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Heidelberg Retina Tomography II parameters in evaluating high- and normal-pressure glaucoma progression

Parametri Hajdelberg tomografije II mrežnjače u proceni progresije glaukoma pri visokom i normalnom očnom pritisku

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Abstract

Background/Aim. Heidelberg retina tomography II (HRT II) haves been employed to quantitatively assess the topography of optic discs in eyes with high-pressure glaucoma (HPG) and normal-pressure glaucoma (NPG), in order to determine which of global and segmental optic disc parameters will prove to be most suitable for monitoring the progression of these two conditions. **Methods.** The results of 73 eyes of 73 patients with HPG and NPG were analyzed in relation to age, refractive error, quality of HRT images and stereometric parameters. **Results.** A statistically significant difference ($p < 0.05$) between the global baseline and follow-up results was found in: rim volume, maximum cup depth and cup shape measure (in the HPG group), and C/D ratio, cup volume, rim volume and cup shape measure (in the NPG group). The baseline and follow-up results of the retinal nerve fiber layer in the temporal and inferotemporal sectors show a significant difference in both groups. **Conclusion.** Several HRT stereometric parameters are useful for monitoring the progression of changes of the optic disc and local retina in eyes with HPG and NPG. Both segmental and global scanning is of importance in glaucoma progression analysis.

Key words:
glaucoma; retina; tomography; disease progression.

Apstrakt

Uvod/Cilj. *Heidelberg retina tomography* (HRT II) koristi se za kvantitativnu procenu topografije optičkog diska očiju sa glaukomom kod povećanog intraokularnog pritiska (*high-pressure glaucoma* – HPG) i kod normalnog intraokularnog pritiska (*normal-pressure glaucoma* – NPG) da bi se utvrdilo koji od globalnih i segmentnih parametara optičkog diska mogu biti najpodesniji za praćenje progresije ova dva poremećaja. **Metode.** Urađena je analiza rezultata dobijenih za 73 oka 73 bolesnika sa HPG i NPG u odnosu na starost bolesnika, refraktivnu grešku, kvalitet HRT snimaka i stereometrijske parametre. **Rezultati.** Utvrđena je statistički značajna razlika ($p < 0,05$) između globalnih početnih vrednosti i rezultata praćenja u zapremini oboda, maksimalnoj dubini ekskavacije i parametrima trećeg momenta (grupa HPG) i u odnosu C/D, zapremini ekskavacije, zapremini oboda i parametrima trećeg momenta (grupa NPG). Početne vrednosti i rezultati praćenja retinalnog sloja nervnih vlakana u temporalnom i inferotemporalonom sektoru pokazali su statistički značajnu razliku u obe grupe. **Zaključak.** Nekoliko HRT II stereometrijskih parametara korisno je za praćenje progresije promena na optičkom disku i okolnoj mrežnjači kod bolesnika sa HPG i NPG. Za analizu progresije glaukoma korisno je, prema tome, praćenje i segmentnih i globalnih parametara optičkog diska.

Ključne reči:
glaukom; mrežnjača; tomografija; bolest, progresija.

Introduction

Accurate and prompt detection of optic nerve damage is of tremendous importance in early diagnosis and prevention of blindness from glaucoma. Primary open-angle glaucoma (POAG) is a disorder that demonstrates typical structural changes in the optic disc along with visual field defects. Depending on whether these changes are accompanied by increased intraocular pressure or not, POAG is divided into two subgroups: normal-pressure glaucoma (NPG) and high pressure glaucoma (HPG). Assessment of the optic disc is included in the standard examination of patients with suspected or manifest glaucoma. It is difficult to detect early changes of glaucoma with standard procedures because

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nerve fiber degeneration and loss of visual field do not progress in parallel in the early stage of glaucoma. A number of studies have shown that visual field abnormalities are detected only after 20−50% of the retinal ganglion cells have been lost [1–3]. The early changes in patients with POAG are those in the thickness of the nerve fiber layer and in the morphology of the optic disc [4, 5]. All these data speak in favor of how it is important to know the real principles of early detection and precise monitoring of progression of glaucoma, as well as diagnostic procedures that make use of it. To assess and follow these changes, modern instruments based on laser confocal and other systems have been developed [6–9]. Heidelberg retina tomograph II (HRT II, Heidelberg Engineering, GmbH, Heidelberg, Germany) uses confocal scanning laser ophthalmoscopy to evaluate quantitatively the three-dimensional surface topography of the optic nerve head and the surrounding nerve fiber layer [10–13]. HRT II is an instrument we used in our study for collecting data. The aim of this study was to determine which stereometrical HRT parameters are most suitable for monitoring progression of glaucoma in both HPG and NPG group, as well as to find out which of the 6 sectors of neuroretinal rim significantly changed over time in both groups, and how the damaged zone of the neuroretinal rim area is changed over time.

