

Measurements of the parapapillary atrophy area and other fundus morphological features in high myopia with or without posterior staphyloma and myopic traction maculopathy

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Abstract

• **AIM:** To investigate the affecting factors of parapapillary gamma and delta zones and other fundus morphological features in high myopia.

• **METHODS:** Seventy high myopia patients were included in this retrospective observational study and 47 patients were female. Patients were divided into three groups: no posterior staphyloma (no PS), PS with myopic traction maculopathy (PS with MTM), and PS without MTM using 3-dimensional magnetic resonance imaging and optical coherence tomography. MTM patients were further classified into three types [epiretinal membrane, macular hole, and macular retinoschisis (MRS)]. Diameters of the gamma and delta zones were measured among other morphometric variables using fundus photographs.

• **RESULTS:** Of the 70 individuals (127 eyes), the mean age was 57.46±13.56y. In univariate analysis, morphological features changed most dramatically in PS with MTM patients, who had the largest gamma zone diameters, the largest disk-fovea distance (DFD) and disk-fovea angle, and the smallest angle kappa and vertical distance of temporal arterial arcade. However, their horizontal delta zone diameter was smaller than in the patients with PS yet without MTM. In multivariate analysis, with axial length

(AL) and age adjusted, the horizontal diameter in the delta zone of the PS without MTM group was still significantly larger than in the PS with MTM group ($P=0.024$). Comparing the three subtypes of MTM patients, the diameters of the gamma zone and DFD in MRS group were the largest.

• **CONCLUSION:** The characteristics of the gamma and delta zones change inconsistently in different stages of high myopia. These changes may be associated with anatomical changes caused by local traction. Factors such as PS, AL and age play an important role. These findings may provide a hint about the pathogenesis of traction in high myopia.

• **KEYWORDS:** high myopia; myopization; myopic traction maculopathy; parapapillary delta zone; parapapillary gamma zone; posterior staphyloma

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INTRODUCTION

High myopia is a major cause of visual impairment that is estimated to affect approximately 1.6 billion people worldwide, and the prevalence is predicted to increase to 9.8% of the global population by 2050^[1]. Myopic maculopathy is a leading cause of visual impairment and blindness, especially in East Asian populations. In China, it is estimated that pathologic myopia may be responsible for low visual acuity in up to 7.1 million people^[2]. The characteristic ocular changes in high myopia include an excessive increase in axial length (AL), the deformation of posterior staphyloma (PS), and the development of a range of retinal and choroidal lesions, especially in elderly patients^[3-5].

Myopic traction maculopathy (MTM) is a high myopia-related complication caused by several mechanisms, with

traction as a common pathway^[6]. There are a number of different manifestations because of differences in AL, PS, and vitreous conditions, including the development of an epiretinal membrane (ERM), macular retinoschisis (MRS), macular hole (MH), and MH retinal detachment^[7]. It is generally believed that MTM is mainly related to the mechanical traction of the inner and outer layers of the eyewall^[8]. Usually, AL, age, and eyeball shape (mainly referred to as PS) are considered to be main risk factors for the progression of fundus diseases in high myopia, but mechanisms for the development of MTM still remain unclear.

The parapapillary region of the optic disc has recently been divided into four zones, including the alpha, beta, gamma and delta zones^[9-11]. Gamma zone was characterized by the absence of Bruch's membrane and also retinal pigment epithelium (RPE). The delta zone, a part of the gamma zone, is located at the border of the optic disc (defined as the end of the lamina cribrosa) on an elongated and thinned peripapillary scleral flange^[12-13]. Studies have found that some morphological features of the fundus may be related to the progression of fundus lesions in high myopia patients^[14-16]. With extension of the AL, the diameter and area of parapapillary atrophy (PPA) increases. Also, the gamma-delta area may be related to the size and number of chorioretinal atrophies^[17]. However, it is still unknown how PPA and other anatomical features change with the deformation of PS and progression of MTM and whether the changes in different zones of PPA would vary with different subtypes of MTM. We, therefore, conducted this study to measure the diameters of PPA and other anatomical features of high myopia patients at different stages of progression based on PS and MTM and we analyzed the associations between the anatomical features and risk factors to help understand the process of myopization.

SUBJECTS AND METHODS

Ethical Approval The study protocol was approved by the Office of Research Ethics Committee at Beijing Friendship Hospital Affiliated to Capital Medical University (2018-P2-009-01), and it was performed in accordance with the principles of the Declaration of Helsinki. All subjects provided written informed consent after the purpose of the study was explained to them in detail.

Study Population This retrospective study enrolled 70 patients (127 eyes) with high myopia aged 22 to 84 (57.46±13.56)y, including 23 males and 47 females who were examined between June 2017 and January 2019 at Beijing Friendship Hospital of Capital Medical University. High myopia was defined as a myopic refractive error (spherical equivalent) of no less than -6.0 diopters (D) and/or an AL longer than 26.5 mm. Patients with previous refractive surgery, episcleral or macular buckling surgery that could cause

iatrogenic variation of the AL, severe systemic conditions and poor quality of fundus images were excluded from the study.

