

Optic nerve damage in highly myopic eyes with chronic open-angle glaucoma

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PURPOSE. *To compare the amount of optic nerve damage in relation to intraocular pressure in highly myopic eyes with chronic open-angle glaucoma versus non-highly myopic eyes with chronic open-angle glaucoma.*

METHODS. *The comparative clinical observational study included 1841 eyes of 1100 patients with chronic open-angle glaucoma. The highly myopic study group consisted of 25 eyes with a myopic refractive error equal to or higher than -8 diopters. It was subdivided into eyes with an optic disc size larger than 2.7 mm² and eyes with an optic disc smaller than 2.7 mm². The control group included the remaining, non-highly myopic eyes (n=1816). For all patients, a morphometric analysis of color stereo optic disc photographs was performed. Main outcome measures were morphometric optic disc measurements and intraocular pressure.*

RESULTS. *In the highly myopic, large-optic-disc study group compared with the control group, maximal and minimal intraocular pressure readings were significantly ($p < 0.05$) lower and neuroretinal rim area corrected for optic disc size was slightly ($p = 0.16$) smaller. Comparing the total highly myopic study group with a control group adjusted for optic disc area, neuroretinal rim area was significantly ($p = 0.039$) smaller in the study group with no significant difference in intraocular pressure measurements between the groups.*

CONCLUSIONS. *At a given intraocular pressure in chronic open-angle glaucoma, optic nerve damage may be more pronounced in highly myopic eyes with large optic discs than in non-highly myopic eyes. This may suggest a higher susceptibility for glaucomatous optic nerve fiber loss in highly myopic eyes than in non-highly myopic eyes. (Eur J Ophthalmol 2005; 15: 41-7)*

KEY WORDS. *Chronic open-angle glaucoma, Myopia, High myopia, Intraocular pressure, Optic disc, Optic nerve head, Neuroretinal rim*

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INTRODUCTION

The role of axial myopia as a risk factor for the development of chronic open-angle glaucoma as well as a risk factor for the amount of glaucomatous optic neuropathy is unclear. Epidemiologic studies have shown that myopic subjects compared with hyperopic subjects have a statistically significantly higher probability to show glaucomatous optic nerve dam-

age (1, 2), in agreement with preceding studies in which axial myopia was considered to be a risk factor for glaucomatous optic neuropathy (3-10). In contrast, Quigley and colleagues did not find a clear relationship between myopia and the eventual development of glaucomatous visual field in the follow-up examination of 647 ocular hypertensive subjects (11). Recent randomized clinical trials revealed varying results suggesting that myopia may or may not be a

predictive factor for the development and progression of glaucomatous optic nerve damage (12-16).

Since the ophthalmoscopic appearance and the histology of the optic nerve head in normal eyes as well as in eyes with glaucoma is markedly different between subjects with high myopia versus subjects without high myopia (17-20), we evaluated whether the amount of glaucomatous optic nerve damage in relation to intraocular pressure varies between chronic open-angle glaucoma eyes with high myopia versus non-highly myopic eyes with chronic open-angle glaucoma. The hypothesis was that in optic discs of comparable size in eyes with established glaucoma, the glaucomatous damage may be larger in highly myopic eyes than in eyes with no myopia, and that the damage to the optic nerve may be more pronounced in the highly myopic eyes despite similar intraocular pressure measurements. If there is a difference with more marked optic nerve damage in the highly myopic eyes, it could point towards a higher glaucoma susceptibility in highly myopic eyes, and could explain the discrepancies between the studies examining the role myopia may play in glaucoma, since in most studies a distinction of high myopia versus moderate myopia has not been made.

PATIENTS AND METHODS

The comparative clinical observational study included 1841 eyes (915 right eyes) of 1100 patients (541 women) with primary or secondary open-angle glaucoma. All patients had an open anterior chamber angle and were prospectively and consecutively evaluated. The total study population was divided into a highly myopic study group consisting of 25 eyes ((10 right eyes; 19 patients (10 women)) and a non-highly myopic control group including 1081 patients ((531 women; 1816 eyes (905 right eyes)). High myopia was defined as a myopic refractive error equal to or higher than -8 diopters. The highly myopic study group was further subdivided into a subgroup with an optic disc area of more than 2.70 mm² and another subgroup including the remaining eyes with an optic disc area of 2.70 mm² or less (Tab. I). Mean age was significantly lower in both study groups than in the non-highly myopic control group (Tab. I). 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). The institutional Review Board/Ethics Committee had approved the study.

