·Clinical Research·

Optic disc area in different types of glaucoma

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Abstract

• AIM: To evaluate the possible relationship of optic disc area with retina nerve fiber layer in different glaucoma subtypes.

• METHODS: One eye each was chosen from 45 patients with ocular hypertension, 45 patients with primary open angle glaucoma, 45 patients with pseudoexfoliation glaucoma and 45 healthy controls followed in our hospital. The records of the patients were reviewed retrospectively. Optic disc area and circumpapillary retina nerve fiber layer measurements were obtained using optical coherence tomography. Central corneal thickness was measured by ultrasound pachymetry.

• RESULTS: The median disc area in the patients with primary open angle glaucoma was significantly higher than the patients with ocular hypertension (2.19 *vs* 1.90 mm^2, *P*=0.030). The median retina nerve fiber layer was thinner in the patients with primary open angle glaucoma and pseudoexfoliation glaucoma than the patients with ocular hypertension for superior, inferior and temporal quadrants. After adjustment for age, no difference in central corneal thickness was found between the groups. Greater disc area was associated with thicker retinal nerve fiber layer for superior, inferior and nasal quadrants in the patients with primary open angle glaucoma. There was no correlation between disc area and central corneal thickness measurements of the groups.

• CONCLUSION: Disc size affects the retinal nerve fiber layer thickness in eyes with primary open angle glaucoma and is a possible risk factor for glaucomatous optic nerve damage.

• **KEYWORDS:** central corneal thickness; ocular hypertension; optic disc area; primary open angle glaucoma; pseudoexfoliation glaucoma; retina nerve fiber layer
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INTRODUCTION

Glaucoma is a multifactorial neuro-degenerative disease which causes progressive retinal nerve fiber layer (RNFL) loss. It is thought that the number of nerve fibers in the RNFL depends on the disc area. However, the association between optic disc area (ODA) and RNFL thickness remains controversial; some studies implicated a significant positive correlation between ODA and RNFL thickness [1-2], whereas other studies reported no such correlation[3-5].

Optical coherence tomography (OCT) enables imaging of optic nerve head and retinal layers and is effective for detecting abnormal RNFL thickness in glaucomatous eyes. Spectral domain OCT has currently the most advanced commercially available technology. This system is 100 times faster than time domain OCT and acquires 40 000 A-scans per second. The increased speed and number of scans provide higher resolution. The Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA) is a spectral domain OCT instrument that measures the optic disc and peripapillary RNFL in a 6 mm^2 area consisting of 200×200 pixels.

The aim of this study is to investigate the possible relationship between ODA and RNFL thickness in patients with glaucoma and ocular hypertension (OHT) as well as healthy subjects.

SUBJECTS AND METHODS

Forty-five patients with OHT, 45 patients with primary open angle glaucoma (POAG), 45 patients with pseudoexfoliation glaucoma (PEXG) and 45 healthy controls followed in our hospital were enrolled to the study. The records of the patients were reviewed retrospectively.

Patients underwent a complete ophthalmic examination by a glaucoma specialist including best corrected visual acuity, slit-lamp evaluation and gonioscopy. The measurements of intraocular pressure (IOP) were obtained using the Goldmann applanation tonometry. Central corneal thickness (CCT) was measured by ultrasound pachymetry (Ocuscan PXP Alcon USA) and the average of three consecutive measurements was calculated. Following dilation, a detailed posterior-segment examination was performed with 90 diopter lens. Visual field testing was performed using a field analyzer (Humphrey Automated; Carl Zeiss Meditec, Dublin, CA, USA). Circumpapillary RNFL and ODA measurements were obtained using OCT (Cirrus high-definition OCT; Carl Zeiss, Dublin, California, USA).

The study was conducted in compliance with the Declaration of Helsinki. The patients signed an informed consent before proceeding with all the examinations and treatments. One eye of each participant was selected randomly for the analysis. Exclusion criteria included advanced lens opacities, prior ocular surgery or laser treatment, ocular trauma, corneal pathology, uveitis, retinal or macular pathology.

OHT was defined as the presence of an IOP greater than 21 mm Hg with normal optic nerve head appearance and normal visual field. Healthy controls had at least one reliable normal visual field perimetry with normal disc appearance and IOP less than 21 mm Hg. Patients with POAG had IOPs greater than 22 mm Hg on more than three occasions, an open normal angle, characteristic glaucomatous optic nerve damage and associated visual field loss in the corresponding location. Patients with pseudoexfoliation glaucoma had IOPs greater than 22 mm Hg, typical pseudoexfoliation material within the angle and upon the lens, a glaucomatous optic disc and glaucomatous visual field defects.

Statistical analyses were performed using SPSS software (SPSS 15.0, SPSS Institute Inc, Chicago, IL, USA). Partial correlation test was used for age adjustment. Kruskal-Wallis test was used to compare the parameters between the groups. Spearman correlation method was used to analyse the correlation of ODA with RNFL and CCT. Multipl regression analysis was made to evaluate the effect of ODA on RNFL. A P value less than 0.05 was considered as statistically significant.

