Fellow Eye Prognosis in Patients With Severe Visual Field Loss in 1 Eye From Chronic Open-Angle Glaucoma

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Objectives: To examine the prognosis for the fellow eye of patients with severe visual field loss in 1 eye from chronic forms of open-angle glaucoma, and to identify risk factors for visual field progression in such eyes.

Methods: Review of 36 patients followed in an academic medical center with monocular severe visual field loss (Advanced Glaucoma Intervention Study score ≥12) from open-angle glaucoma either at initial Humphrey visual field testing or during follow-up. Change in Advanced Glaucoma Intervention Study visual field score and clinical evaluation were used to determine visual field progression. Kaplan-Meier survival analysis and Cox proportional hazards survival regression were used to estimate visual field progression in fellow eyes and assess possible risk factors.

Results: During 67 ± 32 months (mean ± SD), 12 of 36 first-affected eyes (33%) and 6 fellow eyes (17%) had significant visual field progression. The Kaplan-Meier estimate of visual field progression in the fellow eye was 12.4% at 5 years after severe visual field loss in the first eye. Compared with stable fellow eyes, fellow eyes with visual field progression had significantly larger initial cup-disc ratio, smaller between-eyes difference in the initial Advanced Glaucoma Intervention Study score, and lower calculated ocular perfusion pressure. Ocular perfusion pressure was the only variable significantly associated with visual field progression by Cox proportional hazards survival regression ($P = .019$). During an average of 10.2 years of disease, 2 patients (6%) became bilaterally blind from glaucoma.

Conclusions: In this predominantly white population, fellow eyes of patients with severe visual field loss in 1 eye from open-angle glaucoma were not at particularly high risk for further visual field progression, and few patients became bilaterally blind. Fellow eye visual field progression was associated with lower calculated ocular perfusion pressure.


GLAUCOMA IS a leading cause of blindness in the world.1,2 Population-based studies in the United States have found glaucoma to cause 2.5% to 6.3% of bilateral blindness in white patients,2-3 with levels many times higher in African American patients.6,6 When automated perimetric data are examined in patients with treated glaucoma, most studies have noted rates of glaucomatous visual field progression ranging from 9% to 30% during periods of 2 to 7 years,7-18 though others describe higher rates.19,22 However, these studies are almost entirely based on 1-eye results. Some authors estimate that progression of glaucomatous visual field loss does not frequently result in bilateral blindness during the average course of the disease.5,23 Prognostic information is important to patients who have severe damage in 1 eye from glaucoma. Grant and Burke24 reviewed cases of blindness from glaucoma and noted that pairs of eyes tended to behave alike, but outcomes for the fellow eye of patients with severe monocular visual field damage have not been systematically studied. We investigated visual field progression and severe visual field loss in fellow eyes of patients with 1 eye severely damaged from chronic forms of open-angle glaucoma (OAG) to obtain prognostic data and risk factors for fellow eye visual field loss.

RESULTS

Of 294 patients identified using information from the database on the Humphrey perimeters, 205 (70%) had glaucoma; of these, 36 (18%) fulfilled inclusion criteria (21 men and 15 women). Reasons for exclusion included an AGIS score less than 12 in the worse eye in 66 patients (32%); insufficient follow-up, 64 (31%); other

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The authors do not have any proprietary interest in any product mentioned in this article.
PATIENTS, MATERIALS, AND METHODS

We reviewed the databases of the Humphrey perimeters (Humphrey Instruments, Dublin, Calif) at the University of Washington Eye Center, Seattle, to identify patients with severe glaucomatous visual field loss in at least 1 eye on program 24-2 or 30-2 perimetry. Our screening criteria included (1) depression of points at least 10 dB below normal in at least 3 of 4 quadrants to within 20° of fixation; (2) loss of at least 10 dB below normal in at least 10° of fixation; (3) testing with either the 10-2 program or with a size V stimulus; or (4) testing of only 1 eye. Inclusion criteria included (1) diagnosis of primary OAG (POAG), pseudoxfoliative (PXG), pigmentary, or normal-tension glaucoma (NTG) with open angles documented on gonioscopy; (2) visual acuity and/or visual field loss attributable to glaucoma rather than other causes (media opacity, retinal or vascular disease, nonglaucomatous optic neuropathy, neuro-ophthalmic causes); (3) length of follow-up with Humphrey visual field testing of 2 years or more; (4) visual field tests that fulfilled published criteria for reliability25; and (5) patients without bilaterally severe glaucomatous visual field loss (defined as an Advanced Glaucoma Intervention Study [AGIS] score of 12 or more on a scale of 0-20)26 at initial visual field testing. We included patients undergoing treatment for NTG because a recent randomized clinical trial provides strong evidence that treated NTG has similar visual field progression rates as treated POAG.18

