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Evaluation of peripapillary retinal nerve fiber layer thickness in patients with primary open-angle glaucoma

Евалуација дебљине перипапиларног слоја ретиналних нервних влакана код пацијената са примарним глаукомом отвореног угла

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SUMMARY

Introduction/Objective Determination of the difference in peripapillary retinal nerve fiber layer (RNFL) thickness in patients with open-angle glaucoma (POAG) in comparison to the healthy population and according to the progression of the disease.

Methods Four groups were formed among 120 patients: group without glaucoma, early, moderate POAG and preperimetric glaucoma group. Visual field and optical coherent tomography were performed.

Results RNFL thickness value was found to be the highest in inferior quadrant, second highest in superior, third in nasal, the lowest in temporal quadrant. The highest average value of RNFL thickness was in superior quadrant of the healthy group (124.3 ± 17.8μm), and the lowest was in temporal quadrant of the moderate group (46.5 ± 10.8μm). Other RNFL thickness values per quadrants among groups were distributed between these two endpoints. AvgThic in patients with moderate POAG was lesser than in patients with early POAG, which was lesser than in the healthy subjects (59.6 ± 10.6μm *vs.* 73.4 ± 12.1μm *vs.* 105.5 ± 11.3μm). AvgThic in preperimetric glaucoma group was 83.6 ± 9.2μm. Pearson correlation showed high positive correlation between MD values and following parameters: AvgThic, S, I, Smax, Imax, Savg, Iavg. ROC curves found that the parameter with the best diagnostic ability was AvgThic, with area of 0.803(< 0.0005), sensitivity of 67% and specificity of 83.3%.

Conclusion Peripapillary RNFL thickness parameters: AvgThic, S, I, Smax, Savg, Iavg, Imax have excellent ability to discriminate between healthy eyes and eyes with POAG. The parameter with the highest specificity and sensitivity is AvgThic, which makes it the best for early detection and monitoring of POAG.

Keywords: retinal nerve fiber layer; primary open-angle glaucoma; optical coherent tomography; AvgThic

САЖЕТАК

Увод/Циљ Циљ је био одредити разлику у дебљини перипапиларног слоја ретиналних нервних влакна (СРНВ) код пацијената са примарним глаукомом отвореног угла (ПГОУ) у поређењу са здравом популацијом, и према прогресији болести.

Методе Свих 120 пацијената су подељени у четири групе: пацијенати без глаукома, са почетним, са средње узнапредовалим и са препериметријским глаукомом. Комплетан офталмолошки преглед, видно поље и оптичка кохерентна томографија су урађени код сваког пацијента.

Резултати Дебљина СРНВ је највећа у доњем квадранту, мања у супериорном, још мања у назалном, најмања у темпоралном квадранту. Највећа просечна дебљина СРНВ била је у горњем квадранту у групи здравих (124,3 ± 17,8 микрона), а најмања у темпоралном квадранту групе са средње узнапредовалим глаукомом (46,5 ± 10,8 микрона). Остале вредности дебљине СРНВ по квадрантима распоређене су између ове две крајње тачке. Параметар средња дебљина код пацијената са средње узнапредовалим глаукомом био је мањи него у групи са почетним, који је био мањи него код групе здравих испитаника (59,6 ± 10,6 према 73,4 ± 12,1 према 105,5 ± 11,3 микрона). Параметар средња дебљина у препериметријској групи је 83,6 ± 9,2 микрона. Пеарсонова анализа показала је високу позитивну корелацију глобалних индекса видног поља и параметара: средња дебљина, супериорне и инфериорне максималне и средње вредности. Упоређивањем РОК крива, параметар са најбољом дијагностичком способношћу је средња дебљина, са површином од 0,803, осетљивошцћу 67% и специфичношћу 83,3%.

Закључак Параметри дебљине перипапиларе СРНВ: средња дебљина, супериорне и инфериорне максималне и средње вредности имају одличну способност разликовања здравих пацијената од оних са ПГОУ-а. Параметар са највећом специфичношћу и осетљивошћу је средња дебљина, те је најбољи за рано откривање и праћење ПГОУ-а.

