# Age-Related Macular Degeneration

## *Prevalence and Risk Factors from Korean National Health and Nutrition Examination Survey, 2008 through 2011*

*Sang Jun Park, MD,[1] Ju Hyun Lee, MS,[2] Se Joon Woo, MD, PhD,[1] Jeeyun Ahn, MD,[3] Jae Pil Shin, MD, PhD,[4] Su Jeong Song, MD, PhD,[5] Se Woong Kang, MD, PhD,[6] Kyu Hyung Park, MD, PhD,[1] on behalf of the Epidemiologic Survey Committee of the Korean Ophthalmologic Society*

***Objective:*** To investigate the prevalence and risk factors of age-related macular degeneration (AMD) in the Korean population.

***Design:*** A cross-sectional study using a complex, stratified, multistage, probability-cluster survey, which can produce nationally representative estimates.

***Participants:*** Using the database of Korean National Health and Nutrition Examination Survey from 2008 through 2011, 14 352 participants 40 years of age or older with gradable fundus photographs were included.

***Methods:*** Age-related macular degeneration was determined by fundus photograph. Prevalences of AMDs were estimated. Risk factor analyses were conducted using logistic regression analyses (LRAs).

***Main Outcome Measures:*** Prevalence and risk factors of AMD.

***Results:*** The prevalence of AMD was 6.62% (95% confidence interval [CI], 6.15%−7.09%) in the Korean population: 6.02% (95% CI, 5.56%−6.48%) were early AMD and 0.60% (95% CI, 0.45%−0.75%) were late AMD. The prevalence of early AMD in women (6.73%; 95% CI, 6.11%−7.35%) was higher than that in men (5.25%; 95% CI, 4.61%−5.89%; $P<0.001$), and the prevalence of late AMD in women (0.37%; 95% CI, 0.22%−0.52%) was lower than that in men (0.85%; 95% CI, 0.59%−1.12%; $P<0.001$). However, in multiple LRAs both early and late AMD had no association with gender, house income, residence, sun exposure, or systemic comorbidities, including hypertension, diabetes mellitus, and cardiovascular diseases. Early AMD had positive associations with older age groups ($P<0.001$), lower education ($P = 0.027$), occupation ($P<0.001$), anemia ($P = 0.027$), hepatitis B surface antigen carrier status ($P<0.001$), not being overweight (body mass index [BMI], $P = 0.032$; waist circumference, $P = 0.041$, in separate analyses), and higher serum high-density lipoprotein (HDL) level ($P = 0.046$), but not with smoking status. Late AMD had positive associations with age groups ($P<0.001$), current smokers ($P = 0.022$), and lower BMI ($P = 0.037$).

***Conclusions:*** The results suggest that there are 1.21 million individuals with early AMD and 121 000 individuals with late AMD in Korea. Nonoverweight status and higher HDL levels, generally assumed as positive health indicators, as well as anemia and hepatitis B infection had harmful associations with AMD in our study, implying a possible different pathophysiologic process of AMD in Asians compared with that of white persons. *Ophthalmology 2014;■:1−10 © 2014 by the American Academy of Ophthalmology.*

*Supplemental material is available at www.aaojournal.org.*

Age-related macular degeneration (AMD) is the leading cause of blindness in industrialized countries and is responsible for more than 3 million blind people in the world.[1] As a consequence of population aging, the prevalence and absolute number of persons with AMD are likely to increase, and the health expenditure for AMD has sharply increased already.[2] Numerous studies have investigated the epidemiologic factors of AMD over the past 30 years largely in white persons, and recently in Asians. It generally has been assumed that AMD is less frequent in Asians than in white patients; however, recent studies have shown conflicting results.[3] A recent meta-analysis reported that early AMD signs were less common in Asians compared with white persons, whereas the prevalence of late AMD was comparable.[4] On the contrary, in other studies, late AMD prevalence was lower in Asians than that in white persons, whereas early AMD prevalence was comparable.[5] In addition, proportions of late AMD subtypes may be different between Asians and white persons as well as overall AMD prevalence; polypoidal choroidal vasculopathy (PCV), a distinct subtype of wet AMD, accounts for 50% of wet AMD in Asian populations, whereas it accounts for only 8% to 13% in the white population.[6] Hence, a reliable, large, population-based study is needed to investigate the difference in prevalence and risk factors for AMD between East Asians and white persons. However, despite the socioeconomic importance and burden of AMD, epidemiologic studies



ISSN 0161-6420/14/$ - see front matter
http://dx.doi.org/10.1016/j.ophtha.2014.03.022

representing a nationwide population have been scarce. There have been prevalence studies only from the United States, based on the National Health and Nutrition Examination Survey, and to date, no study has been conducted in the Asian population.[7]

Korea is one of the newly industrialized countries in Asia and one of the most populous countries in the world. As the issue of an aging population has emerged in Korea, as in other industrialized countries, several nationwide, government-led surveys have been conducted. The Korea National Health and Nutrition Examination Survey (KNHANES) is one of these national surveys initiated in 1998 and represents the entire Korean population of approximately 50 million. Using the data of the KNHANES from 2008 to 2011, we estimated the prevalence and risk factors of AMD and investigated racial or ethnic differences in AMD epidemiologic factors.

## Methods

### Study Design and Population

The KNHANES is an ongoing, population-based, cross-sectional survey in South Korea conducted by the Korea Centers for Disease Control and Prevention and the Korean Ministry of Health and Welfare. The present study analyzed the data of the 2008 through 2011 KNHANES. The detailed design of the KNHANES has been described elsewhere.[8] In brief, the 2008 through 2011 KNHANES annually selected 4600 households in 200 enumeration districts (2008–2009, KNHANES IV) and 3840 households in 192 enumeration districts (2010–2011, KNHANES V), which represented the civilian, noninstitutionalized Korean population using rolling sampling designs involving a complex, stratified, multistage, probability-cluster survey. The quoted design, not a simple random sample, is used widely in health surveys to sample a fraction of a large finite population while accounting for its size and characteristics. In this design, sampling is always multistage, using strata (separate sampling from population subgroups), cluster (considering possibility of group of observations), and weight (considering oversampling or undersampling).[9] In KNHANES, both the 1-year data surveys and the integrated data of the 2008 through 2011 surveys represent the entire population of Korea. Response rates were 77.8%, 82.8%, 81.9%, and 80.4% in 2008, 2009, 2010, and 2011, respectively. A total of 16 108 eligible subjects (6952 men and 9157 women) 40 years of age or older participated during the 4-year study period. The participants having a gradable fundus photograph from at least 1 eye were included in the present study. The Institutional Review Board of the Seoul National Bundang Hospital approved the present study, which was conducted in accordance with the Declaration of Helsinki.

