Predictive Factors of the Optic Nerve Head for Development or Progression of Glaucomatous Visual Field Loss

Jost B. Jonas,1,2 Peter Martus,3 Folkert K. Horn, Anselm Jünemann, Mathias Korth, and Wido M. Budde1,2

PURPOSE. To evaluate which morphologic features of the optic disc are predictive factors for the development or progression of visual field loss in chronic open-angle glaucoma.

METHODS. The prospective observational clinical study included 763 eyes of 416 white subjects with ocular hypertension and chronic open-angle glaucoma. During the follow-up time (mean, 67.4 months; median, 65.1; range, 6.2–104.5), all patients underwent repeated qualitative and morphometric evaluation of color stereo optic disc photographs and white-on-white visual field examination. Progression of glaucomatous visual field damage was defined by point-wise regression analysis for each of the 59 locations in the visual field. Outcome measures were qualitative and quantitative morphologic optic nerve head parameters.

RESULTS. Development or progression of glaucomatous visual field defects was detected in 106 (13.9%) eyes. At baseline of the study, neuroretinal rim area was significantly (P < 0.002) smaller, the beta zone of parapapillary atrophy (P < 0.003, nasal sector) was significantly larger, and age was significantly higher (P < 0.003) in the progressive study group than in the nonprogressive study group. Both study groups did not vary significantly in size of the optic disc and the alpha zone of parapapillary atrophy. Cox proportional hazard regression analysis revealed that the progression of glaucomatous visual field loss depended significantly on the area of the neuroretinal rim (P < 0.001) and age (P < 0.001), but was independent of diameter of the retinal arterioles and veins.

CONCLUSIONS. Morphologic predictive factors for development or progression of glaucomatous visual field defects in whites are small neuroretinal rim area and large beta zone of parapapillary atrophy. Age is an additional nonmorphologic parameter. Progression of glaucomatous optic nerve head changes is independent of the size of the optic disc and the alpha zone of parapapillary atrophy and retinal vessel diameter. (Invest Ophthalmol Vis Sci. 2004;45:2613–2618) DOI:10.1167/iovs.03-1274

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Morphologic changes in the optic nerve head and functional deficits in the visual field are closely interconnected with each other in patients with chronic open-angle glaucoma. The alterations in the appearance of the optic nerve head such as development of notches in the neuroretinal rim leading to an altered shape of the neuroretinal rim, optic disc hemorrhages, and localized defects or a diffuse loss of retinal nerve fiber layer can precede the development of visual field defects by several years. In addition, longitudinal studies such as the Ocular Hypertension Treatment Study (OHTS) and the Collaborative Initial Glaucoma Treatment Study (CIGTS), have revealed that factors that are predictive of progression of glaucomatous optic nerve damage in patients with chronic open-angle glaucoma are an advanced stage of the disease, as indicated by a small neuroretinal rim; a pronounced defect in the visual field; and a large beta zone of parapapillary atrophy. By performing a prospective examination of eyes that remained stable or that showed deterioration of the visual field during the follow-up, it was the purpose of the present study, similar to preceding investigations, to search for morphologic parameters of the optic nerve head that may indicate an increased risk for eventual development, or further deterioration, of glaucomatous visual field defects.

METHODS

The prospective clinical observational study included 763 eyes (387 right eyes) of 416 (201 women) white subjects. The study was composed of eyes with open-angle glaucoma (498 eyes); 193 normal-pressure glaucoma, 274 primary open-angle glaucoma, 31 secondary open-angle glaucoma due to such conditions as pseudoxefoliation or primary melanin pigment dispersion syndrome) and with ocular hypertension (265 eyes). The subjects were referred by their ophthalmologists for further diagnosis and follow-up of glaucoma and were prospectively and consecutively evaluated. All patients had an open anterior chamber angle and visual acuity of 20/25 or better. At the day of examination, intraocular pressure was equal to or less than 21 mm Hg in all individuals. Exclusion criteria were all eye diseases other than glaucoma, diabetes mellitus, and a myopic refractive error equal to or more than −8 D. The methods applied in the study adhered to the tenets of the Declaration of Helsinki for the use of human subjects in biomedical research. Informed consent was obtained from each subject before enrollment. The patients were part of an ongoing prospective study on the progression of glaucoma (Erlangen Glaucoma Register). Institutional Review Board and Ethics Committee approval had been obtained at the start of the study.

