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CLINICAL INVESTIGATION

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Optic disc morphology in myopic primary open-angle glaucoma

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Abstract ● Objective: To evaluate the morphology of the optic disc in highly myopic eyes with primary open-angle glaucoma. ● Methods: Color stereo optic disc photographs of 44 patients with primary open-angle glaucoma and a myopic refractive error exceeding –8 diopters were morphometrically examined and compared with disc photographs of 571 patients with primary open-angle glaucoma and a myopic refractive error of less than –8 diopters. ● Results: In the highly myopic group, compared to the control group, the optic disc was significantly ($P<0.0001$) larger, the disc shape was significantly ($P<0.0005$) more elongated, and the optic cup depth was significantly ($P<0.0001$) more shallow. The loss of neuroretinal rim was more concentric, and localized retinal nerve fiber layer defects were found significantly less frequently in the highly myopic group than in the control group. In the highly myopic group, zone beta of parapapillary atrophy was significantly ($P<0.0001$) larger. ● Conclusion: The optic disc morphology in primary open-angle glaucoma differs significantly between highly myopic eyes and eyes with hyperopia or low to moderate myopia. The highly myopic eyes are characterized by secondary macrodiscs with elongated shape, shallow and concentric disc cupping, large parapapillary atrophy, and low frequency of localized retinal nerve fiber layer defects. Glaucomatous optic nerve damage in highly myopic eyes, compared to eyes with a normal refractive error, is more diffuse than localized.

Introduction

Independent of the level of intraocular pressure, primary open-angle glaucoma can be defined by an open anterior chamber angle, no obvious reason for an elevation of intraocular pressure, and typical morphologic or psychophysical evidence of optic nerve damage [25, 26]. In this characterization, the refractive error is usually not taken into account. In normal eyes, however, the morphology of the optic disc differs significantly between highly myopic eyes and emmetropic or hyperopic eyes [13]. Additionally, myopia has been reported to be a risk factor for primary open-angle glaucoma [3, 22]. We therefore conducted the present study to evaluate whether, in primary open-angle glaucoma, eyes with high myopia differ from eyes with hyperopia or low to moderate myopia.

Patients and methods

The study included 615 eyes of 615 patients suffering from primary open-angle glaucoma (Table 1). They were evaluated as part of a prospective study on the biomorphometry of the optic nerve involving all patients coming to the hospital with an optic nerve anomaly or disease. The whole group was divided into eyes with a myopic refractive error exceeding –8 diopters ($n = 44$) and eyes with a refractive error of less than –8 diopters ($n = 571$; Table 1). The two groups did not vary significantly in age, gender and neuroretinal rim area.

Table 1 Composition of the study groups (mean±SD); *n.s.* statistically not significant.

	High myopia (n=44)	Control group (n=571)	P-value
Age (years)	59.0±12.8	61.1±15.1	0.21 (n.s.)
Median	59	60	
Refractive Error (diopters)	−11.06±4.05	−0.73±2.44	<0.0001
Range	−8.00 to −24.25	−7.50 to +7.0	
Median	−9.25	0.00	
Men/women	22/22	282/289	

Criteria for the diagnosis of glaucoma, each of which had to be fulfilled, were intraocular pressure of more than 21 mmHg or a history of it, no obvious reason for the elevation of the intraocular pressure, an open anterior chamber angle, and glaucomatous visual field defects. The latter included a mean visual field defect of more than 2 dB or a loss variance of more than 6 dB^2 in the Octopus G1 program. At the time of visual field testing, the patients were not on miotic antiglaucomatous therapy.

