Risk Factors for Visual Field Progression in Treated Glaucoma

Carlos Gustavo V. De Moraes, MD; Viral J. Juthani, MD; Jeffrey M. Liebmann, MD; Christopher C. Teng, MD; Celso Tello, MD; Remo Susanna Jr, MD; Robert Ritch, MD

Objective: To determine intraocular pressure (IOP)–dependent and IOP-independent variables associated with visual field (VF) progression in treated glaucoma.

Design: Retrospective cohort of the Glaucoma Progression Study.

Methods: Consecutive, treated glaucoma patients with repeatable VF loss who had 8 or more VF examinations of either eye, using the Swedish Interactive Threshold Algorithm (24-2 SITA-Standard, Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc, Dublin, California), during the period between January 1999 and September 2009 were included. Visual field progression was evaluated using automated pointwise linear regression. Evaluated data included age, sex, race, central corneal thickness, baseline VF mean deviation, mean follow-up IOP, peak IOP, IOP fluctuation, a detected disc hemorrhage, and presence of beta-zone parapapillary atrophy.

Results: We selected 587 eyes of 587 patients (mean [SD] age, 64.9 [13.0] years). The mean (SD) number of VFs was 11.1 (3.0), spanning a mean (SD) of 6.4 (1.7) years. In the univariable model, older age (odds ratio [OR], 1.19 per decade; \( P =.01 \)), baseline diagnosis of exfoliation syndrome (OR, 1.79; \( P =.01 \)), decreased central corneal thickness (OR, 1.38 per 40 µm thinner; \( P <.01 \)), a detected disc hemorrhage (OR, 2.31; \( P <.01 \)), presence of beta-zone parapapillary atrophy (OR, 2.17; \( P <.01 \)), and all IOP parameters (mean follow-up, peak, and fluctuation; \( P <.01 \)) were associated with increased risk of VF progression. In the multivariable model, peak IOP (OR, 1.13; \( P <.01 \)), thinner central corneal thickness (OR, 1.45 per 40 µm thinner; \( P <.01 \)), a detected disc hemorrhage (OR, 2.59; \( P <.01 \)), and presence of beta-zone parapapillary atrophy (OR, 2.38; \( P <.01 \)) were associated with VF progression.

Conclusions: IOP-dependent and IOP-independent risk factors affect disease progression in treated glaucoma. Peak IOP is a better predictor of progression than is IOP mean or fluctuation.


T HE NATIONAL INSTITUTES OF Health randomized clinical trials (RCTs) of glaucoma treatment have helped elucidate the main risk factors for the development and progression of the disease, one of the major causes of irreversible blindness worldwide.1-7 Yet, the patient populations in these RCTs may not resemble the majority of patients, and their protocol designs may not resemble the clinical conduct typically seen in clinical practice.8-12

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Our study was approved by the New York Eye and Ear Infirmary institutional review board and followed the tenets of the Declaration of Helsinki. We included subjects from the New York Glaucoma Progression Study who were evaluated in the glaucoma referral practice of three of us (J.M.L., R.R., and C.T.) between January 1999 and September 2009. After an initial visit consisting of a complete ophthalmologic examination, standard achromatic perimetry (24-2 SITA-Standard, Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc, Dublin, California), and optic disc stereophotographs, patients were re-examined, usually at 3- to 6-month intervals, and the same tests repeated within 6 to 12 months.
We included patients with glaucomatous optic neuropathy and repeatable visual field (VF) loss who had 8 or more VF examinations of either eye, using the Swedish Interactive Threshold Algorithm (24-2 SITA-Standard, Humphrey Field Analyzer II) because a greater number of VF tests increases the sensitivity and specificity of pointwise linear regression analysis in detecting progression. All eligible eyes were required to have best-corrected visual acuity of 20/40 or better at baseline and a spherical equivalent of less than 6 diopters. If both eyes of the same patient were eligible, the eye with the greater number of VF tests was selected. We excluded subjects with optic disc photographs of poor quality, subjects who were unfamiliar with static perimetry, subjects without reliable baseline results of standard automated perimetry, and subjects whose conditions (other than glaucoma and mild cataract) would likely affect VF testing.

