Myopia-Related Fundus Changes in Singapore Adults With High Myopia

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• PURPOSE: To examine the pattern of myopia-related macular and optic disc changes in Singapore adults with high myopia (spherical equivalent ≤−6.00 diopters).
• DESIGN: Asian adults with high myopia from 3 population-based surveys.
• METHODS: Adults 40 years and older (n = 359) with high myopia were pooled from 3 population-based surveys in Singapore Asians: (1) the Singapore Prospective Study Program (SP2, n = 184); (2) the Singapore Malay Eye Study (SiMES, n = 98); and (3) the Singapore Indian Eye Study (SINDI, n = 77). All study participants underwent standardized refraction and fundus photography, and SiMES and SINDI subjects also completed ocular biometry measurements. Myopia-related macular (posterior staphyloma, lacquer cracks, Fuchs spot, myopic chorioretinal atrophy, and myopic choroidal neovascularization) and optic disc (optic nerve head tilt, optic disc dimensions, and peripapillary atrophy) changes were evaluated.
• RESULTS: The most common myopia-related macular finding in adults with high myopia was staphyloma (23%), followed by chorioretinal atrophy (19.3%). There were few cases of lacquer crack (n = 6, 1.8%), T-sign (n = 6, 1.8%), retinal hemorrhage (n = 3, 0.9%), active myopic choroidal neovascularization (n = 3, 0.9%), and no case of Fuchs spot. The most common disc finding associated with high myopia was peripapillary atrophy (81.2%), followed by disc tilt (57.4%). Staphyloma and chorioretinal atrophy increased in prevalence with increasing age, increasing myopic refractive error, and increasing axial length (all $P < .001$). Ethnicity comparisons demonstrated the highest proportion of staphyloma ($P = .04$) among Malays, the highest proportion of peripapillary atrophy ($P = .01$) and disc tilt ($P < .001$) among Chinese, and the largest cup-to-disc ratio ($P < .001$) among Indians.
• CONCLUSIONS: Staphyloma and chorioretinal atrophy lesions were the most common fundus findings among Asian adults with high myopia. In this population, tilted discs and peripapillary atrophy were also common, while choroidal neovascularization and Fuchs spot were rare. In contrast with Singapore teenagers, in whom tilted disc and peripapillary atrophy were common while staphyloma and chorioretinal atrophy were rare, pathologic myopia appears to be dependent on the duration of disease and, thus, age of the individual. (Am J Ophthalmol 2013;155: 991–999. Crown Copyright © 2013 Published by Elsevier Inc. All rights reserved.)

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PATHOLOGIC MYOPIA, DEFINED AS PRESENCE OF a spectrum of myopia-related retinal and optic disc changes, is a leading cause of visual impairment and blindness in Asian countries.[1–3] The socioeconomic impact of blindness and visual impairment from myopia and high myopia is considerable, as it typically affects individuals during their productive years.[1]

In the Australian Blue Mountains Eye Study, the prevalence of myopia in excess of −5.00 diopters (D) was 2.49% in their cohort of 3654 white population 49 years or older, myopic retinopathy was 1.2%.[1] The Beijing Eye Study found a higher prevalence of myopia in excess of −5.00 D, at 3.29% among 4439 adults 40 years or older, at 2.64% with myopia in excess of −6.00 D, with overall myopic retinopathy prevalence at 3.1%.[2] In rural China, the Handan Eye Study conducted on 6830 individuals 30 years and older found myopic retinopathy prevalence to be 0.9%.[4] More recently, the Hisayama Study, conducted on a Japanese cohort (n = 1892) older than 40 years, found the prevalence of myopic retinopathy to be 1.7%.[5] In a clinic setting, a Japanese study of highly myopic individuals with greater than −8.00 D of spherical refractive myopia, several progressive patterns of pathologic myopia were seen—the initial finding of tessellated fundus, followed by staphyloma developing at approximately 40 years of age, and later with progression to diffuse atrophy and lacquer cracks.[3] The number of cases from a single population-based survey is limited while clinic-based studies are not representative of the population. Although

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pathologic myopia typically progresses with increasing age and higher degrees of myopia,[1–7] few studies have evaluated the pattern of pathologic myopia lesions and associations with axial length and refractive error.

