Prevalence and Associated Risk Factors of Age-Related Macular Degeneration in an Elderly Chinese Population in Taiwan: The Shihpai Eye Study

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Purpose. To assess the prevalence and associated risk factors of age-related macular degeneration (AMD) in an elderly Chinese population in Taiwan.

Methods. The Shihpai Eye Study was a survey of vision and ocular disease in an elderly Chinese population 65 years of age or older residing in Shihpai, Taipei, Taiwan. Of 2045 elderly residents randomly sampled from the household registration databank, 1361 (66.6%) underwent a detailed ophthalmic examination that included fundus color slides by fundus camera after pupil dilatation. Photographs were graded according to the Wisconsin Age-Related Maculopathy Grading System.

Results. Fundus photographs were available for 1105 (54.0% in the eligible, 81.2% in the ocular examined) participants. The 47 (4.3%) participants who had ungradable fundus images were older and had more lens opacity. Of the 1058 gradable photographs, the prevalence of early AMD was 9.2% (95% confidence interval [CI], 7.8–10.8); of late AMD, 1.9% (95% CI, 1.3–2.7); of soft drusen, 42.2% (95% CI, 39.7–44.8); of soft indistinct drusen, 4.1% (95% CI, 3.1–5.2); and of any pigmentary change, 8.6% (95% CI, 7.2–10.2). Age was the most significant factor associated with both early and late AMD. The prevalence of early AMD rose from 5.0% in the 65- to 69-year age group to 24.4% in those 80 years of age and older; and for late AMD, from 1.0% to 9.0%. Those who currently drank alcohol had a lower rate of early AMD than did the nondrinker (adjusted odd ratio 0.32, 95% CI: 0.11–0.93, $P = 0.037$).

Conclusions. AMD is a common eye disease in the elderly Chinese people in Taiwan. The adjusted prevalence rate of exudative AMD is comparable to that in the Chinese people in the Multiethnic Study of Atherosclerosis (MESA) in the United States but is higher than in the Chinese people in the Beijing study in China. Further studies are needed to clarify the incidence and associated risk factors. (*Invest Ophthalmol Vis Sci.* 2008;49:3126–3133) DOI:10.1167/iovs.08-1803

Age-related macular degeneration (AMD) is a well-known leading cause of blindness in the Western world. In Asia, AMD is the leading cause of blindness in only a few areas.[1,2] Furthermore, the distribution of AMD in different geographic regions and different ethnicity varies, even with similar grading methods and definition in population-based studies. For example, a pooled study of the similar race of white people across three continents revealed that the prevalence of advanced AMD is similar.[3] However, the Inuit of Greenland[4] and the Chinese in Beijing[5] both may have similar Mongoloid ancestors,[6] but are at opposite extremes in prevalence of AMD. On the other hand, while living in the same region and community, people of different races have a diverse prevalence of AMD. Black people have a lower prevalence,[7,8] less severe forms,[9,10] and less involvement of the central macula[10] than do white people. Hispanics have prevalence of early AMD similar to that of whites, but they have less-advanced disease.[7,11,12] These differences impose not only different social needs associated with this blinding eye disease but also provide a potential way to sort out the causes of AMD.

Among the different races, the Chinese were reported to have a low prevalence in a previous study.[13] Population-based data on prevalence in the Chinese people were not available until the publication of two recent reports. The two studies in which Chinese people residing in China[5] or the United States[7] were examined revealed conflicting results. Although based on the same grading system, the prevalence rate of early AMD in the Beijing study was one third that in the Chinese subjects in the U.S. study, and the prevalence of late AMD was only one fifth that in the U.S. study. Both studies cited that age is a significant associated factor for AMD yet the prevalence rate among those 65 years of age and older differed by a factor of two- to fourfold. The reason for the difference is not clear.

The studies included the adult population older than 40[5] or 45[7] years, and the constitution of the age groups and the ratio of elderly people (>65 years old) in the study populations were different. It will be interesting to focus on the elderly population to see whether AMD is a prevalent disease in ethnic Chinese based on the same grading method. The Shihpai Eye Study, a population-based prevalence survey of ocular diseases among people 65 years of age or older, may provide a reference in addition to the Beijing and U.S. studies. The purpose of this study was to describe the prevalence and associated factors of AMD in the elderly Chinese living in the Shihpai area, Taipei, Taiwan.

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METHODS

Study Population

The population and methods of the Shihpai Eye Study have been described elsewhere.[2,14] In brief, residents 65 years of age and older in Shihpai, Taiwan, were identified from the household registration databank provided by the government Household Registration Office. According to the official household registration in 1999, the total number of residents 65 years of age or older in Shihpai was 4750. Excluding vacant households ($n = 658$), residents who died before they could be contacted ($n = 48$), and inpatients and residents who were paralyzed or otherwise disabled ($n = 298$), 3746 residents were eligible for the study. Among them, 2045 residents were randomly selected and invited to participate in the survey. Of the 2045 randomly selected individuals, 1361 (66.6%) participated in the ophthalmic examination. These participants were younger (72.2 years vs. 74.3 years), more often men, and had a higher educational level than did those who were not examined.[2]

Procedures

A home interview with a structured questionnaire was conducted before the ocular examination. The structured questionnaire was used to obtain information based on demographic data, personal medical history, and lifestyle. Those who were interviewed were invited to the study hospital for a detailed ophthalmic examination.