The control group consisted of 274 (274/1816=15.1%) eyes with preperimetric glaucoma defined by glaucomatous abnormalities of the optic nerve head and normal white-on-white visual fields, and 1542 (1542/1816 =84.9%) eyes with chronic open-angle glaucoma with glaucomatous visual field defects.

Definition criteria for glaucoma were glaucomatous changes of the optic nerve head including 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 being vertically higher than horizontally, and localized or diffuse retinal nerve fiber layer defects (21). The control group included eyes with primary open-angle glaucoma (n=1146; 63.1%), secondary open-angle glaucoma due to reasons such as pseudoexfoliation or primary melanin pigment dispersion syndrome (n=453; 24.9%), and normal-pressure glaucoma (n=217; 11.9%). In the eyes with primary open-angle glaucoma, no obvious reason for the elevation in intraocular pressure could be detected. Criteria for the diagnosis of normal-pressure glaucoma were maximal intraocular pressure readings equal to or less than 21 mmHg in at least two 24-hour pressure profiles obtained by slit lamp applanation tonometry and containing measurements at 5 PM, 9 PM, midnight, 7 AM, and noon.

The highly myopic study group included 14 (56%) eyes with primary open-angle glaucoma without evident reason for an increase in elevation of intraocular pressure, 7 (28%) eyes with normal-pressure glaucoma, and 4 (16%) eyes with pseudoexfoliative glaucoma. Results of visual field examinations were not taken to characterize the patients of the study group since high myopia by itself might have led to perimetric defects. For the diagnosis of glaucoma in the study group, the same diagnostic criteria for glaucoma were used as in the control group. Study group and control group did not vary significantly ($p>0.05$) in their composition with respect to the various types of chronic open-angle glaucoma.

Intraocular pressure was measured by Goldmann applanation tonometry. For 1607 (87.4%) of all 1841 eyes included in the study, at least one day-and-night

intraocular pressure profile was performed containing measurements at 5 PM, 9 PM, midnight, 7 AM, and noon. The percentage of eyes with intraocular pressure profiles did not vary between the study group (23/25 or 92%) and the control group (1586/1816 or 87.3%). For the statistical analysis, we took the highest intraocular pressure measurements and the lowest measurements (Tab. I).

For all eyes, 15° color stereo optic disc transparencies were taken using a Zeiss telecentric fundus camera (30° fundus camera, equipped with a 15° converter; Zeiss, Oberkochen, Germany).

The disc slides were morphometrically analyzed as described previously (22, 23). Outcome measures were size of the optic disc, optic cup, and alpha zone and beta zone of parapapillary atrophy. All statistical analyses were performed using SPSSWIN (release 11.5).

RESULTS

In the study group, optic disc size was significantly ($p < 0.001$) larger, and alpha zone and beta zone of parapapillary atrophy were significantly larger ($p < 0.001$) than in the control group. Neuroretinal rim area was smaller, however not significantly ($p = 0.18$) smaller, in the study group than in the control group ($1.02 \pm 0.50 \text{ mm}^2$ versus $0.94 \pm 0.65 \text{ mm}^2$) (Tab. I).

Taking into account the physiologic correlation between optic disc size, optic cup area, and neuroretinal rim size in normal eyes (24), a control group was formed adjusted for optic disc size with the study group. This second control group consisted of 579 eyes of patients with a mean age of 60.4 ± 16.2 years and a mean refractive error of -0.38 ± 1.55 diopters (-7.75 diopters to $+3.63$ diopters).

Comparing the study group with the control group adjusted for optic disc area showed that the neuroretinal rim area was significantly ($p = 0.039$) smaller in the study group than in the adjusted control group ($0.94 \pm 0.65 \text{ mm}^2$ versus $1.13 \pm 0.55 \text{ mm}^2$).

Mean maximal intraocular pressure measurements ($19.9 \pm 5.8 \text{ mmHg}$ versus $20.1 \pm 4.9 \text{ mmHg}$; $p = 0.51$) and the mean minimal intraocular pressure measurements ($13.6 \pm 3.5 \text{ mmHg}$ versus $13.7 \pm 3.2 \text{ mmHg}$; $p = 0.99$) were slightly lower, however not significantly lower, in the study group than in the control group. At the same level of intraocular pressure and with both groups

adjusted for optic disc area, the neuroretinal rim area was smaller in the study group than in the control group.