Our aim is to examine the pattern of myopia-related macular and optic disc changes in Singapore adults with high myopia identified from population-based studies, and correlate these findings with refractive error and axial length.

METHODS

WE INCLUDED SINGAPORE ADULTS 40 YEARS AND OLDER with high myopia (spherical equivalent [SE] ≤−6.00 D) from 3 population-based surveys: (1) the Singapore Prospective Study Program (SP2), (2) the Singapore Malay Eye Study (SiMES), and (3) the Singapore Indian Eye Study (SINDI). The selection of adults 40 years and older with high myopia (SE ≤−6.00 D) was done in order to increase the yield of those with fundus changes and still allow for comparison with other published population-based studies. The study followed the principles of the Declaration of Helsinki, with ethics approval obtained from the Singapore Eye Research Institute Review Board. Written consent was obtained from each study participant.

The SP2 involved inviting participants of population-based surveys conducted in Singapore between 1982 and 1998 for repeat examinations between 2004 and 2007. The protocol has been described previously.[8,9] All 3 major ethnic groups were represented, and there was a purposeful disproportionately larger representation of ethnic minorities (Malays and Asian Indians). A total of 5157 subjects underwent a clinical examination that included systemic and ocular assessment, and 4108 underwent fundus photography. SINDI and SiMES were complementary studies with identical methodology. A total of 3280 Malay adults[10] and 3400 Indian adults[11,12] between the ages of 40 and 80 years were recruited.

After informed consent, all subjects from the included projects underwent a detailed and standardized examination, which included measurements of height, weight, blood pressure, and heart rate, and a comprehensive ocular examination.

• **VISUAL ACUITY MEASUREMENT AND REFRACTION:** The presenting visual acuity was measured using the logarithm of the minimal angle of resolution (logMAR) chart (Lighthouse International, New York, New York, USA) at 4 meters, with subjects wearing their current optical correction (glasses or contact lenses). If the largest number could not be identified at 4 meters, the chart was brought closer to the subject, then counting fingers, hand motion, or light perception vision was assessed.

Autorefraction and keratometry were obtained using the Canon RK-5 Autorefractor Keratometer (Canon Inc Ltd, Tokyo, Japan). Refraction was refined by certified study optometrists, and subjects' best-corrected visual acuity in logMAR scores were recorded. SE was calculated as the sum of the spherical power and half of the cylindrical power. The IOL Master (Carl Zeiss Meditec AG, Jena, Germany) was used for ocular biometry that included axial length measurements.

• **FUNDUS PHOTOGRAPHY:** For all studies, a 45-degree digital retinal camera was used. SP2 fundus photographs were obtained after pupillary dilation with tropicamide 1% and phenylephrine 2.5%, using Canon CR-DGi with Canon EOS 10D SLR backing (Canon Inc, Tokyo, Japan). For the SICC, SiMES, and SINDI studies fundus photographs were obtained without preceding pupillary dilation. Canon CR-DGi with the Canon EOS 10D or 20D SLR backing (Canon Inc) system was used for SICC and SiMES, while the Canon CR-DGi with Canon EOS 20D or 40D SLR backing (Canon Inc) was used in the SINDI study systems.

Two fields of each eye were photographed, with one centered at the optic disc and another centered at the fovea, following the Early Treatment for Diabetic Retinopathy Study standard photograph numbers 1 and 2. The high-resolution digital photographs were stored and retrieved digitally on the Singapore Eye Research Institute server.

Fundus photographs were viewed using Photoshop CS5 (Adobe Systems Inc, San Jose, California, USA). An ophthalmologist and trained grader (L.C.), masked to participant characteristics, performed detailed assessment of the fundus photographs using a standardized grading sheet (described in the next section). Because of disc tilt that is often observed in the myopic eye, the longest and shortest disc diameters (orthogonal to one another, irrespective of vertical or horizontal planes) were measured using the pixel ruler. Inter-grader reliability was accessed with additional grading of 50 randomly selected eyes by trained graders (H.H. and V.K.), and reliability was found to be excellent (intraclass correlation coefficient of 0.73). Any discrepancies were reviewed by 2 or more graders including ophthalmologists G.C. and K.O.M.