Patients' medical records were then reviewed for pertinent information: sex, race, diagnosis, age when severe visual field loss was noted in the first eye, ocular history (specifically noting date of glaucoma diagnosis, previous laser or incisional surgery, refractive error [prior to cataract surgery when applicable], medications, and family history of glaucoma), and medical history (specifically noting presence of diabetes mellitus, hypertension, cardiovascular disease, and thyroid disease). Systolic and diastolic blood pressure (BP) measurements were recorded from the clinic notes in the patient's hospital record from the ophthalmology department and other specialty services, and the average was calculated. Ophthalmic data recorded for each eye included visual acuity, disc hemorrhages, medications, and procedures. Not every patient had serial optic disc photographs for review, so cup-disc (C/D) ratios as recorded in the record were used for analysis. Each intraocular pressure (IOP) measurement by Goldmann application tonometry was recorded, and the average for each 3-month period was calculated to derive an overall mean IOP. The highest and lowest IOP in the record was noted for each eye. Most patients had target IOPs set by the treating physician(s), generally based on optic nerve appearance, severity of visual field loss, and starting visual acuity. For patients with non-NTG, the target IOP for undamaged eyes (normal visual field test results) was approximately 21 mm Hg; eyes with early damage (early nasal or arcuate damage) had a target IOP in the upper teens; eyes with moderate damage (more dense arcuate and nasal damage, or both superior and inferior damage) had a target IOP in the mid teens; and eyes with advanced damage (very dense superior or inferior damage, with or without involvement of the opposite hemifield) had a target IOP in the low teens. The target IOP for patients with NTG was generally several milligrams of mercury lower than that for patients with non-NTG. Visual acuity throughout follow-up was compared with initial findings, and final visual acuity was considered unchanged if it was within 2 Snellen lines of initial visual acuity. Noncompliance with treatment was noted if the patient admitted poor compliance with medicines, if multiple follow-up visits were missed, or if the treating physician's notes indicated it was a problem. Ocular perfusion pressure was considered equal to two-thirds the mean arterial pressure − mean IOP27 and was calculated using the following formula:

\[
\frac{\text{(Mean Systolic − Mean Diastolic BP)}}{3} + \frac{\text{(Mean Diastolic BP)}}{2} - \text{Mean IOP}
\]

Visual field tests were generally obtained yearly, although some patients underwent more frequent testing, and others were tested at slightly greater intervals. In some cases in which the visual acuity in the first-affected eye (hereafter referred to as “first eye”) was worse than 20/200, Humphrey visual field testing was not regularly performed in that eye, but the fellow eye continued to be tested regularly. If early improvement in visual field test results (learning effect) was evident, the visual field test used for scoring purposes as the “initial” test was one obtained after this learning effect had stabilized. Generally, if the clinician considered cataract to be serious, visual field testing was deferred until after cataract extraction, with or without trabeculectomy.

For each visual field test, the AGIS score was calculated, and the mean deviation, pattern SD, and corrected pattern SD were recorded. Only visual field tests that met published criteria for reliability27 and that had a total deviation plot were used. The primary methods used to determine the progression of glaucomatous visual field loss were the following: (1) Comparison of initial and final AGIS scores (AGIS criteria); a change of 4 or more AGIS points was considered to be significant, since fewer than 3% of eyes with glaucomatous visual field loss will show long-term fluctuation of 4 or more AGIS points.16 A subsequent article has confirmed that a change of 4 or more points will be confirmed on repeated testing in 95% of cases.17 Although linear regression may be useful in the interpretation of visual field progression,13,14,16,28 it requires many visual field tests and/or many years of follow-up for it to be valid.15,16,28 (2) Clinical evaluation, in which visual field progression was the reason for a lowering of the target IOP.

Comparison of initial and final Collaborative Initial Glaucoma Treatment Study (CIGTS) scores was also used as a secondary method of examining fellow eye visual field progression.29 A change in the CIGTS score of 3 or more points was considered to be significant. We assumed this criteria would detect smaller amounts of visual field progression than might be considered significant by AGIS criteria, although no data have been published on long-term fluctuation using this scoring system.