The study was composed of eyes with primary open-angle glaucoma (n = 291 eyes), secondary open-angle glaucoma due to such conditions as pseudoxefoliation or primary melanin pigment dispersion syndrome (n = 315), or normal-pressure glaucoma (n = 170). In the eyes affected by primary open-angle glaucoma, no obvious reason for the elevated intraocular pressure was detected. Criteria for the diagnosis of normal-pressure glaucoma were maximum intraocular pressure readings equal to or less than 21 mm Hg in at least two 24-hour pressure profiles obtained by slit lamp applanation tonometry.
and containing measurements at 5 PM, 9 PM, 12 AM, 7 AM, and noon. Ophthalmoscopy, medical history, and neuroradiologic, neurologic, and medical examinations did not reveal any reason other than glaucoma for optic nerve damage, such as intrasellar or suprasellar tumors, retinal vessel occlusion, optic disc drusen, or nonarteritic anterior ischemic optic neuropathy. At baseline of the study, the open-angle glaucoma group included 205 (41.2%) eyes with chronic open-angle glaucoma with glaucomatous visual field defects and glaucomatous changes of the optic nerve head, and 293 (58.8%) eyes with preperimetric glaucoma defined by glaucomatous abnormalities of the optic nerve head and normal white-on-white visual field test results. A glaucomatous visual field defect was defined as a tested field (Octopus G1; Interzeag, Schlieren, Switzerland) with (1) at least three adjacent test points having a deviation of equal to or greater than 5 dB and with one test point with a deviation more than 10 dB lower, (2) at least two adjacent test points with a deviation equal to or greater than 10 dB, (3) at least three adjacent test points abutting the nasal horizontal meridian with a deviation equal to or greater than 5 dB, or (4) a mean visual field defect of more than 2 dB. The rate of false-positive and -negative answers had to be equal to or less than 15%. To define the baseline of the visual field examination, two visual field tests were performed before the subject was included in the study. Glaucomatous changes of the optic nerve head included an unusually small neuroretinal rim area in relation to the optic disc size, an abnormal shape of the neuroretinal rim, cup-to-disc diameter ratios higher vertically than horizontally, and localized or diffuse retinal nerve fiber layer defects. Because all eyes examined in the study had to show glaucomatous abnormalities of the optic disc, the inclusion of normotensive eyes with nonglaucomatous optic nerve damage in the normal-pressure glaucoma subgroup was not likely.

Progression of glaucomatous visual field loss was defined by point-wise regression analysis for each of the 59 locations in the visual field. Point-wise progression was assumed, if a difference of larger than 1 dB per test point was observed for the local defect. A point-wise improvement (learning effect or random variation) was assumed if a difference less than −1 dB was observed. An eye was classified as progressive if the number of locations with progression was significantly higher than the number of locations with improvement (binomial test, P = 0.05 two-sided). For each eye, the first follow-up measurement with progression as defined earlier entered the analysis. In subsequent analyses, progression was treated as a time-to-event variable. Kaplan-Meier and simple and multiple Cox regression with forward variable selection were applied. According to the skewed distribution of some variables, for each quantitative variable, categorization according to tertiles was used.