Methods

This retrospective study included 73 eyes of 73 patients from the Ophtalmological Institute of Faculty of Medicine, University of Belgrade. The research followed the Declaration of Helsinki and was approved by the Regional Ethical Review Board. We investigated stereometric parameters of 50 eyes in 50 patients with HPG and 23 eyes in 23 patients with NPG (Table 1). The patients diagnosis was assessed according to the rules of the European Glaucoma Society [14]. The average period of monitoring the patients in the HPG group was 26 months, while in the NPG group it was 23 months, for which period at least three HRT examinations for each patient were done. The restriction of the study to the one eye of each patient for each group was to facilitate statistical analysis. Those eyes with excessive refractive error of more than + 6 diopters or less than – 6 diopters, cataracts, diabetic retinopathy or with any history of surgical treatment or eye trauma were excluded. We used HRT II in our study to get a series of photographies of the cross section of the optical nerve head of different deepness. After 3D reconstruction it produces topographical photographies of the papilla and peripapillar retina [15]. To quantify morphometric rim and cup parameters in optic disc topography, a reference plane is defined, which is stable over each examination, so that the parameters change only when true structural changes in the optic disc occur. The retinal surface located above the reference plane is defined as a rim, and below the reference level as a cup. In order to verify the quality of topographic images we used images with standard deviation less than 40 µm. Ten stereometric parameters [(disc area in mm^2, cup area in mm^2, rim area in mm², cup-to-disc area ratio (C/D ratio), cup volume in mm³, rim volume in mm³, height variation contour in mm, mean cup depth in mm and maximum cup depth in mm and cup shape measure in mm)] of baseline and follow up examinations has been taken into consideration in this study. We also investigated baseline and follow-up data for the mean retinal nerve fiber layer (mRNFL) thickness in each of the 6 sectors to which neuroretinal rim was divided. Moorfields regression analysis (MRA) is a part of HRT programe, representing the method for analyzing regression logarithmic of the global and 6 sectoral rim areas (temporal, inferotemporal, superotemporal, nasal, superonasal, inferonasal) to the matching disc areas and compares the results to a normative database. It defines these areas as damaged, borderline and normal based in the 95% and 99.9% confidence intervals. In our study we examined which of the studied HRT parameters was statistically most suitable for monitoring the progression in both groups, as well which of the 6 sectors of neuroretinal rim showed the greatest change in the mRNFL.

We analyzed the basic demographic characteristics (age, gender), also a refractive error and standard deviation of HRT images and examined stereometrical parametres of the optical disc of both groups, with the aim to establish the existance of a statistically significant difference between the same parametres in baseline and follow-up examinations (statistically significant difference in t test is when $p < 0.05$).

Results

Table 1 shows the basic statistics relating to sex, age, size of refractive error in patients eyes and standard deviation of topographic HRT images. We examined the difference between the aforementioned parameters between the HPG and NPG groups and found that there were no significant differences in refractive error and standard deviation of topographic HRT images among the two groups. There was a statistically significant difference in age between the patients

Table 1

Characteristics of the patients in both studied groups

Parameters	HPG	NPG
Number of eyes, n	50	23
Male/Female, n	20/30	6/17
Age (years), $\bar{x} \pm SD$	60.38 ± 9.41	51.04 ± 6.30
Refractive error (years), $\bar{x} \pm SD$	-0.5 ± 1.5	-0.8 ± 2.5
Topographic standard deviation, $\bar{x} \pm SD$	25.3 ± 6.9	27.2 ± 5.6

HPG – high – pressure glaucoma; NPG – normal – pressure glaucoma

with HPG and NPG. The patients with NPG were significantly younger than the patients with HPG. Tables 2, 3 and 4 show basic statistically summarized results of HRT parameters measurements in both groups (descriptive statistics). Examining the significance of differences among parameters between baseline and the last follow-up examination in the HPG and NPG groups we found different results (statistically significant difference is when $p < 0.05$). In the HPG group stereometrical parameters of follow-up examinations which showed a significant difference from baseline examinations were rim volume, maximum cup depth and cup shape measure (Table 5).