For all eyes, 15-deg color stereo optic disc transparencies had sequentially been taken using the telecentric Zeiss fundus camera. Mixed together with the photographs of more than 500 other patients with glaucomatous or nonglaucomatous optic nerve damage, they were projected in a scale of one to fifteen. They were evaluated in a masked fashion without knowledge of the clinical diagnosis or other clinical data such as refractive error, level of intraocular pressure, and visual field loss. The outlines of the optic cup, optic disc, peripapillary scleral ring and parapapillary chorioretinal 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 magnification was corrected by Littmann's method, taking into account the anterior corneal curvature and the refractive error [21]. The border of the optic disc coincided with the inner side of the peripapillary scleral ring. The optic cup was defined on the basis of contour and not of pallor. The parapapillary chorioretinal atrophy was differentiated into zones alpha and beta. Zone alpha was defined as irregular hypopigmentation and hyperpigmentation and peripheral location. Zone beta was characterized by visible sclera and visible large choroidal vessels close to the optic disc border (Fig. 1). The method has already been described in detail [1, 17]. Using the stereo optic disc diapositives, the optic cup depth was estimated using a relative scale ranging from 0 for "no cupping" to 5 for "very deep cupping."

In all 44 eyes of the highly myopic subgroup and in 280 patients of the non-highly myopic subgroup, the retinal nerve fiber layer was examined on 60-deg red-free photographs of the fundus. The transparencies were projected with a magnification of 15 times after maximal defocusing of the projector. The area of the blurred image of the optic disc was covered, then the projector refocused and the retinal nerve fiber layer evaluated. A localized defect was defined as a wedge-shaped and not spindle-like defect, running towards or touching the optic disc border for not more than 60 deg of the optic disc circumference.

For interindividual comparison, only one randomly selected eye per patient and subject was taken for statistical analysis. The Mann-Whitney test was applied to evaluate the significance of differences in the median of groups, and the chi-square test was used to examine the significance of differences in the frequency of a variable.

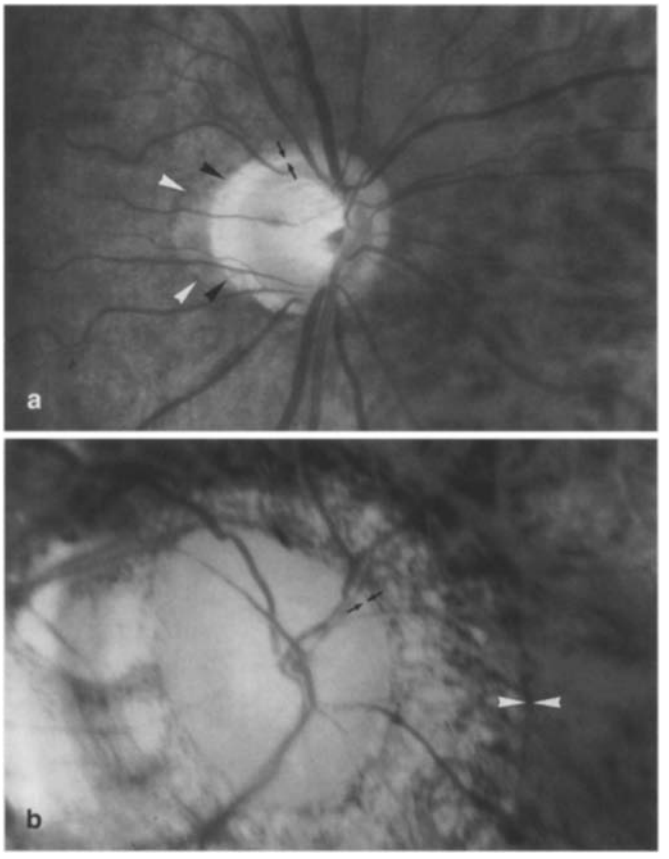

Fig. 1a, b Optic disc photographs of glaucomatous eyes with a refractive error of +1.0 diopters (**a**), and a refractive error of −11.0 diopters (**b**). *White arrowheads* zone alpha, *black arrowheads* zone beta of parapapillary atrophy, *black arrows* peripapillary scleral ring. Note disc hemorrhage in **a**

Results

Area and diameters of the optic disc were significantly greater in the group with high myopia than in the non-highly mopic group (Table 2). This difference in optic disc size was mainly due to a relatively high proportion of very large discs (disc area >3.25 mm^2) in the highly myopic group compared to the non-highly myopic group (50% vs 17%); the proportion of rather small optic discs (disc area <2 mm^2) did not differ markedly between the two groups (16% vs 10%). The optic disc was significantly (P<0.0001) longer in the group with high myopia than in the non-highly mopic group, as indicated by a lower ratio of the minimal to maximal disc diameter (Table 2).

