Prevalence and Associated Risk Factors of Myopic Maculopathy in Elderly Chinese: The Shihpai Eye Study

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Purpose. To assess the prevalence and associated risk factors of myopic maculopathy in an elderly Chinese population in Taiwan.

Methods. Population-based, cross-sectional study. A total of 1361 Chinese aged 65 years or older residing in Shihpai, Taipei, Taiwan, underwent a detailed ophthalmic examination. Of the 1361 participants, 1058 subjects had at least one gradable fundus photograph and were recruited for analysis. High myopia was defined as spherical equivalent of less than –6.0 diopter (D) in the phakic eyes or axial length greater than 26.5 mm in pseudophakic or aphakic eyes. Myopic maculopathy was defined as the appearance of lacquer cracks, focal area of deep choroidal atrophy and macular choroidal neovascularization, or geographic atrophy in the presence of high myopia.

Results. The prevalence of high myopia was 4.2% (44/1058). Signs of myopic maculopathy were present in 32 (72.7%) of the 44 high myopics, representing a prevalence of 3.0% (95% confidence interval, 2.0%–4.0%). Subjects with high myopia with myopic maculopathy had higher systolic blood pressure than those without maculopathy (146.4 ± 16.2 mm Hg vs. 127.0 ± 15.9 mm Hg, $P = 0.001$), and the difference persisted ($P = 0.018$) after adjustment for age, sex, smoking, body mass index, diastolic blood pressure, educational levels, alcohol drinking, and histories of diabetes or taking anti-hypertension medication. Of the 65 high myopic eyes, eyes with maculopathy had a greater myopic degree (–12.8 ± 5.1 D vs. –7.6 ± 1.5 D, $P = 0.001$) and poorer corrected visual acuity (logMAR 0.72 ± 0.6 vs. 0.27 ± 0.2, $P = 0.001$) than those without.

Conclusions. The prevalence of high myopia and myopic maculopathy in this elderly Chinese population group was high. Of the major risk factors examined, high systolic blood pressure may be associated with myopic maculopathy. (*Invest Ophthalmol Vis Sci.* 2012;53:4868–4873) DOI:10.1167/iovs.12-9919

Myopia is common and its prevalence is increasing worldwide.[1–6] High myopia, defined as spherical equivalent of less than –6 diopters (D) or axial length greater than 26.5 mm,[7,8] constitutes approximately 11% to 14% of cases of myopia.[1,9–11] Of the adolescent myopic population, high myopia may account for up to 20%.[2] High myopia is more common in Asians, compared with European-derived populations.[12] However, recent surveys showed that in the past 30 years, the prevalence of high myopia has increased 8-fold in the United States.[6]

In general, high myopia is bilateral and associated with multiple ocular morbidities such as cataract, glaucoma, and retinal detachment.[13] One of the most important complications is myopic maculopathy, which is a common cause of visual impairment.[12] Myopic maculopathy is defined as the presence of a spectrum of signs including lacquer cracks, posterior staphyloma, patchy atrophy, choridal neovascularization, and geographic atrophy.[14] Because of its earlier onset in the working age population, the expected person-years of blindness for people with myopic maculopathy are 7 years more than for those with glaucoma and 12 years more than for those with diabetic retinopathy or age-related macular degeneration.[15,16] The magnitude of public health impact of myopia-related vision loss is therefore substantial.

However, despite its importance, there are few population-based epidemiological studies of the myopic maculopathy. The purpose of this study was to determine the prevalence and associated risk factors of myopic maculopathy in an elderly Chinese population in Taiwan.

Materials and Methods

Populations and Procedures

The study population and methodology in the Shihpai Eye Study have been described elsewhere.[17] The acquisition and grading of fundus photographs have also been reported.[18] In brief, residents 65 years of age and older in Shihpai, Taipei, Taiwan, were identified from the household registration databank provided by the Household Registration Office. Of the 2045 randomly selected individuals, 1361 (66.6%) participated in the ophthalmic examination. Of the participants, 1105 had photographs taken and 1058 had gradable photographs in at least