Table 2

Values of baseline (B) and the last follow-up (F) examination of the studied Heidelberg retina tomography stereometrical parameters in the high-pressure glaucoma (HPG) and the normal-pressure glaucoma (NGP) groups

Sterometrical parameters	HPG		NPG	
	B ($\bar{x}$ ± SD)	F ($\bar{x}$ ± SD)	B ($\bar{x}$ ± SD)	F ($\bar{x}$ ± SD)
Disc area (mm^2)	2.480 ± 0.501	2.480 ± 0.501	2.715 ± 0.631	2.715 ± 0.631
Cup area (mm^2)	0.971 ± 0.590	0.979 ± 0.598	1.087 ± 0.456	1.043 ± 0.453
Rim area (mm^2)	1.508 ± 0.542	1.501 ± 0.540	1.628 ± 0.358	1.671 ± 0.340
Cup/disc area ratio	0.382 ± 0.209	0.385 ± 0.211	0.388 ± 0.106	0.369 ± 0.111
Cup volume (mm^3)	0.319 ± 0.337	0.349 ± 0.300	0.351 ± 0.240	0.312 ± 0.237
Rim volume (mm^3)	0.347 ± 0.204	0.156 ± 0.205	0.390 ± 0.153	0.411 ± 0.133
Mean cup depth (mm)	0.276 ± 0.130	0.283 ± 0.130	0.304 ± 0.118	0.296 ± 0.126
Maximum cup depth (mm)	0.678 ± 0.238	0.850 ± 0.236	0.783 ± 0.225	0.956 ± 0.225
Height variation contour (mm)	0.400 ± 0.201	0.584 ± 0.176	0.386 ± 0.126	0.384 ± 0.107
Cup shape measure (mm)	0.138 ± 0.083	0.299 ± 0.020	0.167 ± 0.060	0.159 ± 0.051

Table 3

Values of baseline and the last follow-up examination of the mean retinal nerve filter layer (mRNFL) in each of the 6 sectors in the high-pressure glaucoma group

Rim area sectors	Baseline mRNFL ($\bar{x}$ ± SD)	Follow-up mRNFL ($\bar{x}$ ± SD)	Baseline *vs* follow-up (values of *t*-test)
Temporal	0.069 ± 0.035	0.039 ± 0.018	2.292*
Temporal superior	0.212 ± 0.115	0.216 ± 0.136	0.162
Temporal inferior	0208 ± 0.128	0.140 ± 0.069	2.681*
Nasal	0.201 ± 0.129	0.198 ± 0.139	0.137
Nasal superior	0.256 ± 0.147	0.254 ± 0.148	0.085
Nasal inferior	0.268 ± 0.148	0.263 ± 0.158	0.165

***p* < 0.05 (statistically significant difference).**

Table 4

Values of baseline and the last follow-up examination of the mean retinal nerve filter layer (mRNFL) in each of the 6 sectors in the normal-pressure glaucoma group

Rim area sectors	Baseline mRNFL ($\bar{x}$ ± SD)	Follow-up mRNFL ($\bar{x}$ ± SD)	Baseline *vs* follow-up (values of *t*-test)
Temporal	0.084 ± 0.029	0.036 ± 0.015	2.435*
Temporal-superior	0.306 ± 0.091	0.312 ± 0.079	0.229
Temporal-inferior	0.217 ± 0.079	0.156 ± 0.098	2.461*
Nasal	0.268 ± 0.102	0.259 ± 0.116	0.262
Nasal-superior	0.359 ± 0.082	0.358 ± 0.094	0.037
Nasal-inferior	0.315 ± 0.106	0.315 ± 0.095	0.007

***p* < 0.05 (statistically significant difference).**

Table 5

Testing significance of the differences between the baseline and follow-up results in both groups

HPG	Baseline *vs* follow-up (*t*-test)	NPG	Baseline *vs* follow-up (values of *t*-test)
Disc area	0.00	Disc area	0.00
Cup area	0.063	Cup area	0.33
Rim area	0.067	Rim area	0.423
Cup/disc area ratio	0.062	Cup/disc area ratio	2.592*
Cup volume	0.184	Cup volume	2.545*
Rim volume	2.286*	Rim volume	2.498*
Mean cup depth	0.282	Mean cup depth	0.202
Maximum cup depth	2.345*	Maximum Cup depth	0.785
Height variation contour	0.123	Height variation Contour	0.086
Cup shape measure	2.005*	Cup shape measure	2.455*
m RNFL	0.445	m RNFL	0.096