Кључне речи: слој ретиналних нервних влакана; примарни глауком отвореног угла; оптичка кохерентна томографија; средња дебљина нервних влакана

INTRODUCTION

Primary open-angle glaucoma (POAG) represents a chronic, progressive and irreversible multifactorial optic neuropathy. It is characterized by cupping of the optic disc, visual field defects, open anterior chamber angle and, in the majority of cases, increased intraocular pressure (IOP). The progressive loss of retinal ganglion cells is the most important characteristic of POAG and it can be quantified by measuring the thickness of peripapillary retinal nerve fiber layer (RNFL) [1, 2].

During the 1970s, Hoyt et al. pointed out the importance of evaluation of RNFL thickness in the diagnosis of glaucoma [3], and along with other researchers showed that the thinning of peripapillary RNFL could even precede the visual field defects as the first sign of glaucoma pathology [4, 5]. Optical coherence tomography (OCT), as a highly objective and reproducible imaging method, was developed at MIT (Massachusetts Institute of Technology) by David Huang et al. in 1991. It represents a non-invasive, non-contact, trans-pupillary method for scanning the retinal structures layer by layer and it is used to analyze different retinal diseases [6]. OCT produces images of high resolution and is able to identify diffuse and focal RNFL defects that occur in glaucoma [7]. Numerous studies have shown that OCT measurement of peripapillary RNFL thickness and macular zone thickness is an excellent method for the diagnosis of glaucoma. However, RNFL thickness has shown itself as a better indicator in glaucoma evaluation [8, 9]. The purpose of this study was to determine the difference in peripapillary RNFL thickness in patients with preperimetric glaucoma and open-angle glaucoma (POAG) in comparison to the healthy population, as well as to determine the difference in thickness of peripapillary RNFL according to the progression of the disease. By accurately determining these differences, we wanted to define the ability of every RNFL thickness parameter in early detection and monitoring of patients with POAG.

METHODS

This research was a prospective and observational type of study. Based on the inclusion criteria, patients were included in the study and they underwent a complete ophthalmologic examination, visual field analysis and optical coherence tomography of the peripapillary RNFL.

One hundred and twenty patients over the age of 18 were included in this study. Pathology of only one eye of the patient was analysed. In cases where both eyes of the patient met the inclusion criteria, the eye included in the study was randomly selected. Based on the clinical findings, four groups were formed with the specified inclusion criteria:

Group 1 (control-healthy group): 30 patients without glaucoma or other eye conditions, with best corrected visual acuity ≥ 0.9, intraocular pressure (IOP) between 10 mmHg and 21 mmHg, normal cup-to-disc ratio (C/D) and normal visual field finding, regardless of gender, race and ethnic background.

Group 2 (early glaucoma group): 30 patients with POAG, with characteristic defects of the optic disc and RNFL, with a mean deviation (MD) lower than -2dB and higher than -6dB in standardized automated perimetry (Hodap classification), with characteristic glaucomatous visual field defects, without other eye conditions, without anamnestic data about previous laser or surgical intervention on the examined eye, with best corrected visual acuity ≥ 0.5, regardless of gender, race and ethnic background.

Group 3 (moderate glaucoma group): 30 patients with POAG, with characteristic defects of the optic disc and RNFL, with a mean deviation (MD) lower than -6dB and higher than -12dB in standardized automated perimetry (Hodap classification), without other eye conditions, without anamnestic data about previous laser or surgical interventions on the examined eye, with best corrected visual acuity ≥ 0.5, regardless of gender, race and ethnic background.

Group 4 (preperimetric glaucoma group): 30 patients with characteristic changes in the optic nerve head that represent glaucoma neuropathy, without functional outbreaks. The standard automated perimetry shows normal values of MD (from -2dB to +2.0dB), with the best corrected visual acuity ≥ 0.9, regardless of the IOP.

Visual field was performed on the Humphrey Visual Field Analyser (Carl Zeiss Meditec-Humphrey Systems, Dublin, CA), using the Threshold C24-2 testing protocol by SITA-FAST strategy. A reliable VF test was defined as one with less than 20% fixation loss, and false-positive and false-negative rates of less than 33%. We used two of VF global indices, Mean Deviation (MD) and Pattern Standard Deviation (PSD) in this study. The VF test was obtained within 4 weeks before the OCT scans.

