Age-Related Macular Degeneration

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

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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.*

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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

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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