### Data Collection

The KNHANES consisted of 3 components: the health interview survey, the health examination survey, and the nutrition survey. The details of data collection have been published elsewhere.[8,10] We used the data from the first 2 surveys: data regarding medical histories, socioeconomic status using a set of structured questionnaires, anthropometry investigations, blood tests, and ophthalmic surveys. Fundus photographs were obtained with a nonmydriatic fundus camera (TRC-NW6S, Topcon, Tokyo, Japan). Patients were defined as having early AMD if the fundus photograph met 1 of the 2 criteria: (1) the presence of soft indistinct drusen or reticular drusen, or (2) the presence of hard or soft distinct drusen with pigmentary abnormalities (increased pigmentation or hypopigmentation of the retinal pigment epithelium) in the absence of signs of late AMD. Late AMD included the presence of signs of wet AMD or geographic atrophy (GA). Wet AMD was defined as retinal pigment epithelial detachment or serous detachment of the sensory retina, subretinal or sub-RPE hemorrhages, and subretinal fibrous scars. Geographic atrophy was defined as a circular discrete area (175 μm in diameter) of retinal depigmentation with visible choroidal vessels, in the absence of signs of wet AMD. Each fundus photograph was graded twice (a preliminary grade and a detailed grade) using the grading protocol of the International Age-Related Maculopathy Epidemiological Study Group.[11] Detailed grading was performed later by 9 retina specialists who (including J.P.S., S.J.S., S.W.K., and K.H.P.) were masked to the patients' characteristics and entrusted by the Korean Ophthalmologic Society. Final grading was based on the detailed grading, and any discrepancies between the preliminary and detailed grading were resolved by 1 reading specialist (J.P.S.).[10] The interrater reliability for AMD grading was 90.2% and 90.7% in 2008, 92.4% and 93.3% in 2009, 94.1% and 95.0% in 2010, and 96.2% and 96.6% (right eye and left eye, respectively) in 2011, respectively (available at: https://knhanes.cdc.go.kr/knhanes/sub04/sub04_03_02.do?classType=8; accessed January 6, 2014). The quality of the ophthalmic survey and fundus photograph readings was verified by the Epidemiologic Survey Committee of the Korean Ophthalmologic Society.[8]

### Variable Definitions and Statistical Analysis

The variables analyzed in this study were defined and categorized as follows. The first category among the categories of each variable defined below was selected as a reference in logistic regression analysis (LRA). Participants were divided into 4 age groups: 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years or older. Smoking status was defined as never smoker, former smoker, or current smoker. House income status was divided into 2 groups: participants with more than 50% household income and those with 50% or less household income according to the equivalent gross household income in each year. Education status was divided into 2 groups: participants with at least a high school degree and those who had graduated from middle school or less. Occupation was categorized as white collar (managers, professionals, clerks, service or sales workers), blue collar (agriculture, forestry, fishery workers, craft and related trade workers, plant and machine operators and assemblers, and simple labor), and no occupation (unemployed, retired, student, and homemaker). Residence was categorized into urban and rural areas based on the address of participants. Sun exposure status was divided into 2 groups: participants with an average of fewer than 5 hours/day and those with 5 hours/day or more. Comorbidities were categorized into participants without history of comorbidities and those with history of comorbidities. Participants were categorized into 2 groups by body mass index (BMI), the ratio of weight (in kilograms) to height (in square meters): those with BMI of less than 25 $kg/m^2$ and those with BMI of 25 $kg/m^2$ or more. Waist circumference (WC) was measured to nearest 0.1 cm at the narrowest point between the lower borders of the rib cage and the iliac crest after normal expiration. Participants were divided into 2 groups: those with a WC of less than 90 cm in men or less than 80 cm in women and those with a WC of 90 cm or more in men or 80 cm or more in women. Hemoglobin, hematocrit, and red blood cells were measured by XE-2100D (Sysmex, Kobe, Japan), and participants with hemoglobin level of less than 13 g/dl in men and less than 12 g/dl in women were designated as anemic. Mean corpuscular volume (MCV) was calculated by dividing the hematocrit (in percent) by the number of red blood cells (millions per microliter), and then multiplying it by 10. Using calculated

Table 2. Weighted Prevalences and Frequencies of Age-Related Macular Degeneration in the Korean Population during the Study Period (2008–2011)

| | All Age-Related Macular Degeneration | Early Age-Related Macular Degeneration | Late Age-Related Macular Degeneration | | |
|---|---|---|---|---|---|
| | | | *All Late Age-Related Macular Degeneration* | *Wet Age-Related Macular Degeneration* | *Geographic Atrophy* |
| Age, weighted mean (SE) | 64.73 (0.43) | 64.71 (0.43) | 64.99 (1.69) | 63.6 (1.9) | 70.5 (3.1) |
| Overall, weighted % (95% CI) | 6.62 (6.15–7.09) | 6.02 (5.56–6.48) | 0.60 (0.45–0.75) | 0.48 (0.34–0.62) | 0.12 (0.06–0.18) |
| Frequency | 1129 | 1034 | 95 | 72 | 23 |
| Age groups (yrs) | | | | | |
| 40–49, weighted % (95% CI) | 1.62 (1.18–2.06) | 1.44 (1.03–1.86) | 0.18 (0.03–0.33) | 0.18 (0.03–0.33) | 0 |
| Frequency | 64 | 57 | 7 | 7 | 0 |
| 50–59, weighted % (95% CI) | 5.16 (4.38–5.95) | 4.75 (4.00–5.51) | 0.41 (0.14–0.69) | 0.37 (0.11–0.63) | 0.05 (0.00–0.14) |
| Frequency | 205 | 192 | 13 | 12 | 1 |
| 60–69, weighted % (95% CI) | 11.68 (10.33–13.04) | 10.65 (9.36–11.94) | 1.03 (0.55–1.52) | 0.83 (0.39–1.28) | 0.20 (0.00–0.40) |
| Frequency | 386 | 358 | 28 | 22 | 6 |
| ≥70, weighted % (95% CI) | 17.96 (16.12–19.80) | 16.26 (14.46–18.07) | 1.70 (1.17–2.23) | 1.15 (0.69–1.60) | 0.55 (0.25–0.86) |
| Frequency | 474 | 427 | 47 | 31 | 16 |

CI = confidence interval; SE = standard error.

MCV, participants diagnosed as anemic were subcategorized as having microcytic anemia (MCV < 80), normocytic anemia (80 ≤ MCV< 100), or macrocytic anemia (MCV ≥ 100). Methods of other blood tests were as follows: hepatitis B surface antigen (HBsAg; electrochemiluminescence immunoassay E-170, Roche, Mannheim, Germany), lipoproteins (total cholesterol, triglyceride, and high-density lipoprotein [HDL]; enzymatic cholesterol assay Automatic Analyzer 7600, Hitachi, Tokyo, Japan), blood urea nitrogen (kinetic ultraviolet assay), creatinine (colorimetric method), and vitamin D (radioimmunoassay; 1470 Wizard gamma-counter, Perkin-Elmer, Turku, Finland). Data regarding HDL collected in 2011 has not yet been released on the grounds of quality control because the measuring method of HDL was changed in 2011.

The data were analyzed with SAS software version 9.2 (SAS Inc, Cary, NC) using proc survey procedures, which can analyze the presented data properly using the variable of strata, cluster, and weight; we used the KNHANES sample weight adjusted for oversampling, nonresponse, and the Korean population from 2008 through 2011.[12] The standard errors of estimates were calculated. *P* values less than 0.050 were considered statistically significant. The comparison of participants included and excluded from the study was conducted. The prevalence of AMD and AMD subgroups were estimated. Simple LRAs were conducted to investigate the associations between AMD prevalence and a set of variables. After that, the LRAs adjusted for age group, gender, and smoking status were performed. Covariates that had a *P* value of less than 0.100 in each LRA adjusted for age group, gender, and smoking status were chosen for multiple LRAs of each subtype of AMD. Age group, gender, and smoking status were always included in multiple LRAs regardless of *P* values. Variables that significantly correlated with each other (e.g., dyslipidemia and lipoproteins, BMI, and WC) were not included simultaneously in multiple LRAs; we chose the most significant covariate among correlated variables for multivariable models, or if significances of correlated variables were similar to each other, we conducted multiple LRAs in separate ways using each variable. When HDL, collected only from 2008 through 2010, had a *P* value of less than 0.100 in the LRA adjusted for age group, gender, and smoking status and was included in multiple LRAs, the multiple LRA was conducted separately based on the analyses from 2008 through 2010 data using the proper sample weight for 3-year analyses. Finally, a multiple LRA was reconducted using the variable of subcategorized anemia instead of the anemia variable when anemia had a significant association in that multiple LRA. We calculated odds ratio and 95% confidence interval (CI) values in all LRAs.

