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Prevalence and factors associated with age-related macular degeneration in a southwestern island population of Japan: the Kumejima Study

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ABSTRACT

Aims To evaluate the prevalence of and factors associated with age-related macular degeneration (AMD) in a rural population of southwestern Japan.

Methods This population-based cross-sectional study of all residents aged 40 years or older was conducted on the island of Kumejima, Okinawa, Japan. Of 4632 eligible residents, 3762 completed a comprehensive questionnaire and underwent ocular examination (participant rate, 81.2%). A non-mydriatic fundus photograph was used to grade AMD lesions according to the Wisconsin protocol. Prevalence of AMD was calculated and factors associated with AMD were identified by logistic regression.

Results Of 3068 subjects with gradable photographs, 469 had early AMD and 4 had late AMD. Age-adjusted prevalence was 13.4% for any AMD, 13.3% for early AMD and 0.09% for late AMD. In multivariate analysis, any AMD was positively associated with age (OR 1.04 per year, 95% CI 1.03 to 1.05), male sex (OR 1.42, 95% CI 1.14 to 1.75) and history of cataract surgery (OR 1.35, 95% CI 1.00 to 1.82) and was negatively associated with longer axial length (OR 0.85 per millimetre, 95% CI 0.74 to 0.96). Early AMD similarly showed significant associations with these same factors.

Conclusions Prevalence of early or late AMD in a southwestern island population of Japan was 13.4% or 0.09%. Our data suggest relatively high prevalence for early AMD and low prevalence for late AMD in this sample of rural Japanese population. Significant factors associated with any or early AMD were mostly similar to that of previous studies.

INTRODUCTION

Age-related macular degeneration (AMD), a major cause of blindness among the elderly in the developed countries,[1] is classified into two stages: early AMD and late AMD.[2] Early AMD is characterised by drusen or abnormalities of the retinal pigment epithelium (RPE). There are two types of late AMD: exudative AMD and geographic atrophy (GA). Despite advancements in the management of late AMD with the introduction of anti-vascular endothelial growth factor (VEGF) drugs, long-term management remains difficult.[1 2] The number of patients with AMD worldwide is increasing especially in Asian populations.[3] It is crucial, therefore, to determine the prevalence of AMD and to identify the factors associated with AMD.

The prevalence of AMD in Asia varies among specific ethnic or geographical groups.[4] Within East Asia, population or cohort-based studies conducted in Japan,[5–8] China,[9 10] Taiwan,[11] South Korea,[12] Singapore,[13] and India[14] show a prevalence of 1.4%–22.8% for early AMD and 0.2%–7.3% for late AMD. In Japan, two population-based surveys[5 6] and two cohort studies[7 8] have investigated the prevalence of and factors associated with AMD. However, the response rate was not high in the population-based studies (44%–49%) and even less in the cohort studies. Furthermore, the contribution of previously identified factors associated with early or late AMD such as history of cataract surgery[15] and sunlight exposure[16] has not been confirmed in East Asian populations.

The Kumejima Study, conducted in 2005–2006, was a population-based study that estimated the prevalence of glaucoma and other major eye diseases affecting rural Japanese residents aged 40 years or older on the island of Kumejima, in the southwest of Okinawa Prefecture.[17] Of 4632 eligible residents, 3762 (81.2%) underwent systemic and detailed ophthalmic examination. Here, we report the prevalence of and factors associated with AMD in the Kumejima population based on comprehensive ocular and systemic evaluations performed in this large-scale study.

PATIENTS AND METHODS

Study population

Participants were residents of Kumejima aged 40 years or older. Kumejima is a 63.2 km^2 rural island located in southwestern Japan (26°N, 126°E), 100 km west of Naha City, Okinawa, 1600 km southwest of Tokyo and 600 km north of Taipei City, Taiwan. The investigation followed the tenets of the Declaration of Helsinki and the municipal laws of Kumejima for protecting privacy of information. The ethics committee of Kumejima Town approved the study protocol. Kumejima had 5249 residents aged 40 years or older in 2005. After excluding residents who had died, moved or could not be located on Kumejima during the study period (n=617), 4632 residents were eligible for the study.