In the highly myopic group, the depth of the optic cup was significantly (P<0.0001) more shallow, and the horizontal and vertical cup-to-disc ratios were significantly (P<0.05 and P<0.0001, respectively) higher. The frequencies of disc hemorrhages (0% vs 4.1%) and localized defects in the retinal nerve fiber layer (2.2% vs 19%) were

Table 2 Optic disc measurements (mean±SD); *n.s.* statistically not significant, *CI 95%* 95% confidence intervals

	High myopia (>−8 diopters)	Control group	*P*-value
Optic disc			
Area (mm^2)	3.61±1.66	2.71±0.63	<0.0001
Range	1.42–8.37	1.26–5.32	
CI 95%	1.58–6.97	1.66–4.17	
Median	3.25	2.61	
Diameter (mm)			
Horizontal	1.97±0.44	1.79±0.24	<0.05
Range	1.25–2.93	1.18–2.95	
CI	95%	1.25–2.90	1.37–2.27
Median	1.94	1.76	
Vertical	2.25±0.61	1.99±0.23	<0.0001
Range	1.20–3.98	1.31–2.83	
CI 95%	1.36–3.73	1.48–2.36	
Median	2.17	1.88	
Minimal	1.92±0.46	1.74±0.21	<0.05
Range	1.12–2.92	1.13–2.46	
CI 95%	1.23–2.87	1.34–2.21	
Median	1.91	1.73	
Maximal	2.35±0.56	1.96±0.26	<0.0001
Range	1.38–3.98	1.33–2.85	
CI 95%	1.59–3.70	1.53–2.46	
Median	2.22	1.94	
Minimal/maximal	0.82±0.11	0.89±0.05	=0.0001
CI 95%	0.58–0.96	0.76–0.97	
Median	0.83	0.89	
Neuroretinal rim			
area (mm^2)	1.25±1.28	1.17±0.70	0.17 (n.s.)
Median	0.90	1.11	
Cup/disc ratio			
Horizontal	0.76±0.24	0.72±0.22	<0.05
CI 95%	0.0–1.0	0.0–1.0	
Median	0.81	0.76	
Vertical	0.77±0.24	0.71±0.23	<0.05
CI 95%	0.0–1.0	0.0–1.0	
Median	0.81	0.76	
Horizontal/vertical	0.99±0.07	1.04±0.42	0.34 (n.s.)
CI 95%	0.85–1.14	0.86–1.25	
Median	0.99	1.01	
Cup depth (relative units)	2.12±0.81	2.91±1.07	<0.0005
Median	2	3	
Parapapzillary atrophy (mm^2)			
Zone alpha	1.27±1.37	0.80±0.67	n.s.
Range	0.00–4.84	0.00–4.84	
CI 95%	0.00–4.41	0.00–2.42	
Median	0.69	0.71	
Zone beta	3.76±2.98	0.71±1.14	<0.0001
Range	0.00–10.8	0.00–9.03	
CI 95%	0.00–10.0	0.00–3.84	
Median	3.27	0.24	

lower in the highly myopic group. The difference between the two study groups was significant for the frequency of localized retinal nerve fiber layer defects (chi-square test). In the highly myopic eyes, zone beta of the parapapillary atrophy was significantly larger than in the eyes of the control group (Table 2).

In the highly myopic group, the optic disc area increased significantly with increasing myopic refractive error (Fig. 2). In the non-highly myopic group, optic disc area was statistically independent of the refractive error (Fig. 3).

