The role of confocal scanning laser ophthalmoscopy in stereometric differentiation of eye papilla in ocular hypertension, normal tension glaucoma and primary open-angle glaucoma

Uloga konfokalne skening laser oftalmoskopije u stereometrijskoj diferencijaciji očne papile kod okularne hipertenzije, normotenzivnog glaukoma i primarnog glaukoma otvorenog ugla

Ranko Gvozdenović*, Dušica Risović‡, Ivan Marjanović*†, Miroslav Stamenković‡, Zorica Joković*, Zihret Abazi‡

*Medical Faculty, University of Belgrade, Belgrade, Serbia; †Institute of Ophthalmology, Clinical Center of Serbia, University in Belgrade, Belgrade, Serbia; ‡Eye Clinic, Medical Center Zvezdara, University of Belgrade, Belgrade, Serbia

Abstract

Background/Aim. Primary open angle glaucoma (POAG) and normal tension glaucoma (NTG) demonstrate the same structural changes in the optic disc along with visual field defects but only POAG includes an abnormal elevation of intraocular pressure. Heidelberg retina tomograph based on confocal scanning laser ophthalmoscopy (HRT) and Moorfields regression analysis (MRA) have been employed to quantitatively assess the topography of eye papilla. We measured stereographic parameters of eye papilla in patients with POAG, NTG, and ocular hypertension (OH) using an HRT in order to determine whether HRT topographic parameters can be used to differentiate those conditions.

Methods. The results of 145 eyes of 145 patients with OH, NTG and POAG were analyzed by age, refractive error, quality of HRT images, stereometric and MRA parameters.

Results. Significant differences were found between NTG and other two groups for a majority of the HRT parameters, and also no differences between OH and POAG patients for a majority of the investigated parameters, except thickness of retinal nerve fiber layer. By reading the MRA no differences were found in the distribution of mostly damaged and mostly preserved neuroretinal rim sectors between NTG and POAG patients, and also all sectors of the neuroretinal rim in OH patients were preserved. Conclusion. HRT stereometric parameters are useful to differentiate patients with OH and NTG, and also for differentiation between NTG and POAG patients, but most of parameters showed no difference between OH and POAG patients. MRA may serve to confirm the diagnosis of OH, but not for precise distinction between NTG and POAG.

Key words: glaucoma; glaucoma, open-angle; ocular hypertension; diagnosis, differential; diagnostic techniques, ophthalmological.

Apstrakt

Uvod/Cilj. Primarni glaukom otvorenog ugla (POAG) i normotenzivni glaukom (NTG) pokazuju jednake strukturne promene u optičkom disku zajedno sa defektom vidnog polja, ali samo POAG podrazumeva abnormno pošten intraokularni pritisak. Heidelbergova retinalna tomografija (HRT) bazirana na konfokalnoj skening laser oštalo-moskopiji i Moorfields regresiona analiza (MRA) korišćeni su u našoj studiji za kvantitativnu procenu topografije očne papile. Primenom HRT mereni su stereometrijski parametri otičkih diskova bolesnika sa okularnom hipertenzijom (OH), NTG i POAG. Cilj rada bio je da se odredi prime-njivost HRT parametara u OH, NTG i POAG. Metode. Rezultati nalaza 145 očiju od 145 bolesnika sa OH, NTG i POAG analizirani su po starosti, refrakcionalnoj grešci, kvalitetu HRT fotografija i stereometrijskim parametrima. Rezultati. Utvrđena je statistički značajna razlika između bolesnika sa NTG i druge dve grupe bolesnika za većinu parametara, kao i odsustvo razlike između OH i POAG grupe za većinu parametara, izuzev za debljnu retinalnog sloja nervnih vlakana. Nalazi MRA pokazali su da nije bilo