**DISC PHOTOGRAPH REVIEW**

Disc photographs of patients in this cohort were reviewed by 2 masked glaucoma specialists searching for disc hemorrhage (DH) and beta-zone parapapillary atrophy (BPPA) using a slide projector. A DH was defined as a splinter-like or flame-shaped hemorrhage on or within the retinal nerve fiber layer or neuroretinal rim. Parapapillary atrophy was defined as an inner crescent of chorioretinal atrophy with visible sclera and choroidal vessels (BPPA) and an outer irregular area of hypopigmentation and hyperpigmentation (alpha-zone PPA). The presence of DH and BPPA at any time in the photographs reviewed was reported. In cases in which the investigators disagreed, a third investigator was used for adjudication.

**VISUAL FIELD ANALYSIS**

A glaucomatous VF was defined if a patient had a glaucoma hemifield test result that was outside the normal limits or if the pattern standard deviation was triggered at P < .05 on at least 2 consecutive baseline VF tests. The 2 baseline tests required reliability indices better than 25% in order to be included. Automated pointwise linear regression analysis was performed using Progressor version 3.3 software (Medisoft, Ltd, Leeds, England), providing slopes (in units of decibels per year) of progression both globally and locally for each point based on threshold sensitivity maps, as well as its level of significance (P values). Details of the software have been described elsewhere. All patients were familiar with 24-2 achromatic perimetry prior to enrollment. Progression was defined as the presence of a test point with a slope of sensitivity over time of a greater than 1.0-dB loss per year, with P < .05. For edge points (nasal-most points of the 24-2), a stricter slope criterion of a greater than 2.0-dB loss per year (also with P < .05) was entered sequentially. Statistical significance was defined at P < .05 in the final model.

**CLINICAL DATA**

Peak intraocular pressure (IOP) was the highest measured IOP during the entire follow-up time. The mean IOP during the entire follow-up period was calculated by averaging all pressure measurements obtained after the date of the first VF test entered in the regression. To avoid the undesired effect that numerous sequential IOP measurements during a short period of time would have on the final average, we used the average IOP for each 6-month period following enrollment to calculate the mean follow-up IOP. Intraocular pressure fluctuation was defined as the standard deviation of this value. Intraocular pressure covariance was calculated by dividing the standard deviation IOP by the mean IOP and then multiplying by 100. We excluded all IOP measurements occurring 4 weeks after any type of incisional surgery or laser procedure to avoid the effect of transitory IOP changes that often occur during this period. Central corneal thickness (CCT) was measured using ultrasonic pachymetry (DGH-350; DGH Technology Inc, Exton, Pennsylvania). Exfoliation syndrome was defined as the presence of characteristic exfoliation material on the pupil border or on the lens capsule following pupil dilation.

**STATISTICAL ANALYSIS**

Categorical variables were compared using the χ² test. Independent-samples t tests were used for comparisons of continuous variables between groups. Pearson correlation coefficients (r) were calculated to assess the relationship between different IOP parameters. First, a logistic regression was used to evaluate the effect of each IOP parameter on the predefined progression outcome. Because greater follow-up time increases the likelihood of detecting progression, all analyses were time adjusted. Also, because IOP-lowering interventions may affect the IOP variability, the model was adjusted for the occurrence of any type of glaucoma-filtering procedure during follow-up. Then, the IOP parameter that best correlated with a progression end point was entered in the model that included all evaluated factors. Each variable was first tested in a univariable model. Those with P < .25 were then entered in the multivariable analysis. The multivariable model was performed using a stepwise approach; that is, significant variables (P < .05) were entered sequentially. Statistical significance was defined at P < .05 in the final model.

**RESULTS**

We selected 587 eyes of 587 patients. Their mean (SD) age at baseline assessment was 64.9 (13.0) years. The mean (SD) number of evaluated VFs was 11.1 (3.0) (range, 8-24), spanning a mean (SD) of 6.4 (1.7) years (range, 2.0-10.2 years). More often they were women (58%) and of European ancestry (90%). The most common diagnosis was primary open-angle glaucoma (46%) (Table 1).

