Primary Open-Angle Glaucoma in a Population Associated with High Prevalence of Primary Angle-Closure Glaucoma

The Kumejima Study

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Purpose: To evaluate the prevalence of and risk factors for primary open-angle glaucoma (POAG) in a rural population of southwestern Japan.

Design: Population-based cross-sectional study.

Participants: All residents 40 years of age and older in Kumejima, Okinawa, Japan.

Methods: Of the eligible 4632 residents 40 years of age and older, 3762 subjects (participant rate, 81.2%) underwent screening examinations, including visual acuity (VA) measurement, slit-lamp examination, Goldmann applanation tonometry, gonioscopy, undilated stereoscopic fundus photographs, autorefractometry, noncontact specular microscopy, pachymetry, and visual field (VF) testing using frequency-doubling technology. If glaucoma or other related ocular disorders were suspected, subjects were referred for definitive examinations including VF testing with the Humphrey Field Analyzer. The diagnosis of POAG was based on the criteria of the International Society for Geographical and Epidemiological Ophthalmology.

Main Outcome Measures: Prevalence and risk factors of POAG.

Results: The prevalence of POAG was 4.0% (95% confidence interval [CI], 3.4%−4.7%); 82% of patients had an intraocular pressure (IOP) less than 22 mmHg, resulting in a prevalence of 3.3% (95% CI, 2.8%−3.9%). Because of POAG, 3 subjects had a VA worse than 20/400 in only 1 eye, and 1 subject had VA loss of worse than 20/400 bilaterally. The average IOP values (mean ± standard deviation) were 14.9±3.2 and 14.6±3.3 mmHg in the right and left eyes, respectively; the IOP values were higher in patients with POAG (15.4±3.3 and 15.2±3.3 mmHg, respectively) than in subjects without glaucoma (14.8±3.1 and 14.4±3.1 mmHg, respectively; $P<0.045$, Student *t* test). Multivariate analysis showed that male gender ($P = 0.003$), older age ($P<0.001$), higher IOP ($P<0.001$), longer axial length ($P<0.001$), and thinner central cornea ($P = 0.006$) were associated with POAG.

Conclusions: High prevalence rates of POAG (4.0%) and POAG with normal IOP levels (3.3%), which were comparable with those on the Japanese mainland, were found in a southwestern rural island of Japan, where the prevalence of primary angle-closure glaucoma (previously reported as 2.2%) was considerably higher than on the Japanese mainland (0.6% in the Tajimi Study) or other countries. The risk factors for POAG included male gender, older age, higher IOP, myopia, and a thinner cornea. *Ophthalmology 2014;■:1−8 © 2014 by the American Academy of Ophthalmology.*

Glaucoma is a leading cause of visual impairment worldwide.[1,2] Primary open-angle glaucoma (POAG) is the most common type of glaucoma in many population-based studies,[3−24] although the prevalence rates differ among studies from a low of 0.5%[6] to very high at 8.8%.[10] Racial variations also have been identified, with high prevalence rates in black people and low prevalence rates in Asian and white populations.[25,26]

In a population-based study of glaucoma on the main island of Japan (the Tajimi study),[27,28] a relatively high prevalence (3.6%) of POAG with an intraocular pressure (IOP) lower than 22 mmHg (normal-tension glaucoma [NTG]), and relatively low prevalence (0.6%) of primary angle-closure glaucoma (PACG) were estimated. Recently, a similarly high prevalence of NTG (2.7%) was reported in Korea,[22] suggesting that there are common high prevalence rates of POAG with normal IOP in those East Asian countries. However, more recently, a high prevalence (2.2%) of PACG was estimated in a population-based study performed in Kumejima, a rural southwestern island of Japan.[29] Ethnic or genetic differences between the Japanese mainland and the southwestern islands and differences in refractive

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error and mean patient ages were thought to be possible explanations for the discrepancy in PACG prevalence rates between studies.[27,29] It should be of interest that the prevalence of POAG, especially POAG with normal IOP, in the Kumejima population compared with that in the Tajimi population. In addition, because the Kumejima population was characterized by demographic data that differed from that of the Tajimi population, such as age, refractive error, blood pressure, and body mass index (BMI), analysis of risk factors for POAG also should be of clinical importance. We investigated the prevalence of POAG including POAG with normal IOP and its risk factors in the Kumejima study.

Methods

The subjects in the current study were identical to those in the previous report of the Kumejima study, which dealt with the prevalence of PACG in this population.[29] Thus, the fundamental methodology is identical to that reported previously and is summarized briefly below.

Study Population

We attempted to screen the entire population 40 years of age and older of Kumejima Island. The study was conducted between May 2005 and August 2006. Kumejima is one of the Ryukyu (Okinawa) islands between Kyushu Island (one of the main Japanese islands) and Taiwan along mainland China. The study followed the tenets of the World Medical Association's Declaration of Helsinki and the municipal law of Kumejima for protecting privacy information. The ethics committee of the town of Kumejima approved the study protocol. All participants provided written informed consent.