Ophthalmic Examination All participants underwent a comprehensive ophthalmic examination, including measurements of best-corrected visual acuity (BCVA), refractive error, and AL (IOL Master; Carl Zeiss, Germany), color fundus photography (Nonmyd α -DIII, KOWA, Japan), B-mode ultrasonography, and spectral-domain optical coherence tomography (SD-OCT, Heidelberg, Germany).

Morphological Characteristics Measurement Using the digitized fundus photographs and the Image J system (National Institutes of Health, Bethesda, MD, USA), we measured the horizontal, vertical, minimal, and maximal diameter of the gamma and delta zones, the distance between the most superior point of the temporal superior arterial arcade and the most inferior point of the temporal inferior arterial arcade (VDA), the angle between the temporal arterial arcade and the optic disc (so-called angle kappa), the distance between the optic disc center and the fovea ("disc-fovea distance", DFD), the angle between the horizontal optic disc axis and the optic disc-fovea line ("disc-fovea angle", DFA), and the distance between the fovea and the outer border of the gamma zone^[17].

Both the parapapillary gamma and delta regions were characterized by a whitish area at the temporal optic disk border without underlying choriocapillaris, medium-sized choroidal arteries, and signs of the RPE (Figure 1)^[12]. The horizontal diameter of the gamma and delta zones was measured on the disc-fovea line. The vertical diameter of the gamma and delta zones was measured through the midpoint of the horizontal line. The maximal diameter was measured where the zone had its largest extension, and the minimal diameter was measured where the zone had its smallest extension, and they all passed through the midpoint of the horizontal line (Figure 2). The gamma/delta ratio was calculated as the ratio of the horizontal gamma diameter to the horizontal delta diameter. Other methods of parameter measurement were based on the recommendations by Jonas *et al*^[18]. Using the Littmann-Bennett method^[19], we corrected the measurements of length and area for their dependence on the magnification of fundus images. All of the image processing and analysis was completed independently by two specialized technicians who were masked to the disease status of the patients, and then the measurements were averaged.

Evaluation of the Posterior Staphyloma and Myopic Traction Maculopathy PS was confirmed using indirect ophthalmoscopy and, for further evaluation, using B-mode ultrasonography and magnetic resonance imaging (MRI) tomography. PS was defined by Spaide *et al*^[20] as "an outpouching of the wall of the eye with a radius of curvature less than the radius of curvature of the surrounding eye wall."

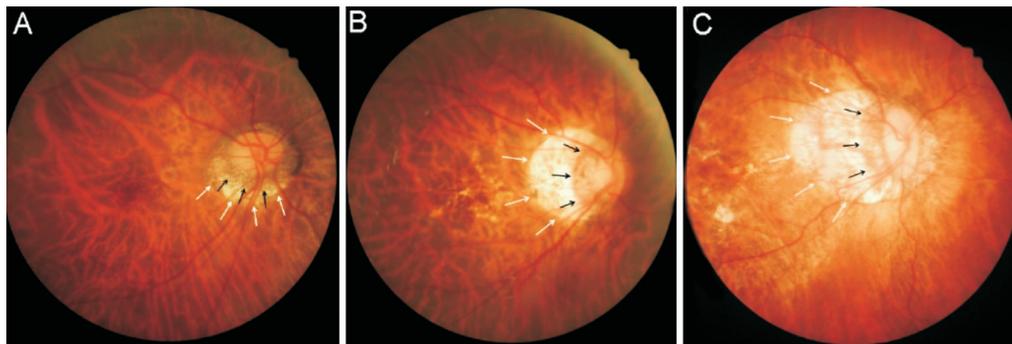


Figure 1 Representative fundus photographs showing the parapapillary gamma zone (white arrows) and the parapapillary delta zone (black arrows) of different groups with high myopia A: No PS or MTM in a 60-year-old woman with AL of 28.3 mm; B: PS without MTM in a 54-year-old woman with AL of 30.1 mm; C: PS with MTM in a 55-year-old woman with AL of 31.3 mm.