For all eyes, 15° color stereo optic disc transparencies had been taken with a telecentric 50° fundus camera equipped with a 1:2 converter (Zeiss, Oberkochen, Germany). The disc slides were projected in a scale of 1 to 15. The outlines of the optic cup, optic disc, peripapillary scleral ring, and alpha and beta zones of parapapillary atrophy were plotted on paper and morphometrically analyzed. To obtain values in absolute size units (i.e., millimeters or square millimeters) the ocular and photographic magnifications were corrected using the Littmann method.20 The optic cup was defined on the basis of contour and not of pallor. The border of the optic disc was identical with the inner side of the peripapillary scleral ring. Parapapillary atrophy was differentiated into a peripheral alpha zone with irregular pigmentation and a central beta zone with visible sclera and visible large choroidal vessels. To assess the configuration and the regional distribution of the neuroretinal rim and parapapillary atrophy, the optic disc and the parapapillary region were divided into four sectors. The temporal inferior sector and the temporal superior sector were right angled and were tilted 13° temporal to the vertical optic disc axis. The temporal horizontal sector and the nasal sector covered the remaining area. The diameters of the retinal arterioles were measured at the optic disc border in the inferotemporal, superotemporal, supranasal, and inferonasal region. The assessment of the optic disc slides was performed in a masked fashion so that the examiners were unaware of the diagnosis, intraocular pressure, and visual field data. The method has been described in detail.18,19

Once or twice a year, all patients included in the study were readmitted to the hospital to measure intraocular pressure in a circular curve with measurements at 5 PM, 9 PM, 12 AM, 7 AM, and 12 PM. In addition, they underwent white-on-white perimetry and stereo photography of the optic nerve head. Mean follow-up time was 67.4 months (median, 65.1 months; range, 6.2 to 104.5 months).

In the statistical analysis, mean and standard deviations of potential predictors are given for the stable eyes and progressive eyes separately. Confirmatory analysis, however, used the Cox proportional hazard regression analysis adjusting for different follow-up times of the patients. Dependency of left and right eyes in the same subject was taken into account conservatively: χ² values were multiplied by the factor, number of patients divided by number of eyes. Thus, significance tests were performed with respect to the number of patients instead of the number of eyes. Only corrected probabilities are presented. With 106 eyes showing progression or new development of visual field loss, hazard rates of 1.87 were detectable (assuming a level of significance of 0.02 two-sided, according to our adjustment for patients contributing two eyes, and a power of 0.8).21 Statistical analysis was performed with a commercially available statistical software package (SPSS for Windows, ver. 11.5; SPSS Science, Chicago, IL).

**RESULTS**

In the whole study population, 106 (13.9%) eyes showed a progressive visual field loss, either as the progression of already-existing perimetric deficits (n = 70) or as new development of glaucomatous visual field defects (n = 36; Fig. 1). The mean and median intraocular pressure was significantly higher in the stable group than in the progressive group (23.3 ± 5.7 mm Hg; P = 0.001). After adjustment for age and neuroretinal rim area, the difference was no longer statistically significant. Both study groups did not vary significantly in the mean minimum intraocular pressure (14.5 ± 3.6 mm Hg vs. 14.0 ± 3.4 mm Hg; P = 0.20).
Optic Disc and Progressive Visual Field Defect in Glaucoma

TABLE 1. Data of Eyes with Progressive Visual Field Loss and Eyes with Stable Visual Fields