• **GRADING SHEET:** The grading sheet was designed to capture all aspects of myopia-related fundus changes. First, the photograph quality was assessed. Staphyloma was determined by visualizing the border of the ectasia, then its location and type were documented based on the Curtin classification.[13] Lacquer crack presence, location, and number were evaluated. With regard to peripapillary atrophy, Curtin and Karlin classification was used.[14] Direction of disc tilt was determined, then the longest and shortest disc diameters were measured using a pixel ruler. The ratio between the longest and shortest disc diameters was calculated and used to compare degree of disc tilt. Direct pixel measurements were not used since there could be magnification differences with respect to refractive error.

The horizontal cup-to-disc ratio was also assessed by the grader. The presence of a T-sign (bifurcation of the central retinal vessels beyond the lamina cribosa),[1,15] Fuchs spot (small pigmented subretinal lesion in the posterior pole, representing the scar phase of myopic choroidal neovascularization),[16] active myopic choroidal neovascularization (CNV), and hemorrhage were also evaluated. Chorioretinal atrophy was characterized based on location and size. Myopic macular chorioretinopathy was given a grade based on Avila classifications (M0-M5)[16]: M0 representing normal fundus, M1 representing fundus pallor and tessellation, M2 representing M1 plus posterior pole staphyloma, M3 representing M2 plus lacquer cracks, M4 representing M3 plus focal deep chorioretinal atrophy, and M5 representing M3 plus large geographic area of deep chorioretinal atrophy.[16]

• **STATISTICAL ANALYSIS:** One eye per subject was chosen based on the highest myopic refractive error. We examined the association of pathologic myopia findings with age, sex, ethnicity, SE, and axial length (AL). The relationship was assessed using the χ^2 test (Fisher exact test if more than 20% of cells have expected count of less than 5) or analysis of variance. SE and AL were also analyzed as continuous variables. Multivariate linear regression and multivariate logistic regression were performed to determine the associations between pathologic myopia findings and SE or AL, with the former as a dependent variable and the latter as independent variables, adjusted for confounders. Two-tailed P values of $<.05$ were considered statistically significant. STATA version 11.0 (StataCorp LP, College Station, Texas, USA) was used for all statistical analyses.

RESULTS

THERE WERE A TOTAL OF 424 SUBJECTS OLDER THAN 40 years and with ≤−6.00 D of myopia from the 3 population-surveys, of which 359 were identified to have fundus photographs. This represents 84.7% of all subjects older than 40 years and with ≤−6.00 D of myopia in the 3 population surveys. Of the subjects with fundus photographs, 332 subjects (92.5%) had gradable photographs. The eye with the highest magnitude of myopic refractive error was used for analyses. Table 1 shows subject distribution with respect to refractive error (−6 to −7.99 D, −8 to −9.99 D, and ≤−10 D), age (40-49 years, 50-59 years, and >60 years), sex, and ethnicity. There was a trend toward higher myopic refractive error with increasing age, though it was not statistically significant ($P = .06$). Sex and ethnicity did not seem to differ with respect to degree of myopia.

The most common myopic fundus finding was staphyloma (76/331; 23.0%), followed by chorioretinal atrophy (64/331; 19.3%) (Table 2). The most common disc finding associated with high myopia is peripapillary atrophy (268/330; 81.2%), followed by disc tilt (190/331; 57.4%). Temporal peripapillary atrophy is the most common (51%; 137/268, data not shown). The most common Avila myopic macular chorioretinopathy grade among adults with high myopia is M1 (196/330; 59.4%), followed by M2 (75/330; 22.7%).