Examinations

All participants provided written informed consent before the examinations. After body weight, height, brachial blood pressure and pulse rate were measured, a structured interview questionnaire

was administered to collect data on history of systemic diseases (hypertension and diabetes), antihypertensive medication, smoking habit, occupation and history of working outdoors.[18] Regarding history of systemic diseases, participants were asked if they had ever been diagnosed with hypertension or diabetes. They were considered as having the condition if they had been diagnosed, whether or not they were on medication at the time of interview. Antihypertensive medication was considered as being taken if any kind of antihypertensive drug was prescribed at the time of interview. Participants were asked if they had ever smoked and their smoking history was categorised into two groups: current/ever smoker and never smoker. Occupation was categorised into six groups: farming, fishing, service industry, office work, home maker or other—and the main occupation of each participant was selected based on self-reporting.[19] Participants were asked if they had a history of working outdoors and to report hours per day and number of years for each occupational activity.[18] Subjects with a history of working outdoors were also asked if they used hats or sunglasses when working outdoors.[18]

An ophthalmic examination performed by experienced examiners and ophthalmologists included measurement of uncorrected visual acuity (VA) and best-corrected VA, refraction, intraocular pressure with Goldmann applanation tonometry, slit-lamp examination of the anterior segment, anterior chamber depth, axial length, ophthalmoscopy and photography of the ocular fundus. The fundus colour photographs were obtained in a dark room through undilated pupils using a digital fundus camera (NW7s; Topcon, Tokyo, Japan) at 45°. The photos were taken in following order: sequential stereo photographs centred on the optic disc in the right eye at 30°, a non-stereo fundus photograph in the right eye at 45°, sequential stereo photographs centred on the optic disc in the left eye at 30° and a non-stereo fundus photograph in the left eye at 45°. The non-stereo fundus photographs at 45° were used for the analysis in this study. Axial length was measured by partial coherence laser interferometry (IOL Master; Carl Zeiss Meditec, Dublin, California, USA).

AMD grading

Grading was performed using Wisconsin Age-Related Maculopathy Grading System.[20] Because we assumed that miosis due to flash photography affected the quality of the significant number of photographs, we first used one eye of each participant and conducted per-eye analysis, according to the previous studies.[21 22] In brief, we used the right eye of the participant if it was gradable. When the right eye was ungradable, we used the left eye if it was gradable (figure 1A). Next, to consolidate our findings, we used both eyes of all participants similar to another previous study,[23] and conducted per-individual analysis using the worse eye of the subjects when both of their eyes were gradable (online supplementary table 3). Subjects with other retinal diseases that would interfere with the precise grading of AMD were excluded.

For the grading, customised software was used to superimpose a Wisconsin grid (a 3000 mm radius centred on the fovea) onto the fundus photograph, as well as the standard reference circles with diameters of 63, 125 and 250 µm. Early AMD was defined as the presence of a large drusen (soft distinct or soft indistinct drusen with diameter ≥125 µm) and/or retinal pigment abnormalities (hyperpigmentation or hypopigmentation) within the grid, in the absence of late AMD. Late AMD was defined as the presence of exudative AMD or GA based on the grading system.

All grades were assigned by three independent ophthalmologists (RO, TI and YY) who were unaware of participants' information. Grading was performed two times for all images. After the first grading, the graders discussed the grading criteria together, and then each graded all of the images again. The agreement ratio and Cohen's Kappa index between each