The examination was conducted according to a standardized protocol that included visual acuity measurement 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; Welch-Allyn, Skaneateles Falls, NY) through a dilated pupil with 1% tropicamide (Alcon-Couvreur, Puurs, Belgium). Lens opacity was graded by slit lamp biomicroscopy according to the modified Lens Opacity Classification System (LOCS) III.[15] Informed consent was obtained from each subject before enrollment in the study. This study was approved by the institutional review board in Taipei Veterans General Hospital and was conducted in accordance with the Declaration of Helsinki.

Both eyes of each participant were photographed with a 35° monoscopic fundus camera (TRC-50IA; Topcon) after pupil dilatation. At least two photography fields were taken in each eye: one centered at the fovea and the other at the optic disc.

Fundus Grading

The Wisconsin Age-Related Maculopathy Grading System was used[16] to evaluate the AMD. The 6000-μm diameter grid consisting of two circles concentric with the center of the macula and four radial lines superimposed over the color slides. The slides were examined on the light box with an 8× magnifying lens. The features evaluated were drusen size, type, number, and area; increased retinal pigment; retinal pigment epithelial depigmentation; geographic atrophy; and signs of exudative macular degeneration (serous detachment of the sensory retina, subretinal hemorrhage, subretinal fibrous scar, retinal pigment epithelial detachment, or laser scar for treatment of exudative AMD). The lesions used to determine the presence and severity of AMD were those that were identified in the macular area circumscribed by the outermost circle of the grading grid. Circles of different size in diameter (63, 125, 250, and 500 μm) were used to define drusen size and area.

Two graders (SJC and KLP) graded all the photographs. The interobserver and intraobserver variability were analyzed by κ statistics. For interobserver agreement, the κ of soft drusen type, number of large drusen (0, 1~9, 10+), depigmentation, and hyperpigmentation were 0.88, 0.66, 0.64, and 0.79, respectively. For intraobserver agreement, the κ for graders 1 and 2 were moderate to high for all these four features. All questionable lesions and all lesions that were classified as neovascular AMD or geographic atrophy were discussed and adjudicated by the two graders.

Definition

Soft drusen were defined as those having a diameter larger than 63 μm. Soft, distinct drusen have distinct sharp margins and uniform density, and soft indistinct drusen have indistinct margins and a softer, less solid appearance. Accordingly, drusen were classified as small hard (<63 μm in diameter), intermediate (63~125 μm), large soft distinct (>125 μm), or large soft indistinct (>125 μm). The number of each different type of drusen within the outermost circle was counted. In defining soft drusen >500 μm in diameter, the areas of the large soft drusen within the outermost circle were pooled as if they were confluent and then the total area estimated, or if the number of large soft drusen exceeded 16. Increased retinal pigment is defined as the deposition of granules or clumps of gray or black pigment in or beneath the retina. Retinal pigment epithelium (RPE) depigmentation is characterized by faint grayish yellow or greenish yellow areas of various density and configuration without sharply defined borders. Early AMD was defined by either the presence of any soft drusen (distinct or indistinct) and pigmentary abnormalities (either increased retinal pigment or RPE depigmentation) or the presence of a large soft drusen ≥125 μm in diameter with a large drusen area (≥500-μm diameter circle) or large soft instinct drusen in the absence of signs of late AMD. Late AMD was defined as the presence of signs of exudative AMD or geographic atrophy. When both eyes of a participant had lesions of different severity, the grade assigned for the participant was that of the more severely involved eye.

Statistical Analysis

The crude prevalence of drusen, pigmentary change, and AMD in participants by age group and sex was expressed in percentages of the study population. The association of early and late AMD with age, sex, hypertension, cigarette smoking, alcohol drinking, BMI, spherical equivalent, and self-reported diabetes was assessed, and adjusted odds ratios were obtained by using multivariate logistic regression models, allowing for control of the mutually confounding effect of these potential risk factors. To compare our results with those in other AMD surveys in Chinese populations, the crude prevalence rates in each study were further age and sex adjusted according to the 1999 Taiwan population[17] to obtain age-standardized prevalences. All data analyses were performed with a commercial statistical software package (Stata; Stata Corp., College Station, TX).