TABLE 1. Distribution of Singapore Adults With High Myopia Based on Age, Sex, Race, and Refractive Error

	Number of Subjects	−6 to −7.99 D n (%)	−8 to −9.99 D n (%)	<−10.0 D n (%)
All	332	191 (57.5)	80 (24.1)	61 (18.4)
Age (y)				
40-49	177	112 (63.3)	32 (18.1)	33 (18.6)
50-59	114	61 (53.5)	33 (28.9)	20 (17.5)
60+	41	18 (43.9)	15 (36.6)	8 (19.5)
Sex				
Male	147	89 (60.5)	36 (24.5)	22 (15.0)
Female	185	102 (55.1)	44 (23.8)	39 (21.1)
Race				
Chinese	135	80 (59.26)	36 (26.67)	19 (14.07)
Malay	104	56 (53.85)	25 (24.04)	23 (22.12)
Indian	89	54 (60.67)	17 (19.10)	18 (20.22)
Other	4	1 (25.00)	2 (50.0)	1 (25.00)

D = diopters.

Staphyloma ($P < .001$), peripapillary atrophy ($P = .02$), disc tilt ($P = .03$), and chorioretinal atrophy ($P < .001$) increased in prevalence with increasing age (Table 2). Avila grading of myopic macular chorioretinopathy also advanced with age ($P < .001$). Lacquer crack (6/333; 1.8%), T-sign (6/333; 1.8%), hemorrhage (3/333; 0.9%), CNV (3/333; 0.9%), and Fuchs spot (0/333) were observed in few subjects. There was a trend of decreasing cup-to-disc ratio with increasing age ($P = .09$).

In general, sex did not alter the prevalence of pathologic myopia findings; however, several differences with respect to ethnicity were seen. Malays were noted to have higher prevalence of staphyloma ($P = .04$, with borderline significance); Chinese were noted to have higher prevalence of peripapillary atrophy ($P = .01$), disc tilt ($P < .001$), and largest ratio between the longest to shortest disc diameters ($P = .006$); and Indians had the largest cup-to-disc ratio ($P < .001$).

Table 3 illustrates the relationship between pathologic findings and SE. The risk of staphyloma increased by 1.56 times for each diopter of increasing myopic refractive error ($P < .001$), adjusting for all other confounders in multivariate logistic regression analysis. Similarly, chorioretinal atrophy increased 1.68 times for each diopter of increasing myopic refractive error ($P < .001$). Multivariate logistic regression analyses for comparing peripapillary atrophy and disc tilt to SE were not as revealing. Lacquer crack increased 1.37 times for each diopter of increasing myopic refractive error ($P = .002$, data not shown) and retinal

TABLE 2. Summary of Myopic Fundus Changes Among Singapore Adults With High Myopia by Age, Sex, and Race (n = 332)

	Staphyloma		Peripapillary Atrophy		Disc Tilt		Chorioretinal Atrophy		Myopic Macular Chorioretinopathy						
	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	M0	M1	M2	M3	M4	M5
All	331	76 (23.0)	330	268 (81.2)	331	190 (57.4)	331	64 (19.3)	330	33 (10.0)	196 (59.4)	75 (22.7)	3 (0.9)	18 (5.5)	5 (1.5)
Age (y)															
40-49	176	23 (13.1)	176	152 (86.4)	177	106 (59.9)	177	20 (11.3)	175	22 (12.6)	123 (70.3)	20 (11.4)	2 (1.1)	7 (4.0)	1 (0.6)
50-59	114	35 (30.7)	113	83 (73.5)	114	69 (60.5)	113	28 (24.8)	114	10 (8.8)	59 (51.8)	35 (30.7)	1 (0.9)	6 (5.3)	3 (2.6)
60+	41	18 (43.9)	41	33 (80.5)	40	15 (37.5)	41	16 (39.0)	41	1 (2.4)	14 (34.1)	20 (48.8)	0	5 (12.2)	1 (2.4)
P_{trend}		<.001		.02		.03		<.001				<.001[a]			
Sex															
Male	146	33 (22.6)	147	123 (83.7)	147	86 (58.5)	146	28 (19.2)	146	12 (8.2)	90 (61.6)	35 (24.0)	1 (0.7)	6 (4.1)	2 (1.4)
Female	185	43 (23.2)	183	145 (79.2)	176	104 (56.5)	185	36 (19.5)	184	21 (11.4)	106 (57.6)	40 (21.7)	2 (1.1)	12 (6.5)	3 (1.6)
P value[a]		.89		.31		.72		.95				.82			
Race															
Chinese	134	24 (17.91)	133	117 (87.97)	135	94 (69.63)	134	27 (20.15)	135	14 (10.4)	84 (62.2)	25 (18.5)	1 (0.7)	6 (4.4)	5 (1.9)
Malay	104	34 (32.69)	104	84 (80.77)	103	57 (55.34)	104	27 (25.96)	102	6 (5.9)	58 (56.9)	32 (31.4)	1 (1.0)	5 (4.9)	0
Indian	89	17 (19.10)	89	63 (70.79)	89	38 (42.70)	89	10 (11.24)	89	13 (14.6)	51 (57.3)	17 (19.1)	1 (1.1)	7 (7.9)	0
Other	4	1 (25.0)	4	4 (100.0)	4	1 (25.00)	4	0	4	0	3 (75.0)	1 (25.0)	0	0	0
P value[a]		.04		.01		<.001		.06				.19			

