Evaluation of morphometric and shape parameters of optic nerve disk in norm and glaucoma based on optical coherence tomography

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Introduction. Morphometrics is a branch of morphology that represents the study of size and shape components of biological form and their variation in the population based on statistical analysis [1]. A considerable amount of work has been published examining the optic nerve disc (OND) size-related parameters and their physiological and pathological associations, however, relatively little information is available describing shape features of OND and their variations in a general population [1]. Assessment of OND, including neuroretinal rim (NRR) and the cup, is one of the most crucial elements in diagnosing and monitoring blindness-related disorders, e.g., glaucoma [2].

The aim of this study was to evaluate morphometric parameters and the shape of OND in a control group, i.e., eyes with no sign of any optic nerve disease, and in a case group, i.e., eyes diagnosed with primary open angle glaucoma (POAG). Data were obtained by optical coherence tomography (OCT), sorted into following groups and analyzed statistically: (1) the control and POAG group, (2) the control and POAG group in four different age ranges, (3) the control and POAG group in female and male genders, (4) the control and POAG group according to a size of OND area, i.e., a small, a medium and a large, (5) the control and POAG group according to an ocular axial length (AL), i.e., a short, a medium and a long. The goal of the work was to identify how age, gender, OND area size and AL affects changes of morphometric parameters and the shape of OND in the control and POAG groups in order to facilitate the solution of glaucoma detection and management.

Materials and Methods. An analysis of an analytical observation case-control study was performed by incorporating tools from geometry, biometrics and computer graphics. The research was conducted in accordance with guidelines of Declaration of Helsinki. The control group comprised 1000 healthy eyes of participants; 45 – 74 years old men and women residing in Kaunas city who were randomly selected. The case group comprised 412 eyes of 45 – 74 years old men and women with POAG residing in Kaunas city. POAG was characterized by an intraocular pressure higher than 21 mm Hg (by a Schiotz tonometer) at diagnosis, the OND glaucomatous structural changes were described and typical glaucomatous visual field defects were approved by two standard automated visual field tests.

OCT of OND was performed by Stratus OCT, a computer-assisted optical instrument, that generates cross sectional 2-dimensional (2D) images (tomograms) of OND with axial and transverse resolutions of 10 μm and 20 μm, respectively. OCT provides cross-sectional images of tissue structure on the micron scale *in situ* and in real time [3]. Similar results could be achieved by the conventional histopathology, which requires removal of a tissue specimen and processing for microscopic examination, but not in real time. Therefore, OCT is like a type of optical biopsy and is a powerful imaging technology for medical diagnostics [3] with high axial resolution, automated outlining of OND margin, and a consistent and stable reference plane for delineation of the NRR boundary [2].

The obtained results of OCT individual radial scan analysis and optic nerve head analysis of the control and POAG groups were divided into four age groups: younger than 60 years old (276 eyes in the control group and 112 eyes in POAG group), between 60 – 65 years (198 and 76), 66 – 70 years (158 and 86), and older than 70 years (368 and 136). Also the data of the control and POAG groups were divided into male (382 and 116) and female (618 and 296) groups. Different OND sizes were considered: the small disk area size was less than 1.5 mm^2 (40 and 13); the medium disk area size was between 1.5 - 2 mm^2 (337 and 114), and the large disk area was considered to be larger than 2 mm^2 (592 and 257). Also different ALs were analyzed; based on the literature review, the range of the average normal AL was considered to be 22.5÷24.5 mm (642 and 237), the short AL was less than 22.5 mm (269 and 109), and the long AL was longer than 24.5 mm (84 and 47).

The obtained data were expressed as mean values with standard deviations (M±SD) in the text. A comparison between and within the control and POAG groups were done by parametric Student t and nonparametric Mann-Whitney-Wilcoxon tests based on the distribution pattern of the data. Analysis of variance (ANOVA) was used to find whether or not the means of several groups were equal. Differences in categorical variables were determined by Post-hoc test analysis. All statistical analysis was performed using the Statistical Package for Social Sciences (SPSS Inc., Ill, version 13 for Windows) and Microsoft Office Excel. Statistical significance was defined as a p value less than 0.05.

Results. Area sizes of OND parameters of different study groups were summarized in Table 1. The statistical significance between and within the data were calculated as p values. The 2D structural visualization of shapes of OND and the cup areas of the control and POAG group was illustrated in Fig.1.

Discussion and Conclusions. Based on OCT, OND and the cup mean areas were significantly larger in POAG group and NRR mean area was significantly larger in the control group. OND mean area in both study groups and NRR also the cup mean areas in the control group were independent of age. But NRR mean area significantly decreased and the cup mean area significantly increased with age in POAG group. OND mean area of the male was

significantly larger in the control group while OND mean area of the female was significantly larger in the POAG group and between the study groups.

Table 1. Areas of OND parameters of different study groups.