## Results

Of the 16 109 participants, 14 352 subjects had a gradable fundus photograph from at least 1 eye (right eye in 13 842 and left eye in 13 778). Comparisons between participants with and without gradable fundus photographs for AMD are demonstrated in Table 1 (available at www.aaojournal.org).

### Prevalence of Age-Related Macular Degeneration

The prevalence of overall AMD was 6.62% (95% CI, 6.15%–7.09%): 6.02% (95% CI, 5.56%–6.48%) were early AMD and 0.60% (95% CI, 0.45%–0.75%) were late AMD (0.48% [95% CI, 0.34%–0.62%] for wet AMD and 0.12% [95% CI, 0.06%–0.18%] for GA). The prevalence of early AMD in women (6.73%; 95% CI, 6.11%–7.35%) was higher than that in men (5.25%; 95% CI, 4.61%–5.89%; $P<0.001$), whereas the prevalence of late AMD in women (0.37%; 95% CI, 0.22%–0.52%) was lower than that in men (0.85%; 95% CI, 0.59%–1.12%; $P<0.001$). Similarly, the prevalence of wet AMD and GA, subtypes of late AMD, are higher in men than in women (wet AMD, 0.67% [95% CI, 0.42%–0.91%] in men and 0.31% [95% CI, 0.16%–0.45%] in women, $P<0.001$; GA, 0.19% [95% CI, 0.08%–0.30%] in men and 0.06% [0.01%–0.12%] $P<0.001$; Table 2 and Fig 1). However, the LRAs revealed that the prevalence of early and late AMD did not differ by gender.

### Risk Factors of Age-Related Macular Degeneration

Results of adjusted LRAs for age group, gender, and smoking status are provided in Table 3 (early AMD), Table 4 (early AMD using the 2008–2010 data; available at www.aaojournal.org), Table 5 (late AMD), Table 6 (wet AMD; available at www.aaojournal.org), and Table 7 (GA; available at www.aaojournal.org). Online-only tables also provide results of simple LRAs for each subgroup of AMD, and the results of simple LRAs for early AMD and late AMD are provided separately in Table 8 (available at www.aaojournal.org).

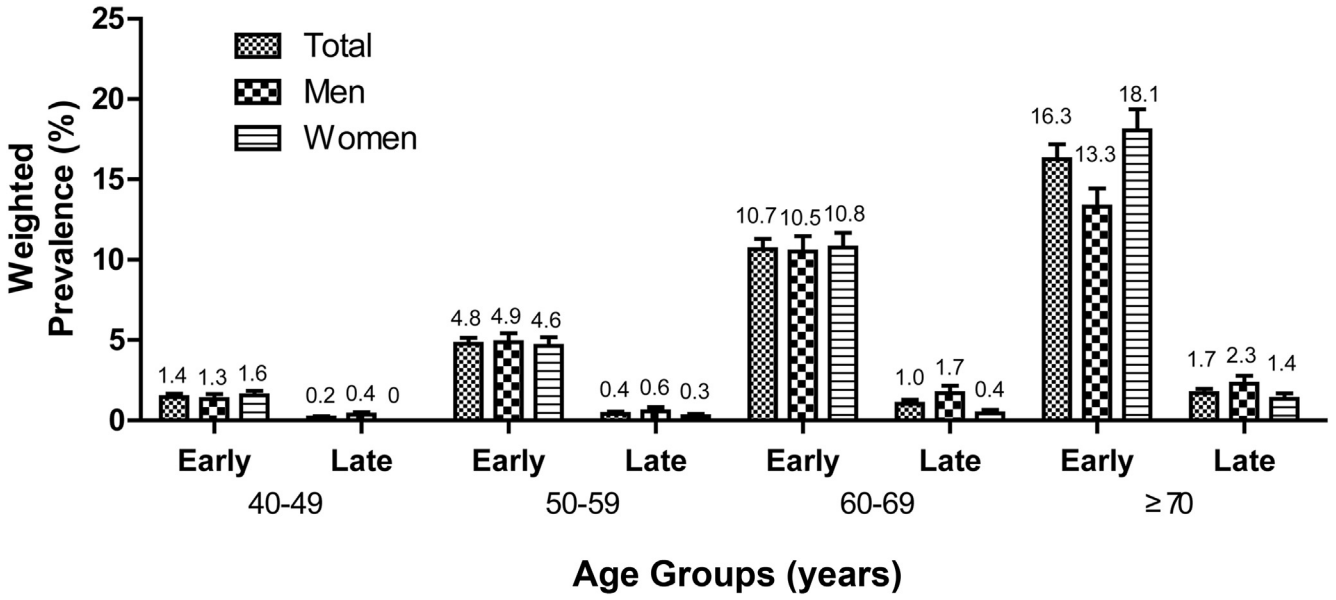


**Figure 1.** Bar graph showing age- and gender-specific weighted prevalence of early and late age-related macular degeneration in Korea during the 4-year study period (2008–2011).

### Multiple Logistic Regression Analyses for Early Age-Related Macular Degeneration

The variables with a *P* value less than 0.100 in LRAs adjusted for age group, gender, and smoking status for early AMD were age group, household income, education, occupation, diabetes mellitus, dyslipidemia, BMI, WC, anemia, HBsAg carrier, triglyceride, HDL, and creatinine. Multiple LRAs were conducted in 3 ways: model 1 (using BMI instead of WC), model 2 (using WC instead of BMI), and model 3 (using HDL and analyzing the 2008–2010 data). Early AMD had similar results in models 1 and 2 and had positive associations with older age groups ($P<0.001$), lower education ($P = 0.027$), occupation ($P<0.001$), anemia ($P = 0.027$), HBsAg carrier ($P<0.001$), lower BMI ($P = 0.032$), and smaller WC ($P = 0.041$; Table 3). In model 3, results of the 3-year data, early AMD also had similar results: positive associations with older age groups ($P<0.001$), lower education ($P = 0.007$), occupation ($P = 0.024$), anemia ($P = 0.035$), HBsAg carrier ($P<0.001$), and higher HDL level ($P = 0.046$; Table 4, available at www.aaojournal.org). In multiple LRAs using the variable of subcategorized anemia instead of anemia, early AMD had a positive association with normocytic anemia ($P = 0.008$), but no association with either microcytic or macrocytic anemia (Table 9, available at www.aaojournal.org).

### Multiple Logistic Regression Analyses for Late Age-Related Macular Degeneration

The variables with a *P* value less than 0.100 in LRAs adjusted for age group, gender, and smoking status for late AMD were age group, smoking status, and BMI. In multiple LRAs, late AMD had positive associations with older age groups ($P<0.001$), current smokers ($P = 0.022$), and lower BMI ($P = 0.037$; Table 5). Multiple LRAs in subgroups of late AMD were provided in supplemental tables (Tables 6 and 7, available at www.aaojournal.org).