[a]*P* value for χ^2 test or Fisher exact test.

TABLE 3. Summary of Myopic Fundus Changes Among Singapore Adults With High Myopia by Spherical Equivalent (n = 332)

	Staphyloma		Peripapillary Atrophy		Disc Tilt		Chorioretinal Atrophy		Myopic Macular Chorioretinopathy			
										M0	M1	M2 and more
SE group	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	n (%)	n (%)
All	331	76 (23.0)	330	268 (81.2)	331	190 (57.4)	331	64 (19.3)	330	33 (10.0)	196 (59.4)	110 (30.6)
−6 to −7.99D	190	21 (11.1)	191	163 (85.3)	191	100 (52.4)	191	10 (5.2)	191	29 (15.2)	131 (68.6)	31 (16.2)
−8 to −9.99D	80	19 (23.8)	78	61 (78.2)	79	50 (63.3)	80	20 (25.0)	80	4 (5.0)	47 (58.8)	29 (36.3)
<−10.0D	61	36 (59.0)	61	44 (72.1)	61	40 (65.6)	60	34 (56.7)	59	0	18 (30.5)	41 (69.5)
P_{trend}	<.001		.05		.09		<.001				<.001[d]	
SE (D)[a], *OR (95% CI),* P												
Unadjusted[b]	1.51 (1.34, 1.71)	<0.001	0.91 (0.83, 1.00)	0.06	1.03 (0.95, 1.15)	0.47	1.54 (1.36, 1.75)	<0.001				
Multivariate adjusted[c]	1.56 (1.37, 1.77)	<0.001	0.92 (0.84, 1.02)	0.1	1.05 (0.96, 1.15)	0.26	1.68 (1.46, 1.95)	<0.001				

CI = confidence interval; D = diopters; OR = odds ratio; *P* = *P* value; SE = spherical equivalent.

[a]Absolute value of SE.

[b]Unadjusted: univariate logistic regression with SE as risk factor and myopic retinopathy factors as dependent variable.

[c]Multivariate adjusted: adjusted for age, sex, and race.

[d]*P* value for χ^2 test.

TABLE 4. Summary of Myopic Fundus Changes Among Singapore Adults With High Myopia by Axial Length (n = 144)

	Staphyloma		Peripapillary Atrophy		Disc Tilt		Chorioretinal Atrophy		Myopic Macular Chorioretinopathy			
										M0	M1	M2 and more
AL group	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	n (%)	n (%)
All	144	38 (26.4)	144	107 (74.3)	144	73 (50.7)	144	27 (18.8)	143	15 (10.5)	80 (55.9)	48 (33.6)
1st Quartile (22.64-25.73mm)	36	6(16.7)	36	22 (61.1)	36	11 (30.6)	36	2 (5.6)	36	10 (27.8)	18 (50.0)	8 (22.2)
2nd Quartile (25.74-26.56mm)	37	4 (10.8)	37	30 (81.1)	37	21 (56.8)	37	2 (5.4)	37	3 (8.1)	27 (73.0)	7 (18.9)
3rd Quartile (26.57-27.67mm)	35	4 (11.4)	35	28 (80.0)	35	21 (60.0)	35	3 (8.6)	35	2 (5.7)	26 (74.3)	7 (20.0)
4th Quartile (27.68-31.69mm)	36	24 (66.7)	36	27 (75.0)	36	20 (55.6)	36	20 (55.6)	35	0	9 (25.7)	26 (74.3)
P_{trend}		<.001		.26		.12		<.001			<.001[c]	
AL (mm), OR (95% CI), *P*												
Unadjusted[a]	1.89 (1.43, 2.50)	<0.001	1.14 (0.91, 1.41)	0.26	1.16 (0.96, 1.41)	0.12	2.56 (1.76, 3.73)	<0.001				
Multivariate adjusted[b]	2.08 (1.53, 2.82)	<0.001	1.09 (0.88, 1.36)	0.43	1.14 (0.93, 1.39)	0.21	3.13 (1.98, 4.95)	<0.001				