RESULTS

Participants

Of the 1361 participants who attended the ocular examination, 1105 (81.2%) had at least one photograph taken in either eye. The 256 subjects who had no photographs in both eyes were older, predominantly female, less educated, and more likely to be living alone or not to be married (Table 1). Among the 1105 subjects who had photographs, 1058 (95.7%) had gradable photographs in at least one eye, the 47 subjects who had no gradable photographs in both eyes were older and had more lens opacity grading (Table 1).

Prevalence

At least one drusen was present in 70.4% (745/1058) of the participants. There was no significant sex difference in their overall frequency ($P = 0.355$). The prevalence of any drusen increased with age ($P = 0.002$), especially in the male population ($P = 0.012$; Table 2). Small hard drusen were the most frequent drusen present in all ages until age 80 (Table 2). Soft drusen were present in at least one eye in 42% of the popula-

TABLE 1. Comparison of Demographic, Social, and Clinical Characteristics of Participants According to the Availability of Gradable Photographs

	Participants without Photographs Taken in Either Eye (n = 256)	Participants with Photographs Taken in Either Eye (n = 1105)		P
		Without Gradable Photos (n = 47)	With Gradable Photos (n = 1058)	
Sex (% male)	63.8	52.0	62.3	0.009
Age, mean y (SD)	73.3 (5.2)	75.8 (6.0)	71.8 (4.8)	<0.0001*
65–69 (%)	27.3	17.0	38.1	
70–74 (%)	35.2	27.7	36.8	
75–79 (%)	25.4	31.9	17.8	
80–84 (%)	9.0	17.0	4.8	
≥85 (%)	3.1	6.4	2.6	
Education level (% ≥9 years)	28.9	31.9	39.4	0.006
Not married or lived alone (%)	35.2	21.3	24.4	0.002
Diabetes (%)	14.1	15.2	15.8	0.797
Hypertension (%)	46.5	51.1	44.9	0.658
LOCS III of nucleosclerosis >grade 3 in right eye (%)	17.3	23.4	11.04	0.002

* χ^2 test for age groups; LOCS III: modified Lens Opacity Classification System III.

tion and in more than 50% of participants over the age of 75 (Table 2). There were age trends with increased prevalence of soft drusen ($P < 0.0001$) but not with the presence of small hard drusen ($P = 0.365$).

Soft distinct drusen were more than ninefold as prevalent as soft indistinct drusen (38% vs. 4%). The prevalence of both types of soft drusen significantly increased with age ($P < 0.0001$; Table 3). There were no sex differences between these two types of soft drusen. For large drusen (>125 μm in diameter), the overall prevalence was 24.4%. The frequency of large drusen increased with age ($P < 0.0001$). There was no difference between the men and the women ($P = 0.163$). The frequency of drusen area greater than 500 μm increased with age, from 3.0% in persons 65 to 69 years of age to 12.8% in those 80 years of age and older ($P < 0.0001$). The large macular drusen area was more prevalent in the women (7.3% vs. 3.2% in males, $P = 0.002$) but were not significant after adjustment for age.

The overall prevalence of retinal pigment abnormalities was 8.6% (Table 4). Prevalence increased with age ($P = 0.022$), with a twofold increase from 7.4% in persons 65 to 69 years of age to 15.7% in those 80 years of age or older. There were no sex differences in the prevalence of retinal pigment abnormalities ($P = 0.441$), yet the men had trends toward increasing prevalence with age ($P = 0.015$), whereas the women did not ($P = 0.586$). Depigmentation was seen more frequently than increased pigment in all age groups in both the men and the women. However, there was no difference between the men and women ($P = 0.780$). The results tended to be significant in the men, but not in the women (Tables 2, 4).

The prevalence of any AMD was 11.1% (117/1058), of which 9.2% (97/1058) was early AMD and 1.9% (20/1058) was late AMD (Table 5). Among the 20 participants with late AMD, only 1 had geographic atrophy; the other 19 had exudative AMD. The prevalence of early AMD increased fivefold with age from 5.0% in those 65 to 69 years of age to 25.5% in those 80 years of age or older ($P < 0.0001$). For late AMD, the prevalence increased with age from 1% in those 65 to 69 to 18.5% in those older than 85 years ($P < 0.0001$).

Among the 19 persons with exudative AMD, 2 (10.5%) were suspected to have polypoidal choroidal vasculopathy (PCV), which was characterized by eccentric fibrosis, and an orange-colored vascular channel as shown in color photographs (Fig. 1). These two patients were relatively young (67 and 68 years) and had no drusen in the affected eyes or fellow unaffected eyes.

