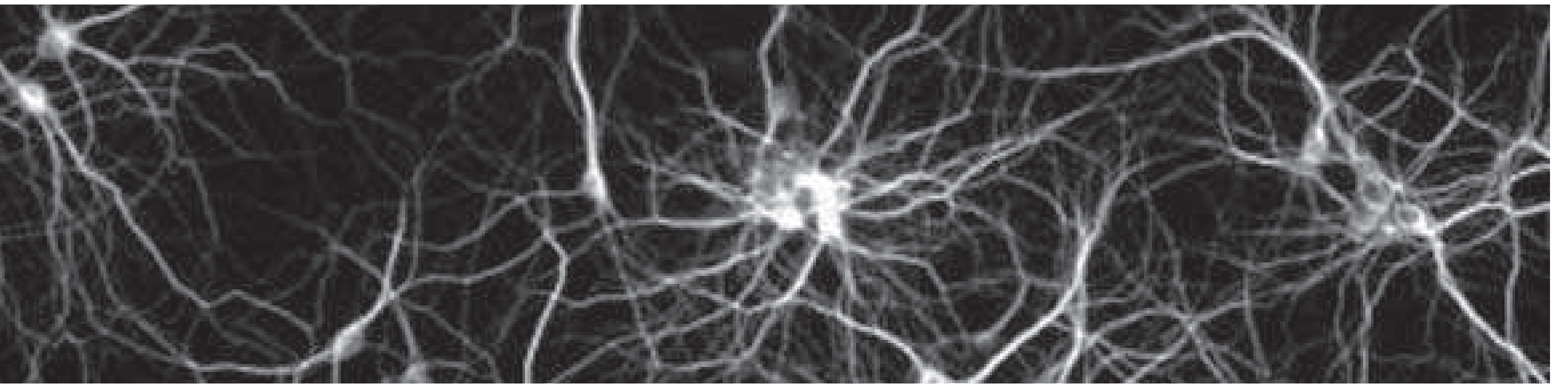

Prediction of glaucomatous optic nerve damage in ocular hypertension with optical coherence tomography

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ABSTRACT – *Purpose:* To assess whether retinal nerve fiber layer (RNFL) thickness value obtained with optical coherence tomography (OCT) in ocular hypertension patients can predict glaucomatous changes in visual field over a 2-year period.

Methods: This comparative analysis included 76 eyes: 36 ocular hypertension (OHT) and 40 healthy. The OCT parameter RNFL thickness and Octopus automated perimetry (SAP) were performed in ocular hypertension and healthy eyes at baseline and after 2 years.

Results: In ocular hypertension group, 6 (16.6%) eyes developed SAP glaucomatous abnormalities in 2-year period. Comparison of RNFL thickness between OHT eyes with and without glaucomatous changes and healthy eyes showed statistically significant thinning of RNFL in the inferior quadrant at baseline in OHT eyes with SAP glaucomatous changes.

Conclusion: Thinner OCT obtained inferior RNFL in OHT eyes is associated with future development of perimetric glaucoma changes.

Key words: glaucoma, retinal nerve fiber layer thickness, optical coherence, ocular hypertension

INTRODUCTION

Optical coherence tomography (OCT), first described in 1991 by Huang *et al.* (1), is a high-resolution cross-sectional imaging technique that allows for *in vivo* measurement of the retinal nerve fiber layer (RNFL). RNFL thickness measurements using OCT have been shown to discriminate between healthy and glaucomatous eyes (2-5), and recently detection of disease progression using OCT has been reported (6). Because there is considerable evidence that RNFL loss precedes visual

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field loss (7-10) and optic nerve head defects (11-13) in patients with glaucoma, it is of interest to quantify this loss in patients with ocular hypertension who are at risk of developing glaucoma. The aim of this study was to determine whether baseline OCT RNFL thickness measurements are associated with the development of glaucomatous changes in ocular hypertension eyes over a 2-year period.

