Diagnostic accuracy of the parameters from ganglion cell complex map, evaluated with SD-OCT in primary open-angle glaucoma

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ABSTRACT

Purpose: To evaluate the sensitivity and specificity of ganglion cell complex (GCC) parameters, obtained with optical coherence tomography (OCT) and to determine their role in diagnosis of primary open-angle glaucoma patients.

Materials and methods: The study included 84 eyes of patients with primary open-angle glaucoma (POAG) and 40 eyes of healthy individuals. All of them underwent complete eye examination, including standard automated perimetry (HFA II) and OCT (RTVue-100). Avg. GCC (average GCC), Sup. GCC (superior GCC), Inf. GCC (inferior GCC), GLV (global loss volume), FLV (focal loss volume) and RNFL (retinal nerve fiber layer — ONH map) were measured. ROC curves were created and sensitivity and specificity were calculated for each of these parameters.

Results: The highest sensitivity and specificity was found for GLV and the lowest for Sup. GCC. The area under the ROC curves (AUC) for GLV was found to be the largest and the smallest for Sup. GCC.

Conclusion: Parameters from GCC map have high sensitivity and specificity. Their diagnostic capability is similar, even slightly better than RNFL. GLV has the highest diagnostic accuracy for primary open-angle glaucoma detection in this study.

Keywords: ganglion cell complex, optical coherence tomography, primary open-angle glaucoma.

Financial Disclosure: None of the authors have a financial or property interest in any materials or methods mentioned. There is no conflict of interests

INTRODUCTION

In the recent years a main focus of research in the field of glaucoma has been the achievement of more precise methods of early diagnosis. The aim of the development of new methods and technologies for detection and monitoring of this disease is to optimize the diagnosis maximizing accessibility and reliability, even for non-glaucoma specialists.

Today optical coherence tomography (OCT) is a widely used and proven imaging modality for evaluation of glaucoma in daily practice. This imaging method gives not only qualitative assessment but also quantitative assessment of these changes. Structural changes in the optic nerve head (ONH), the retinal nerve fiber layer (RNFL) and ganglion cell layer (GCC) in the macular region are now routinely diagnosed with OCT.

A large part of the ganglion cells are located in the macula and this is the reason for detailed examination of the macular region in glaucoma [1, 2]. The monitoring of the macular changes in glaucoma with OCT has changed and progressed in the last 10-15 years, especially with the advent of spectral domain OCT (SD-OCT). Time domain OCT (TD-OCT), also offers the possibility of full macular thickness measurement and some investigations determine its diagnostic accuracy to be good but lower than that for RNFL and ONH [3, 4]. The reason is that TD-OCT with its lower resolution limits the precise segmentation of the retinal layers. We know that in the outer retinal layers no glaucoma changes can be observed [5]. The layers that become thinner are the inner three retinal layers (GCC), which include the dendrites, the bodies and the axons of the ganglion cells. This is why the evaluation of full macular thickness appears to have lower diagnostic accuracy than measuring only GCC [4, 6, 7]. Ganglion cell complex changes

Table. 1. Descriptive statistics.

Parameter	N	Mean	SD
MD	84	−9.33	7.35
PSD	84	6.66	3.38
Avg. GCC	84	75.45	8.25
Sup. GCC	84	77.02	10.35
Inf. GCC	84	73.04	12.07
FLV	84	8.02	3.23
GLV	84	21.46	7.50
Avg. RNFL	84	77.38	12.50
Sup. RNFL	84	77.23	13.28
Inf. RNFL	84	77.53	13.92

Table 2. Sensitivity, specificity and diagnostic ability for GCC parameters.

Parameter	Sensitivity (%)	Specificity (%)	AUC
Avg. GCC	97.50	95.23	0.997
Sup. GCC	92.50	90.48	0.975
Inf. GCC	97.50	95.24	0.990
FLV	98.80	97.50	0.992
GLV	100.00	97.50	1.000

Fig. 1. Two protocols: GCC map и ONH map.

have started to be routinely examined in ophthalmic practice only after the development and wide application of SD-OCT.