Risk Factors for Early and Late AMD

Age was the most significant factor associated with early and late AMD after multivariate adjustment (Table 6). Compared with subjects of age 65 to 69 years, subjects of age 75 to 79, 80 to 84, and 85 years and older had adjusted odds ratios (OR) of 3.3, 7.3, and 5.7 of acquiring early AMD, respectively. For late

TABLE 2. Prevalence of Drusen by Age and Sex

Age Group (y)	Small Hard Drusen				Soft Drusen				Any Drusen			
	Male n (%)	Female n (%)	Total n (%)	P†	Male n (%)	Female n (%)	Total n (%)	P†	Male n (%)	Female n (%)	Total n (%)	P†
65–69	142 (58.0)	85 (53.8)	227 (56.3)	0.411	89 (36.3)	55 (34.8)	144 (35.7)	0.756	168 (68.6)	103 (65.2)	271 (67.2)	0.480
70–74	140 (53.6)	67 (52.3)	207 (53.2)	0.810	102 (39.1)	52 (40.6)	154 (39.6)	0.770	181 (69.3)	87 (68.0)	268 (68.9)	0.782
75–79	60 (59.4)	45 (51.7)	105 (55.9)	0.290	49 (48.5)	47 (54.0)	96 (51.1)	0.451	78 (77.2)	62 (71.3)	140 (74.5)	0.350
80–84	15 (50.0)	12 (57.1)	27 (52.9)	0.615	21 (70.0)	15 (71.4)	36 (70.6)	0.912	25 (83.3)	18 (85.7)	43 (84.3)	0.818
85+	9 (42.9)	3 (50.0)	12 (44.4)	0.756	13 (61.9)	4 (66.7)	17 (63.0)	0.831	18 (85.7)	5 (83.3)	23 (85.2)	0.885
Total	366 (55.6)	212 (53.0)	578 (54.6)	0.406	274 (41.6)	173 (43.3)	447 (42.2)	0.607	470 (71.4)	275 (68.8)	745 (70.4)	0.355
P*	0.295	0.905	0.365		<0.0001	<0.0001	<0.0001		0.012	0.053	0.002	

* χ^2 trend test for age groups.
† Pearson's χ^2 test for sex difference.

TABLE 3. Age- and Sex-Specific Prevalence of Soft Drusen by Size and Type

Age Group (y)	Soft Distinct Drusen				Soft Indistinct Drusen				Drusen >125 μm				Drusen Area >500 μm			
	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†
65–69	86 (35.1)	53 (33.5)	139 (34.5)	0.748	3 (1.2)	2 (1.3)	5 (1.2)	0.971	44 (18.0)	29 (18.4)	71 (17.6)	0.920	5 (2.0)	7 (4.4)	12 (3.0)	0.168
70–74	91 (34.9)	46 (35.9)	137 (35.2)	0.835	11 (4.2)	6 (4.7)	17 (4.4)	0.830	56 (21.5)	34 (26.6)	84 (21.6)	0.262	6 (2.3)	7 (5.5)	13 (3.4)	0.099
75–79	45 (44.6)	39 (44.8)	84 (44.7)	0.970	4 (4.0)	8 (9.2)	12 (6.4)	0.143	26 (25.7)	30 (34.5)	52 (27.7)	0.191	5 (5.0)	10 (11.5)	15 (8.0)	0.099
80–84	18 (60.0)	12 (57.1)	30 (58.8)	0.838	3 (10.0)	3 (14.3)	6 (11.8)	0.640	16 (53.3)	11 (52.4)	27 (52.9)	0.947	3 (10.0)	4 (19.0)	7 (13.7)	0.355
85+	10 (47.6)	4 (66.7)	14 (51.9)	0.410	3 (14.3)	0 (0)	3 (11.1)	0.326	9 (42.9)	3 (50.0)	9 (33.3)	0.756	2 (9.5)	1 (16.7)	3 (11.1)	0.623
Total	250 (38.0)	154 (38.5)	404 (38.2)	0.869	24 (3.6)	19 (4.8)	43 (4.1)	0.378	151 (22.9)	107 (26.8)	258 (24.4)	0.163	21 (3.2)	29 (7.3)	50 (4.7)	0.002
*P**	0.008	0.006	<0.0001		<0.0001	0.003	<0.0001		<0.0001	<0.0001	<0.0001		0.005	0.004	<0.0001	

* χ^2 trend test for age groups.
† Pearson's χ^2 test for sex difference.

AMD, there was an increased trend in OR across the age groups and in subjects older than 85 years, a significant increased OR of 21.35 (95% CI, 4.69–97.12; $P < 0.001$) noted in comparison to the reference group of 65 to 69. Other risk factors such as sex, smoking, BMI, DM, and hypertension had no association with early or late AMD. The spherical equivalent in diopters was not significantly associated with either early AMD (OR = 1.12, 95% CI, 0.97–1.29) or late AMD (OR = 1.01, 95%CI, 0.78–1.31). However, current alcohol drinking was negatively associated with early AMD (OR: 0.32, 95% CI, 011–0.93, $P = 0.037$) yet it was not protective against late AMD.

DISCUSSION

The Shihpai Eye Study provides population-based data on the prevalence of AMD and its associated characteristics in elderly Chinese people in Taiwan. The response rate was 66.6% which is comparable with that in other population-based studies of elderly people.[18] Fundus photographs were read by experienced graders in a masked fashion, and reproducibility of AMD grading was evaluated throughout the study. The data collection and maintenance followed a standard protocol and were carefully monitored.