AL = axial length; CI = confidence interval; OR = odds ratio.

[a]Unadjusted: univariate logistic regression with AL as risk factor and myopic retinopathy factors as dependent variable.

[b]Multivariate adjusted: adjusted for age, sex, and race.

[c]*P* value for χ^2 test.

hemorrhage increased 1.57 times for each diopter of increasing myopic refractive error ($P = .03$, data not shown). The ratio between the longest to shortest disc diameter (a marker for disc tilt) increased by 0.02 for each diopter of increasing myopic refractive error ($P < .001$, data not shown). This shows that the nerve tends to tilt more with increasing myopic refractive error. Logistic regression also showed a trend of decreasing optic nerve head cup-to-disc ratio ($P = .06$) with increasing myopic refractive error (data not shown).

When refractive error was divided into categories (−6 to −7.99 D, −8 to −9.99 D, and ≤−10 D), staphyloma ($P < .001$), chorioretinal atrophy ($P < .001$), peripapillary atrophy ($P = .05$), lacquer cracks ($P < .001$), T-sign ($P = .01$), and CNV ($P = .04$) increased in prevalence with increasing myopic refractive error (Table 3 shows the first 3 results; others are not shown). Avila grading of myopic macular chorioretinopathy also advanced with respect to increasing myopic refractive error in terms of both trend and SE groups (Table 3, $P < .001$).

Using AL data from the SiMES and SINDI studies, 144 subjects were analyzed for myopic fundus changes with respect to AL (Table 4). The risk of staphyloma increased by 2.08 times for each 1 mm increase in AL ($P < .001$) in the multivariate adjusted logistic regression analysis. Similarly, risk of chorioretinal atrophy ($P < .001$) increased by 3.13 times for each 1 mm increase in AL. Risk of lacquer cracks ($P = .01$) increased by 2.03 times for each 1 mm increase in AL (data not shown). The same 3 findings maintained statistical significance when AL was divided into 4 quartile groups (22.64-25.73 mm, 25.74-26.56 mm, 26.57-27.67 mm, 27.68-31.69 mm) (Table 4). Higher Avila grading scores were associated with longer AL ($P < .001$) (Table 4). There was a borderline trend of decreasing cup-to-disc ratio with increasing AL (logistic regression P value of .06). There was an increasing ratio between longest to shortest disc diameter (increasing degree of tilt) with increasing AL ($P = .02$ for trend and $P = .01$ for multivariate adjusted logistic regression analysis).

DISCUSSION

AMONG SINGAPORE ADULTS WITH HIGH MYOPIA FROM population-based surveys, fundus pallor and tessellation (90%), peripapillary atrophy (81.2%), and optic disc tilt (57.4%) are very common findings. The major pathologic findings are staphyloma (23.0%) and chorioretinal atrophy (19.3%). Lacquer crack (1.8%) and T-sign (1.8%) are present in a few individuals. Fuchs spot (0%) and choroidal neovascularization (0.9%) are relatively rare complications of high myopia. The presence of staphyloma and chorioretinal atrophy, in addition to peripapillary atrophy and tilted discs, in Singapore adults contrasts with the results of our Singapore teenager study, whereby staphyloma and chorioretinal atrophy were not present and only peripapillary atrophy and tilted discs were common in young subjects with high myopia.[6] Thus, pathologic myopia may be a disease that is dependent on the duration of disease and there is a lag phase from the onset of high myopia, often in the teenage years, to the presence of common macular lesions such as staphyloma and chorioretinal atrophy in middle-aged to elderly adults. Although we did not collect data in regard to the duration of myopia, we still believe that age is likely to be a surrogate for the duration of myopia as the age of onset of myopia in Singapore is in childhood and the teenage years, with few cases of adult-onset myopia. This could explain why staphyloma and chorioretinal atrophy were not present in the younger generation,[6] as they were children and with a relatively short duration of high myopia.

