

Topographic changes at the optic disc in 33 patients with primary open angle glaucoma

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Abstract

• **AIM:** To show frequency of progression and the progression at the optic disc in primary open angle glaucoma (POAG).

• **METHODS:** A total of 33 patients (66 eyes), 14 male and 19 female, aged 14 to 79 with POAG were imaged using the Heidelberg Retina Tomography II (HRT II) three or more times during follow-up periods of 6 years (2000-2006). Disc progression was determined by regression analysis of global and segmental changes in optic disc parameters. Every patient was tested by Octopus G1 once a year. Imaged optic disc parameters with scanning laser tomography were: rim area (ra), cup/disc (C/D), rim volume (rv), mean RNFL thickness (mRNFL). Imaged segments of the optic disc were global (G), temporal (T), temporal superior (TS), temporal inferior (TI), nasal (N), nasal superior (NS) and nasal inferior (NI).

• **RESULTS:** Global frequency of progression according to c/d ratio existed in 34 eyes (51%), but 32 eyes (48%) were without frequency of progression. Progression existed in 12 eyes (18%) in temporal, 7 eyes (10.6%) in TS, 14 eyes (21%) in TI, 8 eyes (12%) in N, 7 eyes (10.6%) in NS, and 13 eyes (20%) in NI segment. Without progression were 5 eyes (8%).

• **CONCLUSION:** Disc progression in our study is mostly in N and TI segments. Most frequently are stricken TI and NI, but most infrequently NS segment. Most sensitive parameter is c/d ratio. Segmental scanning is of importance in POAG progression analysis.

• **KEYWORDS:** primary open angle glaucoma; Heidelberg retinal tomography II; progression; frequency of progression

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INTRODUCTION

Primary open angle glaucoma (POAG) is an optic neuropathy in which characteristic morphological changes at the optic disc are related to visual field loss. These changes, which reflect the loss of ganglion cell axons that occurs in glaucoma, include an increase in optic cup size and a reduction in neuroretinal rim area. Morphology of the optic nerve head (ONH) is of importance in the diagnosis and follow-up of glaucoma. The laser scanning ophthalmoscope permits to analyze the optic disc topography of the ONH, thereby detecting glaucomatous as well as other changes of the optic disc^[1].

Glaucomatous changes on the ONH are consequence of the focal nerve fibre layer loss which is more readily recognized and perhaps more specific for glaucoma than diffuse loss^[2], and also including ONH cupping and rim area reduction. Since the 1970s it has been recognized that the size of the optic cup is related to the size of the optic disc^[3] in the normal population, and similarly, the area of the neuroretinal rim is related to optic disc size^[4]. For this reason, it is necessary to make actual measurements of the size of optic disc features, rather than relative measurements which vary with optic disc size (such as the cup/disc ratio), in order to distinguish pathological from physiological states. There was no difference between large cup (LC) and normal eyes (NE) in RNFL thickness, rim area, and rim volume. LC was able to be defined as a normal central excavation with a large disc and large cup/disc area ratio with a normal rim area.

It is not possible to measure the dimensions of the optic disc directly in vivo, except during vitreoretinal surgery^[5], and so clinicians have to rely on measurements made on images of the optic disc. The size of an image of a feature in the fundus of the eye is dependent on magnification due to the camera and magnification due to the eye, as well as factors

such as the position of the feature of interest in the fundus (eccentricity)^[6] and the position of the camera with respect to the eye^[7]. Various methods to correct for eye-camera^[8] and eye magnification^[9,10] have been published, and all make assumptions about the optics of the eye to a greater or lesser extent^[11].

To evaluate glaucomatous eyes it is necessary to obtain reliable comparative data and study the topographic morphology of the ONH in normal eyes. The normalized rim: disc area ratio may be useful for glaucoma screening, diagnosis, and follow up. The calculation of this parameter relies on a comparison database with measurements obtained from 100 healthy individuals with a mean age of 36 years^[12]; also in older population where POAG is more common calculation is obtained in same manner. Changes in POAG are described in 6 segments (G, T, TS, TI, N, NS, NI) and through parameters (disc area ratio, rim area, rim volume, C/D area ratio, mean RNFL thickness etc.), where rim/disc area ratio represents useful diagnostic parameter for tracking changes in glaucoma.