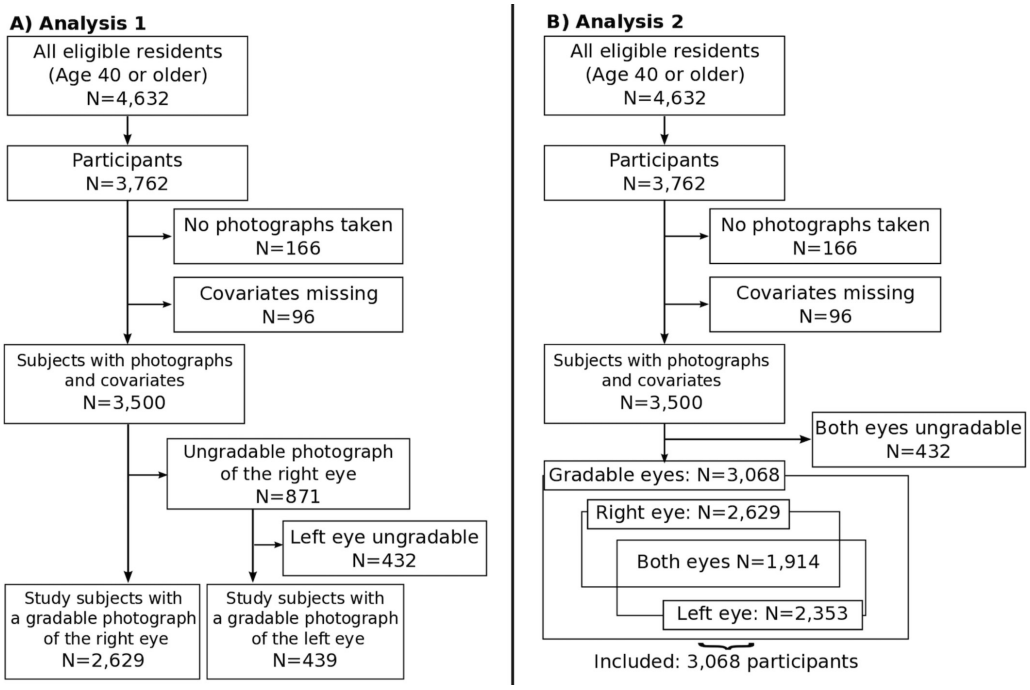

Figure 1 Flow chart showing the inclusion and exclusion of participants in the Kumejima Study for the present analyses. (A) First, we graded the right eye of the participant if it was gradable. However, when the right eye was ungradable, we graded the left eye if it was gradable. (B) Next, to consolidate our findings, we graded left eyes of all participants and conducted per-individual analysis using the worse eye of the subjects when both of their eyes were gradable.

grader is shown in online supplementary table 1. The remaining images for which grading differed among the three graders were discussed to reach a consensus.

Statistical analysis

Age-specific and sex-specific prevalence of early AMD, late AMD and individual AMD lesions were calculated as the ratio of the number of subjects with the condition to the total number of participants who had gradable fundus photographs. After determining crude prevalence, age-adjusted standardised prevalence was assessed using the direct method with reference to WHO standard population figures for 2000–2025 to compare with that described in the previous studies.[24] Multivariate analysis was performed using logistic regression analysis with forward stepwise selection. The minimum corrected Akaike Information Criterion (AICc) was used to choose the best model. In the process of stepwise selection, AICc was calculated and compared each time a variable was entered. This process was repeated until there was no further improvement of the model. We first adopted axial length in the multivariate analysis and excluded spherical equivalent to avoid multicollinearity and to adjust for the fact that approximately 9% of participants had a history of cataract surgery, which might have altered the original spherical equivalent. But we additionally analysed the association between spherical equivalent and early AMD only in eyes that had never underwent cataract surgery in order to verify the association between ocular biometry and AMD. All analyses were performed using JMP Pro software (SAS) V.12.0.0. P values less than 0.05 were considered to be statistically significant.

RESULTS

A flowchart of participants is shown in the figure 1. Of the 4632 eligible residents, 3762 (81.2%) underwent examination. The 3762 participants were younger than the 870 non-participants (59.1±14.9 vs 61.8±14.0 years, P<0.001, unpaired t-test) and the participants were mainly women (male-to-female ratio 1833:1929 vs 555:315, P<0.001, χ^2 test). We excluded 166 participants who had not had any fundus photographs taken because they were examined at home or in assisted-care facilities or they could not provide reliable answers because of mental or physical disorders. An additional 96 participants with missing covariates were also excluded.

