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Evaluation of the significance of some diagnostic parameters in making an early diagnose of primary open-angle glaucoma

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Summary

Background:

The aim of this study was to evaluate diagnostic parameters and analysis of their advantages and limitations in early diagnostics of primary open-angle glaucoma (POAG). Cup/disc ratio (C/D), nerve fiber index (NFI) and mean deviation of retinal sensitivity (MD) were considered.

Material/Methods:

Fifty primary open-angle glaucoma patients (95 eyes), 67 primary open-angle glaucoma suspects (128 eyes), and 77 healthy subjects (148 eyes) underwent full ophthalmologic examination and also HRT, GDx and FDT examinations for determination of C/D, NFI, and MD parameters. Student's t test was used to confirm the statistical significance of the differences between the particular group pairs. Histograms of distribution of the occurrence frequency of the parameter values in the groups were plotted.

Results:

The mean values of C/D were 0.65 ± 0.11 , 0.58 ± 0.11 and 0.43 ± 0.11 , NFI 37.0 ± 22.7 , 18.5 ± 5.6 and 15.1 ± 4.8 and MD -3.00 ± 5.07 , -0.77 ± 2.49 and -0.29 ± 1.94 , respectively. Statistically significant differences between the particular groups were found. There was a partial overlapping of the histograms of distribution of the occurrence frequency of the parameter values.

Conclusions:

The basic diagnostic C/D NFI and MD parameters in primary open-angle glaucoma patients, primary open-angle glaucoma suspects and healthy subjects differed significantly. These parameters are important diagnostic tools in glaucoma diagnosis. A limitation of their applicability is related to a high scatter of the results and their overlapping in particular groups.

key words:

glaucoma • diagnostics • C/D • NFI • MD • standard deviation

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BACKGROUND

Primary open-angle glaucoma (POAG) is a group of chronic, slowly progressive neuropathies of the optic nerve, with distinctive defects in the visual field and morphological changes of the optic disc and of the retinal nerve fibre layer. According to Weinreb et al. [1–3] the course of neuropathy can be divided into 3 stages. The first stage, which is the beginning of the apoptosis of ganglion cells and of the retinal nerve fibre atrophy, is undetectable with available diagnostic methods. In the second stage, changes in the retinal nerve fibre layer thickness and initial changes in the visual field can be ascertained. Diagnosing POAG and initiating its treatment at this stage increases the chance of stopping the progression of the disease. In the third stage the glaucomatous changes in the optic nerve and nerve fibre layer are advanced and although this makes the detection easy, the chance for stopping the progress of the disease is low. The aforementioned reasons make it clear that early diagnosis and initiation of treatment are crucial.

No objective symptoms of POAG are notable until slowly growing defects in the visual field encompass central vision and the patient suddenly loses useful visual acuity. Therefore, an active quest for early features of optic disc glaucomatous damage during an ophthalmological examination is necessary. The recent decade saw a tremendous growth in the development of auxiliary examination techniques that facilitate precise evaluation of the optic disc, the nerve fibre layer and the retinal sensitivity. Currently, methods such as Heidelberg Retinal Tomography (HRT), laser scanning ophthalmoscopy, GDxVCC laser scanning polarimetry and FDT II perimetry are among the more commonly used.

The use of the HRT method allows obtaining a 3D morphological image and determining detailed diagnostic parameters of the optic disc [4], such as the cup/disc ratio (C/D). The GDx laser scanning polarimetry allows the evaluation of retinal nerve fibre layers' thickness in the peripapillary region, expressed as the nerve fibre index (NFI) [4]. The FDT enables the possibility of assessing the visual field and determining the retinal sensitivity mean deviation (MD) [5]. These parameters are widely used in the diagnostics of POAG.

The aim of this study was to evaluate diagnostic parameters (C/D, NFI, MD) and analyze their advantages and limitations in the early diagnostics of POAG.

MATERIAL AND METHODS

During the period 2007–2008, 194 patients (371 eyes) 30–65 years of age were recruited from the outpatient department of the Clinic of Ophthalmology, Medical Center of Postgraduate Education. Subjects were given prophylactic examination, refraction testing or testing for POAG. Tested subjects were divided into 3 groups. Group A consisted of 50 patients (95 eyes, average age 43.7 ± 9.0 years) with diagnosed POAG, confirmed by additional examinations. Group B had 67 POAG suspects (128 eyes, average age 43.2 ± 11.0 years) without glaucomatous visual field defects. Control group C included healthy subjects with normal results on examination for POAG (77 subjects, 148 eyes, average age 46.3 ± 10.9 years). Demographics of the examined subject groups are shown in Table 1.