Scanning laser tomography of the ONH is reproducible^[13-15], but in what way it should be used to evaluate glaucoma progression remains to be determined. To judge progression, measurement variability needs be distinguished from true change, for which a detailed understanding of reproducibility is needed. Variability in Heidelberg retina tomography (HRT) image analysis may be influenced by blood vessels, cardiac pulsation, and the ONH's variably sloped, excavated surface^[13,14]. Progression is not uniform over the ONH^[16] and its detection is likely to be influenced by test conditions and variability in different ONH regions. We studied the reproducibility of different topographic parameters, from which one was selected to assess variability regionally. Vulnerability of the ONH in our study represents level of attenuation (damage) of the mean RNFL thickness in different segments in follow up of POAG changes. Progression is represented in changes in four parameters through six segments of ONH. The purpose of this study was to assess ONH segment with the uttermost progression comparing to first measurement, as well as which ONH segment has ultimate frequency of progression in POAG.

MATERIALS AND METHODS

Patients After obtaining approval from the Institutional Review Board and written, informed consent, we have studied 33 patients (66 eyes), 14 male and 19 female, aged 14 to 79 years, all with POAG, compensated with topical

antiglaucomatous drugs. Follow up period was 6 years (from 2000 to 2006) and all patients were observed in the Institute of eye diseases in Belgrade.

Methods During that period all patients had: Ophthalmologic exam every 4 months, Computerizing visual field exam (Octopus G1) at least once a year, Confocal scanning laser ophthalmoscopy with Heidelberg retinal tomography II (HRT II) at least once a year. The following six optic disc segments were analyzed: Nasal (N), Nasal superior (NS), Nasal inferior (NI), Temporal (T), Temporal superior (TS), Temporal inferior (TI). Global (G) variables were also analyzed. The following optic disc variables (parameters) were analyzed directly by means of HRT software: rim area (ra) (was calculated by subtracting the cup area from the disc area) cup/disc area ratio (C/D) area ratio (was calculated by dividing the cup area by the disc area) rim volume (rv) Mean RNFL thickness (mRNFL). The mean topography of the three images was generated and the disc edge was delineated on the mean image by a single observer (DK), using a mouse drawn contour line. The HRT software was used to analyze both global and segmental optic disc variables. The contour line was then exported from the first HRT mean image (2000.) onto the second HRT mean image (2006.) of the same optic disc.

Optic disc parameters were analyzed directly by means of HRT software: disc area, cup area, cup volume, rim volume, and third moment (cup shape measure) using the standard reference plane. Cup/disc area ratio was calculated by dividing the cup area by the disc area. Rim area was calculated by subtracting the cup area from the disc area. Six optic disc segments were analyzed: N, NS, NI, T, TS, TI. Global variables were also analyzed.

Statistical Analysis Data are presented as mean \pm SD, or as percentages for categorical variables. Normal distribution and homoscedasticity of continuous variables were tested by means of the Kolmogorov-Smirnov test. The data at the different times of the study were evaluated by means of Student's *t* test or Wilcoxon signed ranks test. Frequency of changes at the optic disc parameters were analyzed by Chi-square test.

Statistical evaluations were performed by running the SPSS/PC⁺ software package (SPSS, Chicago, IL) on a personal computer. *P*<0.05 were regarded as statistically significant.

RESULTS

Global frequency of progression according to c/d area ratio existed in 34 of 66 eyes (52%), but 32 of 66 eyes (48%)

Table 1 Statistical significance of ONH segments according to observed parameters

Parameter	T	TS	TI	N	NS	NI	G
Rim area	$z=0.601$; $P>0.05$ SD=0.001	$z=0.94$; $P>0.05$ SD=0.005	$z=2.35$; $P<0.05$ SD=0.008	$z=2.08$; $P<0.05$ SD=0.016	$z=0.82$; $P>0.05$ SD=0.006	$z=1.58$; $P>0.05$ SD=0.003	$z=2.55$; $P=0.01$ SD=0.039
Cup/disc area ratio	$t=0.516$; $P>0.05$ SD=0.004	$t=0.306$; $P>0.05$ SD=0.022	$t=1.99$; $P=0.05$ SD=0.033	$t=2.89$; $P<0.01$ SD=0.036	$t=0.609$; $P>0.05$ SD=0.03	$t=1.82$; $P>0.05$ SD=0.013	$t=3.47$; $P<0.01$ SD=0.022
Rim volume	$z=0.549$; $P>0.05$ SD=0.002	$z=0.42$; $P>0.05$ SD=0.003	$z=1.49$; $P>0.05$ SD=0.004	$z=1.27$; $P>0.05$ SD=0.007	$z=0.46$; $P>0.05$ SD=0.003	$z=1.45$; $P>0.05$ SD=0.004	$z=1.14$; $P>0.05$ SD=0.023
Mean RNFL thickness	$t=1.117$; $P>0.05$ SD=0.02	$t=0.89$; $P>0.05$ SD=0.044	$t=0.03$; $P>0.05$ SD=0.148	$t=1.66$; $P>0.05$ SD=0.015	$t=1.035$; $P>0.05$ SD=0.033	$t=2.14$; $P<0.05$ SD=0.016	$t=1.61$; $P>0.05$ SD=0.024

