Angle Closure in the Namil Study in Central South Korea

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Objective: To assess the prevalence and associated risk factors of angle closure in a defined population as part of the Namil Study.

Methods: In this cross-sectional epidemiologic study for residents aged 40 years or older in Namil-myon, a rural area in central South Korea, the examination included slitlamp biomicroscopy, applanation tonometry, gonioscopy, autorefraction, fundus photography, corneal thickness measurement, visual field test with frequency-doubling technology, and anterior chamber depth (ACD) and axial length (AL) measurements with partial coherence interferometry. Standard automated field test and optical coherence tomography or scanning laser polarimetry were performed to confirm the glaucomatous visual field/optic disc damage. Angle closure included primary angle-closure suspect (PACS), primary angle closure (PAC), and primary angle-closure glaucoma (PACG). Definitions of PACS, PAC, and PACG were based on the recommendations from the International Society for Geographical & Epidemiological Ophthalmology.

Results: Among the 1426 individuals enrolled for the assessment, with exclusion of cataract surgery, the prevalence rates of PACS, PAC, PACG, and overall angle closure in at least 1 eye were 2.0% (95% CI, 1.3%-2.8%), 0.5% (95% CI, 0.1%-0.9%), 0.7% (95% CI, 0.3%-1.1%), and 3.2% (95% CI, 2.3%-4.2%), respectively. Multivariate analysis found that older age (odds ratio [OR], 1.8797; 95% CI, 1.4624-2.4162), shallower ACD (OR, 0.9982; 95% CI, 0.9977-0.9987), and shorter AL (OR 0.9978; 95% CI, 0.9969-0.9988) (P < .001 for each) were significantly associated with angle closure.

Conclusions: The overall prevalence of angle closure was 3.2% in the present study. On the basis of these findings, increasing age, shallower ACD, and shorter AL appear to be associated with angle closure.

Trial Registration: clinicaltrials.gov Identifier: NCT00727168

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The prevalence of angle closure varies according to race and geographic region. The published prevalence rates are the highest among the Eskimo population1,2 and the lowest for the white population,3-5 Asians, including the Chinese,6 Mongol,7 Thai,8 Indian,9,10 Sri-Lankan,11 and Japanese12 populations, have rates between those levels. Recent epidemiologic studies adopting the International Society of Geographical & Epidemiological Ophthalmology (ISGEO) definition9 have demonstrated that female sex, old age, and shallow anterior chamber depth (ACD) are associated risk factors for primary angle-closure suspect (PACS), primary angle closure (PAC), and primary angle-closure glaucoma (PACG).9,10 Increasing age, decreasing axial length (AL), decreasing ACD, and nuclear cataract are associated risk factors for PACS and PAC.11 Finally, old age, family history, high IOP, and constipation are associated risk factors for PACG.12

Because of insufficient population-based prevalence studies in Korea, there is little information on the prevalence and associated risk factors of angle closure in Korea. The Namil Study,13 a population-based prevalence study in Korea, was initiated by the Korean Glaucoma Society, and the results concerning primary open-angle glaucoma (POAG) have been published. As a part of the Namil Study, the prevalence and associated risk factors of angle closure were evaluated in a rural Korean population with the use of the ISGEO definition, and the results were compared with data from other Asian countries.
METHODS

The participants included in this study were the same as those who participated in the previously reported Namil Study. This study was approved by the institutional review board of Chunjang National University Hospital. The work was performed in accordance with the Declaration of Helsinki. Of a total of 3104 residents of Namil-myon (an inland, low-mountainous, rural, and agricultural area of 47.14 km² located in central South Korea), the number of inhabitants aged 40 years or older was 1928. The 1352 persons who participated in the Namil Study represented a response rate of 79.5%.17

The details of the screening examination, definitive examination, and test result evaluations are described in the previous Namil Study report.17 The screening examination, performed by a trained technician, included a medical and ophthalmologic history, autorefration, fundus photography, corneal thickness measurement, visual field test with frequency-doubling technology, and ACD and AL measurements with partial coherence interferometry. The slitlamp examination, IOP measurements with the Goldmann applanation tonometer, binocular optic disc evaluation, and gonioscopy were performed by a glaucoma specialist.

The definitive examinations for glaucomatous visual field/optic disc damage included a visual field test with a visual field analyzer (SITA Standard 30-2; Humphrey Field Analyzer II 720i; Carl Zeiss Meditec) and retinal nerve fiber analysis using optical coherence tomography (Stratus OCT; Carl Zeiss Meditec) or scanning laser polarimetry (GDxVCC; Carl Zeiss Meditec). The same definition for the glaucomatous optic neuropathy and visual field damage was used in this study as in the previous report of the Namil Study for POAG.17 Three separate reading committees evaluated the test results. Each reading committee consisted of glaucoma specialists who were not involved in the examination of the participants.17

The angle status was initially evaluated using a Goldmann-type gonioscopic lens in all participants. An occludable angle was defined as an angle with less than 90° of posterior trabecular meshwork visible.18 The visibility of the posterior trabecular meshwork and angle width was evaluated in primary gaze without digital pressure on the lens.

