual field defects in the patients were not assessed, subjects with glaucoma might not have been entirely removed. Because the students in the present study were of a younger age, the likelihood of confounding diseases, such as glaucoma and cataract, to influence the findings was negligible. Finally, as a cross-sectional study, causal relationships between the morphologic characteristics of optic disc and ChT were not determined. Hence, it remains uncertain whether the progression of optic disc changes can be used as predictors for choroidal thinning or myopic progression. The trends in tilt ratio, PPA area, and other parameters need to be followed in future studies.

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Table 6. Independent Factors Associated With Tilted Optic Discs in All Subjects And Groups With Different Degrees of Myopia

	All Subjects		AL1		AL2		AL3		AL4	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Sex (male:female)	0.45 (0.32, 0.63)	**<0.01**	0.45 (0.16, 1.25)	0.12	0.42 (0.22, 0.79)	**<0.01**	0.51 (0.30, 0.90)	**0.02**	0.43 (0.21, 0.89)	**0.02**
Age, y	0.95 (0.90, 1.01)	0.08	0.83 (0.69, 0.99)	0.04	1.02 (0.92, 1.13)	0.72	0.91 (0.81, 1.02)	0.09	0.97 (0.86, 1.10)	0.67
AL, mm	1.34 (1.14, 1.59)	**<0.01**	0.75 (0.23, 2.43)	0.63	0.55 (0.18, 1.67)	0.29	1.29 (0.48, 3.48)	0.62	1.73 (0.91, 3.31)	0.10
PPA area, 0.1 mm^2	2.33 (1.92, 2.82)	**<0.01**	2.45 (1.37, 4.45)	**<0.01**	2.90 (1.99, 4.21)	**<0.01**	2.14 (1.55, 2.96)	**<0.01**	2.20 (1.46, 3.31)	**<0.01**
pRNFLT, 10 μm	1.05 (0.86, 1.27)	0.66	0.75 (0.43, 1.32)	0.32	0.95 (0.65 6, 1.39)	0.79	1.31 (0.90, 1.90)	0.17	1.15 (0.80, 1.67)	0.45
pChT, 10 μm	1.11 (1.05, 1.17)	**<0.01**	0.98 (0.84, 1.14)	0.78	1.14 (1.02, 1.27)	**0.02**	1.14 (1.03, 1.25)	**<0.01**	1.12 (0.98, 1.28)	0.09
mChT, 10 μm	0.93 (0.89, 0.97)	**<0.01**	0.97 (0.86, 1.10)	0.65	0.94 (0.86, 1.02)	0.15	0.92 (0.85, 0.99)	**0.02**	0.88 (0.79, 0.97)	**0.01**

Factors with statistical significance are shown in boldface.

In conclusion, after investigating the morphologic characteristics of optic disc, including tilted optic discs and PPA area in young myopic patients with different degrees of myopia, we found, for the first time, the presence of tilted optic discs and larger PPA area correlated positively with lower mChT, especially in highly myopic patients. Our findings indicate that young myopic patients, especially those with tilted optic discs and PPA, should be given high priority, and that long-term, regular follow-up is essential. The results of the present study provide a good foundation for continuing research to follow trends in tilt ratio, PPA area, and other ocular parameters.

Acknowledgments

The authors thank the Shanghai Eye Diseases Prevention and Treatment Center for data collection and financial support.

Supported by grants from the Three-Year Action Program of Shanghai Municipality for Strengthening the Construction of the Public Health System (2015-2017; Grant number GWIV-13.1; Shanghai, China), Shanghai Science and Technology Commission Research Project (Grant number 17ZR1426900; Shanghai, China), Shanghai Municipal Planning Commission of Science and Research Fund (Grant number 201640090; Shanghai, China), and Chinese National Nature Science Foundation (Grant number 81703287; Shanghai, China).

Disclosure: **Q. Chen**, None; **J. He**, None; **Y. Yin**, None; **H. Zhou**, None; **H. Jiang**, None; **J. Zhu**, None; **K. Ohno-Matsui**, None; **H. Zou**, None; **Y. Fan**, None; **X. Xu**, None

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