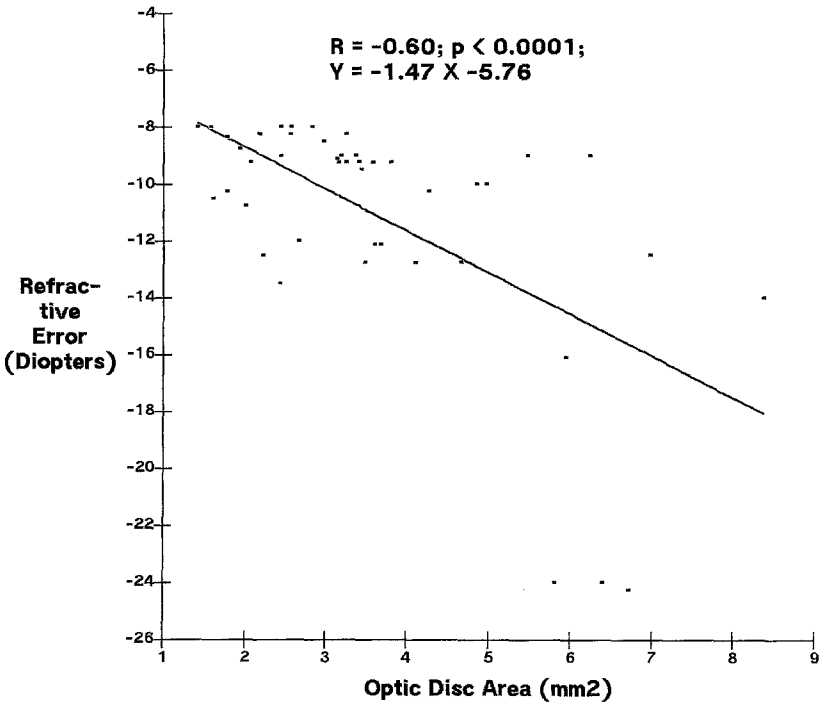

Fig. 2 Scatterplot of refractive error vs optic disc area in the highly myopic study group

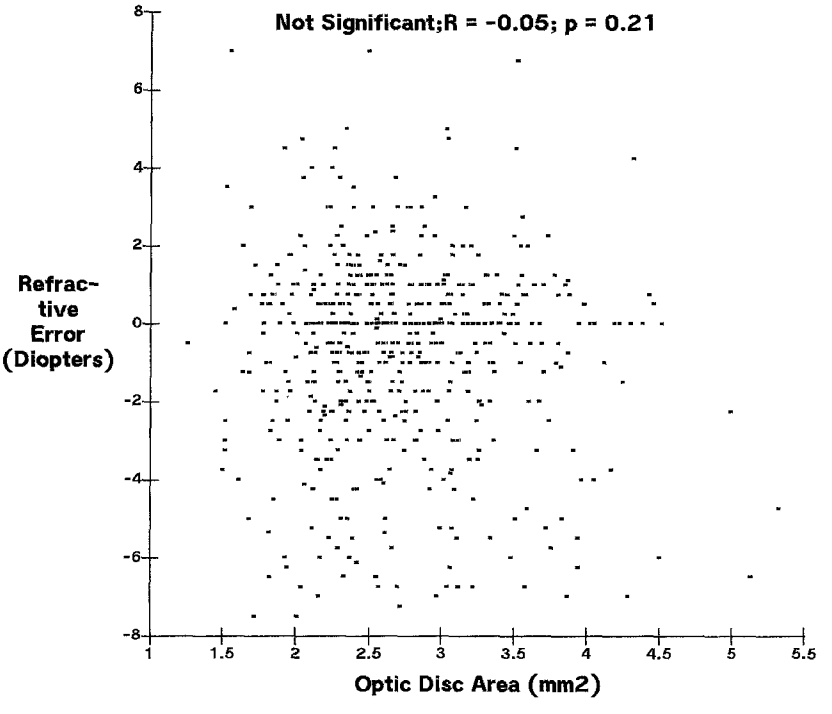

Fig. 3 Scatterplot of refractive error vs optic disc area in the non-highly myopic study group

