The Prevalence of Primary Open-angle Glaucoma in a Population-based Study in The Netherlands

The Rotterdam Study

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Purpose: The objective of this study is to assess the prevalence of primary open-angle glaucoma (POAG) in a defined population in Rotterdam, The Netherlands.

Methods: The Rotterdam Study is a single-center prospective cohort study of a total population of more than 10,000 people, 55 years of age or older. For the current analysis, the first 3062 consecutive, unselected, noninstitutionalized participants were examined according to standard protocols, including perimetry. The diagnosis of POAG was based on the presence of a glaucomatous visual field defect combined with either a vertical cup-disc ratio of 0.5 or more or a cup-disc ratio asymmetry of 0.2 or more, or an intraocular pressure (IOP) more than 21 mmHg, with open and normal anterior chamber angles.

Results: The overall prevalence of POAG in the current study was 1.10% (95% confidence interval [CI]: 1.09,1.11). Age-specific prevalence figures increased from 0.2% (95% CI: 0.16,0.24) in the age group of 55 to 59 years to 3.3% (95% CI: 2.57,4.04) in the age group of 85 to 89 years. Men had a more than three times higher risk of having POAG than women (odds ratio, 3.6). In 52.9% of the patients, POAG had not been diagnosed previously. Of these patients, 38.9% had IOPs of 21 mmHg or lower. In 8.8% of the eyes (2.9% of patients), visual acuity was 20/200 or less due to POAG.

Conclusion: The overall prevalence of POAG in the current study was 1.1%. The prevalence of POAG was higher in men than in women. Of the untreated patients, 38.9% had IOPs of 21 mmHg or lower. Ophthalmology 1994;101:1851–1855

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Glaucoma is a disease of the optic nerve, which is often, but not always, accompanied by an elevated intraocular pressure (IOP). Characteristic of the disease are the generation of typical, progressive visual field defects. The most commonly occurring type of glaucoma is primary open-angle glaucoma (POAG). Overall prevalence figures of POAG in white populations range from 0.4% to 4.1%, depending on the screening procedure and definitions used.1 According to the Model Reporting Area for Blindness Statistics of the United States, glaucoma was responsible for 11.1% of all cases of blindness in the registration.1

The aim of the present study is to describe the prevalence of glaucoma in a defined population in Rotterdam, The Netherlands.
Subjects and Methods

Population

The current study was performed as part of the Rotterdam Study. The Rotterdam Study is a single-center prospective cohort study of more than 10,000 residents who are 55 years of age or older from the suburb of Ommoord, Rotterdam, The Netherlands. The objective of the Rotterdam Study is to investigate the determinants of chronic, disabling cardiovascular, neurogeriatric, locomotor, and ophthalmologic diseases. The study has been approved by the Medical Ethics Committee of the Erasmus University, and written informed consent was obtained from all participants. All participants were randomly selected from the registry office but the invitations to participate were sent according to their postal code.

After informed consent was obtained, home interviews were taken by specially trained interviewers in which information was collected about former and current medical status and family medical history. A medical investigation was carried out in a specially equipped examination center in the center of the suburb.

The overall participation rate was 80% of the eligible persons in the total Rotterdam Study, which was highest in the age group of 55 to 65 years (84%) and declined with age (70% in the age group of 85 years and older). In the current analysis, 3338 persons (77%) of the 4318 eligible persons who were randomly invited to participate in the study from May 1991 until January 1993 were interviewed at home. Of these patients, 3062 (71%) consecutive, unselected, noninstitutionalized persons had an ophthalmologic examination at the research center.