## Discussion

The present study provided detailed data on the prevalence and risk factors of AMD based on the nationwide representing population that included 14 352 participants 40 years of age or older. The prevalences of early and late AMD in Korea were similar to those for Asian populations from a meta-analysis.[4] As with previous studies in Asian populations,[5,13] and not in white populations,[7,14] men had a higher prevalence of late AMD than women in the Korean population, which in part has been explained by the dominance of PCV in Asian men.[4,15] Some authors have explained that the higher frequency of PCV cases in Asian populations brings about the higher ratio of wet AMD-to-GA in Asian populations than that in white populations.[4] The 4-times-higher prevalence of wet AMD to GA in our study was similar to that in Asian populations and higher than that in white populations. Another explanation is that it may be related to higher smoking rates in Asian men compared with that in Asian women,[4,13] which was even observed in our study; more than 90% of women had never smoked, whereas approximately 85% of men had smoked previously or were smoking currently (Table 10), and smoking had a positive association with late AMD. Smoking, although a well-defined risk factor of both early and late AMD,[16] was not associated with early AMD in the Korean population. These findings also were observed in the data from the Seoul National Bundang Hospital AMD Cohort Study, a hospital-based cohort study that included 463 AMD patients and 395 normal controls; smoking had a positive association with wet AMD (n = 314; $P = 0.003$), but an inverse association with early AMD (n = 112; $P<0.001$) in multiple LRAs that included age, gender,

Table 3. Characteristics of Normal and Early Age-Related Macular Degeneration Participants and Associations between Early Age-Related Macular Degeneration and Potential Risk Factors Using Logistic Regression Analysis

| | No Age-Related Macular Degeneration, No. (%) | Early Age-Related Macular Degeneration, No. (%) | Adjusted (Age Group, Gender, and Smoking Status) | | Multivariate Model (Using All Variables with P<0.100 in Adjusted Analysis)* | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | *Model 1* | | *Model 2* | |
| | | | *Odds Ratio (95% Confidence Interval)* | *P Value* | *Odds Ratio (95% Confidence Interval)* | *P Value* | *Odds Ratio (95% Confidence Interval)* | *P Value* |
| Age group (yrs) | | | *P* trend | <0.001 | *P* trend | <0.001 | *P* trend | <0.001 |
| 40–49 | 4168 (41.17) | 57 (9.36) | 1 (reference) | | 1 (reference) | | 1 (reference) | |
| 50–59 | 3758 (30.71) | 192 (23.88) | 3.42 (2.43–4.82) | <0.001 | 2.99 (2.02–4.12) | <0.001 | 3.02 (2.04–4.47) | <0.001 |
| 60–69 | 3038 (16.36) | 358 (30.61) | 8.29 (5.99–11.48) | <0.001 | 6.34 (4.33–9.30) | <0.001 | 6.43 (4.37–9.45) | <0.001 |
| ≥70 | 2259 (11.75) | 427 (36.16) | 13.52 (9.88–18.50) | <0.001 | 9.59 (6.57–14.00) | <0.001 | 9.86 (6.73–14.44) | <0.001 |
| Female gender | 7553 (51.70) | 606 (58.11) | 1.05 (0.81–1.37) | 0.718 | 0.88 (0.63–1.22) | 0.431 | 0.93 (0.66–1.30) | 0.662 |
| Smoking | | | *P* trend | 0.670 | *P* trend | 0.623 | *P* trend | 0.668 |
| Former (to never) | 2833 (22.29) | 224 (22.37) | 0.88 (0.66–1.17) | 0.378 | 0.88 (0.65–1.18) | 0.387 | 0.88 (0.65–1.19) | 0.409 |
| Current (to never) | 2487 (23.23) | 162 (17.56) | 0.94 (0.69–1.28) | 0.684 | 0.87 (0.62–1.22) | 0.428 | 0.87 (0.62–1.22) | 0.432 |
| Household income (≤50%) | 6342 (45.42) | 685 (63.90) | 1.25 (1.05–1.50) | 0.015 | 1.10 (0.91–1.33) | 0.344 | 1.11 (0.91–1.34) | 0.310 |
| Education (≤middle school) | 6733 (45.48) | 768 (74.26) | 1.49 (1.19–1.86) | 0.001 | 1.33 (1.03–1.70) | 0.027 | 1.32 (1.03–1.69) | 0.027 |
| Occupation | | | *P* trend | <0.001 | *P* trend | <0.001 | *P* trend | <0.001 |
| White collar | 3589 (32.21) | 101 (11.04) | 1 (reference) | | 1 (reference) | | 1 (reference) | |
| Blue collar | 4338 (34.33) | 386 (39.66) | 2.00 (1.54–2.58) | <0.001 | 1.82 (1.37–2.41) | <0.001 | 1.82 (1.37–2.42) | <0.001 |
| No occupation | 5117 (32.75) | 530 (49.30) | 1.62 (1.24–2.12) | 0.001 | 1.58 (1.19–2.10) | 0.002 | 1.60 (1.20–2.13) | 0.001 |
| Residence (rural) | 3635 (24.06) | 260 (31.65) | 1.12 (0.95–1.34) | 0.182 | N/A | | N/A | |
| Sun exposure (≥5 hours/day) | 3313 (22.37) | 314 (27.71) | 1.07 (0.89–1.28) | 0.485 | N/A | | N/A | |
| Hypertension | 3838 (25.59) | 421 (41.38) | 1.07 (0.91–1.27) | 0.410 | N/A | | N/A | |
| DM | 1479 (9.89) | 130 (12.40) | 0.78 (0.62–0.99) | 0.039 | 0.82 (0.63–1.07) | 0.144 | 0.83 (0.64–1.08) | 0.161 |
| Dyslipidemia | 1784 (12.33) | 134 (12.23) | 0.77 (0.59–0.99) | 0.043 | 0.85 (0.64–1.13) | 0.254 | 0.85 (0.64–1.13) | 0.256 |
| Stroke | 354 (2.09) | 40 (3.71) | 0.99 (0.64–1.52) | 0.949 | N/A | | N/A | |
| MI or IHD | 453 (2.77) | 54 (5.12) | 1.11 (0.76–1.62) | 0.593 | N/A | | N/A | |
| OA or RA | 2939 (18.63) | 340 (32.64) | 1.14 (0.94–1.39) | 0.191 | N/A | | N/A | |
| Pulmonary Tb | 956 (7.01) | 81 (7.74) | 0.92 (0.68–1.25) | 0.580 | N/A | | N/A | |
| Asthma | 651 (4.53) | 65 (5.74) | 0.85 (0.62–1.16) | 0.296 | N/A | | N/A | |
| Thyroid disease | 631 (4.36) | 50 (3.88) | 0.81 (0.58–1.15) | 0.235 | N/A | | N/A | |
| BMI (≥25 kg/m$^2$) | 4625 (35.52) | 307 (30.36) | 0.79 (0.66–0.95) | 0.013 | 0.81 (0.67–0.98) | 0.032 | N/A | |
| WC (≥90 cm [men], ≥80 cm [women]) | 5614 (40.23) | 442 (43.20) | 0.82 (0.69–0.98) | 0.033 | N/A | | 0.82 (0.68–0.99) | 0.040 |
| Anemia | 1197 (8.70) | 126 (13.31) | 1.39 (1.04–1.86) | 0.025 | 1.39 (1.04–1.87) | 0.027 | 1.39 (1.04–1.86) | 0.028 |
| HBsAg carrier | 446 (3.82) | 52 (5.79) | 1.91 (1.33–2.75) | 0.001 | 1.98 (1.38–2.85) | <0.001 | 1.96 (1.36–2.83) | <0.001 |
| **Serum levels** | | | | | | | | |
| Total cholesterol (mg/dl) | 12 667 (193.40)† | 958 (192.57)† | 1.00 (1.00–1.00)‡ | 0.538 | N/A | | N/A | |
| TG (mg/dl) | 12 667 (148.18)† | 958 (137.78)† | 1.00 (1.00–1.00)‡ | 0.078 | N/A | | N/A | |
| HDL (mg/dl) | 9189 (51.28)† | 626 (51.16)† | 1.01 (1.00–1.02)‡ | 0.057 | N/A | | N/A | |
| BUN (mg/dl) | 12 667 (14.9)† | 958 (15.68)† | 0.99 (0.98–1.01)‡ | 0.277 | N/A | | N/A | |
| Cr (mg/dl) | 12 665 (0.84)† | 958 (0.83)† | 0.61 (0.38–0.98)‡ | 0.042 | 0.77 (0.50–1.19)‡ | 0.243 | 0.77 (0.49–1.21)‡ | 0.255 |
| Vitamin D (ng/ml) | 12 667 (19.0)† | 959 (19.90)† | 1.01 (1.00–1.02)‡ | 0.130 | N/A | | N/A | |