Correspondence to: Ranko Gvozdenović, Desanke Maksimović 6, 22 000 Sremska Mitrovica, Serbia. Phone: +381 22 612 723. E-mail: Ranko2016@gmail.com
the study considering the one eye of each patient for each group was made in order 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. The NTG eyes included in this study were defined as those showing both glaucomatous optic disc changes and IOP never exceeded 21 mmHg on repeated measurements. Subsequently, the eyes enrolled as POAG group included those whose IOP exceeded 21 mmHg prior to or after initiation of therapy. The OH eyes included in this study were defined as those showing no glaucomatous optic disc changes and IOP exceeded 21 mmHg on repeated measurements. We used HRT II in our study for the collection of all necessary data.
By using HRT II we can get a series of photographs of the cross section of the optical nerve head of different deepness and after 3D reconstruction it produces topographical photographs of the papilla and peripapillar retina. To quantify morphometric rim and cup parameters in optic disc topography, a reference plane is defined. The reference plane is parallel to the retinal surface. It needs to be stable so that the parameters change only when true structural changes in the optic disc occur. Within the disc margin, the retinal surface located above the reference plane is defined as rim and below the reference level as cup.

In order to verify the quality of topographic images we used images with standard deviation less than 40 μm. Eight stereometric parameters were taken into consideration in this study: disc area (mm²), cup area (mm²), rim area (mm²), cup-to-disc area ratio (C/D ratio), cup volume (mm³), rim volume (mm³), cup shape measure (mm) and mean retinal nerve fiber layer (mRNFL) thickness (mm). Moorfields regression analysis (MRA), a program contained in the basic package of HRT device was used for comparison of the examined six sectors of neuroretinal rim (1. temporal, 2. supero-temporal, 3. infero-temporal, 4. nasal, 5. supero-nasal, and 6. infero-nasal) with a normative. It defines these sectors as damaged, borderline and normal based on the 95% and 99.9% confidence intervals.

The aim of this study was to find which group has larger damage (in percent) of the of the neuroretinal rim and which segment of the neuroretinal rim is the most frequently and the least frequently represented as the damaged for each group separately. Also, the aim of this study was to find if we can confirm by reading the MRA findings that the neuroretinal rim of OH patients is preserved.

By using SPSS version 20 we analysed the basic demographic characteristics (age, gender), also a refractive error and standard deviation of HRT images and examined eight morphometrical parameters of the optical disc in all three groups, with the aim to establish the existence of statistically significant difference between the same parameters in the groups (statistically significant difference is when \( p < 0.05 \)). We used methods of descriptive statistics, and an analytical statistical methods (t-test).

### Results

Basic statistics relating to sex, age, size of refractive error in patients eyes and standard deviation of topographic HRT images were shown in Table 1. Between all patients who met the entry criteria there were no significant differences in refractive error and standard deviation of topographic HRT images among the three groups. There was statistically significant differences in age between patients with OH and NTG, and patients with OH and POAG. Patients with OH were significantly younger than patients with NTG and POAG. A basic statistical summary of the results of the HRT parameter measurements was shown in Table 2. Examining the significance of differences among parameters between groups we found different values. The mean values of disc area (mm²) were significantly larger in NTG than in the other two groups. The NTG group also showed significantly the largest cup area (mm²), followed in order by POAG and OH group. On the other hand, the mean values of rim area (mm²) were significantly higher in OH than in NTG group. Rim area were not significantly different between OH and POAG patients, and also between NTG and POAG patients. Cup volume (mm³) were significantly higher in HTG than in other groups, and the same parameter were not significantly different between OH and POAG group. The mean values of rim volume (mm³) were significantly larger in OH than in NTG group, but there was no statistically significant differences between other groups in relation to this parameter. Further, the mean values of cup to disc area ratio were significantly larger in NTG eyes than in OH and POAG eyes, though at was not significantly different between OH and POAG group. The NTG patients showed the significantly larger values for cup shape measure (mm) compare to OH and POAG patients, and the same parameter were not significantly different between OH and POAG group. Last investigated parameter of optic disc was mean RNFL thickness (mm), and it was significantly larger in OH than in other two groups of patients. Mean RNFL thickness were not significantly different between NTG and POAG group (Table 2).