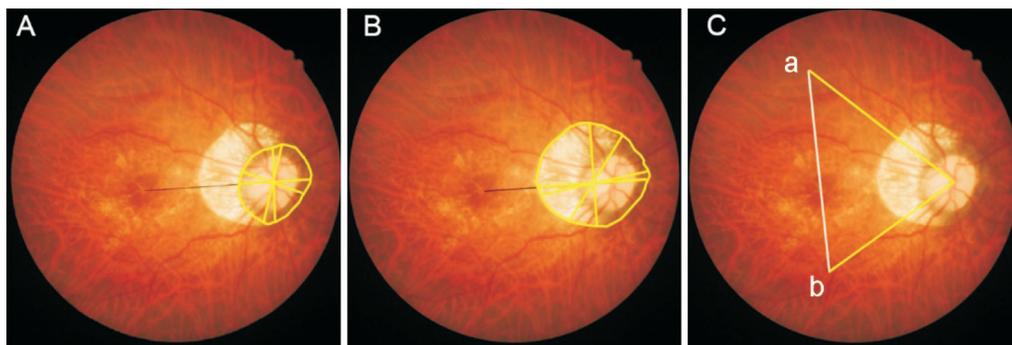


Figure 2 Fundus photograph showing the determination of the diameters of parapapillary delta zone, gamma zone and the angle kappa A: Fundus photograph of a highly myopic eye with the parapapillary delta zone (yellow curve) and the horizontal, vertical, minimal, and maximal diameter (yellow straight line); B: Fundus photograph of a highly myopic eye with the parapapillary gamma zone (yellow curve) and the horizontal, vertical, minimal, and maximal diameter (yellow straight line); C: The angle kappa was determined as the temporal arterial arcade between the optic disk center and the crossing points of a vertical line passing through the fovea and crossing the temporal superior arterial arcade (a) and the temporal inferior arterial arcade (b). The temporal arterial arcade was the distance between a and b.

All of the myopic macular alterations were classified into two groups according to the definition of MTM; that is, the MTM group and the non-MTM group, as analyzed by SD-OCT. According to Panozzo *et al*^[8], the pathologic features generated by traction induced by the ERM and/or residual focal vitreoretinal adhesion in the myopic environment were defined as MTM. ERM refers to the appearance of a fibroproliferative membrane on the surface of the inner limiting membrane of the macular area. The optical coherence tomography (OCT) results are characterized by continuous highly reflective bands of different thicknesses, accompanied by retinal folds^[21]. The MH refers to a partial or full-thickness tissue defect that occurs in the retinal neuroepithelial layer of the macula^[22]. The MRS is the separation of the neurosensory retina into two or more layers, forming one or more cyst-like large gaps^[23]. The PS and MTM were analyzed by two masked observers (Guo XX and Chen X), and they were supervised by a panel of retina specialists (Wang YL and Zhao L).

Magnetic Resonance Imaging The participants were examined using the Discovery MR750 3.0T scanner (GE Healthcare, Milwaukee, WI, USA). The MRI devices were

equipped with an 8-channel phased-array head coil to rapidly scan both eyes, and the T2-weighted CUBE technology was used to obtain a high-contrast delineation of the edges of the eye. Scanning settings were: repetition time =2500ms; echo time =90ms; section thickness =1.0 mm with a 0-mm section gap; flip angle =90°; field of vision =256×230 mm². The scan time of the 3-dimensional (3D) T2-weighted CUBE sequence for each subject was approximately 4.0min. Volume renderings of the images were produced from high-resolution 3D data on a computer workstation (OsiriX 7.0; OsiriX Medical Image Software, Bernex, Switzerland).

Statistical Analysis A commercially available statistical software package (SPSS for Windows, version 22.0; IBM Corporation, USA) was used for the statistical analysis. The mean values and the standard deviations (SD) of the age, AL, SE refractive error, BCVA and other morphological characteristics were calculated for the groups of eyes with different types of MTM. All data are presented as the mean±SD. Fractional visual acuities were converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analyses. A univariate analysis was performed

Table 1 Comparison of clinical and eye characteristics between eyes with and without posterior staphyloma among the eyes with high myopia

Characteristics	Total	No PS	PS			P1	P2
			Total	Without MTM	With MTM		
No. of eyes (%)	127	28 (22.0)	99 (78.0)	42 (42.4)	57 (57.6)	-	-
Age (y)	57.5±13.5	45.6±15.7	60.8±10.9	58.7±11.7	62.3±10.0	0.001	0.157
Axial length (mm)	28.2±2.2	27.0±1.0	28.6±2.3	27.8±1.9	29.1±2.3	<0.001	0.122
BCVA (logMAR)	0.41±0.43	0.16±0.25	0.50±0.45	0.35±0.44	0.60±0.43	0.001	0.730
Refractive error (spherical equivalent; D)	-10.8±4.7	-8.1±2.4	-11.7± 5.0	-10.1±4.3	-12.8±5.2	0.003	0.009
Delta zone, n (%)	99 (78.0)	11 (39.3)	88 (89.9)	36 (85.7)	53 (93.0)	-	-
Gamma zone, n (%)	103 (81.1)	13 (46.4)	90 (90.9)	37 (89.0)	54 (94.7)	-	-
Parapapillary gamma zone, horizontal diameter (mm)	3.21±1.07	2.45±0.44	3.32±1.09	3.05±0.99	3.50±1.12	<0.001	0.363
Parapapillary gamma zone, vertical diameter (mm)	3.11±1.20	2.23±0.29	3.23±1.23	3.17±1.27	3.28±1.21	<0.001	0.712
Parapapillary gamma zone, minimal diameter (mm)	2.80±0.92	2.13±0.30	2.90±0.94	2.80±0.97	2.96±0.92	<0.001	0.729
Parapapillary gamma zone, maximal diameter (mm)	3.56±1.33	2.57±0.45	3.70±1.35	3.49±1.35	3.85±1.35	0.001	0.913
Parapapillary delta zone, horizontal diameter (mm)	2.22±0.71	1.81±0.34	2.28±0.72	2.37±0.85	2.22±0.63	0.113	0.134
Parapapillary delta zone, vertical diameter (mm)	2.46±0.81	1.84±0.37	2.55±0.80	2.48±0.85	2.59±0.78	0.142	0.538
Parapapillary delta zone, minimal diameter (mm)	2.06±0.67	1.60±0.32	2.13±0.67	2.14±0.75	2.12±0.63	0.211	0.266
Parapapillary delta zone, maximal diameter (mm)	2.65±0.91	2.10±0.36	2.72±0.94	2.70±1.05	2.74±0.86	0.028	0.203
Horizontal diameter of gamma/delta ratio	1.49±0.51	1.37±0.20	1.51±0.54	1.33±0.31	1.63±0.63	0.090	0.088
Distance between fovea and outer border of gamma zone (mm)	2.66±0.69	3.27±0.47	2.49±0.64	2.67±0.53	2.35±0.69	0.147	0.178
Disc-fovea distance (mm)	4.73±1.21	4.46±0.33	4.62±0.47	4.48±0.37	4.72±0.51	0.104	0.020
Disc-fovea angle (°)	11.39±6.19	8.34±4.43	12.35±6.35	11.34±5.44	13.09±6.89	0.076	0.028
Vertical distance of temporal arterial arcade (mm)	9.00±10.23	8.19±1.12	7.61±1.26	7.83±1.14	7.45±1.32	0.743	0.043
Angle kappa (°)	77.94±14.69	84.15±8.7	77.93±11.53	81.33±10.2	75.42±11.8	0.146	0.316