Peripheral anterior synecchia was defined as an iridocorneal contact area that could not be detached during gonioscopy. If a satisfactory examination could not be done with the Goldmann-type lens, a 4-mirror lens was used.6 Angle closure was classified into 1 of 3 clinical subtypes, using the definitions reported by the ISGEO19:

1. Primary angle-closure suspect was defined as an eye with an occludable angle and IOP 21 mm Hg or less without peripheral anterior synecchia or glaucomatous change of the optic disc/visual field.

2. Primary angle closure was defined as an eye with any degree of peripheral anterior synecchia or with an occludable angle accompanied by an elevated IOP (>21 mm Hg) and/or iris ischemia (iris whirling and stromal atrophy) but without glaucomatous damage documented on the optic disc/visual field test.20

In aphakic/pseudophakic eyes, the presence of peripheral anterior synecchia, previous laser iridotomy, and/or iris ischemia was considered a diagnostic clue of PAC; any iris changes related to cataract surgery were not regarded as the diagnostic clue of PAC.

3. Primary angle-closure glaucoma was defined as an eye with glaucomatous change to the optic nerve/visual field in the presence of PAC.

In this study, we excluded individuals who had undergone bilateral cataract extraction if both eyes did not have any diagnostic clue for angle closure. The prevalence of angle closure was calculated based on an individual rather than an eye. If a participant had one eye with PACS and the other eye with PACG, he or she was categorized as having the severe subtype, PACG. By the same token, if one eye had PAC and the contralateral eye had PACS, the person was categorized as having PAC.

The assessment of the risk factors and biometric data was based on an eye rather than an individual. Commercial software (SPSS 12.0K; SPSS Inc) was used to analyze differences among the groups using the unpaired 2-tailed t test, analysis of variance, and χ² test. The Bonferroni test for multiple comparisons was used when necessary. Comparison was made between nonglaucomatous eyes and angle-closure eyes when risk factors were estimated and biometric data were analyzed; values in aphakia/pseudophakia were excluded from the ACD evaluation. To minimize the intereye correlation of participants, generalized estimating equation analysis with an unstructured covariance was used to evaluate associated risk factors for angle closure, using commercial software (SAS 9.2; SAS Institute Inc). We performed univariate generalized estimating equation analysis for all predictors, including sex, age, smoking, diabetes mellitus, hypertension, family history of glaucoma, IOP, spherical equivalent, hyperopia, ACD, AL, and corneal thickness. We fitted a multivariate generalized estimating equation model, using all variables that were statistically significant at P < .05 in univariate analyses.

RESULTS

Of the 1532 participants in the Namil Study, 170 individuals (11.1%) underwent cataract surgery in at least 1 eye. Of those with pseudophakia/aphakia, we excluded 106 individuals (6.9%) who underwent bilateral cataract extraction because both eyes did not have any evidence of angle closure. We included 61 persons with unilateral cataract extraction and included 3 with bilateral cataract extraction in whom at least 1 eye had a clue for angle closure. Therefore, 1426 participants were evaluated for the prevalence of angle closure. There were 625 men (43.8%) and 801 women (56.2%), and the distribution was similar to that of the total population of Namil-myon (male, 44.2%; female, 55.8%).

Overall angle closure in at least 1 eye was evident in 46 participants, with a prevalence of 3.2% (95% CI, 2.3%-4.2%) (Table 1). Twenty-nine participants (8 men, 21 women) had PACS in at least 1 eye, and the prevalence was 2.0% (95% CI, 1.3%-2.8%) (Table 1). There were 7 individuals (1 man, 6 women) with PAC in at least 1 eye. The prevalence of PAC was 0.5% (95% CI, 0.1%-0.9%). Ten participants (4 men, 6 women) were identified as having PACG in at least 1 eye, and the prevalence rate was 0.7% (95% CI, 0.3%-1.1%).

Before this survey, no participant had a diagnosis of PACS. One with PAC underwent combined cataract and glaucoma surgery and received β-blocker therapy in 1 eye, 1 participant with phakic PAC underwent surgical iridectomy in both eyes, and 1 participant with pseudophakic PAC underwent laser iridotomy in both eyes. One participant with pseudophakia had PACG and had undergone laser iridotomy in both eyes.

