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Applicability of standard parameters in diagnostics of primary open-angle glaucoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to evaluate the sensitivity, specificity, and likelihood ratio of standard diagnostic parameters C/D, NFI, and MD and their applicability in diagnostics of primary open-angle glaucoma.

Material/Method: This study included 194 subjects (371 eyes), ages 30 to 65 years old, who underwent full ophthalmologic examination and HRT, GDx, and FDT examinations. The values of C/D, NFI, and MD diagnostic parameters were determined. The data were statistically evaluated to determine their sensitivity, specificity, and likelihood ratio.

Results: Values of the positive and negative likelihood ratios were C/D (11.471 and 0.159), NFI (3.739 and 0.152), and MD (6.323 and 0.309), respectively.

Conclusions: The C/D parameter showed the highest sensitivity and specificity, as well as high positive likelihood ratio and near-zero negative likelihood ratio. The NFI and MD parameters showed lower likelihood ratios and their applicability for the diagnosis of primary open-angle glaucoma is limited.

Key words: glaucoma • diagnostics • C/D • NFI • MD • sensitivity • specificity • likelihood

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Background

Contemporary diagnosis of primary open-angle glaucoma is based on evaluation of the optic disc, the neuroretinal rim, and the retinal nerve fiber layers with indirect stereoscopic examination of a dilated pupil using a slit-lamp and Volk lens. Currently, methods such as HRT laser scanning ophthalmoscopy, GDxVCC laser scanning polarimetry, and FDT perimetry [1] are among the more commonly used.

The HRT method uses a confocal laser scanning microscope that allows obtaining a 3D morphological image and determining detailed diagnostic parameters of the optic disc [2], including C/D ratio. The GDx laser scanning polarimetry is based on a measurement of the delay of polarized light components and allows the evaluation of retinal nerve fiber layer thickness in the peripapillary region and determining the NFI [2]. Evaluating the field of vision with the use of FDT enables assessment of retinal sensitivity and determination of its mean deviation [3].

Purpose: The aim of the study was to evaluate the applicability of C/D, NFI, and MD standard diagnostic parameters in diagnosis of primary open-angle glaucoma through determination of sensitivity, specificity, and likelihood ratios.

Material and Method

Our study included 194 patients (371 eyes) ages 30–65 years old who reported to the outpatients department of the Clinic of Ophthalmology at the Medical Center of Postgraduate Education in years 2007–2008 for prophylactic examination, glasses choice, or diagnosis towards primary open-angle glaucoma. These patients were divided into 3 groups. Group A consisted of 50 patients (95 eyes, average age of 43.7±9.0 years old) with diagnosed primary open-angle glaucoma, confirmed by additional examinations. Group B consisted of 67 primary open-angle patients with suspected glaucoma (128 eyes, average age of 43.2±11.0 years old) without distinctive glaucoma lesions in the field of vision. Group C was the control group and included healthy patients with normal results of examination for primary open-angle glaucoma (77 patients, 148 eyes, average age of 46.3±10.9 years old). Detailed characteristics of the examined population have been shown in previous publications [4,5].

All the patients underwent full ophthalmologic examination and then were examined with HRT laser scanning ophthalmoscopy, GDxVCC laser scanning polarimetry, and FDT field of vision examination on Humphrey Matrix perimeter. Standard diagnostic parameters were determined. C/D ratio was determined as the square root of the surface ratio of cup to disc [6]. NFI was determined as the probability of glaucomatous damage to the retinal nerve fiber layer [7]. 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 patient in all examined points [8].

All the basic ophthalmological examinations were performed in the Clinic of Ophthalmology at the Medical Center of Postgraduate Education in Warsaw. GDx, HRT, and FDT examinations were performed in 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). Although no invasive examination methods were used, patients were informed of the aim and course of the study and gave consent to participate in it.

Criteria for qualification of patients were specified in accordance with the guidelines of the European Glaucoma Society [1], described in detail in previous publications [4,5]. Exclusion criteria were: eye refraction error greater than 2 Dsph and media opacity, which lowers the quality of HRT and GDx results, and patients with very small or very large surface of the optic disc (less than 1.69 mm^2 or more than 2.82 mm^2) evaluated in HRT examination.