All data were entered into a spreadsheet computer program (SPSS 6.1; SPSS, Chicago, Ill). Kaplan-Meier survival analysis was used to estimate rates of visual field progression for fellow eyes. Variables considered to be possible risk factors for visual field progression were examined using the independent samples t test, Fisher exact test, and Cox proportional hazards survival regression with forward-stepwise selection. Results are given as the mean ± SD where applicable.
types of glaucoma, 13 (6%); confounding ocular disease, 11 (5%); severe visual field loss bilaterally on initial visual field testing, 8 (4%); and consistently unreliable visual field test results, 7 (3%). Thirty patients were white (primarily of Northern European ancestry), 3 were Asian, and 3 were black. Glaucoma diagnoses included POAG in 18 patients; PXG, 14; NTG, 2; and pigmentary glaucoma, 2. Thirteen of 14 patients with PXG were being treated for glaucoma in both eyes. The diagnosis of glaucoma was made between 1979 and 1984 in 9 patients (25%), between 1985 and 1989 in 15 (42%), and in 1990 or later in 12 (33%). A family history of glaucoma in a first-degree relative was known in 10 of 31 patients for whom this information was noted in the medical record. Myopia was noted in 26 of 35 patients for whom this information could be obtained. One patient died after 46 months’ follow-up. Other demographics and characteristics of the patients studied are given in Table 1.

Among first eyes, all 36 had an AGIS score of 12 or more either on initial Humphrey visual field testing (25), or at final visual field testing (11). The first eye to have severe visual field loss from glaucoma was the right eye in 14 patients and the left in 22. Two first eyes had decreased initial visual acuity from glaucoma. First eye visual field progression was noted in 12 patients (33%)—in 10 (28%) by AGIS criteria and in 2 (6%) by clinical judgment with a change in AGIS score of 3 points. Progression of visual field loss was confirmed with at least 1 further visual field test in 8 eyes; in 4 eyes, no further testing was obtained. Among first eyes, progression of visual field loss was found in 1 of 2 with NTG, in 8 of 18 with POAG, and in 3 of 14 with PXG.

Progression of visual field loss in fellow eyes was noted in 6 patients (17%)—in 5 (14%) by AGIS criteria and in 1 (3%) by clinical judgment with an increase in AGIS score of 3 points. Five of 6 eyes had a final AGIS score higher than or equal to 12. Visual field progression was confirmed with at least 1 more visual field test in 4 of 6 eyes; in the other 2, no further visual field testing was obtained. The average time between severe visual field loss in first and fellow eyes was 37 ± 28 months. Fellow eye visual field progression was found in 3 eyes with POAG, in 2 with PXG, and in 1 with pigmentary glaucoma. When CIGTS scoring was used, 1 additional eye was found to have visual field progression, but no additional visual field testing was performed to confirm progression. Whether using AGIS or CIGTS scoring, Kaplan-Meier survival analysis estimated visual field progression for fellow eyes to be 12.4% at 5 years after severe visual field loss in the first eye (95% confidence interval, 0.9%-23.9%) (Figure).

Four patients had bilateral visual field progression. The Spearman rank correlation coefficient between first and fellow eyes for progression of visual field loss was not significant (R = .316; P = .06), but the between-eye correlation for change in AGIS score was significant (R = .495; P = .002).

Differences between fellow eyes with and without visual field progression are given in Table 2. The slope of change in mean deviation and pattern SD was significantly steeper in eyes with visual field progression. The initial C/D ratio was significantly larger in fellow eyes with visual field progression (P = .01). The mean IOP was not significantly higher in first and fellow eyes with visual field progression. The range, minimum, and maximum IOP were not significantly different for first or fellow eyes with visual field progression (data not shown). The difference in AGIS score between first and second eyes at initial AGIS testing was significantly smaller in patients with fellow eye visual field progression (P = .04) (Table 2).

Notably, the mean ± SD ocular perfusion pressure was significantly lower in fellow eyes with visual field progression.