BMI = body mass index; BUN = blood urea nitrogen; Cr = creatinine; DM = diabetes mellitus; HBsAg = hepatitis B surface antigen; HDL = high-density lipoprotein; IHD = ischemic heart disease; LDL = low-density lipoprotein; MI = myocardial infarction; N/A = not applicable; OA = osteoarthritis; RA = rheumatoid arthritis; Tb = tuberculosis; TG = triglyceride; WC = waist circumference.

*Variables that were significantly related to each other were not included simultaneously in a multiple logistic regression analysis (LRA); multiple LRA in this table were conducted in 2 ways: model 1 (including BMI [instead of WC] and dyslipidemia [instead of lipoproteins] as a covariate) and model 2 (including included WC [instead of BMI] and dyslipidemia [instead of lipoproteins] as a covariate). Adjusted for age group, gender, and smoking status.

†No. (mean).

‡Per 1 unit.

education, diabetes mellitus, hypertension, cardiovascular disease, and dyslipidemia as covariates (Park KH, et al. IOVS 2012;53:ARVO E-Abstract 3304).

In our study, increased age was associated strongly with both early and late AMD, but gender did not have any association. Interestingly, higher serum HDL level was associated positively with early AMD. Some studies have reported positive associations between serum HDL level and AMD,[10,17,18] whereas no association[19] or inverse associations[20] also have been reported. Likewise,

Table 5. Characteristics of Normal and Late Age-Related Macular Degeneration Participants and Associations between Late Age-Related Macular Degeneration and Potential Risk Factors Using Logistic Regression Analysis

| | | | Adjusted (Age Group, Gender, and Smoking Status) | | Multivariate Model (Using All Variables with P<0.100 in Adjusted Analysis) | |
|---|---|---|---|---|---|---|
| | No Age-Related Macular Degeneration, No. (%) | Late Age-Related Macular Degeneration, No. (%) | *Odds Ratio (95% Confidence Interval)* | *P Value* | *Odds Ratio (95% Confidence Interval)* | *P Value* |
| Age group (yrs) | | | *P* trend | <0.001 | *P* trend | <0.001 |
| 40–49 | 4168 (41.17) | 7 (11.79) | 1 (reference) | | 1 (reference) | |
| 50–59 | 3758 (30.71) | 13 (20.75) | 3.31 (1.10–9.93) | 0.033 | 3.25 (1.08–9.77) | 0.035 |
| 60–69 | 3038 (16.36) | 28 (29.67) | 9.46 (3.51–25.47) | <0.001 | 9.37 (3.48–25.23) | <0.001 |
| ≥70 | 2259 (11.75) | 47 (37.78) | 18.34 (7.44–45.22) | <0.001 | 16.71 (6.75–41.33) | <0.001 |
| Female gender | 7553 (51.70) | 37 (32.04) | 0.62 (0.35–1.10) | 0.100 | 0.63 (0.35–1.13) | 0.123 |
| Smoking | | | *P* trend | 0.050 | *P* trend | 0.072 |
| Former (to never) | 2833 (22.29) | 32 (32.97) | 1.55 (0.79–3.04) | 0.208 | 1.54 (0.77–3.06) | 0.219 |
| Current (to never) | 2487 (23.23) | 25 (33.67) | 2.28 (1.18–4.40) | 0.015 | 2.20 (1.12–4.31) | 0.022 |
| Household income (≤50%) | 6342 (45.42) | 63 (59.79) | 0.92 (0.51–1.66) | 0.778 | N/A | |
| Education (≤middle school) | 6733 (45.48) | 60 (56.80) | 0.65 (0.36–1.17) | 0.152 | N/A | |
| Occupation | | | *P* trend | 0.663 | N/A | |
| White collar | 3589 (32.21) | 10 (14.15) | 1 (reference) | | | |
| Blue collar | 4338 (34.33) | 29 (34.71) | 1.18 (0.46–3.03) | 0.733 | | |
| No occupation | 5117 (32.75) | 54 (51.14) | 1.43 (0.58–3.50) | 0.437 | | |
| Residence (rural) | 3635 (24.06) | 33 (28.94) | 0.85 (0.52–1.41) | 0.535 | N/A | |
| Sun exposure (≥5 hours/day) | 1283 (11.91) | 11 (15.52) | 0.83 (0.37–1.86) | 0.655 | N/A | |
| Hypertension | 3838 (25.59) | 45 (38.44) | 0.97 (0.59–1.57) | 0.886 | N/A | |
| DM | 1479 (9.89) | 7 (8.46) | 0.48 (0.18–1.31) | 0.153 | N/A | |
| Dyslipidemia | 1784 (12.33) | 11 (11.69) | 0.85 (0.38–1.90) | 0.699 | N/A | |
| Stroke | 354 (2.09) | 4 (3.86) | 0.89 (0.31–2.56) | 0.833 | N/A | |
| MI or IHD | 453 (2.77) | 4 (6.22) | 1.23 (0.40–3.72) | 0.720 | N/A | |
| OA or RA | 2939 (18.63) | 24 (19.01) | 0.71 (0.41–1.22) | 0.210 | N/A | |
| Pulmonary Tb | 956 (7.01) | 14 (12.96) | 1.43 (0.73–2.79) | 0.295 | N/A | |
| Asthma | 651 (4.53) | 7 (4.90) | 0.70 (0.32–1.54) | 0.375 | N/A | |
| Thyroid disease | 631 (4.36) | 2 (1.03) | 0.32 (0.06–1.75) | 0.189 | N/A | |
| BMI (≥25) | 4625 (35.52) | 26 (20.71) | 0.54 (0.31–0.96) | 0.037 | 0.54 (0.31–0.96) | 0.037 |
| WC (≥90 cm [male], ≥80 cm [female]) | 5614 (40.23) | 39 (33.28) | 0.76 (0.44–1.32) | 0.332 | N/A | |
| Anemia | 1197 (8.70) | 9 (10.01) | 1.13 (0.50–2.60) | 0.766 | N/A | |
| HBsAg carrier | 446 (3.82) | 5 (4.37) | 1.49 (0.51–4.32) | 0.467 | N/A | |
| **Serum levels** | | | | | | |
| Total cholesterol (mg/dL) | 12 667 (193.40)* | 88 (197.01)* | 1.01 (1.00–1.01)† | 0.216 | N/A | |
| TG (mg/dL) | 12 667 (148.18)* | 88 (150.32)* | 1.00 (1.00–1.00)† | 0.874 | N/A | |
| HDL (mg/dL) | 9189 (51.28)* | 58 (48.57)* | 1.00 (0.97–1.02)† | 0.837 | N/A | |
| BUN (mg/dL) | 12 667 (14.9)* | 88 (15.80)* | 0.99 (0.94–1.04)† | 0.581 | N/A | |
| Cr (mg/dL) | 12 665 (0.84)* | 88 (0.89)* | 1.07 (0.54–2.11)† | 0.858 | N/A | |
| Vitamin D (ng/mL) | 12 667 (19.0)* | 88 (19.49)* | 0.99 (0.95–1.03)† | 0.552 | N/A | |