The present study allowed for comparing the results with other studies that used a similar protocol and definition.[5,7] Figure 2 depicts the comparison of the prevalence of early AMD in different ethnic groups and different regions but in the same age groups. The findings of the Beaver Dam Eye Study which used the same definition of AMD but examined stereoscopic fundus photographs were also included for comparison. The crude prevalence of AMD in those 65 to 74 years of age (6.3%) reported in our study is similar to that in the Chinese (5.0%), Hispanics (4.5%), and whites (5.5%) reported in the Multiethnic Study of Atherosclerosis (MESA), but is higher than that in blacks (2.1%) in the MESA and in Chinese (2.5%) in the Beijing Eye Study. Among those 75 years of age and older, the prevalence of early AMD in the Shihpai Chinese (17.7%) was slightly higher than the MESA whites (13.3%), and other ethnic groups (4.4%–13.3%), but was much lower than that in the Beaver Dam whites (36.8%). It is clearly demonstrated that prevalence in the age group older than 75 years is approximately 2.2- to 2.8-fold that of the group of 65 to 69 years across all races in the MESA study and Shihpai study.

Specific lesions characterizing early AMD, such as soft indistinct drusen, increased pigment and drusen area greater than 500 μm were similar between the Shihpai Chinese and the MESA Chinese (estimated according to Fig. 1 in the MESA study of four racial groups).[7] For large drusen (>125 μm), hypopigmentation, and soft distinct drusen (>63 μm), the Shihpai Chinese had more frequent presentation than did the MESA Chinese. Although the same grading scheme was used, the nonmydriatic digital images used in the MESA study may underestimate the pigmentary change or overestimate the large drusen when compared with the film images.[19] It is also possible that drusen borders are more readily seen against the slightly more pigmented fundus of Chinese in the color films. Another reason for the increased prevalence of hypopigmentary lesion in Shihpai Chinese compared with MESA Chinese may be the more common occurrence of central serous chorioretinopathy.[20] Central serous chorioretinopathy may present with spots or patches of hypopigmentation masquerading as the pigmentary abnormalities of AMD. However, these hypopigmentary lesions were rarely associated with large drusen and were excluded from early AMD based on our diagnostic criteria.

As shown in Figure 3, for age greater than 75 years, the prevalence of late AMD in the Shihpai Chinese (4.1%) was

TABEL 4. Age- and Sex-Specific Prevalence of Pigmentary Changes

Age Group (y)	Increased Pigment				Depigmentation				Any Pigmentary Change			
	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†
65–69	5 (2.0)	3 (1.9)	8 (2.0)	0.920	14 (5.7)	8 (5.1)	22 (5.5)	0.779	19 (7.8)	11 (7.0)	30 (7.4)	0.767
70–74	10 (3.8)	2 (1.6)	12 (3.1)	0.224	15 (5.7)	7 (5.5)	22 (5.7)	0.911	21 (8.0)	8 (6.3)	29 (7.5)	0.526
75–79	2 (2.0)	3 (3.4)	5 (2.7)	0.533	7 (6.9)	9 (10.3)	16 (8.5)	0.403	9 (8.9)	11 (12.6)	20 (10.6)	0.408
80–84	4 (13.3)	0 (0)	4 (7.8)	0.081	5 (16.7)	1 (4.8)	6 (11.8)	0.194	7 (23.3)	1 (4.8)	8 (15.7)	0.073
85+	1 (4.8)	0 (0)	1 (3.7)	0.586	3 (14.3)	0 (0)	3 (11.1)	0.326	4 (19.0)	0 (0)	4 (14.8)	0.247
Total	22 (3.3)	8 (2.0)	30 (2.8)	0.202	44 (6.7)	25 (6.3)	69 (6.5)	0.780	60 (9.1)	31 (7.8)	91 (8.6)	0.441
*P**	0.059	0.936	0.096		0.036	0.437	0.032		0.015	0.586	0.022	

* χ^2 trend test for age groups.
† Pearson's χ^2 test for sex difference.

similar to that in the MESA whites (2.9%) and MESA Chinese (5.2%), whereas the MESA Hispanics (0.6%) had the lowest prevalence and the Wisconsin whites the highest (7.1%).

Table 7 shows the comparison of the prevalence of AMD in Chinese across the present study, the Beijing Eye Study, and the Chinese in the MESA study. The adjusted prevalence of early and late AMD was similar between the MESA and Shihpai studies, whereas the Beijing study had an obvious lower rate of early and late AMD. AMD was the third (5/48, 10.4%) leading cause of visual impairment in the Shihpai elderly, whereas it was the fifth (1/49, 2%) leading cause in the Beijing eye study.[21] Prevalent dense cataract that prevents the evaluation of fundus photographs,[5] the ethnic difference between the Chinese living in mainland China and Taiwan,[22] between-center variability,[23] and other environmental differences may account for the discrepancy. Yet, the comparable prevalence of AMD between the Chinese living in Taiwan and the United States suggests that the interaction of genetic and environmental factors plays an important role.