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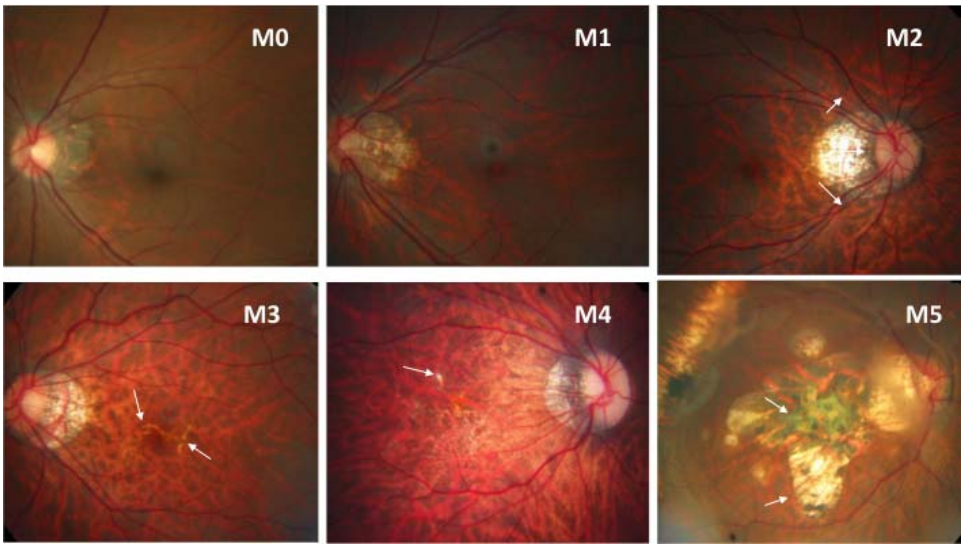

Figure 1. Grading examples of the fundus photographs of myopic maculopathy. **M0**, normal appearing posterior pole; **M1**, tessellation and choroidal pallor pattern in macular area; **M2**, appearance of border of a posterior staphyloma (*arrows*) near disc area; **M3**, yellowish lacquer cracks in Bruch's membrane (*arrow*); **M4**, focal areas of deep choroidal atrophy (*arrow*); and **M5**, geographic areas of atrophy of retinal pigment epithelium and choroids (*lower arrow*), or evidence of choroidal neovascularization in active stage or with fibrosis (*upper arrow*).

one eye. Subjects ($n = 303$) who had no photos or gradable photos in both eyes were older and more likely to have denser lens opacity.[18]

A structured questionnaire was used to collect information on basic demographic data, education, and medical history. The ophthalmic examinations included measurements of visual acuity with Snellen charts at a distance of 6 m, autorefraction (RK-8100; Topcon, Tokyo, Japan), noncontact tonometry (CT-60; Topcon), slit-lamp biomicroscopy (Model BQ900; Haag-Streit, Bern, Switzerland), and indirect ophthalmoscopy (Model 12500; Skaneateles Falls, NY) through a dilated pupil with 1% tropicamide (Alcon, Couvreur, Puurs, Belgium). Lens opacity was graded using slit lamp biomicroscopy with the modified Lens Opacity Classification System (LOCS) III.[19] In addition, ultrasound biometry (AL-1000, Tomey Corporation, Aichi, Japan) was performed for those with pseudophakia or aphakia. Informed consent was obtained from each subject before his or her enrollment in the study. This study was conducted according to the tenets of the Declaration of Helsinki and approved by the institutional review board in Taipei Veterans General Hospital.

Both eyes of the participants were photographed using a 35° monoscopic fundus camera (TRC-50IA; Topcon) at least 30 minutes after pupil dilatation. Two photography fields were taken in each eye, with one centered at the fovea and the other at the optic disc. Blood pressure was measured from the right arm, with the participant in a seated position using manual sphygmomanometer, for three times at least 5 minutes apart. The average of the three measurements were used for analysis. Body height and weight were measured and the body mass index (BMI) was calculated.