The mean (SD) rate of global VF change for the entire population was −0.45 (0.72) dB/y. One hundred seventy eyes (29%) reached a progression end point. Progressing eyes and stable eyes had a mean (SD) global rate of VF change of −1.0 (0.8) dB/y and −0.20 (0.4) dB/y, respectively (P < .01). The Figure shows the distribution of global and pointwise slopes between progressing and stable eyes. Fifty-three eyes (9%) reached at least 1 detected DH, and 370 eyes (63%) had BPPA. Other clinical data are shown in Table 1. Two hundred six eyes (35%) underwent at least 1 incisonal glaucoma surgery during the follow-up period.

Peak and mean IOP showed the strongest correlation coefficient (Pearson r = 0.74; P < .01). The correlation coefficient for peak IOP and IOP standard deviation was also strong and significant (r = 0.69; P < .01). A significant but still weaker correlation coefficient was observed for mean IOP and standard deviation IOP (r = 0.18; P < .01).

In the time-adjusted logistic regression, all IOP parameters were significantly associated with progression...
deviation IOP than did eyes that did not undergo sur-
sion. Eyes that underwent surgery had greater standard
deviation IOP than did eyes that did not undergo sur-

dering eyes only). However, in the multivariable model, only
peak IOP remained significantly associated with progres-
sion. Eyes that underwent surgery had greater standard
deviation IOP than did eyes that did not undergo sur-
gery (3.3 [1.5] mm Hg vs 2.1 [1.0] mm Hg; \(P < .01\)). Using
a predefined cutoff value, eyes with a peak IOP higher
than 18 mm Hg had an odds ratio (OR) of 1.81 (95% con-
fidence interval, 1.22-2.68) \(P < .01\) associated with a progres-
sion outcome.

The results of the logistic regression looking at factors
associated with VF progression in the entire population are
shown in **Table 3**. In the univariable model, older age,
baseline diagnosis of exfoliation syndrome, decreased CCT,
detected DH, presence of \(\beta\)PPA, and IOP peak were asso-
ciated with increased risk of progression. In the multivariable
model, we found that higher peak IOP (OR, 1.13; 
\(P < .01\)), thinner CCT (OR, 1.45 per 40 \(\mu\)m thinner;
\(P < .01\)), DH detection (OR, 2.59; \(P < .01\)), and presence
of \(\beta\)PPA (OR, 2.38; \(P < .01\)) remained significant factors
associated with progression. Older age (OR, 1.14; \(P = .09\))
and presence of exfoliation syndrome (OR, 1.64; \(P = .07\))
reached borderline significance. Eyes with peak IOP mea-
surements of 18 mm Hg or greater progressed at a mean
(SD) global rate of \(-0.52 (0.8)\) dB/y, and eyes with peak
IOP measurements of less than 18 mm Hg progressed at a
mean (SD) global rate of \(-0.28 (0.5)\) dB/y \(P < .01\).

We then separated the entire population into 2 simi-
larly sized groups based on a median split of the mean
follow-up IOP (median, 15.32 mm Hg). Group A con-
sisted of those with a mean follow-up IOP of 15.32 mm Hg
or greater, and group B consisted of those with a mean
follow-up IOP of less than 15.32 mm Hg. Univariable and
multivariable models were also created for these groups.

In group A, peak IOP (OR, 1.13; \(P < .01\)), decreased
CCT (OR, 1.41; \(P = .02\)), and presence of \(\beta\)PPA (OR, 2.45;
\(P < .01\)) were associated with progression in the multi-
variable model (**Table 4**). In group B, female sex was
protective (OR, 0.54; \(P = .04\)), whereas older age (OR, 1.28;
\(P = .04\)), peak IOP (OR, 1.10; \(P = .02\)), decreased
CCT (OR, 1.53; \(P < .01\)), DH detection (OR, 4.53; \(P < .01\)),
and presence of \(\beta\)PPA (OR, 2.54; \(P = .01\)) were associated
with progression. Presence of exfoliation syndrome reached
borderline significance (OR, 2.40; \(P = .07\)) (**Table 5**)