BMI = body mass index; BUN = blood urea nitrogen; Cr = creatinine; DM = diabetes mellitus; HBsAg = hepatitis B surface antigen; HDL = high-density lipoprotein; IHD = ischemic heart disease; LDL = low-density lipoprotein; MI = myocardial infarction; N/A = not applicable; OA = osteoarthritis; RA = rheumatoid arthritis; Tb = tuberculosis; TG = triglyceride; WC = waist circumference.
Adjusted for age group, gender, and smoking status.
*No. (mean).
†Per 1 unit.

2 genome-wide association studies implied that some alleles associated with increased serum HDL level increase the risk of AMD,[21] whereas other alleles with inverse association also were reported.[22,23] Deposition of cholesterol and lipids underneath the retinal pigment epithelium is one of the defining features of drusen that characterizes early AMD,[24,25] and our study shows that HDL may increase the risk of early AMD. Further investigation regarding ethnic differences and genuine associations of HDL-related AMD pathophysiologic features is needed.

Obesity has been regarded as a risk factor of AMD.[26,27] However, a study from the white population reported that the association between obesity and AMD may differ by gender,[28] and some studies were unable to reveal the association even in Asian population, although the study by Chen et al[29] had a relatively small sample size (n = 1105). Interestingly, in our study, early AMD was associated inversely with obesity indices in model 1 and 2, and late AMD was also associated inversely with BMI. These inverse associations with obesity, the obesity

Table 10. Smoking Status among the Korean Population from 2008 through 2011

| Age Group (yrs) | Smoking Status | Total | Men | Women |
|---|---|---|---|---|
| | | *Frequency (Weighted Percent [%])* | | |
| 40–49 | Never smoker | 2432 (52.01) | 278 (14.77) | 2154 (90.53) |
| | Former smoker | 739 (19.74) | 653 (35.22) | 86 (3.73) |
| | Current smoker | 1020 (28.25) | 897 (50.01) | 123 (5.73) |
| 50–59 | Never smoker | 2410 (54.77) | 273 (15.72) | 2137 (93.07) |
| | Former smoker | 747 (21.50) | 696 (40.96) | 51 (2.40) |
| | Current smoker | 769 (23.74) | 683 (43.31) | 86 (4.53) |
| 60–69 | Never smoker | 2008 (56.88) | 242 (15.30) | 1766 (93.78) |
| | Former smoker | 848 (26.40) | 790 (52.56) | 58 (3.18) |
| | Current smoker | 528 (16.73) | 466 (32.14) | 62 (3.05) |
| 70+ | Never smoker | 1560 (59.67) | 177 (14.84) | 1383 (87.69) |
| | Former smoker | 755 (26.78) | 653 (58.87) | 102 (7.17) |
| | Current smoker | 357 (13.55) | 274 (26.29) | 83 (5.76) |
| All ages | Never smoker | 8410 (54.70) | 970 (15.17) | 7440 (91.31) |
| | Former smoker | 3089 (22.35) | 2792 (42.41) | 297 (3.78) |
| | Current smoker | 2674 (22.95) | 2320 (42.43) | 354 (4.91) |

paradox, also have been observed in other diseases.[30] There are several plausible explanations for these inverse associations. First, old age brings about selected populations of nonobese individuals because obese individuals have higher mortality rates than nonobese individuals.[31] Second, ethnic differences may influence the association between obesity and AMD as with different associations reported in other diseases.[32,33] In addition, participants 50 years of age or older, born in 1958 or earlier, grew up in a destitute country enduring the Korean War. Because overall diet quality and micronutrient intake are associated with AMD,[34] such impoverished states may affect these associations. The overweight among those aged Koreans may suggest a better general health status with an increased metabolic reservoir.[35]

One of the most distinct variables associated with early AMD was HBsAg. Only 1 epidemiologic study has been published regarding the association between hepatitis B and AMD, which was also conducted in Korea and revealed a positive association.[36] Unlike white persons, hepatitis B infection is still highly prevalent in Asian populations; the prevalence of HBsAg carrier was 3.9% in our study. Hepatitis B virus was detected in subretinal fluids as well as in tears and the aqueous humor,[37–39] and it may increase the risk of uveoretinal pathologic features and may associate cross-reactivity with retinal S-antigen, which can cause inflammatory processes.[36,40,41] It may partially explain ethnic differences and the role of chronic inflammation in the pathogenesis of AMD.

Anemia also was associated with early AMD. There has been no study regarding the association between anemia and AMD to date, whereas a study in white persons reported that hematocrit level had no association with early AMD.[17] The prevalence of anemia in our study was 9.0%, higher than that in developed countries. The proinflammatory state of aging, independent of disease, may be a cause for anemia.[42] Moreover, inflammation is the second most frequent cause of anemia and accounts for one-third of cases of anemia in older persons.[43,44] Because inflammation plays an important role in the pathogenesis of AMD, it partially explains the association between anemia and AMD. In addition, genetic susceptibility, namely the complement factor H polymorphism, activates the alternative complement pathway and is known to have associations with several chronic conditions, including hemolytic uremic syndrome, microangiopathic hemolytic anemia, and AMD.[45] These inflammatory pathways and their relation to AMD parallel our detailed analysis of the subtypes of anemia, where normocytic anemia was associated with early AMD. Common causes of normocytic anemia include anemia of chronic diseases, chronic inflammation, and hemolytic anemia (e.g., microangiopathic anemia).[46] However, the concurrence of iron and vitamin $B_{12}$ or folate deficiencies could result in normocytic anemia, which has a usual association with microcytic anemia and macrocytic anemia, respectively.[46] Recent studies suggested that deficiencies in vitamin $B_{12}$, folate, or both, which are one of the causes of anemia, may increase the risk of AMD incidence.[47,48] Because the KNHANES lacks the information regarding the blood level of vitamin $B_{12}$ or folate, we could not conduct further anemia differentiation. Further investigation is warranted to reveal not only the pathophysiologic features of the association between early AMD and anemia, but also its differences between Asians and white persons.

Education and occupation were associated with early AMD. Although several studies have reported no association between education and AMD,[49] other studies have showed inverse associations between education and AMD as in our study,[26] suggesting that AMD is affected by behaviors and lifestyles as well as risk factors that cannot be amended.