The number of residents 40 years of age and older in Kumejima was 5249 based on the registration in the municipal office as of May 2005. At the end of the screening period in August 2006, 617 subjects were identified as nonresidents or had moved or died; ultimately, 4632 subjects were identified as the target population for this study. All residents were encouraged to undergo examinations held at the Kumejima Public Hospital. Home visits and examinations were performed for inpatients and for paralyzed and disabled residents.

Screening Examination

First, a medical history interview, including past ocular diseases, was conducted. Height, weight, and arterial blood pressure were measured, and ophthalmologists and trained examiners performed the following ophthalmic examinations. Refractive status was measured using an autorefractometer (ARK-730; Topcon, Tokyo, Japan), and visual acuity (VA) was measured using a chart of Landolt rings at a distance of 5 m with refractive correction using the data obtained initially with an autorefractometer. The central corneal thickness (CCT) was measured using a noncontact specular-type pachymeter (SP-2000P; Topcon). The axial length and central anterior chamber depth were measured by partial coherence laser interferometry (IOL Master; Carl Zeiss Meditec, Dublin, CA). Intraocular pressure was measured 3 times by Goldmann applanation tonometry under topical anesthesia, and the median value was adopted. The angle width was evaluated according to the van Herick method and gonioscopy using a Goldmann 2-mirror lens (Haag-Streit, Koeniz, Switzerland). Sequential stereo fundus color photographs were obtained in a dark room through undilated pupils using a digital fundus camera (NW7S; Topcon) with angles of 30 and 45 degrees. The visual fields (VFs) were evaluated using a frequency-doubling technology screener (Carl Zeiss Meditec) with the C-20-1 screening test.

When participants were unable to come to the facility, the doctors visited them at their homes and performed the examinations using a handheld slit lamp, direct and indirect ophthalmoscopes, and a Perkins applanation tonometer in most cases or a Tono-Pen XL (Bio-Rad Laboratories, Inc., Hercules, CA) in the remaining cases for which Perkins tonometry could not be performed, and gonioscopy.

To screen for glaucomatous fundus findings, 3 glaucoma specialists (S.S., A.I., G.T.) (the Photograph Screening Committee) independently evaluated the stereo fundus photographs. When at least 1 of 3 examiners noted any findings suggestive of the presence of an abnormality, including glaucomatous changes, the subjects were recruited for a definitive examination.

Definitive Examination

Subjects considered to be glaucoma suspects or those with other ocular diseases were referred for a definitive examination when their screening findings met 1 or more of the following criteria: corrected VA worse than 20/30; IOP more than 19 mmHg (to refer all subjects whose IOP was statistically outside the normal limits); vertical cup-to-disc ratio of the optic nerve head of 0.6 or more; difference in the vertical cup-to-disc ratio of 0.2 or more between both eyes; superior rim width (from the 11-o'clock to the 1-o'clock position) or inferior rim width (from the 5-o'clock to the 7-o'clock position) of less than 0.2 of the disc diameter; nerve fiber layer defects or splinter disc hemorrhages; any abnormal findings in the slit-lamp examination or sequential stereo fundus color photographs; angle width less than grade 2 (van Herick method); gonioscopically occludable angle, peripheral anterior synechiae formation, or both; or at least 1 abnormal test point in the frequency-doubling technology VF test.

The definitive examination included slit-lamp examination, applanation tonometry, and optic nerve head evaluation in a dark room with a Goldmann 2-mirror lens and VF testing using the Humphrey Field Analyzer central 24-2 Swedish Interactive Threshold Algorithm standard program (Carl Zeiss Meditec). Unless gonioscopy showed a narrow occludable angle, the pupil was dilated to enable detailed observation of the optic disc and ocular fundus by direct and indirect ophthalmoscopy. When gonioscopy showed a narrow angle with the possibility of angle closure, these observations were carried out without pupil dilation. Three glaucoma specialists performed the slit-lamp examination, applanation tonometry, gonioscopy, and optic nerve head evaluation.

Glaucoma Diagnosis

Six glaucoma specialists (S.S., A.I., T.Y., H.A., G.T., M.A.) determined the final glaucoma diagnosis based on the results of the screening and definitive examinations and the subject's clinical history. The diagnostic scheme was described previously[29] and is summarized in Table 1. An abnormal (glaucomatous) VF result was determined when at least 1 of the hemifields was judged to be abnormal. The hemifield was considered abnormal when the pattern deviation probability plot showed a cluster of more than 3 contiguous points having sensitivity with a probability of less than 5% in the upper or lower hemifield and in 1 of these with a probability of less than 1%.[30]

Risk Factors

The factors evaluated were gender, age, IOP, spherical equivalent refractive error, axial length, CCT, history or presence of diabetes mellitus and hypertension, BMI (weight [kg]/height [m^2]), and mean ocular perfusion pressure: 2/3×mean blood pressure (defined as the diastolic pressure+1/3×[systolic pressure−diastolic pressure]−IOP). Data from eyes diagnosed with POAG were