Since highly myopic eyes are characterized by a secondary or acquired macrodisc (17, 18), we further divided the study group into eyes with an optic disc area of more than 2.70 mm^2 and eyes with an optic disc area equal to or less than 2.70 mm^2 (Tab. I). We chose an optic disc area of 2.70 mm^2 as cut-off point, since it was approximately the mean optic disc area in the control group (Tab. I).

As for the total study group, the study group with a large optic disc area differed significantly in area of beta zone of parapapillary atrophy from the control group (Tab. I).

Neuroretinal rim was smaller, however not significantly smaller, in the newly formed study group compared with the control group ($0.92 \pm 0.81 \text{ mm}^2$ vs $1.02 \pm 0.50 \text{ mm}^2$; $p = 0.16$).

Maximal and minimal intraocular pressure measurements and the mean maximal and mean minimal intraocular pressure values were significantly lower in the highly myopic study group with a large optic disc area than in the control group (Tab. I).

Applying Bonferroni's method to correct for performing multiple statistical comparisons revealed that the differences in optic disc size and size of parapapillary atrophy between study group and control group remained statistically significant. In a similar manner, the majority of the differences in intraocular pressure between study group and control group remained significant or borderline significant (Tab. I).

Within the control group, neuroretinal rim area was not significantly correlated with refractive error (correlation coefficient $r = 0.03$; $p = 0.41$) as has already been shown in a previous study (25).

Correspondingly, a multiple logistic regression analysis including the parameters maximal intraocular pressure, minimal intraocular pressure, optic disc size, neuroretinal rim area, and refractive error showed that neuroretinal rim area was not significantly ($p = 0.97$) associated with the refractive error. In a parallel manner, the moderately myopic eyes with a myopic refractive error ranging between 0 diopters and -8 diopters did not differ significantly in neuroretinal rim area from non-myopic eyes ($0.94 \pm 0.52 \text{ mm}^2$ vs $1.00 \pm 0.47 \text{ mm}^2$; $p = 0.33$).

DISCUSSION

In the lamina cribrosa of the optic nerve, tissue pressure is reduced from the pressure level of the intraocular space to the pressure level of the retrolaminar space (25-27). Since the lamina cribrosa is not indefinitely thin (28), the pressure reduction does not occur in an indefinitely thin layer of the lamina cribrosa, but the pressure may decrease gradually or in steps along the whole thickness of the lamina cribrosa. The pressure gradient across the lamina cribrosa is dependent on the difference in pressure between the intraocular pressure and the pressure in the retrobulbar space surrounding the optic nerve – i.e., the cerebrospinal fluid space – and the thickness of the lam-

ina cribrosa. At a given difference between intraocular pressure and cerebrospinal fluid pressure, the pressure gradient will be steeper in eyes with a thinner lamina cribrosa. Assuming that a steep pressure gradient may be related to the barotraumatic damage to the optic nerve within the lamina cribrosa, one may postulate that eyes with a thin lamina cribrosa may be more glaucoma susceptible than eyes with a thick lamina cribrosa.

Due to the stretching of the globe in high myopia, the optic nerve head is secondarily enlarged (17, 18). It leads to a stretching and thinning of the lamina cribrosa (20). The pathophysiologic consequence may be that the trans lamina pressure difference occurs over a shorter distance resulting in a steeper pressure gra-

TABLE I - COMPOSITION OF THE STUDY GROUP AND CONTROL GROUP (Mean ± SD)