For example, the rapid industrialization of Taiwan has increased the average daily calories and fat intake in the past three decades,[24] and dietary fat and glycemic index have been reported recently to be associated with late AMD and the pigmentary changes in early AMD, respectively.[25,26] The lipid profile of the people in Taiwan is lower than that in the Western countries but higher than in China.[27,28] It will be interesting to see whether the economic development in China and the consequent lifestyle change and westernization of diet has an impact on the prevalence of AMD.

Genetic susceptibility played another role in the development of AMD. The frequency of 1277C in the complement factor H (*CFH*) gene, which is involved in chronic inflammatory response and drusen formation,[29] is much lower in Chinese than in white patients with or without AMD.[30,31] The difference in prevalence of early AMD among the Shihpai Chinese and the MESA Chinese and the MESA whites may indicate that CFH plays a less significant role in drusen formation in ethnic Chinese.

Another genetic factor—*HTRA1*, which is involved in the formation of CNV—was detected in the Chinese[32] and Caucasian[33] patients with late AMD at a similar frequency (55%[32] to 40%,[33] respectively). This genetic factor may be important in the high prevalence of late AMD in the MESA and Shihpai Chinese as well as in the whites. Further prospective research in individuals with different ethnicity who carry the allele is needed to understand the genetic mechanism.

PCV, another explanation for the high prevalence of late AMD, is common in Asians.[34–36] PCV is characterized by submacular or extramacular fibrovascular tissue with orange excrescence or channels, yet is rarely associated with drusen. The two patients with suspected PCV in our studies, although identified by follow-up fluorescein angiography rather than indocyanine green angiography, showed the fundus features of PCV.[37] The prevalence of PCV (10.5%) among patients with exudative AMD in our survey is much lower than in the clinical studies in Japan (54.7%)[36] or our institute (16%; Chen S.-J., unpublished data based on 403 patients with exudative AMD, 2004). The lower prevalence may be explained by the selection bias in the epidemiologic study rather than the hospital-based studies, the onset of PCV in younger age adults, the extramacular lesion of polyps, and the lack of indocyanine green angiography. However, our present study demonstrated that PCV is a frequently occurring eye disease in Asian populations.

TABLE 5. Prevalence of Early and Late Age-Related Macular Degeneration by Age and Sex

Age Group (y)	Early AMD				Late AMD				Any AMD			
	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†	Male *n* (%)	Female *n* (%)	Total *n* (%)	*P*†
65–69	14 (5.7)	6 (3.8)	20 (5.0)	0.387	3 (1.2)	1 (0.6)	4 (1.0)	0.559	17 (6.9)	7 (4.4)	24 (6.0)	0.299
70–74	20 (7.7)	10 (7.8)	30 (7.7)	0.959	4 (1.5)	1 (0.8)	5 (1.3)	0.536	24 (9.2)	11 (8.6)	35 (9.0)	0.846
75–79	12 (11.9)	16 (18.4)	28 (14.9)	0.211	3 (3.0)	1 (1.1)	4 (2.1)	0.388	15 (14.9)	17 (19.5)	32 (17.0)	0.394
80–84	7 (23.3)	6 (28.6)	13 (25.5)	0.673	2 (6.7)	0 (0)	2 (3.9)	0.227	9 (30.0)	6 (28.6)	15 (29.4)	0.912
85+	6 (28.6)	0 (0)	6 (22.2)	0.138	4 (19.0)	1 (16.7)	5 (18.5)	0.895	10 (47.6)	1 (16.7)	11 (40.7)	0.174
Total	59 (8.9)	38 (9.5)	97 (9.2)	0.771	16 (2.4)	4 (1.0)	20 (1.9)	0.097	75 (11.4)	42 (10.5)	117 (11.1)	0.651
*P**	<0.0001	<0.0001	<0.0001		<0.0001	0.111	<0.0001		<0.0001	<0.0001	<0.0001	

* χ^2 trend test for age groups.
† Pearson's χ^2 test for sex difference.