All peripapillary RNFL thickness measurements were done on the Stratus OCT 3000, Carl Zeiss Meditec apparatus, honouring the fast-scanning protocol for optical disc and peripapillary RNFL. Afterwards, an automatic analysis was applied using the previously implemented software version (3.0 Stratus OCT analysis software). OCT measurements were made along a circle concentric with the optic disc at a radius of 1.73 mm, using a scanning mode that samples 512 data points (RNFLThickness 3.4 acquisition protocol). Maximum two scans of the peripapillary zone were used (with 3 consecutive scans), provided that the quality of the scan was equal or higher than 7. For data analysis, we chose the better one of the two scan

The study protocol was approved by the institutional Ethics Committee.

In our research descriptive statistics were used: arithmetic mean, standard deviation, median, quartiles, frequencies, and percentages. Means comparison analysis of paired parameters between the groups was evaluated by one-way ANOVA including the Levene's homogeneity of variance test. Post-Hoc adjustment for multiple comparisons was performed by the Games-Howell method, if variances in groups were not equal, and by the Tukey's honest significant difference test, when variances in groups were equal. Connection between RNFL thickness and visual field parameters was characterized by bivariate correlation analysis computing the Pearson correlation coefficients. The Pearson correlation coefficients with absolute values ≥ 0.5 suggesting a strong association with $p < 0.01$ were accepted as statistically significant. Receiver Operating Characteristic (ROC) curves were used to describe the accuracy of each OCT parameter to differentiate glaucoma from the healthy group. The diagnostic sensitivity and specificity were examined with the area under ROC curve (AUC). The results were analyzed using the SPSS for Windows software, Version 11.5 (SPSS, Chicago, II, USA) and relations were considered significant if p value was < 0.05.

RESULTS

The demographic characteristics of the patients enrolled in the study are presented in Table 1. The four study groups were homogeneous in the number, but not in the gender of subjects. There was a predominance of female patients in Groups 1, 2 and 4, while in the Group 3 there were more male than female patients (57% *vs.* 43%). Overall, there were 73 (60.83%) female and 47 (39.17%) male patients, with an average age of 55.9 ± 13.7 years.

According to the age analysis, the youngest group of patients was Group 1 with the average of 50.7 ± 12.7 years and the oldest group was Group 3 with average of 64.1 ± 10.1 years.

The distribution of the patients according to the age group is shown in Figure1.

The majority of the patients belonged in the 50-59 years age-group, 36 (30%), followed by 60-69 years, 33 (26.6%), while the smallest number, 7 (6.6%), belonged to the group of under 30 years of age. In the eldest group (70+ years of age) there were 17 (14%) patients.

The mean values of visual field parameters (MD, PSD) and RNFL quadrant thickness for each study group are presented in Table 2.

The results of the RNFL thickness distribution by quadrants showed the highest values in the healthy group, followed by the preperimetric group, early POAG group, and the moderate POAG group. The highest average value of RNFL thickness was in the upper quadrant of the healthy group (124.3 ± 17.8 μm), and the lowest average value of RNFL thickness was in the temporal quadrant of the moderate POAG group (46.5 ± 10.8 μm). Other RNFL thickness values per quadrants are distributed between these two endpoints.

The mean values for all parameters of RNFL thickness and statistical differences for each study group are presented in Table 3.

For the parameters: Max-Min, Smax, Imax, Savg, Iavg, and AvgThic the highest average values are in the healthy group, slightly lower in the preperimetric group, even lower in the early glaucoma group and the lowest values are in the moderate glaucoma group. All these parameters show very high statistically significant differences between the groups (p< 0,001).

Since AvgThic is the most commonly used parameter, its mean value for the Group 1 was 105.5 ± 11.3 μm, for the Group 4 was 83.6 ± 9.2 μm, for the Group 2 was 73.4 ± 12.1 μm, for the Group 3 was 59.6 ± 10.6 μm and represents the parameter with the highest statistical significance of differences between the groups.

The relationships between VF global indices and RNFL thickness parameters were evaluated by the Pearson correlation analysis for all groups and presented in Table 4.

It was found that there is a high positive correlation between the MD values and the following RNFL thickness parameters: AvgThic, S, I, Smax, Imax, Savg, Iavg. A low positive correlation between the MD values and Max-Min parameter was demonstrated. Other parameters do not show statistical significant correlation, and their change during MD value change is not significant. This statistical analysis showed that the RNFL parameters that have a high statistical correlation with MD values among different groups are parameters that change with glaucoma progression, but they are also parameters that occur at the outset of POAG even in preperimetric phase of disease. The AvgThic parameter has the highest statistical significance relations with MD values ($p < 0.0005$).