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No Progression</th>
<th>Progression</th>
<th>P (Without Adjustment for Age)</th>
<th>P (With Adjustment for Age)</th>
<th>P (Multivariate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes (n)</td>
<td>657</td>
<td>106</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females/males</td>
<td>311/346</td>
<td>56/50</td>
<td>0.41 (NS)</td>
<td>0.41 (NS)</td>
<td></td>
</tr>
<tr>
<td>Right/Left Eyes</td>
<td>334/323</td>
<td>53/53</td>
<td>0.59 (NS)</td>
<td>0.59 (NS)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>48.0 ± 12.3</td>
<td>56.0 ± 11.0</td>
<td>0.005</td>
<td>0.005</td>
<td>0.007</td>
</tr>
<tr>
<td>Refractive error (D)</td>
<td>−0.92 ± 2.27</td>
<td>−1.02 ± 2.82</td>
<td>0.77 (NS)</td>
<td>0.77 (NS)</td>
<td></td>
</tr>
<tr>
<td>Optic disc area (mm²)</td>
<td>2.72 ± 0.66</td>
<td>2.75 ± 0.59</td>
<td>0.63 (NS)</td>
<td>0.63 (NS)</td>
<td></td>
</tr>
<tr>
<td>Minimal disc diameter (mm)</td>
<td>1.74 ± 0.23</td>
<td>1.76 ± 0.20</td>
<td>0.61 (NS)</td>
<td>0.61 (NS)</td>
<td></td>
</tr>
<tr>
<td>Maximum disc diameter (mm)</td>
<td>1.97 ± 0.23</td>
<td>1.99 ± 0.20</td>
<td>0.38 (NS)</td>
<td>0.38 (NS)</td>
<td></td>
</tr>
<tr>
<td>Neuroretinal rim area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (mm²)</td>
<td>1.32 ± 0.40</td>
<td>1.07 ± 0.40</td>
<td>0.002</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Temp. Horizontal</td>
<td>0.18 ± 0.08</td>
<td>0.15 ± 0.07</td>
<td>0.003</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Temp. Inferior</td>
<td>0.34 ± 0.13</td>
<td>0.27 ± 0.15</td>
<td>0.002</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Temp. Superior</td>
<td>0.32 ± 0.11</td>
<td>0.25 ± 0.11</td>
<td>0.002</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Nasal</td>
<td>0.47 ± 0.14</td>
<td>0.40 ± 0.14</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parapapillary Atrophy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha Zone (mm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.76 ± 0.73</td>
<td>0.74 ± 0.64</td>
<td>0.24 (NS)</td>
<td>0.24 (NS)</td>
<td>0.084 (NS)</td>
</tr>
<tr>
<td>Temp. Horizontal</td>
<td>0.31 ± 0.26</td>
<td>0.28 ± 0.24</td>
<td>0.11 (NS)</td>
<td>0.11 (NS)</td>
<td>0.15 (NS)</td>
</tr>
<tr>
<td>Temp. Inferior</td>
<td>0.18 ± 0.18</td>
<td>0.18 ± 0.17</td>
<td>0.15 (NS)</td>
<td>0.15 (NS)</td>
<td>0.98 (NS)</td>
</tr>
<tr>
<td>Temp. Superior</td>
<td>0.17 ± 0.19</td>
<td>0.18 ± 0.18</td>
<td>0.09 (NS)</td>
<td>0.09 (NS)</td>
<td>0.90 (NS)</td>
</tr>
<tr>
<td>Nasal</td>
<td>0.11 ± 0.24</td>
<td>0.11 ± 0.20</td>
<td>0.73 (NS)</td>
<td>0.73 (NS)</td>
<td>0.82 (NS)</td>
</tr>
<tr>
<td>Beta Zone (mm²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.28 ± 0.50</td>
<td>0.66 ± 1.31</td>
<td>0.19 (NS)</td>
<td>0.19 (NS)</td>
<td>0.11 (NS)</td>
</tr>
<tr>
<td>Temp. Horizontal</td>
<td>0.12 ± 0.19</td>
<td>0.18 ± 0.29</td>
<td>0.35 (NS)</td>
<td>0.35 (NS)</td>
<td>0.29 (NS)</td>
</tr>
<tr>
<td>Temp. Inferior</td>
<td>0.08 ± 0.16</td>
<td>0.20 ± 0.35</td>
<td>0.11 (NS)</td>
<td>0.11 (NS)</td>
<td>0.07 (NS)</td>
</tr>
<tr>
<td>Temp. Superior</td>
<td>0.05 ± 0.11</td>
<td>0.13 ± 0.30</td>
<td>0.25 (NS)</td>
<td>0.25 (NS)</td>
<td>0.16 (NS)</td>
</tr>
<tr>
<td>Nasal</td>
<td>0.03 ± 0.19</td>
<td>0.16 ± 0.55</td>
<td>0.003</td>
<td>0.003</td>
<td>0.05 (NS)</td>
</tr>
<tr>
<td>Arteries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temp. Inferior</td>
<td>0.097 ± 0.032</td>
<td>0.093 ± 0.022</td>
<td>0.15 (NS)</td>
<td>0.15 (NS)</td>
<td>0.18 (NS)</td>
</tr>
<tr>
<td>Temp. Superior</td>
<td>0.098 ± 0.035</td>
<td>0.090 ± 0.030</td>
<td>0.01</td>
<td>0.01</td>
<td>0.05</td>
</tr>
<tr>
<td>Nasal superior</td>
<td>0.086 ± 0.030</td>
<td>0.079 ± 0.024</td>
<td>0.02</td>
<td>0.02</td>
<td>0.09 (NS)</td>
</tr>
<tr>
<td>Nasal Inferior</td>
<td>0.087 ± 0.051</td>
<td>0.078 ± 0.019</td>
<td>0.02</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Veins</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temp. Inferior</td>
<td>0.132 ± 0.043</td>
<td>0.131 ± 0.034</td>
<td>0.90 (NS)</td>
<td>0.90 (NS)</td>
<td>0.81 (NS)</td>
</tr>
<tr>
<td>Temp. Superior</td>
<td>0.131 ± 0.051</td>
<td>0.135 ± 0.034</td>
<td>0.87 (NS)</td>
<td>0.87 (NS)</td>
<td>0.65 (NS)</td>
</tr>
<tr>
<td>Nasal superior</td>
<td>0.111 ± 0.037</td>
<td>0.107 ± 0.038</td>
<td>0.70 (NS)</td>
<td>0.70 (NS)</td>
<td>0.80 (NS)</td>
</tr>
<tr>
<td>Nasal inferior</td>
<td>0.110 ± 0.039</td>
<td>0.102 ± 0.031</td>
<td>0.05</td>
<td>0.05</td>
<td>0.11 (NS)</td>
</tr>
</tbody>
</table>