	Control group	Total study group	p1 value	Study group, disc area >2.7 mm ²	p2 value
No.	1816	25		15	
Age (yr)	62.3±15.8	47.5±13.8	<0.001	45.3±14.9	<0.001
Refractive error (D)	-0.35±1.47	-10.88±4.27	<0.001	-11.97±5.14	<0.001
Range	-7.88 to+3.75	-24.25 to -8.0	<0.001	-24.25 to -8.00	
Optic disc area (mm ²)	2.73±0.73	3.59±1.70	<0.001	4.52±1.59	<0.001
Min. diameter (mm)	1.75±0.23	1.86±0.39	<0.001	2.07±0.34	<0.001
Max. diameter (mm)	1.97±0.27	2.38±0.70	<0.001	2.75±0.68	<0.001
Neuroret. rim (mm ²)	1.02±0.50	0.94±0.65	0.18 (n.s.)	0.92±0.81	0.16
Parapap. atrophy (mm ²)					
Alpha zone	0.77±0.69	1.24±1.29	<0.001	1.56±1.53	0.16
Beta zone	0.74±1.71	2.66±3.07	<0.001	3.59±3.58	<0.001
Intraocular pressure (IOP) (mmHg)					
Mean highest IOP	20.9±5.9	20.1±4.9	0.87 (n.s.)	17.7±4.1	0.028
1 st highest IOP value	23.8±7.4	22.4±7.1	0.29 (n.s.)	19.6±4.1	0.014
2 nd highest IOP value	21.5±6.3	20.7±5.0	0.77 (n.s.)	18.4±4.1	0.044
3 rd highest IOP value	20.2±5.8	19.5±4.9	0.74 (n.s.)	17.2±4.1	0.024
4 th highest IOP value	19.3±5.6	18.7±4.6	0.93 (n.s.)	16.5±4.0	0.046
5 th highest IOP value	18.6±5.5	18.0±4.4	0.88 (n.s.)	15.9±3.8	0.034
Mean minimal IOP	13.7±3.7	13.7±3.2	0.77 (n.s.)	12.2±2.3	0.038
1 st lowest IOP value	12.7±3.9	12.4±2.8	0.82 (n.s.)	11.1±2.2	0.077
2 nd lowest IOP value	13.2±3.5	13.0±2.8	0.77 (n.s.)	11.1±2.2	0.050
3 rd lowest IOP value	14.0±3.6	13.9±3.4	0.69 (n.s.)	12.2±2.4	0.025
	Non-highly myopic control group	Total highly myopic study group	p1 value	Highly myopic study group, disc area > 2.7mm²	p2 value
4 th lowest IOP value	14.7±3.8	14.6±3.8	0.67 (n.s.)	12.9±2.8	0.028
5 th lowest IOP value	15.2±4.0	15.1±3.8	0.64 (n.s.)	13.4±2.6	0.035

p value= Statistical significance of difference between the non-highly myopic control group and the whole highly myopic study group (p1 value), and between the non-highly myopic control group and the highly myopic study group with an optic disc area > 2.7 mm² (p2 value)

dient. One may, therefore, assume that highly myopic eyes with a large optic disc as compared with non-highly myopic eyes may have a higher glaucoma susceptibility at a given intraocular pressure.

This assumption is supported by the results of the present study. The highly myopic study group with a large optic disc had vary significantly lower intraocular pressure measurements than the control group, whereas both groups did not vary significantly in neuroretinal rim area (Tab. I). As a corollary, neuroretinal rim was significantly smaller in the study group than in the eyes of a control group adjusted for optic disc size with the study group. Additionally, intraocular pressure measurements were lower, however not significantly lower, in the study group. This suggests that at the same level of intraocular pressure and with both groups adjusted for optic disc area, neuroretinal rim area was significantly smaller in the highly myopic eyes than in the non-highly myopic eyes. Pointing towards a higher glaucoma susceptibility in highly myopic eyes with large optic discs compared with non-highly myopic eyes, this may fit with the histomorphometry of the lamina cribrosa in highly myopic eyes and with the pathophysiologic role the anatomy of the lamina cribrosa may play. Correspondingly, moderately myopic eyes with chronic open-angle glaucoma and normal-sized optic discs do not differ in neuroretinal rim area from non-myopic eyes (29).

There are limitations of the present study. Study group and control group included patients with primary open-angle glaucoma and secondary chronic open-angle glaucoma, such as pseudoexfoliative glaucoma and pigmentary glaucoma. Since intraocular pressure is usually higher in pseudoexfoliative glaucoma than in primary open-angle glaucoma, a difference in the composition of the patient groups might have led to a bias. Study group and control group, however, did not vary significantly in the proportion of primary open-angle glaucoma versus secondary open-angle glaucoma. Additionally, due to the bright fundus reflex in highly myopic eyes, pseudoexfoliative material on the lens surface may have been more difficult to be detected in the highly myopic eyes, falsely decreasing the percentage of pseudoexfoliative glaucoma in the highly myopic group. The study included all patients with glaucoma who attended the eye department in the study period, and for whom morphometric optic disc measurements obtained by planimetry of optic disc