**COMMENT**

This retrospective cohort resembles a “pragmatic” clinical
trial\(^{21-26}\) that may be useful in ophthalmology.\(^{27}\) We
tested the hypothesis that, in clinical practice, risk fac-
tors for VF progression may not always resemble those
reported by major glaucoma RCTs owing to stringent in-
clusion and exclusion criteria and standardized treat-
ment plans and goals. We confirmed the effect of many
of these parameters\(^{1-7}\) and also found significant risk as-

nected with peak IOP and presence of \(\beta\)PPA. Our re-
sults complement and add to the high level of evidence
generated by these RCTs, provide information about the
behavior of glaucoma patients receiving therapy, and may
help clinicians decide how aggressively to treat specific
patients to slow the rate of glaucoma progression.

We found a significant effect of IOP in all subgroup anal-
yses, consistent with the majority of clinical trials,\(^{14}\) and
we demonstrated that for each increase in millimeters of
mercury in IOP, there is a significant increase in the risk
of progression for treated glaucoma patients. Even though
all IOP parameters were related to progression, peak IOP

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**Table 1. Demographic Characteristics of the Study Population**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient Population (n=587)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>64.9 (13.0)</td>
</tr>
<tr>
<td>Women, No. (%)</td>
<td>345 (58.7)</td>
</tr>
<tr>
<td>Ethnicity, No.</td>
<td>White 504, African 24, Latino 23, Asian 16</td>
</tr>
<tr>
<td>Type of glaucoma, No.</td>
<td>POAG 275, NTG 81, XFG 84, JOAG 37, ACG 76, PG 34</td>
</tr>
<tr>
<td>CCT, (\mu)m</td>
<td>540.9 (37.3)</td>
</tr>
<tr>
<td>Follow-up IOP, mean (SD), mm Hg</td>
<td>15.2 (3.1)</td>
</tr>
<tr>
<td>Peak IOP, mean (SD), mm Hg</td>
<td>19.9 (4.5)</td>
</tr>
<tr>
<td>Baseline (MD), dB</td>
<td>–7.1 (5.1)</td>
</tr>
<tr>
<td>Global rate of VF change, mean (SD), dB/y</td>
<td>–0.45 (0.7)</td>
</tr>
<tr>
<td>Eyes reaching progression end point, No. (%)</td>
<td>170 (28.9)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ACG, angle-closure glaucoma; CCT, central corneal thickness; IOP, intraocular pressure; JOAG, juvenile open-angle glaucoma; MD, mean deviation; NTG, normal-tension glaucoma; PG, pigmentary glaucoma; POAG, primary open-angle glaucoma; VF, visual field; XFG, exfoliative glaucoma.

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**Figure.** A, Distribution of global slopes in the entire study population (ie, 587 eyes of 587 patients). B, Distribution of localized slopes (representing progressing eyes only).

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This retrospective cohort resembles a “pragmatic” clinical trial\(^{21-26}\) that may be useful in ophthalmology.\(^{27}\) We tested the hypothesis that, in clinical practice, risk factors for VF progression may not always resemble those reported by major glaucoma RCTs owing to stringent inclusion and exclusion criteria and standardized treatment plans and goals. We confirmed the effect of many of these parameters\(^{1-7}\) and also found significant risk associated with peak IOP and presence of \(\beta\)PPA. Our results complement and add to the high level of evidence generated by these RCTs, provide information about the behavior of glaucoma patients receiving therapy, and may help clinicians decide how aggressively to treat specific patients to slow the rate of glaucoma progression.