Mean ± SD; P: statistical significance of difference between the two study groups adjusted for age.

In the descriptive analysis, we looked for differences in the optic disc’s appearance, at baseline of the study, between eyes with progressive visual field defects and eyes with stable visual fields. The group of eyes with progressive visual field defects was older than the group without progression (Table 1; Fig. 2). No differences in gender were observed. At the baseline of the study, the group of eyes with eventual progression and the group of eyes without progression did not vary in size of the optic disc and measured separately in each of the four optic disc sectors, was smaller, and the beta zone of parapapillary atrophy, measured in the nasal parapapillary sector, was significantly larger (Table 1; Fig. 3). The diameter of the retinal arteries at the optic disc border was thinner in the eyes with a progressive visual field defect than in the eyes with a stable visual field (Table 1).

In the confirmatory analysis, simple and multiple Cox regression analyses were performed, with the event of development or progression of visual field defect as the dependent parameter, and age, size of neuroretinal rim, total area of beta zone, and temporal inferior arterial diameter at the optic disc border as independent parameters. The univariate analysis revealed that age, neuroretinal rim area, nasal sector of the beta zone, and arterial diameters were significantly associated with progression. The multivariate analysis showed that only age (P < 0.001) and neuroretinal rim area in the temporal superior sector (P < 0.001), kept a statistically significant association with the progression of visual field damage.

In a subgroup of patients with a follow-up of more than 60 months, the prognostic value of neuroretinal rim area (total area and area in the disc sectors) was higher than in the entire study group, whereas the prognostic impact of the diameter of the retinal arterioles was no longer significant. The prognostic value of the beta zone of parapapillary atrophy was higher in the subgroup of patients with a follow-up of longer than 60 months than in the whole study group. Correspondingly, in the subgroup of patients with a follow-up of longer than 60 months, the nasal sector of the beta zone of parapapillary atrophy had a statistically significant association with the progression of glaucoma in the multivariate analysis adjusting for the patient’s age and neuroretinal rim area (P = 0.054). The results for the other variables remained unchanged if, instead of the whole study group, the subgroup of patients with a follow-up of longer than 60 months was used for statistical analysis.