Measurements

The glaucoma screening was performed in three phases by two ophthalmology residents and three perimetrists. In the first phase of the glaucoma study, after keratometry and autorefraction (Topcon RMA 2000, Topcon Corp, Tokyo, Japan), the best-corrected visual acuity was determined (Distance Visual Acuity Chart, The Lighthouse, NY, 2nd edition). If this visual acuity improved with a pinhole, the pinhole visual acuity was noted. Abnormalities of the anterior chamber angle, cornea, iris, and lens were the focus on slit-lamp examination. The method of van Herick et al² was used to determine the width of the chamber angle. The IOP was measured with the Goldmann applanation tonometer (Haag-Streit, Bern, Switzerland), and the median of three consecutive measurements was taken.³ Within the timeframe of the tight examination schedule, subjects were given 200 ml of a 75-g glucose solution 20 minutes before the IOP measurement for a glucose tolerance test that was needed for the cardiovascular study. The 76-point suprathreshold screening test of the Humphrey perimeter (Humphrey Visual Field Analyzer, Humphrey Instruments, Inc, San Leandro, CA) was used to detect visual field defects in the central 30°. A near-refractive correction, appropriate for age, was used. The perimetry screening was performed on both eyes. Three or more contiguously missed points on the screening test were taken as evidence for a visual field defect. The blind spot and outer test points were not counted as missed points. The reliability of a test result was given by the perimeter, but the judgment of the technician about the patient’s responses and fixation was decisive. After perimetry, one drop of 0.5% tropicamide and one drop of 5% phenylephrine hydrochloride were administered in both eyes. After 40 minutes, color slides were taken from the macular area and the optic disc. Direct and indirect ophthalmoscopy then was performed to assess the vertical cup:disc ratio in relation to the contour of the cup. In most cases, the investigator estimating the vertical cup:disc ratio did not know the IOP or the results of the visual field screening. These subjective assessments were used in the analyses. Any other abnormality of the optic discs and macular area was noted. Finally, one drop of 5% thymoxamine was administered in both eyes. The subjects were advised to get directly in contact with the research center in case of blurred vision or ocular discomfort. The IOP was measured again in mydriasis in subjects with narrow angles and a history of possible acute glaucoma and in subjects with eye complaints developing during mydriasis. Subjects who showed a rise in IOP of more than 7 mmHg were referred to the ophthalmologic department of the Erasmus University in Rotterdam.

In the second phase of the glaucoma study, which was planned 2 weeks after the first phase, visual fields were retested with the same 76-point screening test in subjects with a visual field defect or unreliable visual field test in the first phase.

In the third phase of the glaucoma study, which was conducted a few weeks later, subjects with a visual field defect or unreliable visual field test in the second phase of the study were recalled for perimetry on both eyes with the Goldmann perimeter made by a skilled perimetrist, following standard criteria, without knowledge of former visual field defects. Intraocular pressure was measured with the previously described technique. Gonioscopy was performed when a glaucomatous visual field defect was present. A Goldmann three-mirror contact lens was used to judge if the anterior chamber angle was open following the Shaffer grading system and to determine the degree of pigmentation and the presence of other abnormalities.

A random sample of 44 subjects with a normal 76-point suprathreshold Humphrey test also had a visual field examination in the second and third phases.

The subjective determination of the vertical cup:disc ratio of 25 randomly selected optic discs was compared, in a masked way, with the results of the analyses of photographs of the same optic discs with an automated system.

Classification of Glaucomatous Visual Fields

Glaucomatous visual field defects on the Goldmann perimeter included the following types of field defects that could not be explained by other ocular or neurologic abnormalities: a paracentral or full arcuate scotoma of at least 0.4 log units in depth; nasal step of at least 10° in width present to at least two isopters; and central and/or temporal islands.⁴
Criteria for Primary Open-angle Glaucoma

The diagnosis of POAG was based on the presence of a glaucomatous visual field defect on Goldmann perimetry combined with either a vertical cup:disc ratio of 0.5 or more or a difference in vertical cup:disc ratio of 0.2 or more, or an IOP greater than 21 mmHg, with open and normal anterior chamber angles.

Data Analysis

The mean IOP of both eyes was calculated by 5-year age categories for men and women separately. The association among IOP, age, and sex was evaluated with linear regression analysis. The prevalence of POAG was calculated by 10-year age categories for men and women separately, and by 5-year age categories for men and women together. The association among POAG, age, and sex was evaluated further with logistic regression analysis. The association of narrow anterior chamber angles with age and sex also was evaluated with logistic regression analysis. The odds ratio, obtained from logistic regression analysis, was the indication of the relative risk.

Results

The average IOP for both eyes was 14.6 mmHg (median, 14.0 mmHg). The relation between average IOP and sex is shown in Figure 1. Average IOP did not change significantly with age (coefficient of linear regression, −0.004 mmHg/year; 95% confidence interval [CI]: 0.016, 0.024) and it was 0.3 mmHg lower in women than in men (95% CI: 0.5, 0.3). The percentage of eyes with an IOP of more than 21 mmHg was 22% (95% CI: 22.2, 22.2). A difference of more than 2 mmHg between both eyes was observed in 7% (95% CI: 6.8, 7.2) of the subjects.

The median vertical cup:disc ratio was 0.3 for both eyes and both sexes. The ratio did not increase significantly with age (coefficient, 0.001 disc diameter/year; 95% CI: 0.000, 0.002), and there were no significant differences between both sexes (coefficient, −0.015 vertical cup:disc ratio for women; 95% CI: −0.028, 0.002). There was a vertical cup:disc ratio of 0.5 or greater in at least one eye in 19.2% of the study population; thus, the ratio was 0.8 or greater in 2.2%. A difference of 0.2 disc diameter or more between both eyes occurred in 5.0% of the subjects. Optic disc hemorrhages were noted in 0.2% of the subjects. No significant difference existed between the subjective and automatic determination of the 25 randomly selected optic discs (paired Student's t-test; P < 0.05).