Table 2 Frequency of ONH segments change according to observed parameters

Parameters	Ultimate frequency			Least frequency			Statistical significance ANOVA
	ONH segment	Eyes	%	ONH segment	Eyes	%	
Rim area	TI	44	66,7	NS	30	45,5	$F=1.199$; $P>0.05$
Cup/disc area ratio	TI	44	66,7	NS	30	45,5	$F=1.139$; $P>0.05$
Rim volume	NI	39	59,1	NS	23	34,8	$F=0.916$; $P>0.05$
Mean RNFL thickness	NI	41	62,1	NS	32	48,5	$F=0.317$; $P>0.05$

Table 3 Average change between supreme and least parameter values in observed ONH segments

Parameter	Supreme	Change	Least	Change	Statistical significance ANOVA
Rim area (mm ²)	T/TI	0.28	NI	0.16	$F=1.199$; $P>0.05$
Cup/disc area ratio	TI	0.78	N	0.36	$F=1.139$; $P>0.05$
Rim volume (mm ³)	N	0.16	TS	0.06	$F=0.916$; $P>0.05$
Mean RNFL thickness (mm)	N	0.66	T	0.17	$F=0.317$; $P>0.05$

were without frequency of progression. The rim area, cup/disc area ratio, rim volume and mean RNFL thickness, with ONH segments change (%) were 53.8, 53.8, 46.7 and 55.3, but without ONH segments change (%) were 46.2, 46.2, 53.3 and 44.7. According to ONH segments: Progression existed in 12 eyes (18%) in T, 7 eyes (10.6%) in TS, 14 eyes (21%) in TI, 8 eyes (12%) in N, 7 eyes (10.6%) in NS, and 13 eyes (20%) in NI segment. Without progression were 5 eyes (8%). Statistical significance: Pearson Chi-square: in rim area, cup/disc area ratio, rim volume, mean RNFL thickness were $\chi^2=7.162$; $P>0.05$, $\chi^2=7.162$; $P>0.05$, $\chi^2=12.224$; $P<0,05$ and $\chi^2=3.52$; $P>0.05$ (Tables 1-3).

DISCUSSION

According to our results, most vulnerable segments of the ONH are nasal (N) and temporal inferior (TI). Most sensitive parameter in tracking POAG changes is C/D ratio. Progression according to C/D ratio was most frequent in the temporal inferior (TI) segment (in rim area and C/D ratio) and nasal inferior (NI) segment (in rim volume and mRNFL), but most infrequent in the nasal superior (NS) segment (in all parameters). These results are explained by anatomical arrangement of nerve fibres around ONH.

According to authors most vulnerable segment was nasal inferior (NI) and second most vulnerable segment was temporal inferior (TI) segment or temporal superior (TS) segment [17]. Three global optic disc variables were found to change over time in: cup area, C/D area ratio, and rim area. These results correspond with what we would expect to observe in glaucomatous changes [18-20]. Rim area is reproducible and potentially useful as a marker of progression. These features can be expected in standard reference plane analysis of HRT II images and should be considered when evaluating progression [20].

The results indicate that segmental as well as global analysis of optic disc images is required for detection of glaucomatous change, and suggest that the HRT may be able to detect change in areas such as the nasal superior, nasal inferior, and temporal superior segments which may not be detected clinically.

According to literature global parameters of the ONH showed progression in 21 of 56 eyes (37.5%) while ultimate progression was in temporal superior (TS) in 30 eyes (53.6%), and the least was in the nasal superior (NS) segment in 21 eyes (37.5%) [17]. Our study results correspond

to other studies on early topographic changes at the ONH in POAG. Segmental scanning is of importance in POAG progression analysis.

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