Our series found staphyloma in 76 subjects (23.0%) 40 years and older with myopic refractive error greater than −6.00 D. This percentage is lower than that seen in the Blue Mountains Eye Study, where the average SE was −6.10 D, and 35 of 67 eyes (52.2%) had staphyloma.[1] Our study found that staphyloma increased in prevalence with respect to increasing age, increasing myopic refractive error, and increasing axial length. In a Japanese cohort with myopia greater than −8.00 D or axial length greater than 26.5 mm, staphyloma was identified in 90% of subjects and in 96.7% of those 50 years of age and older.[17] Progression of type II staphyloma to type IX was seen, along with an associated increased incidence of lacquer cracks, supporting the theory of progressive mechanical expansion of the globe.[17] In a cross-sectional study in Hong Kong, highly myopic eyes with the presence of posterior pole lesion were reported to have significantly longer AL (28.84 vs 26.59 mm) and greater degree of myopia (−16.8 D vs −9.4 D).[18] In the Shihpai Eye Study in Taiwan, highly myopic eyes with maculopathy had a greater myopic degree (−12.8 vs −7.6 D, $P < .001$) than those without.[19] Understanding the associations of myopic refraction and AL with staphyloma is important from a clinical perspective, as vitreoretinal interface pathology in pathologic myopia with posterior staphyloma encompasses a spectrum of conditions whose baseline functionality, prognosis, rate, and amount of progression vary significantly.[20]

Chorioretinal atrophy is an area of well-circumscribed chorioretinal degeneration in the posterior pole. Chorioretinal atrophy was seen in 64 subjects (19.3%) in our study. This number is lower than in the Japanese study, where diffuse chorioretinal atrophy was seen in 491 eyes (60.9%) and patchy chorioretinal atrophy in 163 eyes (20.2%).[3] The difference is mainly attributable to higher refractive error among the Japanese subjects from a high myopia clinic. Of our subjects with greater than −6.00 D of myopic refractive error, 42.3% had refractive error greater than −8.00 D, and within this subgroup, 39.0% had chorioretinal atrophy. Chorioretinal atrophy is also more prevalent in older adults and in adults with more severe refractive error and longer axial length. In the Beijing Eye Study, increased prevalence of myopic

chorioretinopathy was associated with increasing myopic refractive error, and a significant rate of progression was seen even at 5 years.[7] Posterior staphyloma was reported to be a causative factor for chorioretinal atrophy.[3] However, the correlation between posterior staphyloma and chorioretinal atrophy was not high, possibly because of the small number of cases in our study.

We identified only 6 subjects (1.8%) with lacquer cracks, but more so in those with higher myopic refractive error ($P < .001$) and longer AL ($P = .04$). This suggests that these breaks in the Bruch membrane are highly associated with advanced myopia and axial elongation. High prevalence of lacquer cracks (29.1%) was found in a clinic-based Chinese study (n = 337 subjects or 604 eyes with SE ≤−6.0 D), where both fluorescein angiography and indocyanine green angiography were used.[21] It is likely that our study represents an underestimation of the true prevalence of lacquer cracks because of not using angiographic diagnostic tools. Another imaging modality for detecting lacquer cracks that could be considered for future studies would be autofluorescence.

In our study, only 3 subjects had definite CNV with macular hemorrhage. The rate of CNV was much higher in the Japanese study, with more severe myopic refractive error seen in 91 eyes (11.3%) at initial presentation.[3] In addition, early CNV could have been missed from our study by examining fundus photographs without the aid of fluorescein angiography. Fuchs spot was not observed in eyes included in our study. One case of Fuchs spot was seen in the contralateral eye with the less severe myopic SE. An explanation for the infrequent observation of Fuchs spot could be its transient nature, which typically follows active CNV and could later be enveloped by chorioretinal atrophy.