We found a significant effect of IOP in all subgroup analyses, consistent with the majority of clinical trials,\(^{14}\) and we demonstrated that for each increase in millimeters of mercury in IOP, there is a significant increase in the risk of progression for treated glaucoma patients. Even though all IOP parameters were related to progression, peak IOP
was more important than the mean follow-up IOP. To our knowledge, few trials investigating the effect of IOP parameters (mean, fluctuation, and range) on glaucoma progression have focused on peak IOP. Most RCTs have established target or peak IOP rather than trying to limit means or fluctuation. Zeimer et al suggested the importance of peak IOP on progression in 1991. In a post hoc analysis of the Advanced Glaucoma Intervention Study, eyes that consistently had a peak IOP of less than 18 mm Hg had more stable VF throughout follow-up. In our study, 21% of eyes with a peak IOP of 18 mm Hg or greater progressed, with a mean rate of VF change almost twice that of eyes with peak IOP of less than 18 mm Hg. Moreover, a peak IOP of greater than 18 mm Hg increased the risk of progression by 81%. During water-drinking IOP stress tests, eyes with higher IOP peaks have been reported to be more likely to have worse VF damage and an increased likelihood of progression using event analysis.

### Table 2. Logistic Regression Testing for Association Between Each Intraocular Pressure Parameter and a Progression End Point

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariable Model</th>
<th>Multivariable Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean IOP, per mm Hg higher</td>
<td>1.10 (1.04-1.17)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peak IOP, per mm Hg higher</td>
<td>1.10 (1.06-1.15)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>SD IOP, per 0.1 mm Hg higher</td>
<td>1.03 (1.01-1.04)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Covariance IOP, per mm Hg higher</td>
<td>1.02 (1.01-1.03)</td>
<td>.01</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IOP, intraocular pressure; OR, odds ratio; SD, standard deviation.

*a All patients were included in the analysis.

*b Adjusted for follow-up time and surgical IOP-lowering interventions only. A stepwise multivariable model was used.

### Table 3. Logistic Regression Testing the Association Between All Baseline and Intercurrent Factors With a Progression Outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable Model</th>
<th>Multivariable Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>0.87 (0.60-1.25)</td>
<td>.45</td>
</tr>
<tr>
<td>African or Latino</td>
<td>0.77 (0.38-1.55)</td>
<td>.46</td>
</tr>
<tr>
<td>Presence of exfoliation syndrome</td>
<td>1.79 (1.11-2.90)</td>
<td>.01</td>
</tr>
<tr>
<td>Age, per decade older</td>
<td>1.19 (1.03-1.38)</td>
<td>.01</td>
</tr>
<tr>
<td>CCT, per 40 µm thinner</td>
<td>1.38 (1.13-1.68)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peak IOP, per mm Hg higher</td>
<td>1.10 (1.06-1.15)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Baseline MD, per dB better</td>
<td>1.01 (0.96-1.03)</td>
<td>.86</td>
</tr>
<tr>
<td>Detection of disc hemorrhage</td>
<td>2.31 (1.30-4.10)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Presence of βPPA</td>
<td>2.17 (1.45-3.24)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviations: βPPA, beta-zone parapapillary atrophy; CCT, central corneal thickness; CI, confidence interval; IOP, intraocular pressure; MD, mean deviation; OR, odds ratio.

*a Only peak IOP was entered in the model because it showed the best association (Table 2). All 587 patients were included in the analysis.

*b Adjusted for all variables with \( P < .25 \) in the univariable model.

### Table 4. Logistic Regression Testing for Association Between All Baseline and Intercurrent Factors With a Progression Outcome for Group A Eyes Only

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable Model</th>
<th>Multivariable Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>1.02 (0.61-1.69)</td>
<td>.92</td>
</tr>
<tr>
<td>African or Latino</td>
<td>0.87 (0.32-2.38)</td>
<td>.79</td>
</tr>
<tr>
<td>Presence of exfoliation syndrome</td>
<td>1.43 (0.79-2.57)</td>
<td>.31</td>
</tr>
<tr>
<td>Age, per decade older</td>
<td>1.10 (0.91-1.34)</td>
<td>.31</td>
</tr>
<tr>
<td>CCT, per 40 µm thinner</td>
<td>1.46 (1.01-1.99)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peak IOP, per mm Hg higher</td>
<td>1.12 (1.05-1.21)</td>
<td>.01</td>
</tr>
<tr>
<td>Baseline MD, per dB better</td>
<td>1.00 (0.94-1.05)</td>
<td>.97</td>
</tr>
<tr>
<td>Detection of disc hemorrhage</td>
<td>1.41 (0.60-3.31)</td>
<td>.42</td>
</tr>
<tr>
<td>Presence of βPPA</td>
<td>2.23 (1.33-3.73)</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Abbreviations: βPPA, beta-zone parapapillary atrophy; CCT, central corneal thickness; CI, confidence interval; IOP, intraocular pressure; MD, mean deviation; OR, odds ratio.