Two participants with PACS had a visual acuity of less than 20/400 (World Health Organization criterion for blindness)27 in at least 1 eye. However, the reason for decreased vision in these 2 individuals appeared not to be related to glaucoma because no participant with PACG had a visual acuity of less than 20/400.
Mean age, ACD, and AL were significantly different between angle-closure eyes and nonglaucomatous eyes (all \(P < .05\), t test). However, those variables were not significantly different among the subgroups of angle closure (Table 2).

Women had a shorter ACD vs men (mean [SD], 2.98 [0.34] mm vs 3.12 [0.35] mm; \(P < .001\), t test) and AL (23.08 [0.98] mm vs 23.60 [0.78] mm; \(P < .001\), t test) in nonglaucomatous eyes. In angle-closure eyes, ACD tended to be shallower in women than men, although the difference did not reach a level of significance (2.39 [0.17] mm vs 2.51 [0.25] mm; \(P = .08\), t test); however, AL was significantly shorter in women (22.49 [0.62] mm) than in men (23.25 [0.66] mm; \(P < .001\), t test) (Table 3).
Table 4. Univariate and Multivariate Analyses for the Association With Angle Closure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.4888 (0.2537-0.9416)</td>
<td>.03</td>
</tr>
<tr>
<td>Age, per 10-y change</td>
<td>1.9332 (1.5412-2.4249)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>0.6393 (0.2459-1.6623)</td>
<td>.36</td>
</tr>
<tr>
<td>Smoker</td>
<td>0.5468 (0.2361-1.2665)</td>
<td>.16</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.6511 (0.1991-2.1286)</td>
<td>.48</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.0213 (0.5291-1.9715)</td>
<td>.95</td>
</tr>
<tr>
<td>Family history of glaucoma</td>
<td>2.7861 (0.9599-13.0254)</td>
<td>.19</td>
</tr>
<tr>
<td>Intraocular pressure, per SD change, mm Hg</td>
<td>1.1130 (0.7530-1.6447)</td>
<td>.59</td>
</tr>
<tr>
<td>SE, per SD change</td>
<td>1.0001 (1.0000-1.0003)</td>
<td>.04</td>
</tr>
<tr>
<td>Hyperopia, SE &gt; 0</td>
<td>1.0002 (0.9999-1.0004)</td>
<td>.12</td>
</tr>
<tr>
<td>Anterior chamber depth, per SD change</td>
<td>0.9979 (0.9975-0.9983)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Axial length, per SD change</td>
<td>0.9918 (0.9837-0.9999)</td>
<td>.047</td>
</tr>
<tr>
<td>Corneal thickness, per SD change</td>
<td>1.0275 (0.8397-1.2573)</td>
<td>.79</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; SE, spherical equivalent.
*Ellipses indicate that multivariate analysis was not performed for the variables smoking, diabetes mellitus, hypertension, family history, intraocular pressure, hyperopia, and corneal thickness.

Sex, age, spherical equivalent, ACD, and AL were significantly different in univariate analysis for the associated factors of overall angle closure. In multivariate analysis, older age (odds ratio [OR], 1.8797; 95% CI, 1.4624-2.4162), shallower ACD (OR, 0.9982; 95% CI, 0.9977-0.9987), and shorter AL (OR, 0.9978; 95% CI, 0.9969-0.9988) were also significant (P < .001 for each).

Therefore, the prevalence of overall angle closure may be about half that of the overall POAG prevalence, including suspect and ocular hypertension. However, the prevalence of POAG was 3.5% and that of PACG was 0.7%. Thus, the prevalence of POAG was 5 times higher than that of PACG in Namil-myon, Korea.

Regarding the proportions of POAG to PACG in the Asian glaucoma prevalence studies based on the ISGEO classification, the ratio was 0.8:1 in the Meiktila Eye Study in Myanmar, nearly equal in a population-based survey in Kailu County, Inner Mongolia, northern China, 1:4:1 in Liwan in China; 2.6:1 in the Beijing Eye Study in China; 2.6:1 in Rom Klao in Thailand; and 3:1 for Chinese in the Tanjong Pagar study. Our study showed a ratio of 5:1 and the Japanese Tajimi Study reported a ratio of 6.5:1. In contrast, the ratio was more than 10:1 in the West Bengal Glaucoma Study and 24:1 for Malay participants in the Singapore Malay Eye Study.

Table 5. Prevalence With or Without Exclusion of Participants Who Underwent Cataract Extraction

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Participants</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude prevalence excluding cataract surgery cases</td>
<td>1426</td>
<td>2.04 (1.30-2.77)</td>
</tr>
<tr>
<td>Crude prevalence including cataract surgery cases</td>
<td>1532</td>
<td>1.89 (1.21-2.58)</td>
</tr>
<tr>
<td>Prevalence including cataract surgery casesa</td>
<td>1532</td>
<td>1.85 (1.20-2.60)</td>
</tr>
</tbody>
</table>

Abbreviations: PAC, primary angle closure; PACS, primary angle-closure suspect; PACG, primary angle-closure glaucoma; PAC, primary angle-closure suspect.
aEllipses indicate that multivariate analysis was not performed for the variables smoking, diabetes mellitus, hypertension, family history, intraocular pressure, hyperopia, and corneal thickness.