Correcting the probabilities of the significant association with the Bonferroni adjustment for multiple statistical comparisons essentially revealed the same results.
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disease than in eyes with less pronounced damage of the optic

damage was more marked in eyes at a more advanced stage of the

risk of further progression of glaucomatous optic nerve damage

open-angle glaucoma are a small size of neuroretinal rim and

found that a high cup-to-disc diameter ratio has a statistically significant

on the progressive visual field defects in patients

with normal-pressure glaucoma. Martinez-Bello et al.25 demonstrated that patients who showed progression in high-pass

resolution perimetry had more damaged baseline fields than

did those who remained stable. Tezel et al.24 reported that eyes

with advanced glaucomatous optic disc damage compared with eyes with less advanced optic nerve damage are more

likely to progress, despite receiving treatment to reduce in-

tracular pressure. Correspondingly, in recent randomized

controlled trials such as the OHTS, baseline vertical and hori-

zontal cup-to-disc ratio and pattern standard deviation, besides age and intraocular pressure, were good predictors of the

onset of primary open-angle glaucoma.17 An additional explanation for the finding of a significantly smaller rim area in the

progressive study group than in the stable group may be that in the

progressive group, the neuroretinal rim was already so

much reduced that it sustained little more optic nerve damage than was already present to make visual field defects evident.

Summarizing all these studies suggests clinically that patients

with a small neuroretinal rim may exhibit an increased risk of

glaucoma progression and may need more intensive antiglau-

coma treatment than patients with early loss of the neuroreti-

nal rim. The clinical–histologic correlate of the presumed

higher risk for the development of glaucomatous visual field
defects in eyes with smaller neuroretinal rim may be anatomic

changes in the lamina cribrosa in the course of the glaucoma-
tous process.25

Patients with eventual progression of glaucomatous visual

field defect had a significantly larger beta zone of parapapillary

atrophy than patients with a stable visual field during the

follow-up period in the present study, which may suggest that

a large area of parapapillary atrophy is a predictive factor for

worsening of glaucoma. This notion concurs with findings in

studies performed by Tezel et al.,26 in which presence and size of

parapapillary atrophy were related to the development of

subsequent visual field damage in patients with ocular hyper-
tension. The same authors showed that the extent and location

of visual field abnormalities that developed in ocular hypertensive

eyes with progression to glaucoma exhibited a concor-
dance with the extent and location of progressive parapapillary

atrophy noted in the ocular hypertension period.27 They also

reported that the progression of parapapillary chorioretinal

atrophy may be an early glaucomatous finding in some patients

with ocular hypertension and may indicate progression of

glaucomatous damage of the optic nerve.24 Uchida et al.28 and

colleagues reported that progression of peripapillary atrophy is

associated with progressive optic disc damage and progressive

visual field loss in glaucoma and may be used as a marker for

progressive glaucomatous damage. Daugeliene et al.29 and

Araie et al.32 reported that parapapillary atrophy is one among

other predictive factors of progression of visual loss in normal-

pressure glaucoma. In a study on subjects with ocular hyper-
tension, Quigley et al.11 reported that the presence of a disc

crescent was one of the attributes that were significantly asso-

ciated with the incidence of field loss, which suggests clinically

DISCUSSION

The results of the present study suggest that morphologic

predictive factors for development or progression of glauco-

matous visual field defects in white patients with chronic

open-angle glaucoma are a small size of neuroretinal rim and

large area of beta zone of parapapillary atrophy. Progression of

glaucomatous optic nerve head changes was statistically inde-

dependent of size of the optic disc, size of alpha zone of para-

papillary atrophy, and retinal vessel diameter.

The finding that a small neuroretinal rim area is a predis-

posing factor for eventual progression of glaucomatous visual

field loss fits with other longitudinal studies in which the risk

of further progression of glaucomatous optic nerve damage

was more marked in eyes at a more advanced stage of the

disease than in eyes with less pronounced damage of the optic

nerve.17–19 To mention examples, Araie et al.32 found that a

high cup-to-disc diameter ratio has a statistically significant

influence on the progression of visual field defects in patients

with normal-pressure glaucoma. Martinez-Bello et al.25 demon-

strated that patients who showed progression in high-pass

resolution perimetry had more damaged baseline fields than

did those who remained stable. Tezel et al.24 reported that eyes

with advanced glaucomatous optic disc damage compared with eyes with less advanced optic nerve damage are more

likely to progress, despite receiving treatment to reduce in-

traocular pressure. Correspondingly, in recent randomized

controlled trials such as the OHTS, baseline vertical and hori-

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onset of primary open-angle glaucoma.17 An additional explanation for the finding of a significantly smaller rim area in the

progressive study group than in the stable group may be that in the

progressive group, the neuroretinal rim was already so

much reduced that it sustained little more optic nerve damage than was already present to make visual field defects evident.