*a Group A consisted of those with mean follow-up IOP of 15.32 mm Hg or higher.

*b The only IOP parameter entered in the multivariable model was peak IOP (as described in the fourth paragraph of the “Results” section). The multivariable model was adjusted for all variables with \( P < .25 \) in the univariable model.
There is disagreement on the effects of IOP variation and fluctuation and whether IOP variation and fluctuation are risk factors for progression. It is suggested that these factors are due largely to the intrinsic relationship between IOP variation and the effect of intervention. For instance, if progression is suspected over time, additional procedures (incisional surgery, laser surgery, or medication) will result in lowering of the IOP with a consequent treatment-induced increase in the IOP fluctuation.

Some RCTs established target peak IOP, even though this parameter was not incorporated into their risk models. For instance, in the Ocular Hypertension Treatment Study, the treatment goals for subjects randomly assigned to medication were IOPs of 24 mm Hg or less and a 20% reduction in IOP from the average of the qualifying and baseline IOP. Medical therapy was advanced to achieve the targeted IOP reduction. For the Early Manifest Glaucoma Trial, a standard IOP-lowering protocol was initially applied to all patients in the treatment arm.

Our data demonstrated a significant correlation among all IOP parameters. Peak and mean IOP showed the strongest association, suggesting that patients with a higher mean IOP during follow-up also tend to be those having the highest peaks. One advantage of using peak IOP in clinical practice is its ease of assessment because of its intrinsic relationship to target IOP. Peak IOP can be reassessed at each visit, whereas mean IOP determination requires longitudinal data collection and may be affected by the interval between visits. For instance, if a patient presents with a high IOP at one visit, IOP checks may occur more frequently, falsely elevating the mean. Also, establishing a target peak IOP is clinically easier than seeking to establish a target mean IOP or target IOP fluctuation. Of note, peak IOP remained a significant factor for progression even among eyes with lower mean follow-up IOP in our study.

Three major RCTs confirmed a strong association between DH and future VF development and progression. However, the etiology of DH remains unclear. Disc hemorrhage may be a primary vascular event, or it may result from an ongoing degenerative process at the optic nerve head. Supporting the latter hypothesis, we have reported that sustained, localized, spatially consistent VF loss precedes the onset of DH and continues in the same region. The development of DH could therefore be an indirect sign that the optic nerve complex (optic nerve head and parapapillary region) is particularly susceptible to damage. Disc hemorrhage more often occurs adjacent to areas of neuroretinal rim thinning and retinal nerve fiber layer loss and within areas of greater βPPA width. This also suggests that DH occurs in areas of existing structural damage and increases the likelihood of subsequent VF progression.

The βPPA has been associated with subsequent VF loss in patients with ocular hypertension and in patients with established glaucoma. Using a different cohort, we have also shown that both the presence and the size of βPPA affect the risk for progression. Park et al also reported that βPPA is a significant risk factor in young patients having normal-tension glaucoma with moderate to severe VF loss. Nevertheless, to our knowledge, no RCT has examined the effect of βPPA on glaucoma development or progression. One disadvantage of βPPA assessment is the difficulty in differentiating glaucomatous βPPA from myopic parapapillary degeneration. We minimized this by excluding eyes with high myopia and including only eyes with confirmed glaucomatous optic neuropathy.

One reason βPPA may have had a strong association with progression in our sample is that we defined its presence by looking at the entire set of disc photographs. Previous studies have suggested that PPA enlarges as glaucoma progresses. Structural progression increases the likelihood of future VF progression. Therefore, βPPA could be a surrogate for previous structural progression, which dramatically increases its association with subsequent VF progression. Also, the microstructural changes within the optic nerve complex may predispose to a faster rate of future structural loss. This is partly corroborated by the fact that DHs are more commonly seen in eyes with βPPA and within areas where βPPA is the widest.