Many investigations find high diagnostic accuracy of GCC, comparable to that of RNFL [8, 9]. Others show that evaluating macular changes in glaucoma is very important and valuable, particularly in cases with early and pre-perimetric glaucoma [10, 11]. On the contrary, some studies demonstrate that the diagnostic ability of GCC to be not as high and focus on the weaker diagnostic potential of this parameter.

PURPOSE

The purpose of this study is to evaluate the sensitivity and specificity of ganglion cell complex (GCC) parameters, obtained with optical coherence tomography (OCT) and to determine their role in the diagnosis of primary open-angle glaucoma (POAG) patients.

Materials and methods

In the study we enrolled 84 eyes of POAG patients and 40 eyes of healthy individuals. All underwent complete eye examination, standard automated perimetry (HFA II), contact ultrasound pachymetry (OcuScan RxP, Alcon) and optical coherence tomography (RTVue-100). The inclusion criteria were — primary open-angle glaucoma with perimetric changes; visual acuity above 0.2 and high-quality
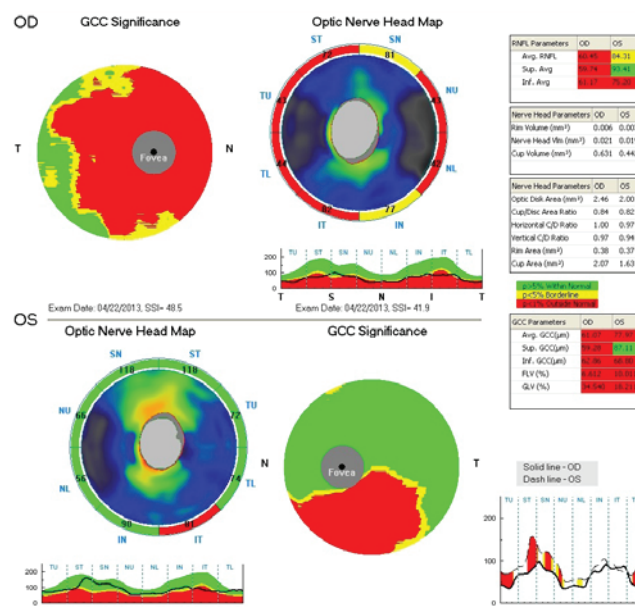
imaging. The exclusion criteria for the selection of patients were — age under 40 and over in 85 years old; best corrected visual acuity under 0.2; spherical equivalent of refractive disorders above +3.00 dpt or below –5.00 dpt. From the study were excluded patients with angle closure glaucoma, non-glaucomatous optic neuropathies, diabetic retinopathy, macular pathology, and previous ocular surgery, different from cataract extraction.

We used an optical coherence tomography (RT-Vue-100), a SD-OCT model with axial resolution of 5 μm, speed 26000 A-scans/sec and wavelength 840 nm.

The protocol for GCC measures the thickness of the inner three layers of the retina in the macular region. It was developed for diagnosis of glaucoma, takes 0.6 sec, covers 15000 points, and includes 15 vertical line scans (A-scans) and one horizontal, which cover area of 7 mm² with center 1 mm temporal from the fovea. The parameters from the GCC map are — Avg. GCC (average GCC thickness for the whole area); Sup. GCC (average GCC thickness for the superior half of the area); Inf. GCC (average GCC thickness for the inferior half of the area); FLV (focal loss volume measures the average amount of statistical significant loss of volume over the entire GCC map in %); GLV (global loss volume measures the average amount of GCC thickness loss over the entire GCC map in %) (Fig. 1).