Discussion

The open-angle glaucomas are a spectrum of entities that can be differentiated from one another by a variety of variables such as the morphology of the anterior chamber angle, the predisposing risk factors, the cause for the elevation of intraocular pressure, the average age at onset, the preponderance of males or females, and the average intraocular pressure [25 ,26]. Recent studies have shown that, parallel to this variability of characteristics, the morphology of the optic disc also differs among the glaucomas. As mentioned, an abnormally large optic disc and a relatively large optic cup have been described for nor-

mal-pressure glaucoma in some studies [2, 8, 20, 27, 30] while another investigation suggested that this finding could be an artifact of the selection of patients [18]. Parapapillary atrophy was significantly more extensive in eyes with the age-related atrophic type of primary open-angle glaucoma than in normal eyes or than in eyes with the focal type of normal-pressure glaucoma [9]. For eyes with pseudoexfoliative glaucoma, a slightly small optic disc size has been described [11, 30]. In patients younger than 40 years and suffering from primary open-angle glaucoma, the optic cup was significantly deeper and steeper, and parapapillary atrophy was significantly smaller than in patients with primary open-angle glaucoma and an age of more than 40 years [10]. Spaeth et al. [28] coined the term "focal ischemic glaucoma" to describe a subgroup of low-tension glaucoma patients who displayed focal emaciation of the neuroretinal rim, typically in the inferotemporal disc sector. Greve and Geijssen [6, 7] differentiated between a "focal ischemic low-tension glaucoma" and a "senile sclerotic glaucoma" characterized by a large parapapillary atrophy and a high degree of fundus tessellation.

According to the results of the present study, eyes with primary open-angle glaucoma and a myopic refractive error of more than -8 diopters also show morphologic characteristics differentiating them in several ways from eyes with primary open-angle glaucoma and low to moderate myopia or hyperopia. The optic disc was significantly larger in the highly myopic group than in the control group. In the highly myopic glaucoma group, the optic disc area enlarged with increasing myopic refractive error (Fig. 2). Similar results were reported for normal eyes with high myopia [13]. In contrast, in eyes with a myopic refractive error of less than –8 diopters the optic disc size is independent of the refractive error (Fig. 3) [14]. One may infer that the postnatal enlargement of the globe in highly myopic eyes stretches the optic disc, leading to an acquired or secondary macrodisc. If the scleral tissue has not yet lost its elasticity, this process may be reversible, as has been described for infants with congenital glaucoma in whom, after reduction of the intraocular pressure, the optic disc and cup decrease in size [23]. The elongated shape of the optic disc in the highly myopic eyes suggests that the myopic stretching of the disc is not uniform but that some regions of the disc are more stretched than others. How this deformation of the lamina cribrosa influences the susceptibility for glaucomatous optic nerve fiber loss is yet unclear.

The secondary macrodiscs in the highly myopic eyes can be differentiated from primary macrodiscs in eyes with low to moderate myopia or hyperopia. The latter show a deep and large physiologic cupping and an unremarkable parapapillary atrophy [16]. In both types of macrodiscs, the cup-to-disc ratios increase with disc size. This explains why, in the present study, the highly myopic eyes had significantly larger cup-to-disc ratios than the eyes of the control group although the neuroretinal rim area did not vary significantly. The ratio of the horizontal and vertical cup/disc ratios, however, did not differ between the highly myopic group and the control group because this parameter is independent of disc size and disc shape. This finding underlines the importance of this ratio in the morphometric description of the optic disc [15].