PS: Posterior staphyloma; MTM: Myopic traction maculopathy; BCVA: Best-corrected visual acuity; P1: The comparison of the no PS and PS group; P2: The comparison of the without MTM and with MTM group.

to compare the differences between the groups. Then, we performed a multivariate analysis and calculated the AL-and-age-adjusted unstandardized regression coefficient B of the main outcomes, with dummy variables being set for group variables in the linear regression models. All *P*-values were considered to be statistically significant if their value was less than 0.05.

RESULTS

The study included 70 patients (127 eyes) with an average age of 57.5±13.5y (range: 22-84y). The mean AL was 28.2±2.2 mm (range: 24.1 to 34.9 mm) and the mean refractive error (spherical equivalent) was -10.8±4.7 diopters (range: -4.75 to -24.75 diopters; Table 1).

A PS was detected in 99 of 127 eyes (78.0%): 42 eyes (42.4%) without MTM and 57 eyes (57.6%) with MTM. Patients with PS were older, had a longer AL, and higher prevalence of delta and gamma zones than patients without PS. The horizontal diameters of the gamma zone in the no PS, PS without MTM, and PS with MTM groups were 2.45±0.44 mm, 3.05±0.99 mm, and 3.50±1.12 mm, respectively. The horizontal diameters of the delta zone were 1.81±0.34 mm, 2.37±0.85 mm, and 2.22±0.63 mm, respectively. The mean prevalence of the gamma zone was 103 of 127 (81.1%), and the mean prevalence of the delta zone was 99 of 127 (78.0%; Table 1). In 4 of

103 (3.9%) eyes without a delta zone, a gamma zone was present. Morphological features changed most dramatically in the PS with MTM group, which had the largest horizontal diameter in the gamma zone, the smallest distance between the fovea and an outer border of the gamma zone, the largest DFD and DFA, and the smallest VDA and angle kappa. However, the PS without MTM group had the largest horizontal diameter in the delta zone.

In univariate analysis, the vertical diameters of the gamma zone (*P*=0.01), the horizontal and vertical diameters of delta zone (*P*=0.01, both), and DFA (*P*=0.04) were significantly larger in the eyes of the PS without MTM group than the no PS group. The distance between the fovea and outer border of the gamma zone was smaller in the PS without MTM group and the difference was statistically significant (*P*<0.001). Eyes in the PS with MTM group had larger horizontal and vertical diameters of the gamma zone (*P*=0.001, and 0.004, respectively), larger vertical diameters of the delta zone (*P*=0.002), larger horizontal diameter of the gamma/delta ratio (*P*<0.001), and larger DFD (*P*=0.01) and DFA (*P*=0.001) than the no PS group. The distance between the fovea and outer border of the gamma zone (*P*<0.001), VDA (*P*=0.01) and angle kappa (*P*=0.001) were smaller than in the no PS group and the differences were statistically significant. The horizontal

Table 2 The association of the three groups and the fundus morphological features in univariate and multivariate analysis