photographs were available. Since normal-pressure glaucoma in non-highly myopic subjects was one of the primary scientific foci of the department, there was a tendency towards taking optic disc photographs preferentially from patients with normal-pressure glaucoma. This may have led to a falsely high proportion of normal-pressure glaucoma patients, and thus a reduction of the mean intraocular pressure, in the non-highly myopic control group. This serves, however, to support the conclusion of the study. In the highly myopic study group, elevated intraocular pressure may have been the primary diagnostic parameter to detect glaucoma, since the abnormal appearance of the optic nerve head and the difficult interpretation of visual field examinations in highly myopic patients may relatively decrease the importance the optic disc examination and perimetry may have for detection of glaucoma. This may have artificially increased the mean intraocular pressure in the highly myopic study group. This possible flaw in the study may serve to support the conclusions of the study. In addition to stretching and thinning of the lamina cribrosa, it is possible that high myopia causes stretching and thinning of the cornea and may affect the measurement of intraocular pressure because a thin cornea may lead to an underestimation of intraocular pressure. In a recent histomorphometric study, however, corneal thickness was statistically independent ($p=0.36$) of the axial length of the globe (own data). Highly myopic eyes may develop glaucoma much sooner than non-highly myopic eyes, and hence the differences in neuroretinal rim area may reflect the longer duration of glaucoma in highly myopic eyes. Indeed, the data presented in Table I suggest that glaucoma in highly myopic eyes develops earlier, since the patients in the highly myopic study group were significantly younger than the patients in the non-highly myopic control group. Simultaneously, however, this suggests that even if glaucoma develops earlier in highly myopic subjects, diagnosis of glaucoma was made earlier in the highly myopic patients than in the non-highly myopic subjects so that the duration of glaucoma may have been comparable between both groups, or at least not longer in the study group than in the control group.

In conclusion, the results of the present study may suggest that highly myopic eyes with chronic open-angle glaucoma may have lower intraocular pressure

measurements than non-highly myopic eyes with chronic open-angle glaucoma at a given amount of glaucomatous optic nerve damage. This agrees with the Early Manifest Glaucoma Trial in which the prevalence of glaucoma increased with increasing myopia, and in which the association between myopia and glaucoma was strong at lower intraocular pressure levels, and weakened gradually with increasing intraocular pressure (13). Pathogenetically, the situation for highly myopic eyes with myopic stretching and thinning of the lamina cribrosa (20) may be similar as for eyes

with advanced glaucoma in which the lamina cribrosa is also decreased in thickness (30, 31), and for which an increased risk for further progression of glaucoma as compared to eyes with early glaucoma has been shown (15, 32-34).

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REFERENCES

1. Leske MC, Connell AM, Wu SY, et al. Risk factors for open-angle glaucoma. The Barbados Eye Study. *Arch Ophthalmol* 1995; 113: 918-24.
2. Mitchell P, Hourihan F, Sandbach J, et al. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. *Ophthalmology* 1999; 106: 2010-5.
3. Podos S, Becker B, Morton W. High myopia and primary open-angle glaucoma. *Am J Ophthalmol* 1966; 62: 1039-43.
4. Greve EL, Furuno F. Myopia and glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1980; 213: 33-41.
5. Daubs JG, Crick RP. Effect of refractive error on the risk of ocular hypertension and open angle glaucoma. *Trans Ophthalmol Soc UK* 1981; 101: 121-6.
6. Phelps CD. Effect of myopia on prognosis in treated primary open-angle glaucoma. *Am J Ophthalmol* 1982; 93: 622-8.
7. Perkins ES, Phelps CD. Open angle glaucoma, ocular hypertension, low-tension glaucoma, and refraction. *Arch Ophthalmol* 1982; 100: 1464-7.
8. David R, Zangwill L, Stone D, et al. Epidemiology of intraocular pressure in a population screened for glaucoma. *Br J Ophthalmol* 1987; 71: 766-71.
9. Chihara E, Liu X, Dong J, et al. Severe myopia as a risk factor for progressive visual field loss in primary open-angle glaucoma. *Ophthalmologica* 1997; 211: 66-71.
10. Quigley HA. Open-angle glaucoma. *N Engl J Med* 1993; 328: 1097-106.
11. Quigley HA, Enger C, Katz J, et al. Risk factors for the development of glaucomatous visual field loss in ocular hypertension. *Arch Ophthalmol* 1994; 112: 644-9.
12. Drance S, Anderson DR, Schulzer M, Collaborative Normal-Tension Glaucoma Study Group. Risk factors for progression of visual field abnormalities in normal-tension glaucoma. *Am J Ophthalmol* 2001; 131: 699-708.
13. Grodum K, Heijl A, Bengtsson B. Refractive error and glaucoma. *Acta Ophthalmol Scand* 2001; 79: 560-6.
14. Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002; 120: 714-20.
15. The Advanced Glaucoma Intervention Study (AGIS). 12. Baseline risk factors for sustained loss of visual field and visual acuity in patients with advanced glaucoma. *Am J Ophthalmol* 2002; 134: 499-512.
16. Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. *Arch Ophthalmol* 2003; 121: 48-56.
17. Jonas JB, Gusek GC, Naumann GOH. Optic disk morphometry in high myopia. *Graefes Arch Clin Exp Ophthalmol* 1988; 226: 587-90.
18. Jonas JB, Dichtl A. Optic disc morphology in myopic primary open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1997; 235: 627-33.
19. Dichtl A, Jonas JB, Naumann GO. Histomorphometry of the optic disc in highly myopic eyes with absolute secondary angle closure glaucoma. *Br J Ophthalmol* 1998; 82: 286-9.
20. Jonas JB, Berenshtein E, Holbach L. Lamina cribrosa thickness and spatial relationships between intraocular space and cerebrospinal fluid space in highly myopic eyes. *Invest Ophthalmol Vis Sci* 2004; 45: 2660-5.
21. Jonas JB, Budde WM, Panda-Jonas S. Ophthalmoscopic evaluation of the optic nerve head. *Surv Ophthalmol* 1999; 43: 293-320.