Table 1. The studied population according to the sex and number of persons (number of eyes).

Group	Sex		Total
	Men	Women	
A	27 (51)	23 (44)	50 (95)
B	21 (40)	46 (88)	67 (128)
C	14 (27)	63 (121)	77 (148)
Total	62 (118)	132 (253)	194 (371)

Inclusion criteria for A group were specified in accordance with the guidelines of the European Glaucoma Society [1] and described in detail in previous publications [6,7]: age over 35 years, regular anterior chamber angle, glaucomatous damage of the optic nerve head, as well as abnormal results of GDx and visual field examinations. For inclusion to group B, glaucoma-suspicious appearance of optic head nerve and GDx results, but normal results of visual field examination, were adopted. The subjects included to group C did not show any glaucoma-related abnormalities. Exclusion criteria were: eye refraction error greater than 2 Dsph and media opacity, which lowers the quality of HRT and GDx results. Subjects with very small or very large optic disc area (less than 1.69 mm^2 or more than 2.82 mm^2) evaluated in HRT examination were also excluded.

Patients underwent detailed ophthalmological examinations and HRT (HRT II Heidelberg Engineering, Germany), GDx VCC (Laser Diagnostic Technologies, USA) and FDT (Humphrey Matrix, Zeiss, Germany) examinations, to determine standard diagnostic parameters. C/D ratio was determined as square root of surface ratio of cup-to-disc [8]. NFI was determined as the probability of glaucomatous damage of the retinal nerve fibre layer [9]. MD value was determined as the difference between retinal sensitivity in a healthy eye (taking age into consideration) and retinal sensitivity values measured in the examined subject in all examined points [10].

All the basic ophthalmological examinations were performed at the Clinic of Ophthalmology, Medical Center of Postgraduate Education in Warsaw while GDx, HRT and FDT examinations were performed at the Institute of Glaucoma and Eye Diseases in Warsaw. The study was approved by the Bioethics Commission of the Medical Center of Postgraduate Education in Warsaw (resolution of 2 March 2005 and of 30 January 2008). The tested subjects were informed about the study and agreed to participate.

The significance of differences between the particular group pairs was tested by using Student's t test. Histograms showing the frequency of occurrence of those parameters in individual groups were also drawn [11].

RESULTS

Results of the measurements of the nerve fibre layer thickness index (NFI), cup-to-disc ratio (C/D) and mean deviation of retinal sensitivity (MD) in POAG patients (group A), POAG suspects (group B) and in healthy subjects (group

Table 2. Results of the measurements of C/D, NFI and MD in particular groups.

	C/D	NFI	MD
Group A (glaucoma patients, 95 eyes)			
Mean value	0.65	37.0	−3.00
Standard deviation	0.11	22.7	5.07
Group B (glaucoma suspects, 128 eyes)			
Mean value	0.58	18.5	−0.77
Standard deviation	0.11	5.6	2.49
Group C (healthy subjects, 148 eyes)			
Mean value	0.43	15.1	−0.29
Standard deviation	0.11	4.8	1.94

Table 3. Student's t test values for comparison of mean NFI, C/D and MD values in particular group pairs.

Group	B	C
NFI		
A	8.97	11.50
B	-	5.40
C/D		
A	4.53	15.68
B		12.10
MD		
A	3.62	4.36
B		1.34

Critical values of the t test (177).

Compared groups	Total number of eyes	Critical value t (p=0.001)
A and B	223	3.34
A and C	243	3.339
B and C	276	3.338

C) are shown in Table 2. Results of the evaluation of the significance of differences between the group pairs of examined subjects are shown in Table 3. Histograms showing the frequency of occurrence of selected parameters (C/D, NFI and MD) in individual groups are shown in Figures 1–3.