Among the remaining 3500 participants, 2629 participants had gradable photographs in the right eye. Of the remaining 871 participants, 439 were gradable in the left eye. In total, 3068 of 3500 (88%) participants were graded (figure 1A). The main causes of ungradable photos were insufficient light due to miosis and marked opacity of the medium. The background characteristics of the participants judged as gradable or ungradable for AMD diagnosis are shown in table 1. Forty-nine eyes were excluded from AMD grading because of other retinal diseases or findings accompanied by multiple haemorrhages, fibrous scarring, chorioretinal atrophy or photocoagulation scarring within the grid such as diabetic retinopathy (n=19), retinitis pigmentosa-like widespread chorioretinal atrophy (n=13), retinal vein occlusion (n=9), pathological myopia (n=3) and miscellaneous diseases (n=5).

Of the 3068 participants, 469 had early AMD (378/2629 in the right eye, 91/439 in the left eye) and 4 had late AMD (4/2629 in the right eye). Prevalence of any AMD, early AMD, late AMD and AMD lesions are shown in table 2 and figure 2. There was a significant positive age trend in the prevalence of any, early or late AMD and large drusen, but not pigment abnormality

Table 1 Background characteristics

	No (%) or Mean±SD		Univariate analysis
	Gradable (n=3068)	Ungradable (n=432)	P value
Sex			
Male	1522 (49.6)	179 (41.4)	
Female	1546 (50.4)	253 (58.6)	0.001*
Age, years	59.5±0.2	73.7±0.6	<0.001*
BMI	25.1±0.1	24.6±0.2	0.004*
Systemic BP, mm Hg	141.5±0.43	146.6±1.1	<0.001*
Diastolic BP, mm Hg	78.9±0.2	74.5±0.6	<0.001*
Pulse rate	77.6±0.2	76.7±0.6	0.16
Hypertension	1235 (40.3)	241 (55.8)	<0.001*
Antihypertensive medication	1011 (33.0)	226 (52.3)	<0.001*
Diabetes	273 (8.9)	70 (16.2)	<0.001*
Smoking history†	1274 (41.5)	152 (35.2)	0.01*
Axial length, mm	23.4±0.0	23.1±0.0	<0.001*
Cataract surgery	333 (10.9)	76 (17.6)	<0.001*
History of working outdoors‡	1946 (63.4)	323 (74.8)	<0.001*
Cumulative time of working outdoors	111±2.6	180±6.9	<0.001*
Hat use	1727 (56.3)	306 (70.8)	<0.001*
Sunglasses use	242 (7.9)	14 (3.2)	<0.001*
Main occupation§			
Farming	743 (24.2)	122 (28.2)	0.07
Fishing	99 (3.2)	10 (2.3)	0.29
Office work	521 (17.0)	10 (2.3)	<0.001*
Service industry	303 (9.9)	21 (4.9)	<0.001*
Home maker	622 (20.3)	141 (32.6)	<0.001*

*P<0.05.
†Smoking history represents being current or ever smoker.
‡Outdoor works included full time and part time.
§Main occupation is based on participant self-report.
BMI, body mass index; BP, blood pressure.

(figure 2). Men showed higher prevalence of any or early AMD and pigment abnormality. Of note, all of the eyes with late AMD were categorised into the neovascular AMD subtype.

Because there were few subjects with late AMD, multivariate analysis was conducted for factors associated with any or early grade of AMD only (table 3 for any AMD, online supplementary table 2 for early AMD). Presence of any as well as early AMD was positively associated with male sex, age and history of cataract surgery, and was negatively associated with axial length and office work. After excluding the pseudophakic eyes, spherical equivalent showed significant positive association with early AMD in both age–sex-adjusted analysis (OR 1.1 per dioptre, 95% CI 1.03 to 1.18, P=0.004) and multivariate analysis (OR 1.1 per dioptre, 95% CI 1.02 to 1.18, P=0.007).