The Receiver Operating Characteristic (ROC) curves area for parameters were calculated to discriminate glaucomatous from healthy eyes. The surfaces determined by ROC curves, cut-off, sensitivity and specificity and p-values for each individual parameter are displayed in Table 5.

By comparing the surface area under the ROC curve, it can be concluded that the parameter which has the best diagnostic ability is AvgThic, with area under the ROC curve of 0.803 (< 0.0005), the sensitivity of 67% and the specificity of 83.3%. The following parameters are S and Iavg with the same surface area under the ROC curve of 0.736 (< 0.002). For the parameter S, the sensitivity was 63.3% and the specificity was 73.3%, while for the parameter Iavg sensitivity was 73.3% and the specificity 73.3%. For the parameter I, the surface area of the curve was 0.733 ($p = 0.002$), the sensitivity 70% and the specificity 73.3% (Figure 2). ROC curve shows that parameter T has pure ability to discriminate glaucomatous from healthy eyes.

DISCUSSION

Even though gender is not considered as a risk factor for POAG, Framigham, Barbados, Blue Mountains and other studies have shown that a greater number of males than females suffer from POAG [9,10]. Analysis of the gender structure of our 120 study participants shows that the majority of participants were females (60.8%). Only the moderate POAG group had more males (56.6%). However, if we look only at the patients with early and moderate POAG, there is an equal number of males and females. The average age in the whole sample was 55.9 ± 13.7 years. The eldest group was the moderate POAG group with an average of 64.1 ± 10.1 years.

Analysis of the mean values of the MD visual field parameter showed a statistically significant decrease from the healthy, through the preperimetric and early glaucoma group to the moderate POAG group. Testing of differences between MD and PSD values among study groups, ANOVA and Post-Hoc analysis showed that there was a statistically significant difference between the groups 1,2 and 3 ($p < 0.001$) except between the healthy and the preperimetric group ($p = 0.384$) which suggests that these groups cannot be distinguished according to the parameters of the visual field but this can be done using OCT analysis. The investigation of Li et al. [10] as well as some other researchers [11-13] have shown a high correlation between MD values and the stage of POAG.

The mean value of RNFL thickness for the healthy group in our study was 105.5 ± 11.3 μm, which was the highest value compared to other groups. The lowest value of RNFL thickness was in the moderate POAG group (59.6 ± 10.6 μm). RNFL thickness value decreases with the progression of POAG, which was confirmed by the statistical analysis of the AvgThic parameter differences between groups ($p < 0.0005$). Scientific studies of Patel et al [9]. and Sihota et al. [11] have shown similar values of RNFL thicknesses for healthy populations, varying between 90-128 μm, and they also found that thickness of RNFL in patients with POAG and preperimetric glaucoma are statistically significantly lower compared to the healthy population.

The results obtained by OCT measuring of RNFL thickness per quadrants showed the same distribution in all study groups. RNFL thickness value was found to be the highest in the inferior quadrant, second highest in the superior quadrant, third in the nasal quadrant, while it was the lowest in the temporal quadrant. Taking into account all values the greatest RNFL thickness was found in the healthy group and the lowest in the moderate POAG group**.** Research by Aydogan et al. [12] has shown that the average RNFL thickness in healthy individuals is 112.7 ± 8.7 µm, for temporal quadrant 82.3 ± 9.6 µm, for superior 139.9 ± 18.0 µm, for nasal 83.0 ± 10.6 µm and for inferior quadrant 145.9 ± 14.6 µm. Patel et al. [9] have published that the thinning of RNFL by quadrants follows the progression of glaucomatous disease. The high congruence between the results of our research and other researchers [9-12], both in average values and quadrant thickness distribution, confirms the applicability of the ISNT rule in all stages of glaucoma.

Stefanova et al.[13] reported that both inferior and superior RNFL quadrants are the specific glaucomatous sites for early POAG damage, which was also confirmed by the study of Singh et al.[14] analysing OCT finding among the healthy group of 50 subjects and 55 patients with early POAG. In the study that involved 98 healthy individuals, 285 patients with ocular hypertension, and 66 patients with glaucoma, Mayoral et al. [15] have found that the RNFL thickness across quadrants decrease from healthy, over OHT patients to POAG patients. This means that as the disease progresses the RNFL thickness decreases by quadrants.