HPG – high-pressure glaucoma; NPG – normal pressure glaucoma; mean retinal nerve filter layer (m RNFL);
***p* < 0.05 (statistically significant difference).**

In the NPG group stereometrical parameters of follow-up examinations which showed a significant difference from baseline examinations were C/D ratio, cup volume, rim volume and cup shape measure (Table 5). Analyzing the progression of mRNFL damage in each of the 6 sectors of the neuroretinal rim in the HPG group, we found statistically significant differences between baseline and follow-up examinations in the temporal and inferotemporal sector (Table 3). The same sectors showed a statistically significant difference between baseline and follow-up examinations in the NPG group (Table 4). Reading of the MRA findings of both groups, showed that the size of the damage (in percent) of the neuroretinal rim was higher in the group with NPG (10.5%), than in the group with HPG (7.5%), observing only baseline examinations. Also, observing only baseline MRA examinations we found that in the group with HPG the most often clasified as damaged was nasal segment while the least one was temporal, also in the group with NPG the most often clasified as damaged was the nasal segment, and the least one was the temporal (Table 6).

Table 6

Moorfields regression analysis (MRA) results: Damaged sectors distribution by the baseline and follow-up results in both groups [(50 eyes in the high-pressure glaucoma (HPG) and 23 eyes in the normal pressure glaucoma (NPG) group]

Groups	MRA tmp (n)	MRA tmp/sup (n)	MRA tmp/inf (n)	MRA nsl (n)	MRA nsl/sup (n)	MRA nsl/inf (n)
HPG						
baseline	3	8	5	10	9	5
follow-up	9	9	10	12	10	8
NPG	MRA tmp	MRA tmp/sup	MRA tmp/inf	MRA nsl	MRA nsl/sup	MRA nsl/inf
baseline	1	2	2	4	3	2
follow-up	5	2	9	4	3	2

tmp – temporal; sup – superior; inf – inferior; nsl – nasal.

Discussion

Structural alterations of the optic disc nerve fiber layer complex provide the earliest reliable signs of damage from glaucoma [15–17]. Accurate and objective quantitative measurements of the optic nerve head and nerve fiber layer are required to improve our ability to regularly recognize early glaucomatous progression. The quest for more accurate and objective methods has caused several qualitative and quantitative systems to be proposed to detect optic disc changes. The reproducibility and effectiveness of confocal scanning lasers using HRT II, as in our study, has already been reported [16–19]. According to our HRT results, the mRNFL was most vulnerable in the temporal and temporal inferior segments of the optic disc. The same results were found in both studied groups. According to the authors, the most vulnerable segment was the nasal inferior, and the second most vulnerable segment was the temporal segment or superotemporal segment [20]. Similar results were published by Marjanovic et al. [21]. The most sensitive parameters in tracking HPG progression in our study were for the three parameters of global optic disc: rim volume, maximum cup depth and cup shape measure. The most sensitive parameters in tracking NPG progression in our study were four parameters of global optic disc: C/D ratio, cup volume, rim volume and cup shape measure. Similar results can be found in other authors [22–24]. According to Uchida et al. [25] the parameters that best defined the presence of glaucomatous damage were those which analyze the cup, followed by those that analyze the neuroretinal ring, and finally those that are dependent on RNFL measurements. The parameters with highest diagnostic value were cup shape measure and the C/D ratio [25]. Other studies show that the 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 glaucoma progression [24]. There seems to be great variability in the appearance and progression of initial glaucomatous optic disk and nerve fiber layer abnormalities in patients with glaucoma. Our study indicate that segmental as well as global analysis of optic disc images are required to detect a glaucomatous change, and suggest that HRT may be able to detect a change in the mRNFL in areas such as the temporal and inferotemporal segments, and also in a few global parameters in both studied groups, which may not be detected clinically.

Conclusion

Retinal nerve fiber layer progression in our study is mostly represented in the temporal and inferotemporal segments of the optic disc, and this applies to both high preasure glaucoma (HPG) and normal-pressure glaucoma (NPG) group. Considering the global parameters, the most frequently stricken in the HPG group were rim volume, maximum cup depth and cup shape measure, and in the NPG group C/D ratio, cup volume, rim volume and cup shape measure. Based on the baseline MRA results in both groups the most often clasified as damaged were the nasal segment, and the least often the temporaline. Thus, both segmental and global scanning are of importance in HPG and NPG progression analysis.

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