We also performed the sex-stratified analysis. In men, the presence of any AMD was positively associated with age (OR 1.04 per year, 95% CI 1.03 to 1.06, P<0.001) but negatively associated with longer axial length (OR 0.82 per millimetre, 95% CI 0.67 to 0.98, P=0.03), hat use (OR 0.68, 95% CI 0.49 to 0.95, P=0.02) and office work (OR 0.62, 95% CI 0.49 to 0.95, P=0.04). In women, the presence of any AMD was positively associated with age (OR 1.05 per year, 95% CI 1.04 to 1.07, P<0.001).

Multivariate analyses to determine the associations between each constituent of early AMD lesions (ie, large drusen and

Table 2 Prevalence of age-related macular degeneration (AMD) and AMD lesions

	N	Any AMD (%)	Early AMD (%)	Late AMD (%)	Large drusen (%)	Pigment abnormality (%)
Crude prevalence						
Total 40+	3068	15.4 (14.1–16.7)	15.3 (14.0–16.6)	0.1 (0–0.3)	12.0 (10.8–13.1)	2.4 (1.8–2.9)
Total 50+	2176	19.5 (17.9–21.2)	19.3 (17.7–21.0)	0.2 (0–0.4)	15.1 (13.6–16.6)	2.7 (2.0–3.3)
Age-adjusted†						
Total 40+†	3068	13.4 (12.2–14.6)	13.3 (12.1–14.5)	0.09 (0–0.2)	10.7 (9.6–11.8)	2.3 (1.7–2.8)
Total 50+†	2176	18.0 (16.4–19.7)	17.9 (16.2–19.5)	0.14 (0–0.3)	14.4 (12.9–15.9)	2.6 (1.9–3.3)
Men						
Total 40+†	1523	15.9 (14.1–17.7)	15.7 (13.9–17.5)	0.2 (0–0.4)	12.1 (10.5–13.7)	3.4 (2.5–4.3)
Women						
Total 40+†	1545	14.9 (13.2–16.7)	14.9 (13.1–16.7)	0.1 (0–0.2)	11.8 (10.2–13.5)	1.4 (0.8–1.9)
P value between sexes		0.03	0.049	0.13	0.29	<0.001

*Crude prevalence.
†Standardised to the age distribution of the world population. Difference between sexes was determined by Cochran-Mantel-Haenszel test.

pigment abnormality) and the background characteristics revealed that presence of large drusen was significantly associated with age (OR 1.03 per year, 95% CI 1.02 to 1.04, P<0.001), axial length (OR 0.86 per millimetre, 95% CI 0.75 to 0.98, P=0.03) and hat use (OR 0.62, 95% CI 0.42 to 0.95, P=0.03). Pigment abnormality showed a significant association with male sex (OR 2.89, 95% CI 0.1.68 to 5.13, P<0.001), history of cataract surgery (OR 2.14, 95% CI 1.10 to 3.91, P=0.03), farming (OR 0.44, 95% CI 0.23 to 0.80, P=0.007) and office work (OR 0.45, 95% CI 0.18 to 0.96, P=0.04).

Lastly, we conducted per-individual analysis using worse eyes of subjects when both eyes were gradable (1914 (62%) subjects had bilateral gradable eyes and 1154 (38%) participants had single gradable eye (figure 1B)). We then found 585 participants had early AMD and 6 had late AMD. As expected, prevalence of any AMD, early AMD, late AMD and AMD lesions was slightly higher compared with per-eye analysis (online supplementary table 3). In the multivariate analysis, factors associated with any grade of AMD were similar, but slightly different, from those found in per-eye analysis: similar to per-eye analysis, any AMD was positively associated with age (OR 1.04 per year, 95% CI 1.03 to 1.05, P<0.001), male sex (OR 1.41, 95% CI 1.14 to 1.75, P=0.002), cataract surgery (OR 1.37, 95% CI 1.03 to 1.83, P=0.03) and negatively associated with longer axial length (OR 0.84 per millimetre, 95% CI 0.75 to 0.94, P=0.002). In addition, sunglasses use (OR 1.44, 95% CI 1.02 to 2.00, P=0.04) and farming (OR 1.26, 95% CI 1.00 to 1.59, P=0.048) were found to be associated with any AMD. Factors associated with early AMD were the same as per-eye analysis: early AMD was positively associated with age (OR 1.04 per year, 95% CI 1.03 to 1.05, P<0.001), male sex (OR 1.42, 95% CI 1.14 to 1.75, P=0.001) and cataract surgery (OR 1.38, 95% CI 1.03 to 1.84, P=0.03) and negatively associated with longer axial length (OR 0.84 per millimetre, 95% CI 0.75 to 0.94, P=0.002).