Detection of an early stage glaucoma was confirmed by the study of Komaratih et al. [11], as well as Li et al. [10] who recommended that the best parameter for recognition of an early POAG is AvgThic parameter. Yalvac et al. [16] conducted an interesting study of patients with ocular hypertension using Stratus OCT. Patients were divided into three groups: at low, medium, and high risk of developing POAG. The best parameters for differentiating the risk level of glaucoma developement were Iavg and Imax. Thereby, they emphasized the lower part of the RNFL as the site of pathological knockout and the place where the earliest POAG occurs. Guedes et al. [17] studied the ability of early detection of glaucoma by the OCT apparatus. They compared the changes that occur in the thickness of the macular zone and the peripapillary RNFL zone and concluded that in the competition of numerous parameters, the average thickness of RNFL is far the best at detecing patients with early glaucoma. They hinted that there are almost 100% ganglia retinal cells in the peripapillary zone, and in the macular zone their number is about 50%, and the parameters of the thickness of RNFL are better for determining glaucoma than the parameters of the macular region. The area of ROC curve for AvgThic was 0.93 in the above-mentioned study, which was higher than the results obtained in our study (0.803). Our study showed that quadrant S has the highest, quadrants I and N high ability, for discrimination between the healthy and preperimetric glaucoma patients.

ROC curves were calculated and constructed to discriminate healthy from glaucomatous eyes. A study by Stagg and Medeiros [18] showed the areas under the ROC curves for discriminating POAG from normal eyes were 0.89 for global RNFL and 0.75 for global MRW ($p = 0.006$). Similarly, according to this study, the best parameter of the RNFL thickness group is AvgThic with a largest area under the ROC curve 0.803, cut-off value of 63.9, sensitivity of 67%, and specificity of 83.3%. Hsieh et al. [19] reported that the largest area below the ROC curve were with: AvgThic, quadrant I and quadrant S. Singh et al. [14] also confirmed that the surface of the ROC curve is the largest for AvgThic and quadrant S parameter (Area = 0.963, Area = 0.943), and a slightly smaller area in the case of quadrant I, but with high values of sensitivity of 89% and specificity of 81%. These results are almost the same as results in our study which has underlined the importance of parameter Avg Thic, S, Smax, I and Iavg for the earliest possible diagnosis of glaucoma.

CONCLUSION

In summary, peripapilary RNFL thickness parameters: AvgThic, S, I, Smax, Savg, Iavg and Imax have excellent ability to discriminate between healthy eyes and eyes with POAG. However, the parameter with the highest specificity and sensitivity is the parameter AvgThic, which makes it the best for early glaucoma detection and monitoring of POAG. Finally, the determination of thickness of peripapillary RNFL in patients with POAG using optical coherence tomography represents the method which distinguishes between patients with POAG, preperimetric glaucoma and healthy population hence it can be used in glaucoma diagnostics and follow-up. We believe the current high precision and reliability of OCT parameters can be even better, and perhaps the answer lays in future studies of related influences of OCT parameters through mathematical models.

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A part of this work can be found at the researchsquare platform as a preprint.

Conflicts of interest: None declared.

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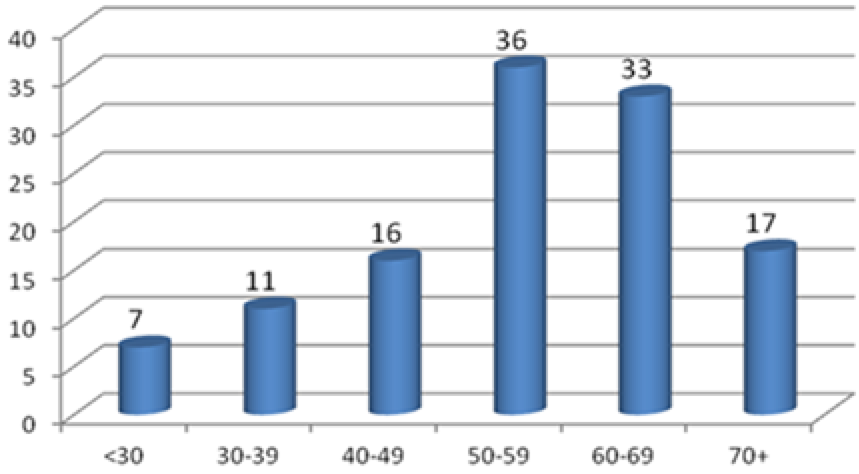