SUBJECTS AND METHODS

One eye was randomly selected from each of 40 healthy and 36 subjects with ocular hypertension (OHT), who met the inclusion criteria as defined below. All recruited cases were examined at University Department of Ophthalmology, Zagreb University Hospital Center, Zagreb, Croatia. An informed consent was obtained from all participants and the methods were approved by the Ethics Committee of the Zagreb University School of Medicine. All study eyes had the best-corrected visual acuity of at least 20/40.

All subjects underwent ophthalmologic examination including visual acuity, biomicroscopy, direct and indirect ophthalmoscopy, intraocular pressure (IOP) measurement by Goldman aplanation, and visual field testing prior to OCT image acquisition at baseline and two visual fields at 2-year follow up.

Optical coherence tomography (SOCT Copernicus; OPTOPOL Technology S.A.) was employed to measure RNFL thickness. Haag-Streit Octopus 101/G2 glaucoma program was used for perimetry. The perimetry parameters of mean deviation (MD) and corrected loss variance (CLV) were used on visual field interpretation.

Study eyes were classified as OHT or healthy based on the following criteria: ocular hypertensive eyes had a measured IOP of 24 mm Hg or more on at least 2 occasions. These eyes had intact rims, no evidence of hemorrhage, notch, excavation, or RNFL defect, and had symmetric optic disks (asymmetry of vertical cup or disk <0.2). Visual field results on the Octopus automated perimetry glaucoma program showed a corrected pattern SD within the 95% normal limits.

Healthy eyes had the highest measured IOP of 20 mm Hg or lower with no history of elevated IOP. Other criteria were the same as those for OHT eyes.

The primary endpoint of the study was evidence of glaucomatous change defined as development of glaucomatous visual field damage on two or more consecutive tests. Glaucomatous visual field damage was identified by MD and CLV values over 6 db.

The RNFL average system was used to measure the values of superior, inferior, nasal and temporal RNFL thickness and their averages used as parameters. Student's t-test was used for continuous variables of RNFL thickness.

RESULTS

The age of healthy and ocular hypertension subjects was similar (62±9.3 years in healthy and 61±5 years in ocular hypertension group). There were 58% of female subjects in the group of healthy subjects (22 of 40) and 62% in the group of OHT subjects (22 of 40). The mean intraocular pressure value was 16.3±5.0 mm Hg in healthy group and 24.4±2.8 mm Hg in OHT group. There were no sta-

Table 1. *Baseline demographic and ocular factors in healthy and ocular hypertension (OHT) subjects*

	Normal (n=40)	OHT (n=36)
Sex (% female)	58	62
Age (yrs)	62±9.3	61±5.0
Baseline IOP (mm Hg)	16.3±5.0	24.4±2.8
MD (db)	1.3±0.2	1.4±0.7
CLV (db)	1.3±0.4	1.3±1.1

IOP = intraocular pressure; MD = mean deviation; CLV = corrected loss variance

Table 2. *Demographic and ocular factors in healthy and ocular hypertension (OHT) subjects with and without glaucomatous change at 2-year follow up*

	Healthy (n=40)	OHT eyes without glaucomatous change (n=30)	OHT eyes with glaucomatous change (n=6)
Sex (% female)	58	60	62
Age (yrs)	64±8.3	61±2.5	63±5.2
IOP (mm Hg)	16.8±4.0	24.5±3.8	24.4±3.2
MD (db)	1.4±0.3	2.4±3.3	8.2±2.1 (*P*<0.01)
CLV (db)	2.0±0.7	2.5±4.0	9.6±4.3 (*P*<0.01)

OHT eyes with and without glaucomatous change
IOP = intraocular pressure; MD = mean deviation; CLV= corrected loss variance

Table 3. *Baseline retinal nerve fiber layer thickness (RNFL) in eyes with and without glaucomatous change and healthy eyes*