Definitions

High myopia was defined as a spherical equivalent of less than –6.0 D in the phakic eyes, low to moderate myopia as a spherical equivalent of –0.5 to –5.9 D, and no myopia as a spherical equivalent of greater than –0.5. In participants with pseudophakia or aphakia, high myopia was defined if axial length was greater than 26.5 mm.[7,8] The grade of myopia was defined according the more severely affected eye for each participant. The grading of myopic maculopathy was done by a retinal specialist (SJC) based on fundus photographs (Fig. 1) and myopic maculopathy was categorized according to the Avilla's grading method[14]: M0, normal appearing posterior pole; M1, tessellation and choroidal pallor pattern in macular area; M2, appearance of a posterior staphyloma; M3, yellowish lacquer cracks in Bruch's membrane; M4, focal areas of deep choroidal atrophy secondary to lacquer cracks or posterior staphyloma; and M5, geographic areas of atrophy of retinal pigment epithelium and choroids, and choroidal neovascularization (CNV; active CNV or fibrosis, or Fuchs' spot). This grading system with step-wise severity level of maculopathy has been shown to be functionally correlated with greater visual impairment in more severe grading after long-term follow-up.[8] In addition, more than 50% of patients with high myopic retinopathy of lacquer cracks alone would lose their vision after 10 years.[8] Therefore, we defined those with maculopathy equal to or greater than M3 as clinically significant myopic maculopathy in this study. When two eyes of a participant were discrepant for the severity of myopic maculopathy, the grade assigned for the participant was that of the more severe eye. Other retinal pathology, such as age-related macular degeneration, epiretinal membrane, or previous retinal detachment surgery, was excluded.

Statistical Analysis

The prevalence of high myopia and myopic maculopathy by age group and sex was expressed in percentages of the study population. The χ^2 test was used for evaluating the trend of prevalence in age groups. The associations of myopic maculopathy with age, sex, education, cigarette smoking, alcohol drinking, BMI, self-reported diabetes, systolic and diastolic blood pressure, and taking anti-hypertension medication were assessed. Multivariate logistic regression analysis was used to obtain adjusted odds ratios (OR) of having myopic maculopathy, allowing for controls of the mutually confounding effects of these potential risk factors. All data analyses were performed using a commercial statistical software package, SPSS 17.0 (Chicago, IL).

Results

There were 44 (4.2%) subjects with high myopia among the 1058 participants with gradable retinal photographs. Twelve high myopics had no myopic maculopathy (three in grade M0, five in grade M1, and four in grade M2). A total of 32 participants (7 in grade M3, 8 in grade M4, and 17 in grade M5) had myopic maculopathy equal to or greater than stage M3, corresponding to a prevalence of 3.0% (95% confidence interval, 2.1%–4.2%). Table 1 presents the distribution of no myopia, low to moderate myopia, and high myopia by sex and

Table 1. Prevalence of No Myopia, Low and Moderate Myopia, and High Myopia by Age and Sex

		No Myopia						Low and Moderate Myopia						High Myopia					
		Men		Women		Total		Men		Women		Total		Men		Women		Total	
Age Groups, y	*n*	*n*	%*	*n*	%*	*n*	%†	*n*	%*	*n*	%*	*n*	%†	*n*	%*	*n*	%*	*n*	%†
65–69	403	189	77.1	115	72.3	304	75.4	50	20.4	36	22.8	86	21.3	6	2.4	7	4.4	13	3.2
70–74	389	180	69.0	94	73.4	274	70.4	72	27.6	30	23.4	102	26.2	9	3.4	4	3.1	13	3.3
75–79	188	63	62.4	51	58.6	114	60.9	35	34.7	29	33.3	64	34.0	3	3.0	7	8.0	10	5.3
80-84	51	17	56.7	10	47.6	27	52.9	11	36.7	10	47.6	21	41.2	2	6.7	1	4.8	3	5.9
85+	27	13	61.9	0	0	13	48.2	5	23.8	4	66.7	9	33.3	3	14.3	2	33.3	5	18.5
P			0.001		<0.001		<0.001		0.023		0.002		<0.001		0.022		0.05		0.003

* Percentage among the same sex in the age group.

† Percentage in the age group.

age groups. There was an age-related trend in the prevalence of high myopia ($P = 0.003$) and low and moderate myopia ($P < 0.001$). Table 2 presents the status of myopic maculopathy in the high myopics. In subjects with high myopia, there was a significant age trend for myopic maculopathy ($P = 0.004$), in particular in women ($P = 0.028$).