Summarizing all these studies suggests clinically that patients

with a small neuroretinal rim may exhibit an increased risk of

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coma treatment than patients with early loss of the neuroreti-
nal rim. The clinical–histologic correlate of the presumed

higher risk for the development of glaucomatous visual field
defects in eyes with smaller neuroretinal rim may be anatomic

changes in the lamina cribrosa in the course of the glaucoma-
tous process.25

Patients with eventual progression of glaucomatous visual

field defect had a significantly larger beta zone of parapapillary

atrophy than patients with a stable visual field during the

follow-up period in the present study, which may suggest that

a large area of parapapillary atrophy is a predictive factor for

worsening of glaucoma. This notion concurs with findings in

studies performed by Tezel et al.,26 in which presence and size of

parapapillary atrophy were related to the development of

subsequent visual field damage in patients with ocular hyper-
tension. The same authors showed that the extent and location

of visual field abnormalities that developed in ocular hypertensive

eyes with progression to glaucoma exhibited a concor-
dance with the extent and location of progressive parapapillary

atrophy noted in the ocular hypertension period.27 They also

reported that the progression of parapapillary chorioretinal

atrophy may be an early glaucomatous finding in some patients

with ocular hypertension and may indicate progression of

glaucomatous damage of the optic nerve.24 Uchida et al.28 and

colleagues reported that progression of peripapillary atrophy is

associated with progressive optic disc damage and progressive

visual field loss in glaucoma and may be used as a marker for

progressive glaucomatous damage. Daugeliene et al.29 and

Araie et al.32 reported that parapapillary atrophy is one among

other predictive factors of progression of visual loss in normal-

pressure glaucoma. In a study on subjects with ocular hyper-
tension, Quigley et al.11 reported that the presence of a disc

crescent was one of the attributes that were significantly asso-

ciated with the incidence of field loss, which suggests clinically

FIGURE 2. Progresion of glaucomatous visual field defects according to age at baseline. The sample was divided into three groups of equal size; according to the observed distribution of age. Bottom, middle, and top lines: oldest, middle and youngest age groups, respectively.

FIGURE 3. Progression of glaucomatous visual field defects according to the area of the neuroretinal rim at baseline. The sample was divided into three groups of equal size according to the observed distribution of neuroretinal rim area. Bottom, middle, and top lines: groups with smallest, midsized, and largest rim areas, respectively.
that, independent of the size of the neuroretinal rim, a large beta zone of parapapillary atrophy may be taken as a relative indicator for an increased risk of further progression of glaucoma, suggesting the need of a more intensive treatment. In contrast to the beta zone of parapapillary atrophy, the size of the alpha zone did not play a major role as a predictive factor of the eventual loss of neuroretinal rim, which is in agreement with previous studies in which measurement of the beta zone was markedly more important than measurement of the alpha zone for the detection of glaucomatous optic nerve damage.30