Parameters	No PS vs PS without MTM				No PS vs PS with MTM				PS without MTM vs PS with MTM				AL	Age
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis			
	P	B	P	B	P	B	P	B	P	B	P	B		
Parapapillary gamma zone, horizontal diameter (mm)	0.07	0.61	0.72	0.11	0.001	1.06	0.59	0.17	0.04	0.45	0.74	0.06	<0.001	0.007
Parapapillary gamma zone, vertical diameter (mm)	0.01	0.94	0.48	0.24	0.004	1.05	0.75	-0.11	0.66	0.11	0.10	-0.35	<0.001	<0.001
Parapapillary gamma zone, minimal diameter (mm)	0.002	0.67	0.39	0.23	0.003	0.84	0.82	0.07	0.38	0.17	0.32	-0.17	<0.001	0.006
Parapapillary gamma zone, maximal diameter (mm)	0.03	0.92	0.83	0.08	0.002	1.27	0.83	-0.08	0.20	0.36	0.48	-0.16	<0.001	<0.001
Parapapillary delta zone, horizontal diameter (mm)	0.01	0.56	0.26	0.27	0.06	0.41	0.89	-0.03	0.33	-0.15	0.04	-0.30	0.004	0.03
Parapapillary delta zone, vertical diameter (mm)	0.01	0.64	0.21	0.32	0.002	0.75	0.45	0.20	0.50	0.11	0.43	-0.12	<0.001	0.03
Parapapillary delta zone, minimal diameter (mm)	0.01	0.55	0.20	0.28	0.01	0.52	0.74	0.08	0.84	-0.03	0.13	-0.21	<0.001	0.04
Parapapillary delta zone, maximal diameter (mm)	0.04	0.59	0.58	0.17	0.02	0.64	0.89	-0.04	0.80	0.05	0.26	-0.21	<0.001	0.009
Horizontal diameter of gamma/delta ratio	0.85	-0.04	0.50	-0.15	<0.001	1.59	<0.001	1.28	<0.001	1.63	<0.001	1.43	<0.001	0.68
Distance between fovea and outer border of gamma zone (mm)	<0.001	-0.59	0.006	-0.41	<0.001	-0.92	<0.001	-0.56	0.009	-0.32	0.22	-0.15	0.14	<0.001
Disk-fovea distance (mm)	0.92	0.01	0.26	-0.12	0.01	0.26	0.88	0.02	0.005	0.25	0.11	0.14	0.05	0.001
Disk-fovea angle (°)	0.04	3.00	0.09	2.72	0.001	4.74	0.006	4.71	0.15	1.75	0.12	1.99	0.37	0.28
Vertical distance of temporal arterial arcade (mm)	0.23	-0.36	0.72	-0.11	0.01	-0.74	0.52	-0.22	0.13	-0.38	0.68	-0.01	0.48	<0.001
Angle kappa (°)	0.28	-2.82	0.80	0.67	0.001	-8.73	0.47	-2.04	0.008	-5.91	0.20	-2.71	0.08	<0.001

PS: Posterior staphyloma; MTM: Myopic traction maculopathy; AL: Axial length; B: Non-standardized regression coefficient B.

diameter of the gamma zone ($P=0.04$), the gamma/delta ratio ($P<0.001$), and DFA ($P=0.005$) were significantly larger in the eyes of the PS with MTM group than in the PS without MTM group. Also, the distance between the fovea and outer border of the gamma zone ($P=0.009$) and angle kappa ($P=0.008$) were smaller in the PS with MTM group and the difference was statistically significant (Table 2).

The largest horizontal diameter of the gamma zone was found in the PS with MTM group, while the largest horizontal diameter of the delta zone was found in the PS without MTM group, which suggested that the changes in the gamma and delta zones were inconsistent in these two groups. Furthermore, the changes in the gamma area and delta area were consistent in the no PS group and PS without MTM group and presented as a wider gamma and wider delta. In the PS with MTM group, the diameter of the gamma area became relatively large, but that of the delta area did not change as much; that is, the two diameters showed inconsistent changes.

Since AL and age are well-known risk factors of myopization besides PS, and the AL and age of the three groups showed a trend of increasing with the progression of high myopia, we conducted a multivariate analysis that included the main ocular parameters as dependent variables and AL and age in the univariate analysis as independent variables. The distance

between the fovea and outer border of the gamma zone still showed significant differences ($P=0.006$) between the no PS group and the PS without MTM group, but the differences in the gamma, delta parameters and DFA were not significant ($P>0.05$). In the no PS group and the PS with MTM group, the horizontal diameter of the gamma/delta ratio ($P<0.001$), the distance between the fovea and outer border of the gamma zone ($P<0.001$) and the DFA ($P=0.006$) still showed significant differences. In the PS without MTM group and PS with MTM group, the horizontal diameter of the gamma/delta ratio still showed significant differences ($P<0.001$). The difference of horizontal diameter of delta zone between the PS without MTM group and PS with MTM group was not significant in univariate analysis. However, in multivariate analysis, the difference was significant ($P=0.04$; Table 2).