22. Littmann H. Zur Bestimmung der wahren Größe eines Objektes auf dem Hintergrund des lebenden Auges. *Klin Monatsbl Augenheilkd* 1982; 180: 286-9.
23. Jonas JB, Gusek GC, Naumann GOH. Optic disc, cup and neuroretinal rim size, configuration, and correlations in normal eyes [published erratum appears in 1991; 32: 1893]. *Invest Ophthalmol Vis Sci* 1988; 29: 1151-8.
24. Caprioli J, Miller JM. Optic disc rim area is related to disc size in normal subjects. *Arch Ophthalmol* 1987; 105: 1683-5.
25. Morgan WH, Yu DY, Cooper RL, et al. The influence of cerebrospinal fluid pressure on the lamina cribrosa tissue pressure gradient. *Invest Ophthalmol Vis Sci* 1995; 36: 1163-72.
26. Morgan WH, Yu DY, Alder VA, et al. The correlation between cerebrospinal fluid pressure and retrolaminar tissue pressure. *Invest Ophthalmol Vis Sci* 1998; 39: 1419-28.
27. Morgan WH, Chauhan BC, Yu DY, et al. Optic disc movement with variations in intraocular and cerebrospinal fluid pressure. *Invest Ophthalmol Vis Sci* 2002; 43: 3236-42.
28. Bellezza AJ, Hart RT, Burgoyne CF. The optic nerve head as a biomechanical structure: initial finite element modeling. *Invest Ophthalmol Vis Sci* 2000; 41: 2991-3000.
29. Jonas JB, Martus P, Budde WM. Anisometropia and degree of optic nerve damage in chronic open-angle glaucoma. *Am J Ophthalmol* 2002; 134: 547-51.
30. Jonas JB, Königsreuther KA, Naumann GOH. Optic disc histomorphometry in normal eyes and eyes with secondary angle-closure glaucoma. I. Intrapapillary region. *Graefes Arch Clin Exp Ophthalmol* 1992; 230: 129-33.
31. Jonas JB, Berenshtein E, Holbach L. Anatomic relationship between lamina cribrosa, intraocular space, and cerebrospinal fluid space. *Invest Ophthalmol Vis Sci* 2003; 44: 5189-95.
32. Araie M, Sekine M, Suzuki Y, et al. Factors contributing to the progression of visual field damage in eyes with normal-tension glaucoma. *Ophthalmology* 1994; 101: 1440-4.
33. Tezel G, Siegmund KD, Trinkaus K, et al. Clinical factors associated with progression of glaucomatous optic disc damage in treated patients. *Arch Ophthalmol* 2001; 119: 813-8.
34. Jonas JB, Martus P, Budde WM, et al. Small neuroretinal rim and large parapapillary atrophy as predictive factors for progression of glaucomatous optic neuropathy. *Ophthalmology* 2002; 109: 1561-7.

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