RESULTS

Baseline characteristics of the patients are summarized in Table 1. The mean age in the control group was 60.96±10.5y, compared with 62.09±10.8y in OHT, 67.42±12.4y in POAG and 68.07±6.8y in PEXG groups. It was significantly higher in POAG (P=0.006) and PEXG (P=0.002) groups than healthy controls. There was no significant difference in the refractive status and sex between the groups.

CCT measurements are also shown in Table 1. Glaucoma patients further exhibited thinner corneal thickness than the patients with OHT and healthy subjects. However, the differences between groups became insignificant after further adjustment for age.

Disc area measurements are shown in Table 2. The median disc area in the control group was similar to the disc sizes in the POAG, PEXG and OHT groups. However, it was significantly higher in patients with POAG than OHT group.

Quadrantic RNFL thickness measurements are also shown in Table 2. Quadrantic RNFL thicknesses in the superior, inferior and temporal quadrants were significantly lower in the POAG and PEXG groups than the corresponding values in the OHT and control groups. The measurements in the nasal quadrant were significantly lower in the POAG and PEXG groups than the values in the control group.

Table 1 Baseline characteristics of subjects by groups

Groups	Age (a)	Sex (M:F)	Refraction (SE)	CCT (μm)
PEXG	68.07±6.8	0.66	-0.65±1.6	534.78±36.59
POAG	67.42±12.4	0.79	-0.52±1.7	532.00±39.94
OHT	62.09±10.8	0.45	-0.39±1.1	546.47±32.60
Controls	60.96±10.5	0.61	-0.51±1.5	551.93±26.45

SE: Spherical equivalent; CCT: Central corneal thickness; PEXG: Pseudoexfoliative glaucoma; POAG: Primary open angle glaucoma; OHT: Ocular hypertension.

The comparison of disc areas and quadrantic RNFL thicknesses between the groups revealed significant differences (Table 3). There was a positive correlation between the disc areas and the RNFL thicknesses of superior, inferior and nasal quadrants in POAG group. Additionally, disc area measurements are positively correlated with RNFL thicknesses of temporal quadrant in OHT group and superior quadrant in healthy subjects. No correlation was found between ODA and CCT in any group (Table 3).

Table 4 shows the regression analysis of RNFL quadrants versus age, CCT and ODA in eyes with POAG. Variance inflation factor (vif) values are less than 5, so the predictors are not correlated. ODA is an independent variable for superior, inferior and nasal RNFL thicknesses in POAG.

DISCUSSION

Optic nerve head size shows considerable variability between individuals ranging between 2.10-2.35 mm^2 [6-8]. Actual disc size varies with demographic factors such as age and race. Disc size is also associated with variations of the optic nerve head and the RNFL.

Disc size-dependent variations may influence the susceptibility to glaucoma or cause misdiagnosis. There are different hypotheses based on the anatomical features that are responsible for the increased susceptibility. Some studies [9-10] sustain that smaller discs have smaller total lamina cribrosa area and fewer lamina pores than the large discs, causing less space for nerve fibers to travel through and this possibly induces focal compression of the axons. The opposite opinion is that the pressure differential across the lamina cribrosa could produce an increased deformation and displacement of the central tissue in large discs, leading to greater glaucoma susceptibility in large discs [11-12]. In our study, disc size in POAG group was significantly higher than the value in OHT group.

A smaller number of nerve fibers may represent less anatomical reserve. Significant nerve fiber loss may precede the development of visual field defects [13]. Following differentiation between healthy eyes and eyes with glaucoma by RNFL thickness measurements may aid in early diagnosis. In a study by Blumberg *et al* [14], the eyes with POAG had thinner superior, inferior and total RNFL than the healthy individuals. In the study by Eltutar *et al* [15], the eyes with PEXG had thinner inferior, temporal, nasal and total RNFL

Table 2 Quadrantic RNFL thickness and ODA measurements by OCT imaging

Groups	Superior RNFL (μm)	Inferior RNFL (μm)	Nasal RNFL (μm)	Temporal RNFL (μm)	ODA (mm^2)
PEXG	96 (40-140)	105 (48-137)	65 (33-88)	60 (34-111)	1.90 (1.32-3.01)
POAG	90 (12-131)	98 (51-173)	64 (43-90)	56 (34-94)	2.19 (1.39-3.32)
OHT	110 (80-140)	117 (72-146)	67 (49-91)	65 (42-83)	1.90 (1.40-2.71)
Controls	120 (91-166)	124(80-157)	71 (55-105)	64 (49-92)	1.87 (1.45-3.41)
P					
PEXG *vs* POAG	0.765	1.000	1.000	0.957	0.055
PEXG *vs* OHT	0.002	0.002	1.000	0.038	1.000
PEXG *vs* controls	0.000	0.000	0.015	0.047	1.000
POAG *vs* OHT	0.000	0.000	0.459	0.000	0.030
POAG *vs* controls	0.000	0.000	0.002	0.001	0.150
OHT *vs* controls	0.297	1.000	0.364	1.000	1.000

RNFL: Retina nerve fiber layer; ODA: Optic disc area PEXG: Pseudoexfoliative glaucoma; POAG: Primary open angle glaucoma; OHT: Ocular hypertension. Kruskal Wallis test was used.