OND parameters (mm^2)	Mean (±SD) Control group	p* within control group	Mean (±SD) POAG group	p** within POAG group	p between control and POAG
Optic disk area size	2.14±0.39		2.19±0.43		0.02
in age group <60 years	2.10±0.4	0.2	2.15±0.41	0.3*,**, 0.2***, 0.9****-******	0.3
in age group 60-65 years	2.15±0.35		2.21±0.52		0.3
in age group 66-70 years	2.12±0.37		2.21±0.43		0.1
in age group >70 years	2.16±0.42		2.21±0.41		0.2
in male gender group	2.17±0.38	0.03	2.11±0.40	0.02	0.2
in female gender group	2.11±0.40		2.22±0.44		<0.001
in eyes with short AL	2.20±0.40	0.04*, <0.001** <0.001**	2.16±0.36	0.06*, 0.008**, <0.001***	0.4
in eyes with medium AL	2.14±0.37		2.26±0.44		<0.001
in eyes with long AL	1.86±0.43		1.97±0.49		0.2
NRR area size	1.60±0.38		1.33±0.41		<0.001
in age group <60 years	1.58±0.31	0.4	1.43±0.37	0.05*, 0.04**, 0.02***, 0.9****-******	<0.001
in age group 60-65 years	1.64±0.53		1.31±0.44		<0.001
in age group 66-70 years	1.59±0.33		1.30±0.48		<0.001
in age group >70 years	1.60±0.36		1.30±0.37		<0.001
in male group	1.60±0.36	0.8	1.29±0.43	0.2	<0.001
in female group	1.60±0.40		1.35±0.40		<0.001
in eyes with small OND	1.18±0.24	<0.001	1.14±0.27	0.1-0.7	0.7
in eyes with medium OND	1.48±0.26		1.33±0.31		<0.001
in eyes with large OND	1.69±0.36		1.35±0.45		<0.001
in eyes with short AL	1.71±0.39	0.001*, ** **	1.44±0.40	0.01*, <0.001**, 0.01***	<0.001
in eyes with medium AL	1.59±0.36		1.32±0.42		<0.001
in eyes with long AL	1.34±0.4		1.16±0.36		0.01
Cup area size	0.55±0.41		0.86±0.58		<0.001
in age group <60 years	0.52±0.37	0.3	0.72±0.48	0.01*, 0.03**, 0.01***, 0.8****-*****, 0.9******	<0.001
in age group 60-65 years	0.54±0.41		0.93±0.65		<0.001
in age group 66-70 years	0.52±0.38		0.91±0.64		<0.001
in age group >70 years	0.58±0.46		0.91±0.55		<0.001
in male group	0.58±0.41	0.1	0.82±0.53	0.4	<0.001
in female group	0.53±0.41		0.87±0.60		<0.001
in eyes with small OND	0.21±0.18	0.05*, <0.001**, ***	0.16±0.25	0.03*, <0.001**, ***	0.4
in eyes with medium OND	0.33±0.26		0.46±0.30		<0.001
in eyes with large OND	0.69±0.43		1.10±0.55		<0.001
in eyes with short AL	0.52±0.43	0.1*, 0.9**, 0.5***	0.72±0.51	0.001*, 0.4**, 0.1***	<0.001
in eyes with medium AL	0.56±0.40		0.94±0.6		<0.001
in eyes with long AL	0.53±0.47		0.81±0.56		0.003

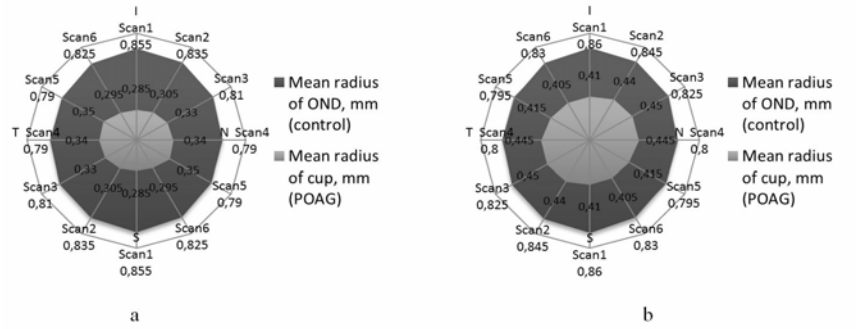

Fig. 1. Visualization of the shapes of OND of the control (a) and POAG (b) groups

There were significant linear correlations between OND mean area and the cup, NRR mean areas, but the cup mean area and NRR mean area of the small disks had no significant difference between the control and POAG groups. The cup mean area did not depended on AL, but the longer was the AL, the significantly smaller were OND mean area and NRR mean area in the control and POAG groups.

Based on OCT, the vertically oval OND was of irregular shape, it was vertically-oblique in the control and POAG groups. The cup shape was horizontally-oblique in the control group and had the more vertically-oblique shape in the POAG group. The diameters (the scans 1-6 of OCT) and the shape of the OND and the cup had no significant dependence on the age and on the gender in both research groups. The structural 2D OND shape was more correctly oval of the small disk in the control group and more vertically oval of the small disk in the POAG group. The shape of OND of the medium and the large disks did not differ significantly between the study groups. There was no significant statistical difference of the cup diameters and the shape between the control and POAG groups when the OND area was small. In the future, structural 3D models for OND analysis could be developed.

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An evaluation of optic nerve disk morphology and size is essential in diagnosis and management of visual impairments, for example glaucoma. A considerable amount of work has been published examining the optic nerve disc size-related parameters and their physiological and pathological associations, however, relatively little information is available describing shape features of the optic nerve disk and their variations in a general population. We applied an optical coherence tomography in order to evaluate morphometric parameters and the shape and their possible changes of the optic nerve disk in a control and primary open angle glaucoma groups. Areas and shapes of the optic nerve disk, a rim and a cup were analyzed. Based on OCT the vertically oval OND had irregular shape, it was vertically-oblique in the control and the glaucoma groups. The cup shape was horizontally-oblique in the control group and had the more vertically-oblique shape in the glaucoma group.