Among the 44 subjects with high myopia, 9 (20.5%) had bilateral myopic maculopathy, 23 (52.3%) had unilateral myopic maculopathy, 2 (4.5%) had bilateral high myopia without myopic maculopathy, and 10 (22.7%) had unilateral high myopia without myopic maculopathy. There were a total of 65 eyes with high myopia. The average best-corrected logMAR visual acuity by grade was 0.29 in M0 (number of the eyes, $n = 4$), 0.33 in M1 ($n = 11$), 0.18 in M2 ($n = 9$), 0.39 in M3 ($n = 12$), 0.37 in M4 ($n = 12$), and 1.1 in M5 ($n = 17$). Of them, eyes with maculopathy had worse corrected visual acuity (logMAR, 0.72 ± 0.6), compared to eyes without maculopathy (0.27 ± 0.2, $P = 0.001$; Table 3). Of the 31 phakic eyes, eyes with myopic maculopathy were associated with more myopic degree than those without (−12.8 ± 5.1 D vs. −7.6 ± 1.5 D, $P = 0.001$). Of the 34 pseudophakic or aphakic eyes, the axial length was not significantly different between the two groups (28.0 ± 1.9 mm vs. 27.1 ± 0.5 mm, $P = 0.072$). The percentage of eyes with lens opacity or eyes that had undergone cataract surgery was not different between the two groups (Table 3).

Univariate analysis suggested that systolic blood pressure (SBP) was significantly higher in the high myopics with maculopathy (146.4 ± 16.2 mm Hg) than those without (127.0 ± 15.9 mm Hg, $P = 0.001$; Table 4). The difference remained significant ($P = 0.02$) after further adjustment for age, sex, diastolic blood pressure, smoking, educational level, BMI, alcohol drinking, history of diabetes, and history of taking antihypertension medication; for each 10 mm Hg increase in SBP, the OR of having myopic maculopathy was 2.46 (95% CI: 1.66–3.64, $P = 0.02$). SBP was also significantly higher in subjects with myopic maculopathy, compared with those with low or moderate myopia ($P = 0.002$; Fig. 2).

Discussion

In this elderly Chinese population in Taiwan, the prevalence of myopic maculopathy was 3.0%, which was similar to that in Beijing Eye Study (BES) (3.1%),[20] but higher than the Blue Mountains Eye Study (BMES) (1.2%).[21] However, direct comparisons may be difficult for several reasons. First, these studies defined myopic maculopathy based on fundus findings without the criteria of refractive error, which may be prone to misclassification. Second, posterior staphyloma was one of the criteria of myopia maculopathy in the other studies but not ours. Finally, our study population (≥65 years) was older than the two studies (≥49 years in BMES and >40 years in BES) (Table 5).

In our study, the definition of refractive error or axial length was a prerequisite for myopic maculopathy cases. The reason for this approach is that we felt it increased the specificity for myopia-related maculopathy and diminished the issue in subjects with ambiguous fundus findings, and thus reduced ascertainment bias. If we included refractive criteria (<−6.0 D) to the above two studies and included posterior staphyloma as a criteria of myopic maculopathy in our study, the proportion of myopic maculopathy in high myopic eyes in our study (73%, 47/65 eyes) is higher than in the BES (65%, 140/214 eyes) and

Table 2. High Myopia by Maculopathy Status*

		Maculopathy <M3						Maculopathy ≥M3					
		Men		Women		Total		Men		Women		Total	
Age Groups, y	*n*	*n*	%†	*n*	%†	*n*	%‡	*n*	%†	*n*	%†	*n*	%‡
65–69	403	1	0.4	3	1.9	4	1.0	5	2.0	4	2.5	9	2.2
70–74	389	3	1.1	1	0.8	4	1.0	6	2.3	3	2.3	9	2.3
75–79	188	2	2.0	0	0	2	1.1	1	1.0	7	8.1	8	4.3
80–84	51	1	3.3	0	0	1	2.0	1	3.3	1	4.8	2	3.9
85+	27	0	0	1	16.7	1	3.7	3	14.3	1	33.3	4	14.8
Total	1058	7	1.1	5	1.3	12	1.1	16	2.4	16	4.3	32	3.0
P			0.061		0.642		0.090		0.057		0.028		0.004

* M3 and above: presence of yellowish lacquer cracks in Bruch's membrane, focal areas of deep choroidal atrophy, or geographic areas of atrophy of retinal pigment epithelium and choroids, and choroidal neovascularization (Fuchs' spot).