The protocol for ONH was created for the evaluation RNFL and also ONH. The tomograph makes 13 circular scans around the optic disc with diameter from 1.3 to 4.9 mm and after analysis a RNFL map is constructed. After that 12 radial scans are made with 3.7 mm length to determine the boundaries of optic disk and its structural parameters. This program automatically determines the center of the ONH and its borders, using data from three-dimensional image of optic disk (3 D-disk reference).

Table 3. Comparison of the results between GCC and RNFL.

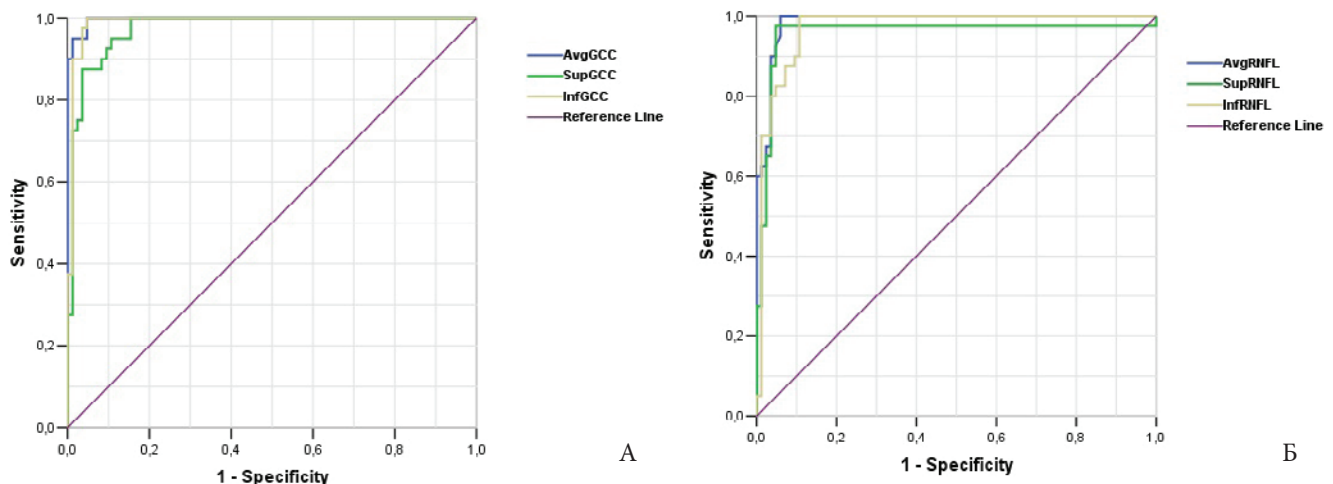| Parameter	Sensitivity (%)	Specificity (%)	AUC	AUC	Sensitivity (%)	Specificity (%)	Parameter
Avg. GCC	97.50	95.23	0.997	0.985	94.05	97.50	Avg. RNFL
Sup. GCC	92.50	90.48	0.975	0.956	95.24	97.50	Sup. RNFL
Inf. GCC	97.50	95.24	0.990	0.971	90.48	90.00	Inf. RNFL

Fig. 2. A) ROC curves for Avg. GCC, Sup. GCC and Inf. GCC; B) ROC curves for Avg. RNFL, Sup. RNFL and Inf. RNFL.

Data processing was made with the software package SPSS 16.0. The results were expressed as arithmetic mean±standard deviation. For each parameter the correlation with MD was evaluated. The sensitivity and specificity were calculated and ROC curves were built for each parameter from the GCC and RNFL map by determining the area under the operating curve (AUC).

RESULTS

Ganglion cell complex and retinal nerve fiber layer were measured successively with two different protocols of RTVue-100 — GCC и ONH map (RNFL), on one and the same day. Table 1 shows the mean values and the standard deviation of the parameters from the two maps.

The parameters of GCC map were found to have high sensitivity and specificity (above 90%), which highlighted their very high diagnostic accuracy for glaucoma (Table 2). The highest AUC had GLV, and the lowest — Sup. GCC.