Table 3 Comparison of the disc size with RNFL and central corneal thicknesses

Groups	Univariant analysis	ODA (mm^2)	Superior RNFL (μm)	Inferior RNFL (μm)	Nasal RNFL (μm)	Temporal RNFL (μm)	CCT (μm)
PEXG	*r*	1.0	0.014	0.232	0.194	0.112	-0.054
	P		0.927	0.126	0.201	0.464	0.724
POAG	*r*	1.0	0.379	0.411	0.369	0.115	0.076
	P		0.010	0.005	0.013	0.454	0.619
OHT	*r*	1.0	0.120	0.176	0.251	0.298	0.141
	P		0.432	0.247	0.096	0.047	0.619
Controls	*r*	1.0	0.323	0.135	-0.009	0.288	-0.086
	P		0.030	0.375	0.953	0.055	0.575

ODA: Optic disc area; RNFL: Retinal nerve fiber layer; CCT: Central corneal thickness; PEXG: Pseudoexfoliative glaucoma; POAG: Primary open angle glaucoma; OHT: Ocular hypertension. Sperman's rho test was used.

Table 4 Correlations of RNFL quadrants with age, CCT and ODA in POAG

Predictors	Superior RNFL			Inferior RNFL			Nasal RNFL		
	Age	CCT	ODA	Age	CCT	ODA	Age	CCT	ODA
SE coef	0.287	0.087	7.612	0.297	0.090	7.887	0.121	0.036	3.22
t	-2.09	1.03	1.97	-1.82	2.91	2.53	0.32	1.50	2.73
P	0.043	0.031	0.050	0.050	0.006	0.015	0.751	0.140	0.009
vif	1.132	1.079	1.058	1.132	1.079	1.058	1.132	1.079	1.058

RNFL: Retinal nerve fiber layer; CCT: Central corneal thickness; ODA: Optic disc area; SE coef: Standard error of the coefficient; vif: Variance inflation factor. Multipl regression analysis was used. A variation inflation factor less than 5 shows that the predictors are not correlated.

compared to healthy controls. Our results are similar to the previous studies. In our study, RNFL thickness measurements both in the POAG and PEXG groups were significantly lower than the values of control group in all quadrants.

Some studies[1-2] report a positive correlation between the disc size and RNFL thickness. On the other hand, some studies[3-5] suggest that such a relationship could be an artifact due to magnification varriation between eyes. Some factors including axial length and refractive status could affect optical magnification of OCT scanning. Additionally, RNFL thickness decreases further away from the optic disc margin. In our study, when the groups were evaluated one by one, a positive correlation was found between the disc area and some quadrantic RNFL thicknesses in POAG, OHT and control groups.

In a study by Kasumovic *et al* [16], OCT parameters were evaluated in normal, preperimetric, developed perimetric and terminal glaucoma. The largest disc was noticed in preperimetric glaucoma group (1.94±0.62) and was statistically higher than control study group (1.75 ±0.66) and terminal glaucoma group (1.58 ±0.10) respectively. There is no significant difference between the size of disc in the developed perimetric glaucoma group (1.80±0.66) compared to control group [16]. According to this study, disc size becomes smaller in later stages of glaucoma. This finding may explain the positive correlation between the disc area and RNFL in POAG.

CCT measurements may also correlate with disc size, because of the anatomic continuity of the cornea, sclera, and optic disc lamina. It has been reported that CCT is correlated

with anterior scleral thickness in patients with glaucoma [17]. Unlikely, some studies [18-19] reported that CCT is inversely correlated to ODA in glaucoma patients. Terai *et al* [20] showed a weak correlation between CCT and optic disc size in patients with POAG. However, they emphasized that they could not detect a clinically relevant correlation. In our study, there was no relationship between the disc area and CCT measurements in any group.

The strength of the present study was that it revealed the relationship between the disc size and the RNFL thickness in different glaucoma subtypes and had a control group for comparison. The study has also several limitations. First, selection of subjects may not be standardized because of the retrospective nature. Second, the magnification was not adjusted for the axial length or refraction. Third, other disc parameters and visual field test were not evaluated in this study.

In conclusion, our results suggest that the disc area is significantly positively correlated with the RNFL thickness in POAG. This relationship may be a possible risk factor for glaucomatous optic nerve damage. However, further studies are necessary to reveal the pathogenesis.

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