† Percentage among the same sex in the age group.

‡ Percentage in the age group.

Table 3. Ocular Characteristics in High Myopic Eyes with or without Maculopathy

	Without Maculopathy ($n = 24$)	With Maculopathy ($n = 41$)	*P*
Best corrected visual acuity in logMAR	0.27 ± 0.2	0.72 ± 0.6	0.001
Pseudophakia or aphakia (%)	15 (63%)	19 (46%)	0.304
Spherical equivalent (D)*	−7.6 ± 1.5	−12.8 ± 5.1	0.001
Axial length (mm)†	27.1 ± 0.5	28.0 ± 1.9	0.072
Cataract (%)‡	18 (75%)	35 (85%)	0.335

Data are mean ± SD for visual acuity and spherical equivalent.

* Spherical equivalents were analyzed only in the 31 phakic eyes.

† Axial length were analyzed only in the 34 aphakic or pseudophakic eyes.

‡ Cataract denotes eyes with nuclear opacity ≥ grade 4, cortical opacity ≥ grade 3, or posterior subcapsular opacity ≥ grade 3, according to the LOCS III grading scheme in the phakic eyes.

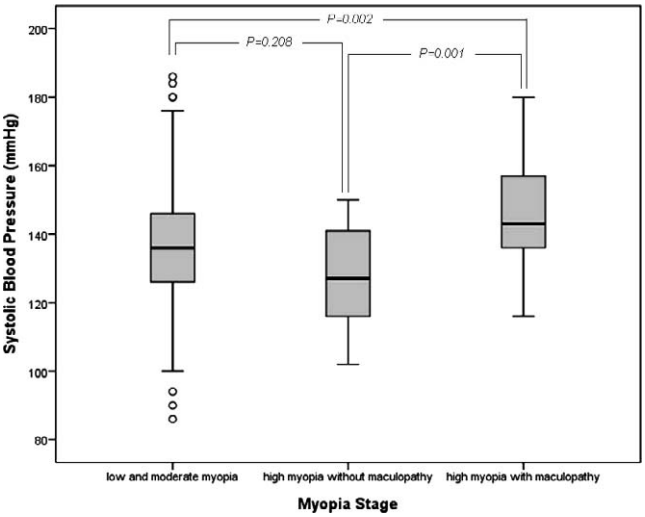

Figure 2. Systolic blood pressure in low and moderate myopia, high myopia without maculopathy, and high myopia with maculopathy.

much higher than in the BMES (25%, 20/79 subjects). Thus, our study suggests that the higher prevalence of myopic maculopathy and higher proportion of maculopathy among the high myopic eyes in the Chinese people might imply a racial difference between Chinese and whites.

As discussed, difference in age may account in part for the higher prevalence of myopia maculopathy in our study. Aging has an impact on the anatomical and functional outcomes in patients with myopic maculopathy. Clinic-based studies have shown that increased severity of maculopathy is associated with increased axial length as well as increased age.[8,22] With aging, the lacquer cracks extend and thus increase the areas of choriocapillary atrophy as well as the chances of CNV ingrowths from ruptured Bruch's membrane.[23] More than half of the patients with lacquer cracks had progression in numbers and severity in an average follow-up after 6 or 12 years.[23,24] The lacquer crack is an initiating factor of subsequent degeneration of retina and CNV development in high myopia.[25] Lacquer cracks are thus the precursor and hallmark of high myopic maculopathy. Because of their prominent and distinct clinical features as well as their prognostic implication, we suggest that lacquer cracks be an important clinical sign in future epidemiological studies. In screening high myopic subjects, appearance of lacquer cracks denotes more frequent future follow-ups in preventing myopic blindness, provided that effective treatment for high myopic CNV is available.