Narrow angles, determined with the method of van Herick et al., were present in 2.4% of the subjects: 2.7% in women and 1.8% in men. The prevalence of narrow angles was not associated significantly with age (logistic regression, odds ratio, 1.03; 95% CI: 1.00, 1.05). The chance of women having narrow angles was two times higher than men (logistic regression, odds ratio, 2.17; 95% CI: 1.27, 3.70). No person with a narrow angle had glaucomatous visual field defects.

A visual field defect or unreliable test was present in 563 (18.4%) of the 3062 subjects, and 530 (94.2%) of these subjects underwent a repetition of the screening test in the second phase. In 239 (7.8%) of the subjects, there were abnormal results of the visual field test in the second phase. Of these subjects, 205 (85.8%) underwent Goldmann perimetry in the third phase. This resulted in a glaucomatous visual field defect in 45 eyes (1.1%) of 34 subjects. Other kinds of visual field defects were not considered. In two patients who had dementia, a reliable Goldmann visual field could not be made. None of the 44 subjects with a normal visual field in phase 1 had glaucomatous visual field loss in phase 2 or 3.

In the current study, 1.1% (95% CI: 1.09, 1.11) (34 patients) had POAG in at least one eye (Table 1). In 53% of the patients, the diagnosis of POAG was new. Of the patients in whom POAG was newly diagnosed, 39% had IOPs of 21 mmHg or lower. No other types of glaucoma were present, nor were there subjects with a glaucomatous field defect who did not meet the other diagnostic criteria for POAG. The prevalence of POAG in men was three times higher than in women (odds ratio, 3.6). The prevalence of POAG increased from 0.2% (95% CI: 0.16, 0.24) in the age group of 55 to 59 years to 3.3% (95% CI: 2.57, 4.04) in the age group of 85 to 89 years (Table 2).

Visual acuity of 20/200 or less due to POAG was found in four eyes (8.8%); only one (2.9%) of the patients with POAG had a visual acuity of 20/200 or less in the better eye.

In three pilot studies in different populations 28 to 74 years of age, the median IOP was lowered by 1.5 mmHg after taking 200 ml of the 75-g glucose solution.

In three patients, angle-closure glaucoma started within 1 day after applying the mydriatics, which was cured without sequelae by neodymium:YAG laser iridotomy.

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Table 1. Prevalence of Primary Open-angle Glaucoma According to the Rotterdam Criteria (n = 3062)

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Total No. of Participants</th>
<th>No. of Participants with POAG (%)</th>
<th>Total No. of Participants</th>
<th>No. of Participants with POAG (%)</th>
<th>Total No. of Participants</th>
<th>No. of Participants with POAG (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>55–64</td>
<td>461</td>
<td>1 (0.2)</td>
<td>657</td>
<td>1 (0.2)</td>
<td>1118</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>65–74</td>
<td>515</td>
<td>12 (2.3)</td>
<td>730</td>
<td>5 (0.7)</td>
<td>1245</td>
<td>17 (1.4)</td>
</tr>
<tr>
<td>75+</td>
<td>250</td>
<td>10 (4.0)</td>
<td>449</td>
<td>5 (1.1)</td>
<td>699</td>
<td>15 (2.2)</td>
</tr>
<tr>
<td>Total</td>
<td>1226</td>
<td>23 (1.9)</td>
<td>1836</td>
<td>11 (0.6)</td>
<td>3062</td>
<td>34 (1.1)</td>
</tr>
</tbody>
</table>

POAG = primary open-angle glaucoma.

Discussion

In this study, we observed an overall prevalence of POAG of 1.1%. The prevalence of POAG was related to age and was higher in men than in women. The diagnosis of glaucoma was made for the first time in 53% of the patients with POAG. Of these patients, 39% had IOPs of 21 mmHg or lower.

The distribution of the IOP corresponds well with other studies. In the study by David et al., the median IOP was 14 mmHg, as in the current study. In other studies, the mean or median IOP was 1 to 2 mmHg higher compared with our study, which could have resulted from the influence of the glucose solution that was given before the IOP measurement. Correction of the possible influence of the glucose on the IOP by adding 2 mmHg did not change the number of patients with POAG. As a consequence, the percentage of eyes with an IOP of more than 21 mmHg in the current study was approximately half the percentage of eyes with elevated IOP in the other studies. The prevalence of IOP differences of more than 2 mmHg between both eyes corresponded well with the estimate of 7.7% obtained in the Framingham Eye Study. In contrast to our study, several studies have found a relation between age and IOP. A possible explanation for this difference in relation between age and IOP is that this relation has been found in study populations that included younger age groups. No sex differences in IOP were found in a few studies. Other studies have found a slightly higher IOP in women than in men. In our study, women had slightly lower IOPs than men, but the differences were small.