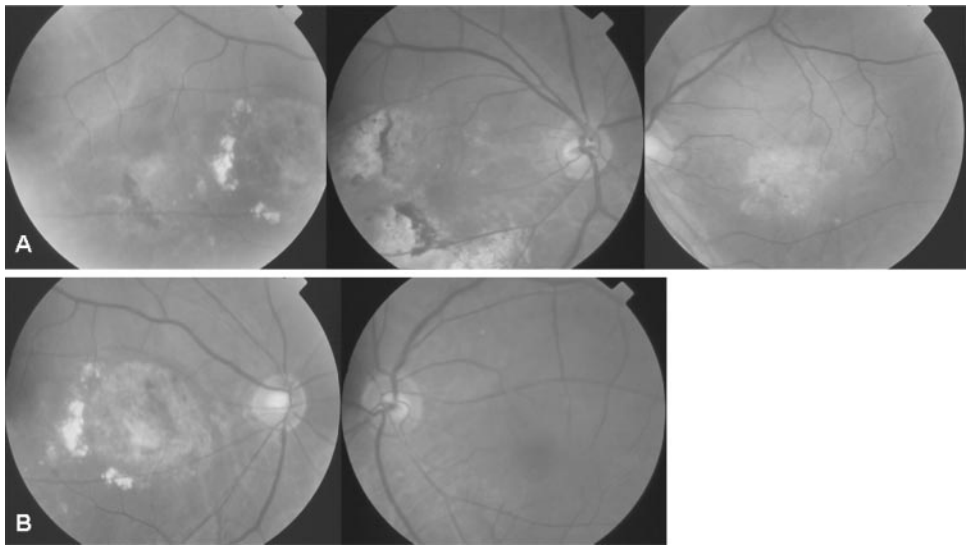

FIGURE 1. Fundus photographs of two suspected cases of PCV. (**A**) Patient 1 was a 67-year-old male with bilateral atrophic scar at the macula and extrafoveal orange-colored elevation in his right eye. (**B**) Patient 2 is a 68-year-old female with right extrafoveal atrophic scar and minimal lipid exudates. Note the prominent choroidal vascular channels adjacent to the atrophic scar. Both cases showed no drusen in the macula.

In the risk factors analysis, age was the most significant factor for early and late AMD after multivariate adjustment. For early AMD, every increase of 5 years doubled the risk, until 85 years. Subjects older than 85 had a nearly 20-fold higher risk of acquiring late AMD than did those aged 65 to 69. On the contrary, current alcohol drinking had a protective role in early AMD. Wine drinking has been reported to be negatively associated with prevalence of any AMD,[38,39] whereas heavy drinking is positively associated with early AMD.[8] The specific kind of alcohol or the amount was not recorded in our study. The role of alcohol in relation with AMD needed further study, especially regarding incidence in follow-up.

Smoking, the most consistent risk factor for AMD in many prevalence studies of white populations,[3,40–42] was not a significant factor in the Shihpai and Asian population studies[43,44] except in one recent report from Japan.[45] The proportion of current smokers in the total participants of these studies were similar: 18.5% white[46] and from 16.1%,[43] 18.0% (present study), and 18.2%,[45] to 23%,[44]—yet only the Funagata study[45] showed marginal significance (OR: 5.03; 95% CI:1.00–25.47) of the association of smoking with late AMD. Smoking was considered the most important risk factor for AMD before the discovery of CFH.[47] The combined effect of both exposures increases the risk 34-fold, which far exceeds the sum of their independent effects.[47] The lower prevalence of CFH Y402H in the Chinese population[30] and Japan[31] probably decreases the interacting and progressing effects of smoking on AMD. Another possible explanation is survival bias. The Chinese/Taiwanese smokers have a shorter life expectancy than do Japanese and white smokers; hence, they do not survive long enough for AMD to develop. However, the life expectancy of the male smokers in Taiwan is 71.4 years[48] which is similar to that in the United States (71.8 years)[49] but is shorter than in Japanese smokers (78.6 years).[50] A further incidence study[51] and a CFH survey at the population level may help in assessing the role of smoking in Asian people.

Our studies were limited by having younger participants with gradable photographs, which may have led to an under-

TABLE 6. Multivariate Regression Analysis of Risk Factors Associated with Early and Late AMD

	Early AMD			Late AMD		
Risk Factors	**Adjusted Odds Ratio**	**95% CI**	***P***	**Adjusted Odds Ratio**	**95% CI**	***P***
Age (vs. 65–69)						
70–74	1.6	0.88–2.92	0.126	1.22	0.32–4.61	0.771
75–79	3.3	1.77–6.15	<0.001	2.39	0.58–9.80	0.226
80–84	7.3	3.21–16.71	<0.001	3.57	0.61–20.84	0.157
85+	5.7	1.99–16.27	0.001	17.48	4.16–73.40	<0.001
Sex (female vs. male)	0.83	0.47–1.47	0.517	0.50	0.14–1.82	0.295
Smoking (vs. nonsmokers)						
Past smokers	0.97	0.51–1.84	0.914	1.94	0.56–6.69	0.294
Current smokers	0.74	0.37–1.47	0.389	1.69	0.48–5.94	0.411
Alcohol (vs. none)						
Past drinkers	0.94	0.33–2.65	0.906	0.47	0.05–4.34	0.502
Current drinkers	0.32	0.11–0.93	0.037	0.54	0.11–2.56	0.436
BMI (vs. <25 kg/m^2)						
25–29.9	1.36	0.85–2.17	0.200	0.42	0.13–1.31	0.134
30+	1.39	0.63–3.06	0.415	—	—	—
DM (yes vs. no)	0.72	0.37–1.40	0.330	1.87	0.56–6.28	0.312
Hypertension (yes vs. no)	1.19	0.75–1.88	0.462	0.84	0.31–2.27	0.729

—, no participant with late AMD has BMI ≥30.