Before conducting multiple LRAs, several systemic risk factors were associated with AMDs. But, systemic risk factors—hypertension, diabetes mellitus, and cardiovascular diseases—were not associated with both early and late AMD in multiple LRAs. The relationships between these systemic risk factors and AMD remain unclear, although they have been investigated in numerous studies. In addition, vitamin D was not associated with AMD, although several studies have reported otherwise.[50] Furthermore, we were unable to reveal the association between sun exposure and AMD, a conflicting issue in the literature.[51,52] Further investigation with thorough evaluation of sun exposure is needed because its measurement in our study depended on only a single question regarding average hours of daily sun exposure.

This study has several limitations. First, KNHANES did not include institutionalized individuals, and we excluded participants without any gradable fundus photographs. It not only may cause underestimation of AMD prevalence and may affect risk factor analyses, but also may cause selection bias in analyzing risk factors of AMD. The results should be interpreted under the consideration of these limitations. Second, although the response rates for the KNHANES during the study period were relatively high, ranging from 77.8% to 82.8%, and the KNHANES sample weight was adjusted for the responding participants to provide nationally

representative estimates, approximately 20% of the population did not complete the KNHANES through the study period, which may result in the selection bias. This limitation, an inherent bias of the survey, also should be considered when interpreting the results. Third, AMD was graded using only fundus photographs; we could not identify PCV, which is more prevalent in Asians.[15] Third, although the largest population-based study including 14 352 participants, the frequencies and prevalence of late AMD and its subtypes were too low to achieve a sufficient statistical power. The KNHANES, a government-led survey for nationally representative estimates, is not solely designated for evaluating the prevalence and risk factors of late AMD, resulting in low statistical power for evaluating late AMD. This is an inherent limitation for the study using pre-existing surveys. Despite lacking sufficient statistical power, these analyses implied that the pathophysiologic and risk factors of wet AMD and GA are somewhat different from each other.

Recently, Cho et al[10] also reported the prevalence and risk factors of AMD in Korea using the 2-year KNHANES database. However, compared with the recent study by Cho et al, our study analyzed all available databases in the KNHANES—the 4-year data of KNHANES—resulting in the larger sample size. In addition, we investigated the prevalences and risk factors with more detailed stratification of AMD and conducted a rigorous study by providing all possible information (e.g., frequencies for each covariate), handling the missing values (e.g., HDL), and in-depth analysis of the risk factors (e.g., subtype analysis of anemia).

In conclusion, the prevalence of AMD was 6.62% in the Korean population 40 years of age or older: 6.02% were early AMD and 0.60% were late AMD, suggesting that there are 1.21 million individuals with early AMD and 121 000 individuals with late AMD in Korea. In addition, we revealed novel risk factors for AMD: not being overweight and having higher levels of HDL, generally assumed to be positive health indicators, as well as anemia and hepatitis B infection. Maintaining good health indicators, such as not being overweight or having higher HDL levels, may not be enough to prevent the occurrence of AMD. Correction of possible low-grade inflammatory conditions may be recommended, taking into account the harmful associations of anemia and hepatitis B infection with AMD. This also implies a possible different pathophysiologic course of AMD in Asians compared with that in white persons.

## References

1. Vision 2020: The Right to Sight. Global initiative for the elimination of avoidable blindness: action plan 2006–2011. Geneva: World Health Organization; 2007:1–2. Available at: http://apps.who.int/iris/handle/10665/43754. Accessed February 24, 2014.
2. Lee PP, Feldman ZW, Ostermann J, et al. Longitudinal prevalence of major eye diseases. Arch Ophthalmol 2003;121:1303–10.
3. Jager RD, Mieler WF, Miller JW. Age-related macular degeneration. N Engl J Med 2008;358:2606–17.
4. Kawasaki R, Yasuda M, Song SJ, et al. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. Ophthalmology 2010;117:921–7.
5. Yang K, Liang YB, Gao LQ, et al. Prevalence of age-related macular degeneration in a rural Chinese population: the Handan Eye Study. Ophthalmology 2011;118:1395–401.
6. Laude A, Cackett PD, Vithana EN, et al. Polypoidal choroidal vasculopathy and neovascular age-related macular degeneration: same or different disease? Prog Retin Eye Res 2010;29:19–29.
7. Klein R, Chou CF, Klein BE, et al. Prevalence of age-related macular degeneration in the US population. Arch Ophthalmol 2011;129:75–80.
8. Yoon KC, Mun GH, Kim SD, et al. Prevalence of eye diseases in South Korea: data from the Korea National Health and Nutrition Examination Survey 2008–2009. Korean J Ophthalmol 2011;25:421–33.
9. Oyeyemi GM, Adewara AA, Adeyemi RA. Complex survey data analysis: a comparison of SAS, SPSS and STATA. Asian J Math Stat 2010;3:33–9.
10. Cho BJ, Heo JW, Kim TW, et al. Prevalence and risk factors of age-related macular degeneration in Korea: the Korean National Health and Nutrition Examination Survey. Invest Ophthalmol Vis Sci 2014;55:1101–8.
11. Bird AC, Bressler NM, Bressler SB, et al; International ARM Epidemiological Study Group. An international classification and grading system for age-related maculopathy and age-related macular degeneration. Surv Ophthalmol 1995;39:367–74.
12. Kim Y, Park S, Kim NS, Lee BK. Inappropriate survey design analysis of the Korean National Health and Nutrition Examination Survey may produce biased results. J Prev Med Public Health 2013;46:96–104.
13. Kawasaki R, Wang JJ, Ji GJ, et al. Prevalence and risk factors for age-related macular degeneration in an adult Japanese population: the Funagata study. Ophthalmology 2008;115:1376–81.
14. Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology 1992;99:933–43.
15. Maruko I, Iida T, Saito M, et al. Clinical characteristics of exudative age-related macular degeneration in Japanese patients. Am J Ophthalmol 2007;144:15–22.
16. Christen WG, Glynn RJ, Manson JE, et al. A prospective study of cigarette smoking and risk of age-related macular degeneration in men. JAMA 1996;276:1147–51.
17. Klein R, Cruickshanks KJ, Nash SD, et al. The prevalence of age-related macular degeneration and associated risk factors. Arch Ophthalmol 2010;128:750–8.
18. VanderBeek BL, Zacks DN, Talwar N, et al. Role of statins in the development and progression of age-related macular degeneration. Retina 2013;33:414–22.
19. Eye Disease Case-Control Study Group. Risk factors for neovascular age-related macular degeneration. Arch Ophthalmol 1992;110:1701–8.
20. Tan JS, Mitchell P, Smith W, Wang JJ. Cardiovascular risk factors and the long-term incidence of age-related macular degeneration: the Blue Mountains Eye Study. Ophthalmology 2007;114:1143–50.
21. Chen W, Stambolian D, Edwards AO, et al; Complications of Age-Related Macular Degeneration Prevention Trial (CAPT) Research Group. Genetic variants near *TIMP3* and high-density lipoprotein-associated loci influence susceptibility to