MTM was detected in 57 eyes of 127 patients (44.9%): 22 eyes (38.6%) with ERM, 17 eyes (29.8%) with MH, and 18 eyes (31.6%) with MRS. The mean age of patients without MTM was 54.0 ± 14.8 y (range: 22-79y) and the mean AL was 27.4 ± 1.7 mm (range: 24.1-32.3 mm). The mean age of patients in the PS with MTM group was 62.3 ± 10.0 y (range: 22-84y) and the mean AL was 29.1 ± 2.3 mm (range: 25.2-34.9 mm). The mean horizontal diameters of the gamma zone in patients with ERM, MH and MRS were 2.97 ± 0.98 mm, 3.22 ± 1.17 mm

Table 3 Clinical characteristics of eyes with and without myopic traction maculopathy

Characteristics	Absent	Myopic traction maculopathy (present)			P	
		Total	ERM	MH		MRS
No. of eyes (%)	68 (53.1)	57 (44.9)	22 (38.6)	17 (29.8)	18 (31.6)	-
Age (y)	54.0±14.8	62.3±10.0	61.1±7.7	62.8±12.3	63.4±10.5	0.758
Axial length (mm)	27.4±1.7	29.1±2.3	28.63±2.14	29.2±2.8	29.7±2.0	0.334
BCVA (logMAR)	0.27±0.39	0.60±0.43	0.38±0.37	0.73±0.51	0.76±0.28	0.018
Refractive error (spherical equivalent; diopters)	-9.1±3.7	-12.8±5.2	-11.4±4.6	-13.1±5.6	-14.7±5.0	0.282
Delta zone, n (%)	44 (64.7)	53 (93.0)	19 (86.4)	16 (94.1)	18 (100)	-
Gamma zone, n (%)	47 (69.1)	54 (94.7)	20 (90.9)	16 (94.1)	18 (100)	-
Parapapillary gamma zone, horizontal diameter (mm)	2.93±0.91	3.50±1.24	2.97±0.98	3.22±1.17	4.25±0.84	0.001
Parapapillary gamma zone, vertical diameter (mm)	2.96±1.18	3.28±1.20	2.89±1.21	2.91±1.18	4.04±0.87	0.003
Parapapillary gamma zone, minimal diameter (mm)	2.65±0.90	2.96±0.92	2.67±0.97	2.67±0.87	3.56±0.62	0.003
Parapapillary gamma zone, maximal diameter (mm)	3.29±1.25	3.85±1.35	3.29±1.43	3.51±1.27	4.76±1.20	0.001
Parapapillary delta zone, horizontal diameter (mm)	2.25±0.79	2.19±0.63	2.10±0.64	2.13±0.68	2.43±0.55	0.236
Parapapillary delta zone, vertical diameter (mm)	2.36±0.79	2.59±0.78	2.42±0.93	2.47±0.65	2.89±0.64	0.135
Parapapillary delta zone, minimal diameter (mm)	2.04±0.70	2.12±0.63	2.01±0.73	2.03±0.58	2.31±0.53	0.295
Parapapillary delta zone, maximal diameter (mm)	2.58±0.96	2.75±0.86	2.55±1.04	2.63±0.77	3.06±0.63	0.151
Horizontal diameter of gamma/delta ratio	1.34±0.29	1.63±0.63	1.44±0.39	1.70±1.02	1.78±0.29	0.220
Distance fovea-outer border of gamma zone (mm)	2.91±0.59	2.35±0.69	2.63±0.66	2.34±0.66	2.02±0.63	0.019
Disc-fovea distance (mm)	4.48±0.35	4.72±0.51	4.55±0.46	4.54±0.38	5.10±0.47	< 0.001
Disc-fovea angle (°)	10.09±5.30	13.09±6.89	11.84±5.77	13.93±7.74	13.81±7.46	0.564
Vertical distance of temporal arterial arcade (mm)	8.01±1.15	7.45±1.32	7.25±1.28	7.57±1.28	7.60±1.44	0.561
Angle kappa (°)	82.58±9.8	75.42±11.86	75.65±11.5	78.67±12.23	72.07±11.6	0.261

ERM: Epiretinal membrane; MH: Macular hole; MRS: Macular retinoschisis; BCVA: Best-corrected visual acuity; P: The comparison of the three groups of myopic traction maculopathy.

and 4.25±0.84 mm, respectively. The mean horizontal diameter of the delta zone was 2.10±0.64 mm, 2.13±0.68 mm and 2.43±0.55 mm, respectively (Table 3).

In univariate analysis, the gamma parameters ($P<0.01$), the vertical diameter of the delta zone ($P=0.03$), and the DFD ($P<0.001$) were significantly larger in MRS patients than ERM patients. And the distance between the fovea and outer border of the gamma zone ($P=0.005$) was significantly smaller in the ERM group than in the MRS group. Gamma parameters ($P<0.01$) and DFD ($P<0.001$) were significantly larger in the eyes of the MRS group than the MH group. The differences in the gamma, delta, and other morphological features were not significant between the MRS and MH group.