RNFL (μm)	Eyes with glaucomatous change (n=6)	Eyes without glaucomatous change (n=30)	Normal eyes (n=40)	p 1	p 2
Mean (TSNIT)	101±17.3	108±16.1	107±16.3	>0.01 (0.98)	>0.01 (0.47)
Temporal Mean	85±12.2	89±11.3	88±13.5	>0.01 (0.12)	>0.01 (0.87)
Superior Mean	117±13.5	121±13.2	119±11.3	>0.01 (0.72)	>0.01 (0.46)
Nasal Mean	95±17.3	97±15.6	97±13.4	>0.01 (0.12)	>0.01 (0.34)
Inferior Mean	115±12.2	131±12.4	126±15.4	<0.01	>0.01

p1 = corresponding pair: eyes with and without glaucomatous change, p2 = corresponding pair: eyes without glaucomatous change and healthy eyes; TSNIT = temporal superior nasal inferior thickness

tistically significant between-group differences according to sex, age, MD and CLV parameters at baseline (Table 1).

At 2-year follow up, there were no statistically significant sex and age differences between healthy eyes and OHT eyes with and without glaucomatous changes. There were no differences in MD and CLV parameters between 40 normal and 30 OHT eyes. Six OHT patients developed glaucomatous changes in their visual fields, with statistically significant differences in MD and CLV values as compared with OHT eyes without glaucomatous changes (Table 2).

There were no statistically significant differences between healthy and OHT eyes with and without glaucomatous visual field changes according to baseline mean, temporal, superior and nasal mean of RNFL (Table 3). The mean rates of change were significantly higher for inferior mean of RNFL thickness in OHT eyes with glaucomatous changes as compared with healthy eyes and OHT eyes without glaucomatous visual field changes.

DISCUSSION

In this study, a significant difference was detected in the baseline parameters of inferior value of RNFL between 40 healthy and 36 OHT eyes without glaucomatous changes as compared with 6 OHT eyes that developed glaucomatous perimetric changes in 2-year period. Our study demonstrated that thinner inferior OCT obtained RNFL measurement at baseline in OHT eyes could predict development of visual field damage.

Numerous experimental and clinical studies have demonstrated that RNFL becomes atrophic in glaucoma (9-16). In a study (14) that quantified and compared RNFL thickness in OHT eyes with that in healthy eyes and glaucomatous eyes by using OCT, there was considerable within-group variability in the measured RNFL thickness. The average RNFL was significantly thinner in OHT eyes than in healthy eyes. Specifically, RNFL was significantly thinner in OHT eyes than in healthy eyes in the inferior and nasal quadrants. RNFL was significantly thinner in glaucomatous eyes than in OHT and healthy eyes in each quadrant and throughout 360° measurement. A significant decrease in retinal height (an indirect measure of RNFL thickness) by almost 30% was found in OHT eyes as compared with normal eyes (15). The specificity of glaucomatous changes increases when OCT parameters from both optic nerve head and RNFL scans are combined (16). In a study on OCT guide progression analysis (17), the rate of RNFL thinning was variable among patients with developed glaucoma. The sector at seven o'clock was the most frequent location that showed progression.

Many studies support the claim that early RNFL and optic disk abnormalities are associated with the development of glaucoma changes in OHT eyes (3-5,10,18). These results reinforce the importance of RNFL examination and monitoring in glaucoma suspect eyes because objective RNFL measurements may provide improvement in glaucoma detection (13).

Although all OHT eyes in our study had normal visual fields and showed no evidence of optic disk or RNFL defects based on ophthalmologic examination at baseline, it is possible that visual field defects might be detected in some of these eyes using other visual function techniques such as short wavelength automated perimetry or frequency doubling perimetry, which should be subjects of our future investigation.

CONCLUSION

According to our results, OCT obtained thinner inferior RNFL in OHT subjects is associated with future development of glaucomatous optic nerve damage, documented by visual field defects. This finding could contribute to early recognition of glaucoma.

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