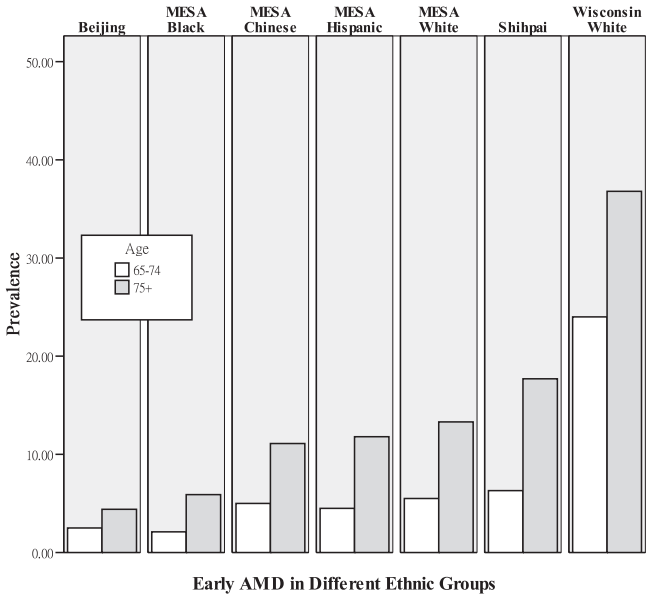

FIGURE 2. Prevalence of early AMD in different ethnic groups in the Beijing Eye Study, MESA, the Shihpai Eye Study, and the Beaver Dam Eye Study.

estimation of the true prevalence in the Shihpai population. However, after adjustment for sex and age of the nonparticipants, the difference was small, both for early AMD (adjusted rate, 9.51% vs. 9.17%) and late AMD (adjusted rate, 1.99% vs. 1.89%). The relatively small number of female participants in the 80+ age group may also hamper the estimation of sex difference, as shown in the age trends of pigmentary change (Table 4). Other than this, there were no sex differences in the prevalence of drusen, pigmentary change, or early AMD in any age groups analysis.

In summary, the Shihpai eye study showed that early and late AMD are common eye diseases among elderly Chinese in Taiwan. The prevalence rate is comparable to the rate in the Chinese people in the MESA in the United States, but is higher than that in the in the Beijing study in China. Further investigation is needed to clarify the relationships between incidence and risk factors.

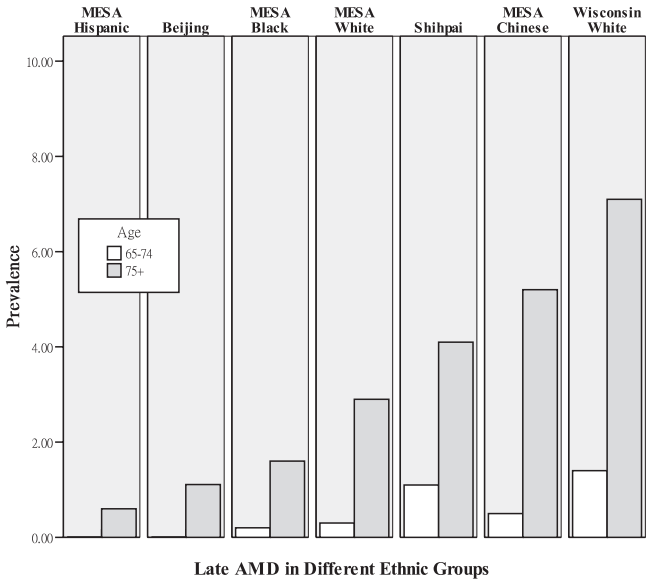

FIGURE 3. Prevalence of late AMD in different ethnic groups in the Beijing Eye Study, MESA, Shihpai Eye Study, and the Beaver Dam Eye Study.

TABLE 7. Adjusted Prevalence of Early and Late AMD among Elderly Chinese from the Shihpai and Other Eye Studies*

	Early AMD Prevalence (Prevalence Ratio)	Late AMD Prevalence (Prevalence Ratio)
MESA study (age 65–85)	6.84% (0.71)	1.92% (1.26)
Beijing study (≥age 65)	3.15% (0.31)†	0.38% (0.18)†
Shihpai study (age 65–85)	9.58% (1.00)	1.52% (1.00)

* Prevalence in persons older than 65 years was estimated by using a direct standardization method, with the 1999 Taiwan population as a reference.

† The adjusted prevalence in the Shihpai survey of early AMD and late AMD is 10.19% and 2.12%, respectively, when including those of age greater than 85.

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