DISCUSSION

In this study, we assessed the prevalence of and factors associated with early or late AMD or AMD-specific lesions in participants of a population-based study conducted on the island of Kumejima. Although located in the southernmost region of Japan, Kumejima shares several socioeconomic factors in common with populations in rural areas in other parts of Japan, such as a higher proportion of elderly people and outdoor workers, lower-income level and limited access to medical facilities.

Prevalence of AMD

In this study, the age-standardised prevalence among aged 40 years or older was 13.4% for any AMD, 13.3% for early AMD and 0.09% for late AMD. We first used only one eye

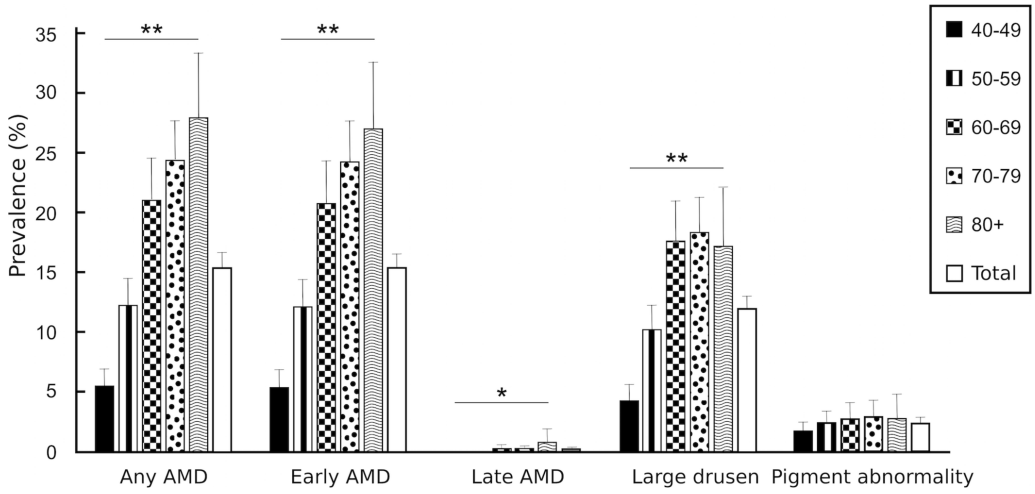

Figure 2 Prevalence of age-related macular degeneration (AMD) and AMD lesions at each age group. Bars indicate the 95% CIs. Age trend was analysed with Cochran-Armitage trend test. *P<0.01, **P<0.001.

Table 3 Results of age–sex-adjusted OR and multivariate analysis for association of background characteristics with any grade of AMD

