· Original article ·

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 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 temporal superior (TS), 14 eyes (21%) in temporal inferior (TI), 8 eyes (12%) in nasal (N), 7 eyes (10.6%) in nasal superior (NS), and 13 eyes (20%) in nasal inferior (NI) segment. Without progression were 5 eyes (8%).

• CONCLUSION: Disc progression in our study was mostly in nasal (N) and temporal inferior (TI) segments. Most frequently were stricken temporal inferior (TI) and nasal inferior (NI), but most infrequently nasal superior (NS) segment. Most sensitive parameter was 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

Table 1 Statistical significance of ONH segments according to observed parameters

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

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 asses 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: nasal, nasal superior, nasal inferior, temporal, temporal superior, temporal inferior. Global variables were also analyzed.

Statistical Analysis Data are presented as mean ± standard deviation, 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

Table 2 Frequency of ONH segments change according to observed parameters

Parameters	Ultimate frequency			Least frequency			Statistical significance
	ONH segment	Eyes	%	ONH segment	Eyes	%	ANOVA
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	$F=0.317;P>0.05$

+ 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%) 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: Progres-sion existed in 12 eyes (18%) in temporal (T), 7 eyes (10.6%) in temporal superior (TS), 14 eyes (21%) in temporal inferior (TI), 8 eyes (12%) in nasal (N), 7 eyes (10.6%) in nasal superior (NS), and 13 eyes (20%) in nasal inferior (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.

REFERENCES

1 Anton A, Yamagishi N, Zangwill L, Sample PA, Weinreb RN. Mapping structural to functional damage in glaucoma with standard automated perimetry and confocal scanning laser ophthalmoscopy. *Am J Ophthalmol* 1998;125(4):436-446

2 Arnold JV, Gates JW, Taylor KM. Possible errors in the measurement of retinal lesions. *Invest Ophthalmol Vis Sci* 1993;34(8):2576-2580

3 Bartz-Schmidt KU, Sengersdorf A, Esser P, Walter P, Hilgers RD, Krieglstein GK. The cumulative normalised rim/disc area ratio curve. *Graefes Arch Clin Exp Ophthalmol* 1996;234(4):227-231

4 Bengtsson B, Krakau CE. Correction of optic disc measurements on fundus photographs. *Graefes Arch Clin Exp Ophthalmol* 1992;230(1):24-28

5 Bennett AG, Rudnicka AR, Edgar DF. Improvements on Littmann's method of determining the size of retinal features by fundus photography. *Graefes Arch Clin Exp Ophthalmol* 1994;232(6):361-367

6 Brigatti L, Weitzman M, Caprioli J. Regional test-retest variability of confocal scanning laser tomography. *Am J Ophthalmol* 1995;120(4):433-440

7 Chauhan BC, McCormick TA. Effect of the cardiac cycle on topographic measurements using confocal scanning laser tomography. *Graefes Arch Clin Exp Ophthalmol* 1995;233(9):568-572

8 Cioffi GA, Robin AL, Eastman RD, Perell HF, Sarfarazi FA, Kelman SE. Confocal laser scanning ophthalmoscope. Reproducibility of optic nerve head topographic measurements with the confocal laser scanning ophthalmoscope. *Ophthalmology* 1993;100(1):57-62

9 Garway-Heath DF, Rudnicka A R, Lowe T, Foster PJ, Fitzke FW, Hitchings RA. Measurement of optic disc size: equivalence of methods to correct for ocular magnification. *Br J Ophthalmol* 1998;82(6):643-649

10 Hermann M M, Theofylaktopoulos I, Bangard N, Jonescu-Cuypers C, Coburger S, Diestelhorst M. Optic nerve head morphometry in healthy

adults using confocal laser scanning tomography. *Br J Ophthalmol* 2004;88(6):761-765

11 Jonas JB, Budde WM, Panda-Jonas S. Ophthalmoscopic evaluation of the optic nerve head. *Surv Ophthalmol* 1999;43(4):293-320

12 Jonas JB, Fern ndez MC, St rmer J. Pattern of glaucomatous neuroretinal rim loss. *Ophthalmology* 1993;100(1):63-68

13 Jonescu-Cuypers CP, Thumann G, Hilgers RD, Bartz-Schmidt KU, Krott R, Krieglstein GK. Long-term fluctuations of the normalised rim/disc area ratio quotient in normal eyes. *Graefes Arch Clin Exp Ophthalmol* 1999;237(3):181-186

14 Kamal DS, Viswanathan AC, Garway-Heath DF, Hitchings RA, Poinoosawmy D, Bunce C. Detection of optic disc change with the Heidelberg retina tomograph before confirmed visual field change in ocular hypertensives converting to early glaucoma. *Br J Ophthalmol* 1999;83(3):290-294

15 Kato A, Sugiyama K, Kono Y, Uchida H, Tomita G, Yamamoto T. Serial topographic changes at the optic disc in normal-tension glaucoma viewed with scanning laser tomography. *Nippon Ganka Gakkai Zasshi* 2003;107(10):597-601

16 Min KH, Seong GJ, Hong YJ, Kim CY. Optic nerve head topographic measurements and retinal nerve fibre layer thickness in physiologic large cups. *Korean J Ophthalmol* 2005;19(3):189-194

17 Tan JC, Garway-Heath DF, Hitchings RA. Variability across the optic nerve head in scanning laser tomography. *Br J Ophthalmol* 2003;87(5):557-559

18 Teal PK, Morin JD, McCulloch C. Assessment of the normal disc. *Trans Am Ophthalmol Soc* 1972;70:164-177

19 Tuulonen A, Airaksinen PJ. Initial glaucomatous optic disk and retinal nerve fibre layer abnormalities and their progression. *Am J Ophthalmol* 1991;111(4):485-490

20 Varma R, Quigley HA, Pease ME. Changes in optic disk characteristics and number of nerve fibres in experimental glaucoma. *Am J Ophthalmol* 1992;114(5):554-559

原发性开角型青光眼视盘形态变化分析33例

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摘要

目的:分析原发性开角型青光眼(POAG)视盘损害的进展和进展频率。

方法:33例(66眼)POAG患者,男14例,女19例,年龄14~79岁,在随访的6a间(2000/2006),3次或更多次进行海德堡视网膜断层扫描仪II(HRT II)检查。对整体和节段的视盘参数进行回归分析判断视盘损害的进展。患者每年进行Octopus G1计算机视野分析检查一次。激光扫描视盘图像参数包括:盘沿面积(ra),杯盘比(C/D),盘沿体积(rv),平均视神经纤维层厚度(mRNFL)。扫描视神经的节段包括总体(G),颞侧(T),颞上(TS),颞下(TI),鼻侧(N),鼻上方(NS)和鼻下(NI)。

结果:根据杯盘比C/D,总体上有34眼(51%)视盘损害进展,32眼(48%)没有进展。12眼(18%)颞侧(T),7眼(10.6%)颞上,14眼(21%)颞下,8眼(12%)鼻侧,7眼(10,6%)鼻上,13眼(20%)鼻下,视盘损害进展。5眼(8%)没有进展。

结论:在鼻侧(N)及颞下方(TI)视盘损害进展最多,进展频率最高在颞下方(TI)和鼻下方(NI),频率最低在鼻上方(NI)。杯盘比C/D最敏感。节段扫描对POAG进展分析有重要意义。

关键词:原发性开角型青光眼,海德堡视网膜断层扫描仪II,进展,进展频率