age-related macular degeneration. Proc Natl Acad Sci U S A 2010;107:7401–6.
22. Reynolds R, Rosner B, Seddon JM. Serum lipid biomarkers and hepatic lipase gene associations with age-related macular degeneration. Ophthalmology 2010;117:1989–95.
23. Zhang X, Li M, Wen F, et al. Different impact of high-density lipoprotein-related genetic variants on polypoidal choroidal vasculopathy and neovascular age-related macular degeneration in a Chinese Han population. Exp Eye Res 2013;108:16–22.
24. Mullins RF, Russell SR, Anderson DH, Hageman GS. Drusen associated with aging and age-related macular degeneration contain proteins common to extracellular deposits associated with atherosclerosis, elastosis, amyloidosis, and dense deposit disease. FASEB J 2000;14:835–46.
25. Curcio CA, Presley JB, Malek G, et al. Esterified and unesterified cholesterol in drusen and basal deposits of eyes with age-related maculopathy. Exp Eye Res 2005;81:731–41.
26. Age-Related Eye Disease Study Research Group. Risk factors associated with age-related macular degeneration. A case-control study in the Age-Related Eye Disease Study: Age-Related Eye Disease Study report number 3. Ophthalmology 2000;107:2224–32.
27. Hogg RE, Woodside JV, Gilchrist SE, et al. Cardiovascular disease and hypertension are strong risk factors for choroidal neovascularization. Ophthalmology 2008;115:1046–52.
28. Adams MK, Simpson JA, Aung KZ, et al. Abdominal obesity and age-related macular degeneration. Am J Epidemiol 2011;173:1246–55.
29. Chen SJ, Cheng CY, Peng KL, et al. Prevalence and associated risk factors of age-related macular degeneration in an elderly Chinese population in Taiwan: the Shihpai Eye Study. Invest Ophthalmol Vis Sci 2008;49:3126–33.
30. Kim BJ, Lee SH, Jung KH, et al; Korean Stroke Registry Investigators. Dynamics of obesity paradox after stroke, related to time from onset, age, and causes of death. Neurology 2012;79:856–63.
31. Allison DB, Fontaine KR, Manson JE, et al. Annual deaths attributable to obesity in the United States. JAMA 1999;282:1530–8.
32. Gatineau M, Mathrani S. Obesity and ethnicity. Oxford, UK: National Obesity Observatory; 2011. Available at: http://www.noo.org.uk/gsf.php5?f=9777&fv=10266. Accessed February 27, 2014.
33. Ma RC, Chan JC. Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States. Ann N Y Acad Sci 2013;1281:64–91.
34. Montgomery MP, Kamel F, Pericak-Vance MA, et al. Overall diet quality and age-related macular degeneration. Ophthalmic Epidemiol 2010;17:58–65.
35. Oreopoulos A, Kalantar-Zadeh K, Sharma AM, Fonarow GC. The obesity paradox in the elderly: potential mechanisms and clinical implications. Clin Geriatr Med 2009;25:643–59. viii.
36. Roh MI, Kim JH, Byeon SH, et al. Estimated prevalence and risk factor for age-related maculopathy. Yonsei Med J 2008;49:931–41.
37. Friberg TR, Williamson D. Hepatitis B surface antigen in human subretinal fluid. Am J Ophthalmol 1983;95:712–3.
38. Temel A, Seber E, Gunay M. Detection of hepatitis B surface antigen in aqueous humor. Acta Ophthalmol (Copenh) 1990;68:205–8.
39. Koksal I, Cetinkaya K, Aker F. Hepatitis B surface antigen in tears and aqueous humor. A comparative study of serum hepatitis B surface antigen levels. Ophthalmologica 1992;204:19–22.
40. Singh VK, Kalra HK, Yamaki K, et al. Molecular mimicry between a uveitopathogenic site of S-antigen and viral peptides. Induction of experimental autoimmune uveitis in Lewis rats. J Immunol 1990;144:1282–7.
41. Slepova OS, Kushnir VN, Zaitseva NS, et al. Clinical and immunological signs of retinal lesions and possibilities of their correction by drugs in patients with chronic diffuse liver diseases of viral etiology and carriers of Australia antigen [in Russian]. Vestn Oftalmol 1994;110:27–9.
42. Roy CN. Anemia of inflammation. Hematology Am Soc Hematol Educ Program 2010;2010:276–80.
43. Guralnik JM, Eisenstaedt RS, Ferrucci L, et al. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. Blood 2004;104:2263–8.
44. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med 2005;352:1011–23.
45. Atkinson JP, Goodship TH. Complement factor H and the hemolytic uremic syndrome. J Exp Med 2007;204:1245–8.
46. Tefferi A. Anemia in adults: a contemporary approach to diagnosis. Mayo Clin Proc 2003;78:1274–80.
47. Rochtchina E, Wang JJ, Flood VM, Mitchell P. Elevated serum homocysteine, low serum vitamin B12, folate, and age-related macular degeneration: the Blue Mountains Eye Study. Am J Ophthalmol 2007;143:344–6.
48. Gopinath B, Flood VM, Rochtchina E, et al. Homocysteine, folate, vitamin B-12, and 10-y incidence of age-related macular degeneration. Am J Clin Nutr 2013;98:129–35.
49. You QS, Xu L, Yang H, et al. Five-year incidence of age-related macular degeneration: the Beijing Eye Study. Ophthalmology 2012;119:2519–25.
50. Seddon JM, Reynolds R, Shah HR, Rosner B. Smoking, dietary betaine, methionine, and vitamin D in monozygotic twins with discordant macular degeneration: epigenetic implications. Ophthalmology 2011;118:1386–94.
51. Pham TQ, Rochtchina E, Mitchell P, et al. Sunlight-related factors and the 10-year incidence of age-related maculopathy. Ophthalmic Epidemiol 2009;16:136–41.
52. Sui GY, Liu GC, Liu GY, et al. Is sunlight exposure a risk factor for age-related macular degeneration? A systematic review and meta-analysis. Br J Ophthalmol 2013;97:389–94.

## Footnotes and Financial Disclosures

Originally received: October 30, 2013.
Final revision: March 8, 2014.
Accepted: March 17, 2014.
Available online: ■■■. Manuscript no. 2013-1816.

[1] Department of Ophthalmology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea.

[2] Medical Research Collaborating Center, Seoul National University Bundang Hospital, Seongnam, Korea.

[3] Department of Ophthalmology, SMG-SNU Boramae Medical Center, Seoul, Korea.

[4] Department of Ophthalmology, Kyungpook National University School of Medicine, Daegu, Korea.

[5] Department of Ophthalmology, Kangbuk Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

[6] Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

Financial Disclosure(s):
The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Supported by the National Research Foundation of Korea, funded by the Ministry of Education, Science, and Technology (grant nos.: NRF-2012R1A1A2008943 and NRF-2013R1A2A2A04015829). The sponsor or funding organization had no role in the design or conduct of this research.

Abbreviations and Acronyms:
**AMD** = age-related macular degeneration; **BMI** = body mass index; **CI** = confidence interval; **GA** = geographic atrophy; **HBsAg** = hepatitis B surface antigen; **HDL** = high-density lipoprotein; **KNHANES** = Korea National Health and Nutrition Examination Survey; **LRA** = logistic regression analysis; **MCV** = mean corpuscular volume; **PCV** = polypoidal choroidal vasculopathy; **WC** = waist circumference.

Correspondence:
Kyu Hyung Park, MD, PhD, Department of Ophthalmology, Seoul National University Bundang Hospital, #300, Gumi-dong, Bundang-gu, Seongnam, Gyeonggi-do 463-707, Korea. E-mail: jiani4@snu.ac.kr; Se Woong Kang, MD, PhD, Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, #81, Irwon-ro, Gangnam-gu, Seoul 135-710, Korea. E-mail: swkang@skku.edu.