Additionally, we determined the sensitivity, specificity and diagnostic accuracy of retinal nerve fiber layer (Avg. RNFL, Sup. RNFL and Inf. RNFL). From the results, presented in Table 3, it was obvious that the two areas of the fundus have comparable diagnostic accuracy for glaucoma, and the ROC curves illustrate this as well (Fig. 2).

DISCUSSION

In the clinical practice, the diagnosis of glaucoma with standard methods is often controversial and unreliable. Sometimes, only when progression is certain and obvious we can be sure that the patient has glaucoma. A large number of patients remain in the group «glaucoma suspects» for many years with various changes in treatment strategy during this time. From this suffers not only the patient, but also the confidence in the physician.

The opportunities that OCT provides for the early diagnosis and monitoring of patients with glaucoma not only progress with time, but also enhance the information that we obtain in terms of diagnostic accuracy and the objective analysis of the results.

Following the successful application of OCT for the evaluation of the changes in the peripapillary RNFL in glaucoma (1995), ideas began to form for its use in diagnosing this disease through examination of the macular area [12]. The pioneer studies in this field from 1998 revealed that in glaucoma the full macular thickness was reduced by a third. The evaluation of the macular volume with TD-OCT has shown it to be slightly diminished in patients with glaucoma and that this correlates directly with the severity of the disease [2]. Several studies were searching for the relationship between structural changes in the entire macular thickness and changes in peripheral vision. They found a good correlation between the macular thickness and the MD (Mean Deviation), and a good correspondence between structural defects in the macula and paracentral scotomas in the visual field [1, 13].

Many other similar studies have shown the potential of analyzing the changes in macular thickness for the diagnosis of glaucoma [1, 3, 4]. They were performed with the TD-OCT device, which has a reduced potential for segmentation of the retinal layers. It measures only the full mac-

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ular thickness and many studies have pointed out the diagnostic ability of this parameter (AUC about 0.80) to be lower than RNFL's one (AUC about 0.94) [3, 4]. A different study, performed later with TD-OCT had similar results — macular thickness (with AUC 0.85) had lower diagnostic potential than RNFL (AUC 0.92). After that, the same authors did a study with SD-OCT, which measured only the GCC (AUC 0.90) and found better performance, compared to RNFL (AUC 0.92) [12, 13]. Other authors also reached similar conclusions [8, 9, 14]. The reason, as noted, is that in glaucoma not all retinal layers, respectively macular layers, are decreased in thickness but only the inner, where the ganglion cells are located [5].

The results from our study do not differ from the most published reports on this subject. We also found very similar diagnostic ability between GCC and RNFL. The highest AUC in this study was found for GLV, which indicates the outstanding diagnostic potential of this parameter. According to some studies, the early glaucoma changes often appear first on the GCC map, and at a later stage can be identified in the RNFL. A similar study among glaucoma patients at different stages of disease determined the GCC and GLV as parameters for the detection of preperimetric structural changes [11, 15]. Paracentral scotomas near the fixation point are typical for the early normal tension glaucoma and in such cases the GCC demonstrates better diagnostic capabilities than the RNFL. With the progression of glaucomatous changes, the correlation between the two parameters become equal [9].

Presently, it is debatable in which cases the structural parameters (from GCC, RNFL and ONH map) have the highest diagnostic ability and whether their reproducibility allows glaucoma monitoring. The accuracy of interpretation of results in patients with macular pathology, myopia, peripapillary atrophy, tilted discs, and abnormal size of the ONH is still controversial. The impact of concomitant ocular pathology on their diagnostic potential as well as their application in monitoring childhood glaucoma and preperimetric glaucoma is a subject of future research.

CONCLUSION

In this study, we analyzed the diagnostic accuracy of the parameters from the GCC map and compared them with RNFL. Very high sensitivity and specificity were found for all the GCC parameters, equal with RNFL. Evaluation of these parameters, combined with evaluation of ONH and the functional changes in the visual field present us a comprehensive and thorough assessment of glaucoma patient' status.

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