The median vertical cup:disc ratio observed in our study corresponds well with other studies. In a study by Klein et al., a grading system for fundus photographs of the optic disc was used, which may result in more accurate outcomes. In the Framingham Eye Study, a subjective interpretation of the cup:disc ratio was made by several investigators, which has probably resulted in a higher variability. The percentage of eyes with a vertical cup:disc ratio of more than 0.4 was 27.8% in the study by Klein et al., 10.9% in the Framingham Eye Study, and 19.4% in the current study. A difference in the vertical cup:disc ratio of 0.2 or more between both eyes occurred in 6.8% of the subjects in the Framingham Eye Study and in 5% of the subjects in our study. An association between cup:disc ratio and age was reported in the Framingham Eye Study. Klein et al. reported a prevalence of optic disc hemorrhage of 0.9%, which was only slightly higher than the 0.2% in the current study and within the confidence limits of our estimate.

The visual field screening procedure resulted in the selection of 1.1% of subjects with glaucomatous visual field defects in one or both eyes. This result is in agreement with the outcome of a study by Bengtsson. Studies from which age-specific prevalence data for POAG are known are tabulated in Table 2. From this table, we can conclude that in patients younger than 65 years of age, half the prevalence of POAG is shown in the current study compared with other studies. The studies in Framingham, Ferndale, and Dalby showed a prevalence of 0.8%, 0.8%, and 0.9%, respectively, in the age group of 55 to 69 years, whereas in the Rotterdam Study the prevalence of POAG in the same age group was 0.4%. Of course, due to the limited sample size, there is some overlap in this age group between the confidence intervals of the point estimates. In the age group of 80 years and older, the prevalences of POAG in the Rotterdam Study were lower than the prevalences of the Framingham Study, but higher than the prevalences of the Baltimore Eye Survey for white Americans. The prevalence of POAG in the age group 80 to 84 years was 4.4% in the Framingham Study and 3.1% in the Rotterdam Study, whereas the prevalence of POAG in the age group 80 to 89 years was 2.16% in the Baltimore Eye Survey and 3.1% in the Rotterdam Study. The Beaver Dam Study showed the highest prevalences of POAG in all age categories. A partial explanation for this difference in prevalence is that in Beaver Dam a visual field defect was not necessary for the diagnosis of POAG, in contrast to the current study. But even when we use their definition of POAG in the Rotterdam Study, it would only increase the overall prevalence from 1.1% to 1.5%, which is still beneath the 2.1% overall prevalence of POAG in Beaver Dam. In addition, differences in visual field testing procedure may have resulted in differences in prevalence; in the Dalby, Baltimore, and Rotterdam studies, visual field defects detected with automatic perimetry were required to be confirmed with Goldmann perimetry. In the Beaver Dam Study, only automatic perimetry was performed. In the current study, 53% of the patients with POAG were newly discovered. This figure is similar to that in a study by...
Hollows and Graham. In Bengtsson’s study, however, none of the patients with glaucoma had been treated previously.

Of the 53% patients with newly diagnosed POAG, 39% had IOPs of 21 mmHg or lower. This percentage would remain the same when corrected for the possible influence of the glucose drink because the IOPs were 18 mmHg or lower. The percentage of patients with untreated POAG and normal IOPs is only slightly lower than the 50% and the 61% observed in other studies.

There is conflicting evidence regarding the association of POAG with sex. In the Framingham Eye Study, a higher prevalence of glaucoma among males was observed, as in our study. Bengtsson found a higher prevalence of POAG among females. In other studies, no sex difference in glaucoma prevalence was observed. The small number of patients with POAG could have resulted in the relation between POAG and sex, as found in the current study. Differences in sex were consistently present in all age categories. In addition, it may be that this prevalent sex difference in POAG is more pronounced in older age groups. Combining prevalence results with younger age groups may equalize the sex difference. If there is a real difference in the prevalence of POAG between men and women, some unknown factors related to sex predispose to or protect for POAG at 55 years of age and older.

In conclusion, the overall prevalence of POAG was 1.1% in this study, which is similar to prevalence figures of glaucoma in other studies on whites. Men had a three times higher risk of having POAG than women. Age-adjusted rates showed a lower frequency of POAG until 65 years of age compared with other studies, which suggests that POAG starts at an older age in the Rotterdam Study.

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References