Localized defects of the retinal nerve fiber layer were found significantly more rarely in the highly myopic eyes, than in the non-highly myopic group. Although this finding may partially be due to the brighter fundus in the highly myopic eyes preventing clear detectability of the retinal nerve fiber layer, it suggests that the optic nerve damage in primary open-angle glaucoma is more diffuse in highly myopic eyes than in non-highly myopic eyes. Similar findings suggesting diffuse optic nerve damage have been reported for eyes with open-angle glaucoma and high intraocular pressure [10]. This contrasts with reports on eyes with normal-pressure glaucoma and a normal refractive error, in which relatively high frequencies of disc hemorrhages and localized retinal nerve fiber layer defects point towards more localized optic nerve damage [4, 12, 19].

There is considerable overlap between the highly myopic group and the non-highly myopic group, so that there is no distinct pathognomonic marker for each group. Despite this overlap, however, the significance of the differences between the groups suggests that in primary open-angle glaucoma, a highly myopic subgroup may be distinguished from the non-highly myopic subgroup.

The abnormally extensive parapapillary atrophy in the highly myopic group does not vary remarkably in size from the parapapillary atrophy in highly myopic eyes without glaucoma [13]. This indicates that the large parapapillary atrophy in highly myopic eyes with glaucoma is mainly due to nonglaucomatous reasons such as the myopic stretching of the globe.

In 57% of the eyes of the highly myopic group, the mean maximal intraocular pressure reading, calculated as the mean of the four highest intraocular pressure measurements, was lower than 20 mmHg. This suggests for some of the highly myopic eyes a hypothetical special type of glaucoma at the low-pressure end of the spectrum of open-angle glaucomas. This has already been described by Geijssen and by Spaeth and coworkers [5, 29]. The low intraocular pressure measurements in the highly myopic eyes correspond with a significantly shallower disc cupping than in the non-highly myopic eyes (Table 2). This agrees with a recent study on primary open-angle glaucoma, in which the optic cup was deeper in eyes with high intraocular pressure than in eyes with only moderately elevated intraocular pressure [10]. Suggesting a higher glaucoma susceptibility in highly myopic eyes, the finding of low intraocular pressure readings in the highly myopic group fits with previous reports in the literature. Quigley and coworkers [24] studied the development of glaucomatous visual field loss in eyes with ocular hyperten-

sion. They classified the eyes into severely myopic, myopic, emmetropic, hyperopic and severely hyperopic, and found that myopic eyes tended to be at greater risk of developing subsequent perimetric loss. This tendency, however, was not significant. Perkins and Phelps [22] reported an accelerated progression of visual field loss in myopic patients compared to emmetropic or hyperopic patients.

In spite of the statistical significance of the findings, the present study has limitaions. It is more difficult to evaluate the retinal nerve fiber layer in highly myopic eyes than in emmetropic eyes due to the relative brightness of the highly myopic fundus and, possibly, because in highly myopic eyes the nerve fiber layer spreads out on a larger fundus area and may thus be thinner. Additionally, it is more difficult to delineate the border between the optic cup and the neuroretinal rim in highly myopic eyes than in non-highly myopic eyes. Accordingly, it is harder to detect neuroretinal rim notches in highly myopic eyes because the neuroretinal rim is thinner and the optic cup is more shallow than in non-highly myopic eyes. The relatively low mean maximal intraocular pressure readings in some of the highly myopic glaucoma eyes may be due in part to the special anatomy of highly myopic eyes leading to falsely low measurements of intraocular pressure or to a better therapeutic reduction of intraocular pressure in the highly myopic group.

Future studies may show whether the parapapillary atrophy in highly myopic eyes with glaucoma differs histologically from the parapapillary atrophy in glaucomatous eyes with a non-highly myopic refractive error. Future investigations may also reveal whether patients with primary open-angle glaucoma and high myopia, as compared to primary open-angle glaucoma patients with low to moderate myopia or hyperopia, have a different rate of progression that may be related to the described differences in the optic disc morphology and the level of intraocular pressure. The relatively young age of the patients of the highly myopic group suggests that this type of primary open-angle glaucoma may have a more severe course.

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