Figure 1. Graphical presentation of the patients according to age groups

Figure 2. Receiver operating characteristic curves for the retinal nerve fiber layer thickness parameters

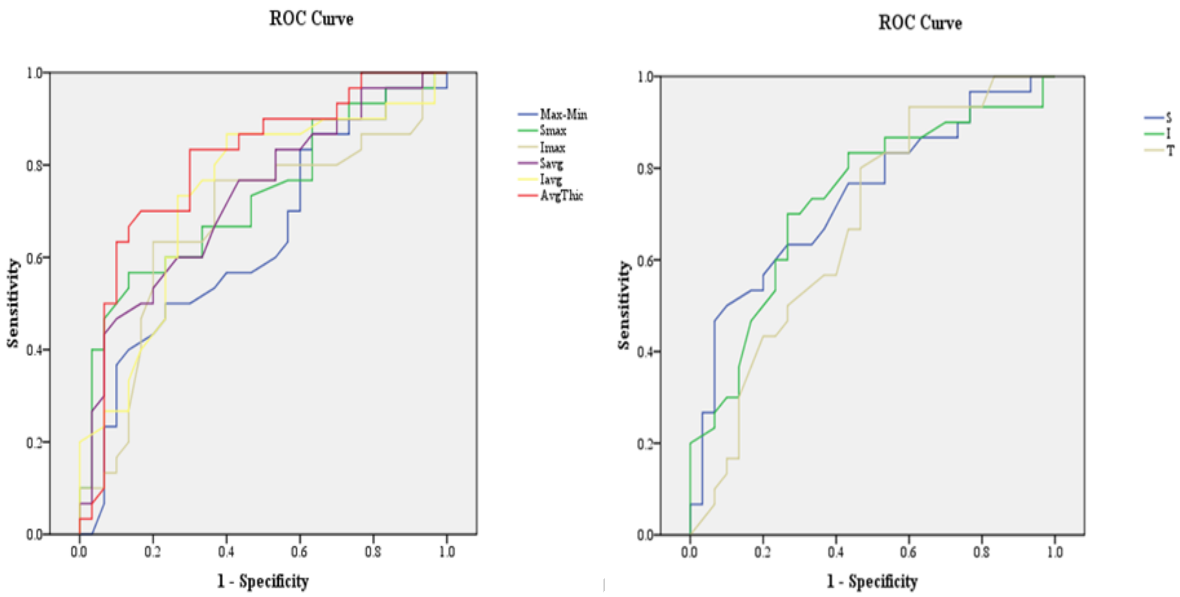

Table 1. Demographic characteristics of the patients

Group		1	2	3	4	Σ
No. of patients		30	30	30	30	120
Sex	Male	8 (26.6%)	13 (43.3%)	17 (56.6%)	9 (30%)	47 (39.1%)
	Female	22 (73.3%)	17 (56.6%)	13 (43.3%)	21 (70%)	73 (60.8%)
Age		50.7 ± 12.7	60.1 ± 13.1	64.1 ± 10.1	51.8 ± 9.5	55.9 ± 13.7

Table 2. Differences in mean values of mean deviation, pattern standard deviation, and retinal nerve fiber layer quadrants thickness

Parameters	Group 1	Group 2	Group 3	Group 4	p1	p2	p3
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD			
MD	-0.29 ± 0.70	-4.18 ± 1.27	-9.89 ± 1.74	-0.80 ± 1.01	< 0.001	< 0.001	0.027
PSD	1.40 ± 0.53	4.34 ± 1.72	9.08 ± 2.02	1.92 ± 0.76	< 0.001	< 0.001	0.002
S	124.3 ± 17.8	84.6 ± 18.4	68.9 ± 19.5	91.6 ± 14.2	< 0.001	< 0.001	< 0.001
N	90.5 ± 22.5	62.7 ± 15.4	54.5 ± 16.8	59.8 ± 19.5	< 0.001	< 0.001	< 0.001
I	133.4 ± 15.3	87.2 ± 22.4	69.2 ± 23.9	113.8 ± 19.1	< 0.001	< 0.001	< 0.001
T	73.73 ± 13.71	55.90 ± 16.12	46.50 ± 10.85	70.63 ± 20.52	< 0.001	< 0.001	0.494