Multivariate analysis showed significant differences in the gamma zone parameters and DFD between the MH and MRS groups ($P<0.05$). However, the differences in delta parameters between the ERM and MRS groups were no longer significant, while other parameters were still statistically different (Table 4). To further analyse the association between risk factors and the fundus morphological features, we found that there was no significant association between DFA and AL or age among No PS, PS with and without MTM patients. The differences in VDA, angle kappa, gamma zone, and DFD were mainly due to the AL and/or age factors. In addition, delta zone and distance between the fovea and outer border of the gamma zone may be affected by other factors besides AL and age, with PS as

the likely factor. Among three subtypes of MTM patients, the differences in the delta zone, VDA, and angle kappa were mainly related to the AL and/or age. For the gamma zone, the distance between the fovea and outer border of the gamma zone and DFD, PS might play a role in the pathogenesis of MTM in addition to AL and age.

DISCUSSION

The present study showed morphological features changed most significantly in the PS with MTM group, which had the largest diameters of the gamma zone, the largest DFD and DFA, and the smallest VDA and angle kappa. However, the horizontal diameter of the delta zone was smaller than in the PS without MTM patients, which suggested that traction had an inconsistent influence on delta and gamma zones. Comparing the three subtypes of MTM patients, the diameters of the gamma zone and DFD in the MRS group were the highest. Furthermore, we conducted a multivariate analysis to reveal the role of AL and age on the comparison of morphological features in the different groups. Some previous studies have suggested this, although they did not directly demonstrate these findings. The results of our study revealed the changes of PPA and other anatomical landmarks of the fundus in different stages of high myopia patients and we further analyzed the role of risk factors such as PS, AL and age in these patients.

For MTM patients, the traction to the retina is the crucial factor in disease development. And the traction comes from

Table 4 Differences in fundus morphological features among the three types of myopic traction maculopathy groups by univariate analysis and multivariate analysis

Parameters	ERM vs MH				ERM vs MRS				MH vs MRS				AL	Age
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis			
	P	B	P	B	P	B	P	B	P	B	P	B		
Parapapillary gamma zone, horizontal diameter (mm)	0.25	0.39	0.45	0.22	<0.001	1.42	<0.001	1.10	0.005	1.03	0.004	0.89	<0.001	0.04
Parapapillary gamma zone, vertical diameter (mm)	0.89	0.05	0.59	-0.15	0.001	1.25	0.003	0.88	0.002	1.20	0.001	1.03	<0.001	0.005
Parapapillary gamma zone, minimal diameter (mm)	0.87	0.05	0.70	-0.09	0.001	1.00	0.003	1.74	0.002	0.95	0.001	0.83	<0.001	0.08
Parapapillary gamma zone, maximal diameter (mm)	0.53	0.25	0.95	0.02	<0.001	1.61	<0.001	1.20	0.002	1.36	0.001	1.18	<0.001	0.002
Parapapillary delta zone, horizontal diameter (mm)	0.81	0.05	0.98	0.01	0.06	0.38	0.15	0.29	0.12	0.33	0.17	0.29	0.006	0.66
Parapapillary delta zone, vertical diameter (mm)	0.90	0.06	0.93	-0.02	0.03	0.534	0.11	0.37	0.07	0.47	0.11	0.39	0.003	0.46
Parapapillary delta zone, minimal diameter (mm)	0.84	0.04	0.94	-0.01	0.09	0.34	0.23	0.24	0.15	0.304	0.22	0.53	0.01	0.66
Parapapillary delta zone, maximal diameter (mm)	0.75	0.09	0.99	-0.01	0.03	0.58	0.12	0.41	0.09	0.50	0.13	0.42	0.008	0.26
Distance between fovea and outer border of gamma zone (mm)	0.17	-0.28	0.27	-0.23	0.005	0.61	0.02	0.50	0.15	0.32	0.21	0.27	0.02	0.92
Disk-fovea distance (mm)	0.97	-0.01	0.71	-0.05	<0.001	-0.55	0.001	0.47	<0.001	-0.56	0.001	-0.52	0.02	0.18
Disk-fovea angle (°)	0.35	2.10	0.36	2.11	0.38	-1.97	0.36	-2.11	0.96	0.13	>0.99	0.01	0.43	0.31
Vertical distance of temporal arterial arcade (mm)	0.46	0.32	0.21	0.50	0.41	-0.35	0.90	-0.68	0.94	-0.03	0.66	-0.18	0.002	0.06
Angle kappa (°)	0.43	3.02	0.15	4.86	0.34	3.58	0.93	0.29	0.10	6.60	0.14	5.15	<0.001	0.01

ERM: Epiretinal membrane; MH: Macular hole; MRS: Macular retinoschisis; AL: Axial length; B: Non-standardized regression coefficient B.