	Age–sex-adjusted		Multivariate model	
	OR (95% CI)	P	OR (95% CI)	P
Age (per year)			1.04 (1.03 to 1.05)	<0.001
Male			1.42 (1.14 to 1.75)	0.001
BMI	1.00 (0.97 to 1.02)	0.74		
Systemic BP, mm Hg	1.00 (0.99 to 1.00)	0.70		
Diastolic BP, mm Hg	1.00 (0.99 to 1.01)	0.68		
Pulse rate	1.00 (0.99 to 1.00)	0.36		
Hypertension	1.04 (0.84 to 1.29)	0.71		
Antihypertensive medication	1.05 (0.84 to 1.30)	0.67		
Diabetes	1.07 (0.76 to 1.48)	0.70		
Smoking history*	1.02 (0.78 to 1.32)	0.90		
Axial length, mm	0.84 (0.74 to 0.95)	0.007	0.85 (0.74 to 0.96)	0.009
Cataract surgery	1.33 (0.99 to 1.79)	0.06	1.35 (1.00 to 1.82)	0.049
History of working outdoors†	1.09 (0.86 to 1.38)	0.47		
Cumulative time of working outdoors	1.00 (1.00 to 1.00)	0.34		
Hat use	0.94 (0.75 to 1.17)	0.58		
Sunglasses use	1.35(0.92 to 1.93)	0.12		
Main occupation‡				
Farming	1.16 (0.91 to 1.47)	0.22		
Fishing	0.92 (0.48 to 1.64)	0.79		
Office work	0.64 (0.43 to 0.92)	0.02	0.66 (0.44 to 0.95)	0.03
Service industry	1.27 (0.88 to 1.79)	0.20		
Home maker	0.91 (0.68 to 1.22)	0.52		

P values between any AMD and no AMD are indicated.
*Smoking history represents being current or ever smoker.
†Outdoor works included full time and part time.
‡Main occupation is based on participant self-report.
BP, blood pressure; BMI, body mass index.

for grading as in the previous studies,[6 21 22] and therefore the prevalence is likely to be underestimated. The underestimation ratio was estimated to be 36% for early AMD and 28% for late AMD.[21 22] Considering the proportion of bilaterally affected patients reported in previous population-based or cohort-based studies was 59%–76% for early AMD and 10%–57% for late AMD,[5 7 25 26] using a single eye would underestimate the prevalence at a rate of 80%–88% for early AMD and 50%–79% for late AMD. In the current per-individual analysis using the worse eye (note that 62% of the subjects had bilateral gradable eyes), the age-standardised prevalence of any, early and late AMD were 16.8%, 16.7%, and 0.14%, respectively and was 25%–56% higher than the results of per-eye analysis, and the difference was comparable to the underestimation ratio from the previous studies.[5 7 21 22 25 26] The prevalence of AMD in Asia has been reported to range from 1.4% to 37.9% for early AMD and from 0.1% to 7.3% for late AMD.[4] The prevalence of early AMD in the present study was similar to the pooled prevalence in European ancestry (11.19%, 95% CI 5.63% to 20.39%)[3] and generally higher than that in most Asian countries. Within Asia specifically, prevalence of early AMD was reported at 4.1%–22.8% in Japan,[5–8] 1.4%–9.5% in China,[9 10] 14.8% in Taiwan,[11] 6.0% in South Korea,[12] 5.1% in Singapore[13] and 16%–21% in India.[14] In addition to Kumejima, a high prevalence of early AMD was reported at 12.7% in Hisayama Town on the island of Kyushu in southwest Japan[5] and at 14.8% in Puzih City, Taiwan,[11] approximately 1500 km from each other. The higher prevalence of early AMD in this area compared with the average prevalence in Asian countries might, at least in part, be associated with the geographical background.

As for the prevalence of late AMD (0.09%), our finding was among the lowest reported in Asia (0.1%–7.3%).[3 5–14] It was still low (0.14%) even when all gradable eyes were analysed. The prevalence of late AMD might have been further underestimated because 12% of the participants were ungradable and were older than those with gradable photographs. We believe that despite the high prevalence of early AMD in Kumejima population, the prevalence of late AMD was at least lower than that in other Asian populations. This low prevalence might be associated with various environmental and genetic factors, which unfortunately could not be assessed in the present analysis. Development of late AMD was negatively associated with intakes of some nutrients such as antioxidant, fish or nuts.[27 28] Considering that Kumejima is a small island located far from the mainland Japan, genetic factors might be one of the contributory factors to this low prevalence of late AMD. It is also noteworthy that all of the eyes with late AMD were of the neovascular AMD subtype, and there were no cases of GA despite the relatively high prevalence of early AMD, in agreement with previous epidemiological studies conducted in Asian countries.[3 29]

AMD and age, sex, axial length, and history of cataract surgery

Factors associated with AMD were previously analysed using age, sex, smoking history, blood pressure or hypertension, diabetes and body mass index, but the association of ocular factors or the environmental characteristics had been unclear in East Asian populations.