p1– p-value between Groups 1 and 2;

p2 – p-value between Groups 1 and 3;

p3 – p-value between Groups 1 and 4

Table 3. Differences in mean values of RNFL thickness parameters

Parameters	Group 1	Group 2	Group 3	Group 4	p1	p2	p3
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD			
Imax/Smax	1.1 ± 0.1	1 ± 0.32	1.1 ± 0.5	1.2 ± 0.2	0.234	0.084	0.02
Smax/Imax	0.9 ± 0.1	1.1 ± 0.4	1.2 ± 0.6	0.8 ± 0.2	0.258	0.034	0.088
Smax/Tavg	2.2 ± 0.4	2.2 ± 0.74	2.1 ± 0.7	1.9 ± 0.5	0.836	0.196	0.008
Imax/Tavg	2.3 ± 0.3	2.1 ± 0.62	2.1 ± 0.8	2.3 ± 0.6	0.102	0.105	0.85
Smax/Navg	1.8 ± 0.4	1.9 ± 0.62	1.8 ± 0.6	2.4 ± 1.1	0.756	0.941	0.057
Max-Min	128.3 ± 15.1	96.6 ± 25.1	83.3 ± 25.7	121.1 ± 19.3	< 0.001	< 0.001	0.111
Smax	160.1 ± 17.2	117.2 ± 25.1	94.1 ± 28.6	128.5 ± 21.7	< 0.001	< 0.001	< 0.001
Imax	169.8 ± 14.5	113.0 ± 25.7	95.1 ± 29.7	150.1 ± 22.1	< 0.001	< 0.001	< 0.001
Savg	124.3 ± 17.8	84.1 ± 17.7	68.7 ± 18.8	92.1 ± 15.5	< 0.001	< 0.001	< 0.001
Iavg	135.6 ± 18.1	87 ± 21.7	69.5 ± 23.5	113.0 ± 17.7	< 0.001	< 0.001	< 0.001
AvgThic	105.5 ± 11.3	73.4 ± 12.1	59.6 ± 10.6	83.6 ± 9.2	< 0.001	< 0.001	< 0.001

p1– p-value between Groups 1 and 2;

p2 – p-value between Groups 1 and 3;

p3 – p-value between Groups 1 and 4

Table 4. Pearson correlation testing between Groups 2 and 3, 1 and 4 in relation to the retinal nerve fiber layer thickness parameters

Parameters	**S**	**N**	**I**	**T**	**Imax/ Smax**	**Smax/ Imax**	**Smax/ Tavg**	**Imax/ Tavg**	**Smax/ Navg**	**Max–Min**	**Smax**	**Imax**	**Savg**	**Iavg**	**Avg. Thic.**
Pearson corr. (2–3)	0.418	0.207	0.421	0.397	-0.093	-0.086	0.071	0.021	0.106	0.276	0.422	0.348	0.432	0.406	0.571
p	0.001	0.112	0.001	0.002	0.482	0.515	0.591	0.873	0.421	0.033	0.001	0.006	0.001	0.001	0.0005
Pearson corr. (1–4)	0.717	0.595	0.498	0.09	-0.303	0.223	0.238	0.025	-0.314	0.208	0.633	0.472	0.698	0.539	0.734
p	0.001	0.001	0.001	0.494	0.019	0.087	0.067	0.85	0.015	0.111	0.001	0.001	0.001	0.001	0.0005

Table 5. Receiver operating characteristic curves, cut-off, sensitivity, and specificity

Parameters	Surface area	Cut-off	Sensitivity (%)	Specificity (%)	p
S	0.736	75	63.3	73.3	0.002
I	0.733	76	70	73.3	0.002
T	0.676	54	80	53.3	0.019
Max–Min	0.637	/	/	/	0.069
Smax	0.727	102.5	60	76.7	0.002
Imax	0.678	96	63.3	80	0.018
Savg	0.728	75	60	73.3	0.002
Iavg	0.736	76.5	73.3	73.3	0.002
AvgThic	0.803	63.9	70	83.3	< 0.0005