### Table 1. Demographics and Characteristics of Patients Studied

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Initial Mean ± SD (Range)</th>
<th>Final Mean ± SD (Range)</th>
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<tbody>
<tr>
<td><strong>Cup-disc ratio</strong></td>
<td></td>
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<tr>
<td>First-affected eye</td>
<td>0.83 ± 0.13 (0.50-1.00)</td>
<td>0.91 ± 0.11 (0.70-1.00)</td>
</tr>
<tr>
<td>Fellow eye</td>
<td>0.61 ± 0.21 (0.15-0.90)</td>
<td>0.69 ± 0.25 (0.15-1.00)</td>
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<tr>
<td><strong>Mean deviation, dB</strong></td>
<td></td>
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<tr>
<td>First-affected eye</td>
<td>−17.9 ± 6.0 (-2.1 to −27.5)</td>
<td>−20.6 ± 4.0 (-14.4 to −29.7)</td>
</tr>
<tr>
<td>Fellow eye</td>
<td>−8.0 ± 4.8 (+1.3 to −15.6)</td>
<td>−7.4 ± 7.4 (+1.9 to −26.1)</td>
</tr>
<tr>
<td><strong>Pattern SD, dB</strong></td>
<td></td>
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<tr>
<td>First-affected eye</td>
<td>10.0 ± 2.5 (3.2-14.2)</td>
<td>10.5 ± 3.0 (2.9-16.7)</td>
</tr>
<tr>
<td>Fellow eye</td>
<td>6.4 ± 3.8 (1.8-14.4)</td>
<td>7.3 ± 4.6 (1.7-17.1)</td>
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<tr>
<td><strong>Corrected pattern SD, dB</strong></td>
<td></td>
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<tr>
<td>First-affected eye</td>
<td>9.3 ± 3.0 (0.0-14.0)</td>
<td>10.2 ± 3.2 (0.0-16.7)</td>
</tr>
<tr>
<td>Fellow eye</td>
<td>5.5 ± 4.1 (0.0-14.3)</td>
<td>6.3 ± 9.8 (0.0-16.7)</td>
</tr>
<tr>
<td><strong>AGIS score</strong></td>
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<td></td>
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<tr>
<td>First-affected eye</td>
<td>13.1 ± 4.2 (2-20)</td>
<td>15.2 ± 2.7 (12-20)</td>
</tr>
<tr>
<td>Fellow eye</td>
<td>4.3 ± 3.9 (0-11)</td>
<td>5.2 ± 5.3 (0-20)</td>
</tr>
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</table>

* AGIS indicates Advanced Glaucoma Intervention Study; age, age at time of initial visual field test showing first-affected eye severe visual loss. All values are given as mean ± SD (range).
Regression compared with nonprogressors (P = .015) (Table 2) and in first eyes of the same patients (50.7 ± 5.6 mm Hg vs 57.6 ± 6.1 mm Hg; P = .02). Cox proportional hazards survival regression revealed increasing ocular perfusion pressure to be the only variable significantly associated with fellow eye stability (β = −0.193; SE = 0.082; relative risk = 0.825; P = .019). This association was essentially unchanged if CIGTS scoring was used to determine visual field progression (relative risk = 0.834; P = .01). Ocular perfusion pressure in first eyes with visual field progression was not significantly lower than in stable first eyes (55.0 ± 8.9 mm Hg vs 57.0 ± 4.8 mm Hg; P = .48).

Of 11 fellow eyes with an initial AGIS visual field score of 0, none showed visual field progression, and only 1 eye had any increase in score at all (final score, 1). Visual field progression occurred in 3 (30%) of 10 fellow eyes with mild damage (AGIS score, 1-5) and 3 (20%) of 15 fellow eyes with moderate damage (AGIS score, 6-11). These differences were not statistically significant (P = .15). The mean length of disease or follow-up time did not differ significantly between groups or between eyes with visual field progression and stable eyes (first or fellow).

Three (4.5%) of 66 eyes improved in AGIS score by 4 or more points during follow-up. None of these patients had dramatic IOP changes during follow-up. No other eyes had an improvement in AGIS score of more than 2 points during follow-up.

Cataract extraction was performed in 5 patients bilaterally prior to initial visual field testing. During the course of follow-up, cataract extraction was performed bilaterally in 4 patients—in the first eye in 3 and in the fellow eye in 1. One patient had a moderate increase in cataract in both eyes, which did not account for the marked progression in visual field loss (AGIS score increase of 16 and 18 points, and worsening of mean deviation by 23 and 24 dB, respectively). All other eyes had only mild or stable lens opacities during follow-up.

During the average duration of disease of 10.2 years in this group of patients, 56% of first eyes and 25% of fellow eyes underwent incisional glaucoma surgery. No association was found between visual field progression and the number, type, or timing (ie, before or during follow-up) of procedures.

Most first and fellow eyes had stable or improved visual acuity during and at final follow-up (Table 3). Reasons for worsened (by 3 or more lines) central visual acuity included glaucoma (3 first eyes); glaucoma with cataract (2 first eyes and 1 fellow eye, including both eyes of the patient with moderate increase in cataracts mentioned in the preceding paragraph); age-related macular degeneration (2 first eyes and 1 fellow eye); and central retinal vein occlusion (1 fellow eye). One fellow eye had severe visual loss because of suprachoroidal hemorrhage after combined phacoemulsification and trabeculectomy. Among fellow eyes, visual acuity was not worse than 20/60 (only 3 eyes worse than 20/40) throughout the period of visual field follow-up (excluding early postoperative periods) in all but 1 fellow eye, which had reduction of visual acuity from macular degeneration. No visual field tests were used with poor reliability in the presence of reduced central visual acuity. All eyes considered to have severe glaucomatous visual field loss were classified as such prior to the reduction of central visual acuity by the mechanisms listed in this paragraph.