multiple sources, including incomplete or abnormal posterior vitreous detachment causing forward axial traction, scleral expansion and/or PS causing backward axial traction, and the posterior vitreous cortex, the inner limiting membrane and ERM causing tangential traction. Tractional force due to vitreoretinal adhesion on the retinal vessels may also be the cause of MTM^[24-25]. Traction is closely related to AL and age. The longer the AL is, the greater traction force will be, resulting in an increase in the incidence of MTM^[26-27]. With age, vitreous liquefaction, ERM formation and the decrease of vascular elasticity can also lead to an increase in traction force. In our study, we found that MTM was strongly associated with PS, since high myopia patients without PS rarely showed the sign of MTM. The presence of a PS might suggest a higher risk of progression. Also, patients with MTM were older, had a longer AL, and the highest prevalence of delta and gamma zones. The gamma zone was defined as the region at the optic disk border without Bruch's membrane (BM)^[8]. Within the area without BM, the delta zone corresponded to the region of the elongated and thinned peripapillary scleral flange, located between the optic disk border and the merging line of the optic nerve dura mater with the posterior sclera^[10]. When the AL was greater than 26.5 mm, the prevalence of gamma and delta zones increased steeply^[28]. Previous studies found a correlation between the size of the gamma region and the delta region;

that is, the wider the horizontal diameter of the gamma, the wider the diameter of the delta region^[17]. Jonas *et al*^[29] found that BM was actively produced and elongated during the process of axial myopization. With the axial elongation and the deformation of PS, the backward pull led to an elongation and thinning of the underlying scleral tissue. While BM may not be markedly stretchable, it is not directly connected with the sclera and may slip away from the optic disk border^[17]. Therefore, it is believed that the development and enlargement of the gamma zone constitutes the early stage of high myopia. With the progression of high myopia, the backward pull affects the peripapillary scleral flange, leading to thinning and expansion of the delta region. Increasing age and AL are relevant risk factors related to the appearance of pathologic alterations in highly myopic patients^[30-32]. It is likely that excessive axial elongation may trigger stress in the posterior that may lead to local or diffuse degeneration of the sclera and/or retina, and these degenerative changes can induce pathological changes. The results of our study revealed that the diameters of the gamma zone, DFD, angle kappa and VDA were mainly related to the AL and/or age. Our study also showed that there was a significant difference in the delta horizontal diameter between the PS without MTM group and the PS with MTM group, even after AL and age correction. Therefore, although axial elongation is generally

believed to play a key role in these degenerative changes^[33], AL is not by itself the only indicator of myopia given that PS has been reported in eyes with high myopia^[34]. Even though PS may not be the primary factor, its appearance does determine more severe alterations and a higher prevalence of myopic maculopathy. Ohno-Matsui *et al*^[35] found that the presence of MTM was more frequent among eyes with irregular, asymmetric staphylomas. Fernandez-Vega *et al*^[36] considered that the RPE alterations, neurosensory retinal detachment, retinoschisis, optic disk and visual field damage were all more common in eyes with PS than no PS eyes. Based on previous studies, we found that, in MTM eyes, there were other factors, in addition to AL and age in the gamma zone, DFD and the distance between the fovea and outer border of the gamma zone, that played a role in the pathogenesis. We speculated it may be related to the characteristic of the PS. However, it requires further investigation whether the difference in the type and location of PS affects the pull force on the eyeball and results in different fundus lesions.

Our study showed that the horizontal diameter of the gamma region was relatively large in the PS with MTM group, indicating that, with lengthening of the AL and progression of the disease, the area of the gamma zone also expanded. However, the largest horizontal diameter of the delta region was in the PS without MTM group, and that of the PS with MTM group was relatively smaller. These findings are mostly new and cannot be directly compared with the results obtained in previous investigations. We speculated on the possible mechanism of high myopia; that is, early on, the gamma and delta zones increase uniformly with progression of the disease, and then the eye shape changes with an increase in the AL, age, and incidence of PS. When the local force of the eyeball is evenly distributed, the gamma and delta regions can progress synchronously and, therefore, a large gamma zone corresponds to a large delta region. In this case, the risk of developing MTM is lower. When the backward pull of the eyeball is uneven, the gamma area may expand and widen, while the delta area does not change significantly, which may lead to the occurrence and progression of MTM. This case suggests that the shape of PS may be a high-risk factor for MTM.

The main limitation of our study is that it was a cross-sectional study and, therefore, we could not obtain data on the dynamic process. Hence, other possibilities may exist. From the progression of no PS to PS without MTM, the eye is subjected to a greater pull force, but the sclera tissue still has resistance to protect it from developing fundus lesions. In this case, the delta area is the largest. However, when the pull force is large enough to exceed the load capacity of the eyeball tissue, MTM emerges. Fortunately, the appearance of MTM reduces the pull force on the eyeball, and the delta area becomes relatively

small. Additionally, our results could have been influenced by measurement errors.

In conclusion, morphological features changed most significantly in the patients with PS and MTM. In different stages of high myopia patients, characteristics of the gamma and delta zones changed inconsistently. In comparison among the three subtypes of MTM patients, the diameters of the gamma zone and DFD in the MRS group were the highest. Furthermore, we found that PS, AL and age had different roles in determining the morphological features of these patients. Understanding these morphological features and affecting factors may provide hints about the pathogenesis of the parapapillary gamma and delta zones, and potentially about the process of myopization.

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