DISCUSSION

The juxtaposition of the results of C/D ratio measurements shows, as expected [1,27,28], a great difference of the parameter's mean value ($p=0.001$) between healthy subjects (group C) and groups B (glaucoma suspects) and A (glaucoma

Figure 1. Distribution of the occurrence frequency of the C/D values in particular populations. **Figure 2.** Distribution of the occurrence frequency of the NFI values in particular populations.

patients). The difference is smallest between the mean values of the parameter in groups A and B, which makes evident the difficulties in differentiation between glaucoma patients and glaucoma suspects based on the evaluation of the optic disc. The results of our study are in agreement in particular with Jonas et al. [12] observations and confirm that linear C/D ratio is of great use in diagnosing primary open-angle glaucoma. Histograms showing the distribution of particular C/D values' frequency occurrence in individual groups (Figure 1) demonstrate partial overlapping of

Figure 3. Distribution of the occurrence frequency of the MD values in particular populations.

curves. However, their shift between the control group of healthy patients and the glaucoma patients group is clearly visible, which is evidenced by a high significance of mean values' differences in these groups (Table 3).

The results of measurements of the retinal nerve fibre layer thickness in the peripapillary region, shown in Table 2, expressed as a probability index of glaucomatous damage NFI, differ statistically significant between individual groups of tested subjects. The acquired results confirm previous observations of da Pozzo et al. [13], who have shown that the NFI is lower than 18 in healthy subjects and does not exceed 31 in glaucoma patients. The diagnostic value of the NFI has also been confirmed by Reus and Lemij [14], Zheng et al. [15] and Medeiros et al. [16]. According to the data collected in the GDx corporate materials [9], the glaucomatous damage probability index NFI below 30 defines this probability as low, NFI of 30–50 as suspicion of glaucoma, and NFI over 50 indicates an increased probability of glaucomatous damage to the retinal nerve fibre layer in the peripapillary region. Histograms showing the distribution of particular NFI values' frequency of occurrence in individual groups (Figure 2) demonstrate overlapping of curves to a larger degree than in the case of C/D parameter; however, their shift between the control group of healthy patients and the glaucoma patients group is also visible, which can be confirmed by the high significance of differences of the NFI mean values in these groups (Table 3). The high dispersion of the NFI indicator observed in primary open-angle glaucoma patients (from 11 to 98) limits its diagnostic usability, which is confirmed by results of other studies [17,18]. Therefore, the suggestion of Medeiros et al. [17] to improve the method of analysis and interpretation of the GDx examination due to a very high dispersion of measurement results, both in healthy subjects as well as in glaucoma patients, is understandable.

Results of the measurements of the mean defect of retinal sensitivity (MD), compiled in Table 2, show, according to the accepted criteria of primary open-angle glaucoma diagnosis [1], a statistically significant difference between the control group of healthy subjects (group C) and the glaucoma patients (group A), as well as between the glaucoma suspects (group B) and glaucoma patients (group A). No statistically significant difference has been observed between the healthy patients (group C) and glaucoma suspects (group B). This is connected with the criteria for selection of patients for

group B, in whom no significant change in the visual field has been observed. The mean value of MD parameter was -0.29 dB in the group of healthy patients and was close to the value given by Bowd et al. [19], who determined an MD value of -0.16 dB for an analogous group of healthy subjects. The mean value of the MD parameter in the group of glaucoma patients was -3.00 dB, which is also close to the values found in the literature. For an analogous group of glaucoma patients, Bowd et al. [19] determined an MD value of -3.8 dB, Boden et al. [20] an MD value of -2.9 dB, and Racette [21] an MD value of -3.69 dB. The cause of these slight discrepancies is probably a difference in the glaucoma stage in the examined subjects. According to the ESG guidelines [1], the MD index in a healthy person is 0 dB. The deterioration of the retinal sensitivity is connected with lowering of the MD value until reaching maximum values of the so-called perimetrically blind field (from -27 dB to -34 dB). Histograms showing the distribution of particular MD values' frequency of occurrence in individual groups (Figure 3) demonstrate clear overlapping of curves, proof of which can be seen in the high significance of differences of the MD mean values in these groups (Table 3). The high dispersion of the MD index in primary open-angle glaucoma patients (from -20 to $+4$) observed in the study indicates that it is necessary to use additional diagnostic parameters.

CONCLUSIONS

Mean values of the basic diagnostic parameters (C/D NFI and MD) in primary open-angle glaucoma patients, primary open-angle glaucoma suspects, and healthy subjects differed significantly. They are an important diagnostic tool in glaucoma diagnosis.

What limits the diagnostic value of these parameters is their wide span and overlapping in populations of primary open-angle glaucoma patients and healthy patients.

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