### Table 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>OH (n = 39)</th>
<th>NTG (n = 45)</th>
<th>POAG (n = 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disc area (mm²)</td>
<td>(1.638–3.226)</td>
<td>2.398²</td>
<td>(1.410–3.922)</td>
</tr>
<tr>
<td>Cup area (mm²)</td>
<td>(0.019–1.652)</td>
<td>0.587²</td>
<td>(0.099–3.354)</td>
</tr>
<tr>
<td>Rim area (mm²)</td>
<td>(0.891–2.572)</td>
<td>1.810²</td>
<td>(0.149–2.515)</td>
</tr>
<tr>
<td>Cup/disc area ratio</td>
<td>(0.053–0.650)</td>
<td>0.230²</td>
<td>(0.071–0.958)</td>
</tr>
<tr>
<td>Cup volume (mm³)</td>
<td>(0.004–0.691)</td>
<td>0.161²</td>
<td>(0.005–1.104)</td>
</tr>
<tr>
<td>Rim volume (mm³)</td>
<td>(0.118–0.967)</td>
<td>0.458²</td>
<td>(0.006–1.194)</td>
</tr>
<tr>
<td>Cup shape measure (mm)</td>
<td>(-0.079–0.305)</td>
<td>-0.195²</td>
<td>(-0.284–0.129)</td>
</tr>
<tr>
<td>Mean RNFL thickness (mm)</td>
<td>(0.080–0.396)</td>
<td>0.235³81</td>
<td>(0.019–0.527)</td>
</tr>
</tbody>
</table>

RNFL – retinal nerve fiber layer; \(^{\text{a1}}p < 0.05\) vs NTG; \(^{\text{a2}}p < 0.01\) vs NTG; \(^{\text{b1}}p < 0.05\) vs POAG; \(^{\text{b2}}p < 0.01\) vs POAG.

By the reading of MRA findings of all three groups, we found that the size of the damage of neuroretinal rim is higher in the NTG group (12.4 %), than in the group of the patients with POAG (6.5 %). We found that in group of the patients with POAG the segment which is most often classified as damaged was nasal, and the least often temporal, also in the group of the patients with NTG the segment the most often classified as damaged was nasal, and the least often temporal (Table 3). All six sectors of neuroretinal rim of each eye in the OH group were classified as normal.

**Discussion**

Since the development of the HRT, many reports have demonstrated its advantages for quantitative assessments of optic disc topography during diagnosis and follow-up of glaucoma patients. Several authors have made comparisons between the topographic parameters of optic discs among patients with glaucoma, individuals with OH, and normal controls. However, there are few reports of studies that have compared those parameters among OH, NTG, and POAG patients. In our study we did not find any HRT parameter which is significantly different among all three groups. In previous reports, disc area showed no significant difference among these disorders; however in our study the NTG patients have significantly largest disc area. In our study the NTG group also showed significantly larger disc area. We found that the size of the damage of neuroretinal rim is higher in the NTG group (12.4 %), than in the group of the patients with POAG (6.5 %). We found that in group of the patients with POAG the segment which is most often classified as damaged was nasal, and the least often temporal (Table 3). All six sectors of neuroretinal rim of each eye in the OH group were classified as normal.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Demaged sectors of neuroretinal rim (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>temporal</td>
</tr>
<tr>
<td>NTG (n = 45 eyes)</td>
<td>2</td>
</tr>
<tr>
<td>POAG (n = 61 eyes)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Conclusion**

Patients with NTG tend to have larger disc, larger cupping, smaller rims, and thinner RNFL as compared to POAG and OH patients. Patients with NTG also had a larger area of damage of the neuroretinal rim, compared to POAG. On the other hand, patients with OH were younger, and had largest rim area and largest cup shape measure. Looking at the size of the all tested parameters, the patients with POAG were positioned in the middle, with respect to all three groups. Thus, HRT topographic parameters are useful to differentiate patients with OH and NTG, and also for differentiation between NTG and POAG patients, but in most of them showed no difference between OH and POAG patients. Also, we can conclude that MRA may serve to confirm the diagnosis of OH, but not for precise distinction between NTG and POAG.

**References**

4. Tuulonen A, Lehtola J, Airaksinen PJ. Nerve fiber layer defects with normal visual fields. Do normal optic disc and normal