If the visual field is judged using the definition of blindness of a concentric visual field defect of 10 dB using the Humphrey size III stimulus within 20°, then 11 of 36 first eyes were blind at initial visual field testing, and 12 more became blind during follow-up. Among fellow eyes, none were initially blind, and 2 became blind during follow-up, resulting in bilateral blindness in 2 patients. Thus, during the average of 10.2 years of disease, the rate of bilateral blindness was 5.6% among all pa-
Our study shows that patients with severe loss of vision in 1 eye from chronic OAG have a 12.4% risk of significant visual field progression in the fellow eye during a 5-year period (Figure). During follow-up of 67 months, fellow eye visual field progression occurred in 6 (17%) of 36 patients, and during 10 years of disease, 2 patients (6%) became bilaterally legally blind from glaucoma. The calculated ocular perfusion pressure was found to be significantly associated with visual field progression in fellow eyes.

Reduced ocular perfusion pressure compared with that found in normal eyes has been previously reported in patients with POAG,

but others have found lower ocular perfusion pressure only in patients with NTG. Tribble and Anderson reported that visual field depression during experimental short-term IOP increases was dependent on ocular perfusion pressure. Low BP and a reduction in BP at night (the "nocturnal dip"), both of which might be associated with a decrease in ocular perfusion pressure, have been noted in patients with progressive glaucoma.

and the nocturnal dip is absent in stable patients. We found ocular perfusion pressure to be significantly associated with visual field progression only in fellow eyes, though first eyes with visual field progression also had a lower ocular perfusion pressure than stable first eyes. This may be attributed in part to small sample size, but it is possible that greater severity of damage present on initial visual field testing may increase susceptibility to further damage, despite a higher ocular perfusion pressure (ie, lower IOP).

Still, most first eyes of patients with fellow eye visual field progression were considered to have progressed, and these first eyes also had a significantly lower ocular perfusion pressure.

Notably, of 23 patients legally blind in 1 eye from OAG either at initial testing or during follow-up, 2 (8.7%) had visual field progression to legal blindness in their fellow eye during a mean disease duration of 10 years. In a community-based study of patients with OAG, Hattenhauer et al found a 9% risk of bilateral blindness at 20 years' follow-up among those patients not blind in either eye from glaucoma at diagnosis. Using the same rate of visual field progression for a single eye, these findings are in close agreement with our findings in patients already blind in 1 eye. The time period covered by our study was more recent than the time period in the study by Hattenhauer et al; although practice patterns may have changed with time and a greater number of treatment options and modalities have been available recently, the results of the 2 studies do not seem to differ greatly. In the present study, the mean follow-up period or disease duration did not differ significantly between eyes with and without visual field progression.

Cataract extraction is known to improve automated visual field mean sensitivity in eyes with glaucoma. Although several eyes in this study had cataract extraction during follow-up, we believe this had little effect on our findings because the overall improvement is usually small when many preoperative and postoperative visual field test results are compared; eyes with severe damage from glaucoma generally show little improvement after cataract extraction. In addition, most patients with considerable cataract seemed to have had visual field testing deferred until after cataract extraction.

Four patients had bilateral visual field progression. Both eyes of most patients (72%) behaved similarly, with 61% of patients remaining stable and 11% having bilateral progression of visual field loss, though this is a skewed population. The correlation between first and fellow eyes with visual field progression was not significant but might have been if more patients were studied. However, the between-eyes correlation for change in AGIS score was significant.

Some of our patients had glaucoma associated with pseudoxefoliation of the lens. Although PXG may clinically seem to be a primarily unilateral disease, all but 1 fellow eye was being treated for glaucoma in our patient group.

This study was retrospective and may be limited by incomplete data and bias of selection and reporting. The number of patients studied was relatively small. Nonetheless, patients in similar (predominantly white) populations with severe visual field loss in 1 eye from OAG may be encouraged to know that rates of visual field progression did not seem to be exceptionally high in the fellow eye while under treatment. The rate of bilateral legal blindness was low, and reduction in fellow eye central visual acuity from glaucoma was uncommon. However, visual field progression occurred in many first eyes; when fellow eye visual field progression occurred, the usual result was severe visual field loss, and some patients had bilateral visual field progression despite treatment. Both eyes of 26 patients (72%) in this study behaved similarly, and those with visual field progression in 1 eye must be observed carefully for visual field progression in the fellow eye. Further study is warranted.