In this study, age and male sex were significantly associated with early AMD. Moreover, pigment abnormality, one of the early AMD lesions, was also more likely to be seen in men. Early AMD and pigment abnormality was seen more frequently in men than women in several previous studies of Asian population.[30] As previously discussed, male predominance in early AMD or pigment abnormality might suggest a particular subtype of AMD in Asian populations.[30]

We found that axial length was negatively associated with early AMD for the first time in a Japanese population. A previous report[31] suggested that there might be possible relationship between ocular biometry and development of AMD. Of the early AMD lesions, large drusen was negatively associated with axial length. The prevailing hypothesis is that shorter eyes are likely to have increased scleral rigidity, leading to impaired transfer of oxygen and nutrients, thereby resulting in damage to the RPE.[32] Relationship between previous cataract surgery and AMD have been controversial in population-based studies from Singapore[15] or South Korea.[33] The present study showed that history of cataract surgery was significantly associated with any or early AMD. However, the result should be interpreted with care because in the subanalysis for each constituents of early AMD, only pigment abnormality, that could be less specific for AMD, was significantly correlated with history of cataract surgery. Although presence of pigmentary abnormality is a well-recognised risk factor for advanced AMD, further studies such as prospective cohort ones will be needed to clarify this finding in detail.

AMD and occupation

We found a significant negative association between office workers and any or early AMD. A few studies investigating the association between socioeconomic status and AMD found that early AMD was most frequently observed in blue-collar workers, followed by non-workers and then white-collar workers.[34] However, using all gradable eyes, office work was not associated with any or early AMD. This inconsistency indicates that no conclusion on this relationship can be drawn based on the current results and future studies are awaited.

Limitations

There are several limitations in this study. First, the fundus photographs were taken through undilated pupils and, 12% of the photographs were ungradable for AMD. When one eye from one subject for grading, the prevalence is likely to be underestimated. In addition, we conducted per-individual analysis; however, only 62% of the participants had bilateral gradable eyes. Therefore, the prevalence from per-individual analysis is also likely to be underestimated.[5 7 21 22 25 26] Second, it is also worth mentioning that the participants with ungradable photos were older and more likely to be men and to have shorter axial length or cataract surgery than those with gradable photos. This might have introduced selection bias, and therefore, such rick factors might have been under/overestimated. This might have also contributed to low prevalence of late AMD in this study. However, the prevalence of early AMD was found to be relatively high, and in the analysis using all gradable eyes, late AMD was additionally seen in only two participants. Therefore, the impact on the prevalence of late AMD should be limited, if any. Third, there were few subjects with late AMD, which makes the analysis of factors associated with late AMD less reliable. Nevertheless, a much higher proportion of eligible residents than in the previous studies in Japan[5–8] were able to undergo AMD grading (81.2%), comparable with the rates of previous population-based studies in Asia, and therefore the calculated prevalence of early AMD in Japanese should be of clinically and epidemiologically valid. Fourth, in the present study we did not find significant association between smoking and AMD. Although smoking might be one of the strong risk factors of AMD, several population-based or cohort studies failed to demonstrate the significant association between smoking and AMD.[5 8 30] Future analyses using categorisation into present/ever smokers and never smokers, or using pack-years[7] may elucidate this problem. Finally, the cross-sectional study design limits inference of the causal relationship based on the results of the study.

CONCLUSION

In conclusion, we investigated the prevalence of AMD and AMD-specific lesions in a population-based study conducted in Kumejima, a rural island in southwest Japan. In this study, with its high response rate, age-adjusted prevalence of early AMD tended to be high and that of late AMD was low compared with the pooled prevalence for all Asian countries. Clinicians and healthcare providers should keep in mind that, in addition to age and sex, axial length, and history of cataract surgery may be associated with the presence of AMD or AMD-specific lesions.

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Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

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Prevalence and factors associated with age-related macular degeneration in a southwestern island population of Japan: the Kumejima Study

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