The prevalence rates in this population-based study were 2.0% for PACS, 0.5% for PAC, and 0.7% for PACG, and the overall prevalence of angle closure was 3.2% in a rural area of Korea. In a previous report on the Namil Study, the prevalence of POAG, including POAG suspect, was 5.6% and that of ocular hypertension with open angle was 0.6% in the same population of Namil-myon.

Therefore, the prevalence of overall angle closure may be about half that of the overall POAG prevalence, including suspect and ocular hypertension. However, the prevalence of POAG was 3.5% and that of PACG was 0.7%. Thus, the prevalence of POAG was 5 times higher than that of PACG in Namil-myon, Korea.

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Table 6 reports the prevalence rates of PACS, PAC, and PACG in selected Asian population-based studies. Concerning the ratio of POAG to PACG and the prevalence, angle closure appears to be more frequent in China and less frequent in West Bengal and in Malay people (Singapore Malay Eye Study) than in our study. Primary angle closure was also lower in preva-
enience in our study, except for that of the Andhra Pradesh Eye Disease Study, and was similar to that in the Tajimi Study. With regard to PAC, the prevalence in China, India, and Thailand also appears to be higher than in our study. The prevalence of PACS in the present study was relatively lower than in other Asian populations and similar to those of the studies of Andhra Pradesh, South India, and Kandy, Sri Lanka. The Beijing Eye Study documented that 2% of the participants were aphakic/pseudophakic, although the researchers did not calculate prevalence according to the lens status. On the other hand, only those with phakia were included in the analysis of the angle-closure prevalence in the Kandy Eye Study. Calculating the prevalence of angle closure including individuals with previous cataract extraction can confound the prevalence result because increasing rates of cataract surgery can be related to the tendency of occurrence of angle closure.

We believe that the prevalence obtained after excluding cataract surgery cases would be closer to reality. Nevertheless, considering the prevalence of angle closure after the exclusion of cataract surgery cases as a real prevalence may also be an oversimplification of reality because we do not know how many individuals with previous cataract surgery had angle closure, especially PACS, before surgery and how cataract surgery prevents angle closure.

After excluding cataract extraction cases, age- and sex-standardized prevalence could not be calculated because we did not know how many nonresponders underwent cataract extraction. Thus, only the crude prevalence rate was calculated (Table 5).

The Meiktila Eye Study and the Kandy Eye Study showed that women with open angles had significantly shorter ACD compared with men; however, the difference in ACD in women with angle closure was not significant from that in men. We found similar findings in our study. Casson et al postulated that angle closure may be related to the shorter ACD in women and that men with a shallow ACD may have a risk similar to women with a shallow ACD.

Age and ocular biometry were not significantly different among the subgroups of angle closure (PACS, PAC, and PACG), although those were different between non-glaucomatous eyes and angle-closure eyes. The Chennai Glaucoma Study and the Handan Eye Study showed similar results. Therefore, factors other than ocular biometry may play a role in the development of more severe forms of angle closure.

In our study, blindness related to PACG was not identified. This finding is in contrast to other population-based studies in which blindness was frequent with respect to PACG. In our study, the number of participants with PACG was small (n=10). A larger population is needed to elucidate the relationship between blindness and PACG in Korea. Blindness associated with PACG might be preventable if there is easy access to the medical care system. The higher incidence of cataract surgery in our study may imply easy access to ophthalmic medical care in the Namil-myon area.

Presently, older age, shallower ACD, and shorter AL were associated with angle closure, which is in line with previous population-based studies. In our study, sex and hyperopia were significant risk factors with univariate analysis but not with multivariate analysis, suggesting that their effects are in part mediated by other variables in our models, such as AL and ACD. Most previous studies have reported female sex to be a risk factor for angle closure, although some studies did...
not show such a statistically significant female predominance in angle closure. Hyperopia may be related to the development of PACG.28 However, recent population-based studies9,10,12 in southern India and Sri Lanka did not demonstrate such a relationship with hyperopia and angle closure. Therefore, further studies are needed to clarify the relationship of sex or hyperopia with prevalence of angle closure in Korea.

In summary, our study shows that the prevalence rates of PACS, PAC, and PACG in at least 1 eye were 2.0%, 0.5%, and 0.7%, respectively, and the overall prevalence of angle closure in at least 1 eye was 3.2%. In addition, increasing age, shallower ACD, and shorter AL were associated with angle closure in men and women aged 40 years or older from Namil-myon, central South Korea.

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REFERENCES


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