Computer-stored measurement data matrix (MS Excel spread sheet) was used for statistical analysis [9]. The significance of differences between mean values of measured parameters in all groups was measured with the t test. Sensitivity and specificity of these parameters and likelihood ratio (LR) in relation to glaucoma patients were determined. Mean values of these parameters determined in patients with suspected glaucoma (group B) were accepted as cut-off values for calculations. Sensitivity of the method was designated as the proportion of glaucoma patients correctly detected as a result of the analysis performed, and specificity as the proportion of healthy patients correctly detected as a result of the analysis. Likelihood ratio of the method was calculated from the value of its sensitivity and specificity. If positive LR is greater than 10 and negative LR is less than 0.1, the method may be used to confirm a diagnosis, but when positive LR values are from 5 to 10 and negative LR values are from 0.1 to 0.2, the method can still be considered as a useful diagnostic device.

Results

Results of the measurements of the nerve fiber layer thickness index (NFI), cup-to-disc ratio (C/D), and mean deviation (MD) of retinal sensitivity in patients with primary open-angle glaucoma (group A), patients with suspected primary open-angle glaucoma (group B), and in healthy patients (group C) are shown in Table 1.

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Table 1. Results of measurements of NFI, C/D and MD of retinal sensitivity in groups A, B and C.

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

Table 2. Juxtaposition of sensitivity values, specificity parameters, C/D, NFI and MD parameters and value of their likelihood ratio.

Result of analysis		A Group	C Group	Total
		C/D		
Positive		81	11	92
Negative		14	137	151
Total		95	148	243
Sensitivity		0.853		
Specificity			0.926	
Likelihood ratio	(+)			**11.472**
	(–)			**0.159**
		NFI		
Positive		84	35	119
Negative		11	113	124
Total		95	148	243
Sensitivity		0.884		
Specificity			0.764	
Likelihood ratio	(+)			**3.739**
	(–)			**0.152**
		MD		
Positive		69	17	86
Negative		26	131	157
Total		95	148	243
Sensitivity		0.726		
Specificity			0.885	
Likelihood ratio	(+)			**6.323**
	(–)			**0.309**

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Calculated values of sensitivity and specificity of individual diagnostic parameters and their likelihood ratio values are shown in Table 2.

Discussion

We found statistically significant differences between individual groups of the examined population in results of the C/D, NFI, and MD measurements (Table 1). The mean value of C/D ration in Group A (glaucoma patients) was 0.65±–0.11 *vs.* 0.43±–0.11 in Group C (healthy control patients). These results acquired are consistent with those of Jonas et al. [10] and confirm that linear C/D ratio is of great use in diagnosing primary open-angle glaucoma. The mean value of NFI in primary open-angle glaucoma patients was 37.0±22.7 *vs.* 15.1±–4.8 in healthy patients. This is consistent with the observations of da Pozzo et al. [11], who have shown that the NFI is lower than 18 in healthy patients and does not exceed 31 in glaucoma patients. The mean value of MD in primary open-angle glaucoma patients was –3.00±5.07 dB and –0.29±–1.94 dB in healthy controls. Bowd et al. [12] determined the MD value of –0.16 dB for an analogous group of healthy patients and –3.8 dB for primary open-angle glaucoma patients.

The analysis of sensitivity and specificity values of the standard diagnostic parameters C/D, NFI and MD and their likelihood ratio value (Table 2) shows that the parameters with the greatest sensitivity and specificity are the C/D ratio (85.3% and 92.6%) and NFI (88.4% and 76.4%). Much lower values were obtained for the MD parameter (72.6 and 88.5). The positive likelihood ratio for C/D parameter was 11.5 and the negative likelihood ratio was 0.16. In the case of NFI and MD parameters, the positive likelihood ratios were 3.74 and 6.32, respectively, and the negative ratios 0.15 and 0.31, respectively. The very high positive likelihood ratio obtained for the C/D parameter (greater than 10) and near-zero likelihood ratio means that confirmation of glaucomatous damage to the optic disc can be obtained through measurement of this parameter. Although the measurement of NFI and MD can reveal certain useful information, it is of lesser diagnostic value.

Conclusions

The C/D parameter showed the highest sensitivity and specificity, as well as high positive likelihood ratio and near-zero negative likelihood ratio. The NFI and MD parameters showed lower likelihood ratios and their applicability for the diagnosis of primary open-angle glaucoma is limited.

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