Table 4. Factors Associated with High Myopic Subjects with or without Maculopathy

	Without Maculopathy ($n = 12$)	With Maculopathy ($n = 32$)	*P*
Age (y)	73.3 ± 6.1	74.3 ± 6.6	0.658
Sex (men, %)	58%	50%	0.622
Education (higher than junior high school, %)	58.3%	46.9%	0.498
Diabetes (%)	16.7%	15.6%	0.933
Smoking (current, %)	25.0%	37.5%	0.436
Alcohol drinking (current, %)	8.3%	0%	0.099
Taking anti-hypertension medication (%)	41.7%	34.4%	0.654
Systolic blood pressure (mm Hg)	127.0 ± 15.9	146.4 ± 16.2	0.001
Diastolic blood pressure (mm Hg)	73.8 ± 10.1	77.8 ± 10.5	0.260
BMI (kg/m^2)	24.0 ± 3.9	24.9 ± 3.4	0.499

Data are mean ± SD for continuous variables.

* *P* value derived using *t*-test for continuous variables and chi-square test or Fisher exact test for categorical variables.

Our study also showed that the modifiable factor of SBP may play a role in high myopic subjects with maculopathy. In our study, for every 10 mm Hg increase in SBP, the odds of acquiring maculopathy were 150% greater in high myopic patients after adjustment for age, taking anti-hypertensive medication, and other potential confounders. Most of all, subjects with the most severe maculopathy of CNV or geographic atrophy had a higher SBP than subjects with other less severe stages. The reason was not clear in this cross-sectional study, although increased SBP has been reported to be associated with exudative AMD.[26,27] Recent studies on the diurnal variation of choroidal thickness in normal subjects showed that SBP played a significant role on the thickness change.[28,29] Higher SBP was associated with thinner choroidal thickness in the afternoon.[29] The high SBP in myopic patients may further compromise the already thinner choroid,[30] hamper the choroidal circulation, and hence increase the severity of maculopathy. Our finding of SBP as a risk factor needs further verification in longitudinal cohort studies. Furthermore, it is still unknown if this finding applies to younger populations. Future interventional studies or clinical studies might consider including blood pressure measurement for analysis.

Our study was limited in several aspects. The 66.6% participation rate is lower than other studies with a younger population.[17] Yet the rate is comparable to other aged population surveys.[31] The participants with gradable photographs were younger than those nonparticipants or participants with ungradable photographs. However, the difference was small.[18] There were two definitions of high myopia in our study, as for aphakic or pseudophakic eyes, but we were unable to acquire data of their spherical equivalent before cataract surgery. For aphakic or pseudophakic eyes, we used a more or less strict definition for high myopia (axial length ≥26.5 mm), thus the prevalence of high myopia might have been underestimated to some extent. However, we believe the

Table 5. Prevalence of Myopic Retinopathy in Different Population-Based Studies

	Blue Mountains 2002	Beijing 2010	Present Study
Population (age, *n*)	≥49 y; 3654	≥40 y; 4319	≥65 y; 1361
Definition	Staphyloma	Staphyloma	SE ≤ −6.0 D or axial length ≥ 26.5 mm
	Lacquer cracks	Lacquer cracks	Lacquer cracks
	Fuchs' spot	Fuchs' spot	Fuchs' spot
	Chorioretinal atrophy	Chorioretinal atrophy	Chorioretinal atrophy
Mean SE (D)	−6.1	−8.9	−12.8
Mean visual acuity (Snellen)	20/40	20/36	20/105
Prevalence	1.2%	3.1%	3.0%

effect of including the axial length as a defining characteristic in the prevalence of myopic maculopathy is minimal if any. There is no consensus on the cutoff value of axial length for high myopia at present.[13] This cutoff was adopted in several studies as the definition of high myopia.[8,32] Furthermore, studies showed that there were significantly more retinal complications in eyes with axial length longer than 26.5 mm.[7,33] Our findings of association between SBP and myopia maculopathy is also limited by the study's small sample and the cross-sectional design. Further studies such as case–control studies are needed to compare the SBP measured in the clinic and monitored at home as well as its relationship with myopic maculopathy.

In conclusion, high myopic maculopathy with lacquer cracks, focal or geographic chorioretinal atrophy, and Fuchs' spot was present in 3.0% of the elderly Chinese people in Shihpai area in Taiwan. It was associated with higher SBP. Eyes with maculopathy were associated with greater myopic degree and lower visual acuity. The association of high SBP and myopic maculopathy needs further verification from other studies with long-term follow-up.

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