Peripapillary atrophy is the most common finding associated with the myopic fundus in our study, observed in 268 subjects (81.2%). Optic disc tilting is thought to be more common in those with astigmatism or high refractive error, particularly myopia.[22] Disc tilt was observed in 190 subjects (57.4%) in our study. A smaller cup-to-disc ratio, another optic disc feature associated with high myopia, was also observed in subjects with higher myopic refractive error in our study, corroborating findings by Wu and associates,[23] Jonas and Dichtl,[24] Xu and associates,[2] and Nonaka and associates.[25]

Avila grade increases with age, myopic refractive error, and longer AL. In our study, the most common Avila myopic macular chorioretinopathy grade was M1, followed by M2. This result differs from those identified in the clinic-based Chinese study in Guangzhou where subjects ranging from 8- to 88-year-olds with myopia greater than −6.00 D presented with M3 Avila grade most commonly, followed by M4. The difference could likely be explained by study selection criteria, where the clinic-based cohort may have more pathology, and angiographic diagnostic tools allowing for improved identification of lacquer cracks, a requirement for the M3 grade.

The clinical implications of the ethnicity differences are unclear, and the only visually blinding complication of pathologic myopia found to be of borderline significance is staphyloma among Malays ($P = .04$). This finding may be explained by sample variation, given the relatively small number of subjects with high myopia in each study ethnic group. Other identified ethnic variations with respect to optic nerve appearance are interesting but may not have visually significant consequences.

Our study has considerable implications. This study comprised a large collection of highly myopic subjects who are fairly representative of the general population; this is in contrast with many previous studies of highly myopic subjects from the clinic. Given the alarming rates of myopia in Asia, there will be an enormous adult population at high risk of developing pathologic myopia. We have documented the 2 most common fundus findings, staphyloma and chorioretinal atrophy, in middle-aged adults. This contrasts with our findings of optic disc tilt and peripapillary atrophy without staphyloma or chorioretinal atrophy in younger Singapore teenagers with high myopia.[7] Finally, the increasing prevalences of staphyloma and chorioretinal atrophy with more severe refractive error in our study emphasizes that preventive strategies to slow the progression of myopia in childhood to prevent the eventual development of extreme myopia in adulthood are important.

There are several limitations to this retrospective study. Our study is cross-sectional in nature and the temporal sequence of progression of lesions cannot be documented. Hayashi and associates found that 40.6% of highly myopic eyes (greater than −8.00 D) showed progression over a mean follow-up period of 12.7 years.[3] Because of the absence of stereophotographs, clues such as presence of a rim or sharp bends in retinal vessels were used to judge whether staphyloma was present.[13] The lack of peripheral and stereoscopic views may have limited the detection and characterization of staphylomata. Some staphylomata are so large that the edge of the ectasia may not be incorporated into the photograph, and thus could be missed and the prevalence underestimated. Second, lacquer cracks can be subtle and missed in fundus photographs without the use of fluorescein angiography or indocyanine green angiography. In addition, fundus examinations of the peripheral retina were not performed and peripheral retinal lesions associated with high myopia were not assessed in our study. Lastly, optical coherence tomography (OCT) was not performed on the study subjects, and findings such as macular retinoschisis and macular hole could also have been missed using fundus photographs alone. Most recently, spectral-domain OCT has been used to study choroidal neovascularization in pathologic myopia, and choroidal thinning has been shown to be more prominent in eyes with myopic CNV.[26] Participants who responded could be different from those who did not, leading to selection bias and underestimation of true prevalence. By the same token, participants with ungradable photographs

could have had worse disease, again leading to underestimation of true prevalence.

Future prospective, longitudinal studies using fluorescein angiography and spectral-domain OCT technologies may better delineate the evolution of pathologic myopia. Clinically, ophthalmologists should be aware that the pattern of pathologic myopia may differ across ages, severity of refractive errors, and ethnic groups. High-risk adults who are older with more severe myopia could be identified for regular screening and early management.

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Biosketch

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