In the present study as well as in preceding investigations, optic disc size was not significantly associated with the frequency of progression of glaucomatous visual field defects.17–19 In accordance with preceding investigations, it suggests that neither a large nor a small optic disc size predisposes the eyes to the progression of glaucomatous visual field loss. Previously, the marked interindividual variability in optic disc area has been reason to raise the question of whether the disc size correlates with the susceptibility for glaucomatous optic nerve damage.1 In some hospital-based studies, optic disc area was significantly larger in non-highly myopic patients with normal-pressure glaucoma than in non-highly myopic patients with high-pressure open-angle glaucoma.31 In a parallel manner, the larger optic disc size in combination with the reportedly higher glaucoma susceptibility in the Afro-American population compared with whites has led to the hypothesis that eyes with large optic discs may be more prone to glaucomatous optic nerve fiber loss than eyes with small optic discs.32–34 Deducing from purely mechanical factors, the pressure gradient across the lamina cribrosa produces a more pronounced displacement of the lamina cribrosa in large optic discs than in small optic nerve heads.32,35 Inside the optic disc, the susceptibility for neuroretinal rim loss is higher in regions with a long distance to the central retinal vessel trunk than in sectors with a short distance.36 These pro factors indicating a higher risk for glaucomatous damage in eyes with large discs are opposed by the con factors. Optic nerve fibers are more crowded in eyes with small optic nerve heads than in eyes with large discs.37 A dense arrangement of the nerve fibers in small optic discs may suggest that the lamina cribrosa, mechanically deformed by the glaucomatous process, may more easily press the optic nerve fibers in small optic discs than in large optic nerve heads.36 Small optic discs have been reported to contain fewer optic nerve fibers than large optic nerve heads.36 It suggests that eyes with small optic discs have a smaller anatomic reserve capacity. Nonarteritic anterior ischemic optic neuropathy and optic disc drusen occur more frequently in small optic nerve heads than in large optic discs.1,38 For both entities, similar pathogenic mechanisms have been discussed as for glaucoma—that is, a perfusion problem, as is present in ischemic optic neuropathy, and a blockade of the orthograde axoplasmic flow, as in the case of optic disc drusen. Results in other studies have suggested that the higher glaucoma susceptibility in the inferior and superior disc regions compared with the temporal and nasal disc sectors is associated with a higher percentage of pore-to-disc area.1,40–42 This ratio increases with decreasing optic disc size.42 In summary, one might infer that the effects of the pro and con factors may compensate for each other. This notion agrees with findings in the present investigation as well as with those in other recent studies, such as the Baltimore Eye Survey, in which Quigley et al.43 and Jonas et al.44 concluded that the optic disc area may be a weak predictive factor for open-angle glaucoma.

The diameter of the retinal arteries varied to some extent between the progressive group and the stable group (Table 1). In a multiple regression analysis with compensation of interparameter interdependencies, however, the retinal arterial diameters were not significantly associated with the development of visual field defects. Although the diameters of the retinal arteries correlate with the loss of neuroretinal rim in cross-section studies of patients with glaucoma,45,46 the interindividual variability in the diameter of the retinal vessels as well as the dependency of the retinal arterial diameter on the amount of glaucomatous optic nerve damage may have been the reason that the relationship between retinal arterial diameter and the risk for eventual development of glaucomatous visual field damage did not reach a statistically significant level. The failure of the retinal artery caliber to remain a statistically significant predictive factor for the progression of glaucoma in the multivariate analysis therefore does not necessarily mean that it is not an important or a primary factor.

There are limitations to the present study. Because it was the purpose of the study to evaluate whether morphologic features of the optic disc are of importance for progression of glaucoma, other factors such as the level of intraocular pressure and the type of chronic open-angle glaucoma were not primarily taken into account. Minimum intraocular pressure measurements, however, did not vary significantly between the progressive study group and the stable study group. In fact, the maximum intraocular pressure measurements were significantly lower in the progressive study group than in the stable group before adjustment for age and neuroretinal rim area. After adjustment, the difference was no longer statistically significant. Another possible limitation of the study is that two instead of three visual field examinations were performed at baseline of the study. A possible learning effect of a third visual field examination at baseline may have artificially reduced the number of patients with progression of their visual field defects during the follow-up. Another limitation of the study may be that differences between the patients in the antiglaucoma treatment influenced the level of intraocular pressure and, due to that, the rate of progression of glaucoma. Because the type of treatment was independent of optic disc parameters such as size and shape of the optic nerve head and because, in case of doubt, a small neuroretinal rim and a large beta zone of parapapillary atrophy might have favored a more intensive antiglaucoma therapy, the possible flaw in the study that the therapy varied among the patients may serve to underline the results that, besides age, a small neuroretinal and a large beta zone of parapapillary atrophy are predictive factors for eventual progression of glaucomatous visual loss. These findings may be of importance in deciding whether patients with chronic open-angle glaucoma need intensified antiglaucoma therapy to decrease the risk of further loss of visual function.

References