Although a thinner central cornea increases the risk of VF progression, the precise pathophysiology of this effect remains unclear. Proposed mechanisms range from...
tension glaucoma. Even though exfoliation syndrome glaucoma progresses almost twice as fast as eyes with normal tension glaucoma, we previously demonstrated that eyes with exfoliative syndrome increased the risk of progression by more than 200%. Even though exfoliation syndrome reach only borderline significance in most of our multivariable analyses, there was a trend for these eyes to progress faster than eyes without exfoliation syndrome (mean [SD] global rate of VF change, −0.65 [0.7] dB/yr vs −0.41 [0.7] dB/yr; P = .008). However, exfoliation syndrome lost its significance once IOP and other parameters were added to the model (Tables 3, 4, and 5).

The Ocular Hypertension Treatment Study and the Early Manifest Glaucoma Trial showed a significant association between baseline mean deviation and an increased rate of progression. The Advanced Glaucoma Intervention Study found that nonprogressing eyes had better VF scores at 4 years than did progressing eyes. In conclusion, we confirmed that, in a population of patients treated for glaucoma, well-known and reported risk factors are indeed relevant for risk assessment. Moreover, additional information provided by simple diagnostic tools (tonometry and ophthalmoscopy) suggest the importance of other IOP-independent factors (such as age) may become more apparent. Aging may increase the susceptibility of the optic nerve complex to IOP stress. Despite population-based studies stating that African ancestry confers susceptibility to glaucoma development and progression, none of the RCTs that investigated the effect of race on progression has found any significant association in multivariable analyses. In our study, nonwhites were underrepresented, preventing us from any interpretation of these results.

Most RCTs have failed to show any association between sex and glaucoma development or progression. In the Ocular Hypertension Treatment Study, men were more likely to convert to glaucoma than were women in the univariable model. In our study, male sex was a risk factor among patients with lower mean follow-up IOP.

Our study is limited by its retrospective nature and by the biases inherent in a tertiary-care referral center; therefore, we suggest that a pragmatic clinical trial be evaluated with care. These limitations, however, are mitigated by the large sample size, the long follow-up period, the large number of VF tests, and a cohort that closely resembles those seen in clinical practice. Our findings may not be applicable to other clinical settings because they reflect a specific population for which certain risk factors may play a more important role than others. The significant biases and limitations of nonstandardized treatment and follow-up protocols may slant the assessment of risk. For example, patients may be treated more or less aggressively depending on the ophthalmologist's perceived risk for further deterioration. This may not be the same for all ophthalmologists or even the same ophthalmologist at another time. Our main purpose, however, was to confirm whether risk factors identified in RCTs are the same as those in clinical practice. Confirmation from other clinical databases could provide even greater clinical relevance for RCTs and enhance their importance.

One advantage of using trend analysis over event analysis was our ability to provide rates of VF change in this population. Depending on the number and frequency of VF tests, trend analysis may provide better sensitivity and specificity to detect progression compared with event analysis. Our population underwent a large number of VF tests, increasing the power of our analyses. We chose a specific definition of progression using pointwise linear regression, which could have been at the expense of lower sensitivity. Yet our definition of progression, requiring 2 adjacent points in the same hemifield, increased our likelihood of detecting true VF progression.

In conclusion, we confirmed that, in a population of patients treated for glaucoma, well-known and reported risk factors are indeed relevant for risk assessment. Moreover, additional information provided by simple diagnostic tools (tonometry and ophthalmoscopy) suggest the importance of peak IOP and the presence of BPPA to assess the future risk of glaucomatous vision loss. Clinicians should be aware of the continued roles played by both IOP-dependent and IOP-independent factors in treated patients.

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Correction

Error in Text. In the Clinical Sciences article titled “Risk Factors for Visual Field Progression in Treated Glaucoma,” by De Moraes et al, published in the May issue of the Archives (2011;129[5]:562-568), the last sentence of the last paragraph in the right column of page 565 should have appeared as follows: “This is partly corroborated by the fact that DHs are more commonly seen in eyes with βPPA and within areas where βPPA is the widest. 40” This article was corrected online.

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