Evaluation of the Retinal Nerve Fiber Layer and Ganglion Cell Analysis Measurements in Healthy Individuals with Large Physiological Cupping

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ABSTRACT

Purpose: To determine the retinal nerve fiber layer thickness (RNFLT) and macular ganglion cell analysis (mGCA) of healthy individuals with large physiological cupping.

Materials and Methods: This cross-sectionally designed study was managed in a single-centered eye clinic. Eyes with large physiological cupping were defined as group 1 with cup to disc ratio (CDR) >0.3. The second group was defined as those CDR £0.3. The mGCA and RNFLT measurements were obtained by spectral-domain optical coherence tomography (SD-OCT).

Results: The mean age of 43 patients (23 women, 20 men) with large physiological cupping was 34.6 ± 15.3 years and 44 patients (25 women, 19 men) with normal cupping was 33.27 ± 14.75 years. The central macular thickness (CMT) values were similar between two groups (p=0.1). The average and three quadrant measurements of RNFL showed significant difference between two groups, except nasal quadrant. However, the average and five quadrant measurements of GCA showed similar results between two groups, except inferotemporal quadrant. While the correlation analysis determined significantly negative correlation between CDR and mean and three quadrants of RNFLT, there was no correlation between CDR and mean and any quadrants of GCA.

Conclusion: As a result the measurements of macular GCA should be thought more valuable parameter than peripapillary RNFLT to evaluate the pathological processes.

Keywords: Large physiological cupping, Ganglion cell analysis, Retinal nerve fiber layer, Optical coherence tomography, Optic nerve.

INTRODUCTION

The optic disc, consist of retinal ganglion cell (RGC) axons, exits from the globe through the lamina cribrosa and separate into the optic cup and the neuroretinal rim[1,2]. The optic cup is a central depression of the optic disc without any axons, and the neuroretinal rim, composed of RGCs, neuroglia, astrocytes, and capillaries, is the tissue between the optic cup and optic disc magrin[1]. The excavation of the optic cup can be seen in glaucoma or as a physiological condition without glaucoma. The term of physiologic large cupping was first introduced by Jonas et al[3]. Previous studies demonstrated the measurements of retinal nerve fiber layer thickness (RNFLT) as a useful parameter to differentiate physiological and pathological processes[4,5,6].

In this current study, we aimed to show whether or not the measurements of the macular ganglion cell analysis (GCA) are more valuable parameter than peripapillary RNFLT to evaluate the pathological conditions of optic nerve and large physiological cupping.

MATERIALS AND METHODS

This cross-sectionally designed study was approved by the Ethics Committee and informed consent was obtained from all participants according to Declaration of Helsinki.

Patients: Eighty-six eyes of 43 healthy individuals with large cupping were defined as group 1 (with cup to disc ratio (CDR) > 0.3) and 88 eyes of 44 age and sex matched healthy individuals with minimal optic disc excavation were defined as group 2 (with CDR £ 0.3). The group classification have done according to the ratio of cup area

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Received: 08.02.2021
Accepted: 12.11.2021

Glo-Kat 2022; 17: 33-36

DOİ: 10.37844/glauc.cat.2022.17.6

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to disc area obtained by spectral-domain optic coherence tomography (SD-OCT). The cup area has been calculated by subtracting the neuroretinal rim area from the disc area. All participants had a detailed ophthalmic examination including best-corrected visual acuity (BCVA), intraocular pressure (IOP, mmHg) measured by applanation tonometry, anterior segment and fundus examination using slit-lamp biomicroscopy, visual field analysis using the Humphrey Field Analyzer (Carl Zeiss Meditec, Jena, Germany) and OCT measurements by using SD-OCT (CIRRUS Spectral Domain OCT; Carl Zeiss Meditec, version 6.0 software). The patients with visual field defects, high intraocular pressure (more than 21mmHg), history of ocular disease or previous ocular surgery were thought as presumed glaucoma and not included in this study.

OCT Measurement Protocol

The central macular thickness (CMT), RNFLT, GCA and CDR measurements were obtained by using SD-OCT after pupil dilation with 0.5% tropicamide. A single macular scan (200 × 200 macular cube scan protocol) and macular GCA of each eye was recorded. The GCA algorithm automatically segmented and calculated the thickness of the macular GCL and inner-plexiform layer (IPL) within a 14.13 mm^2 elliptical annulus area centered on the fovea. The mean and six quadrants of (superotemporal, superior, superonasal, inferonasal, inferior, and inferotemporal) GCA and the mean and four quadrants of (superior, nasal, inferior, temporal) peripapillary RNFLT values were measured, and the mean/ median/ mean rank values were used in the statistical analyses. All of the included SD-OCT scans had a signal strength of at least six.

Statistical Analysis

All statistical analyses were performed using the SPSS software version 21.0 (IBM Corp., Armonk, NY, USA). Continous variables were described as mean ± standard deviation. The variables were investigated by Kolmogorov-Smirnov and Shapiro-Wilk tests to determine whether they were normally distributed. The normally distributed variables were analized with the independent samples t-test and not-normally distributed variables were analized with Mann Whitney U test and Spearman correlation tests. A p-value of less than 0.05 was considered as the statistical significance. A five percent type-I error level was used to infer statistical significance.

RESULTS

The mean age of the individuals (23 women, 20 men) was 34.6 ± 15.3 years (range 10 and 59) in group 1 and that of group 2 (25 women, 19 men) was 33.27 ± 14.75 years (range 11 and 58). The mean BCVA values in both groups were 20/20. The mean IOP value of the group 1 (12,56 ± 2,15 mmHg) was similar to the second group (12,40 ± 2,24 mmHg) (p=0.62 Independent T test). The mean spherical (-0.03 ± 0.88 D and -0.18 ± 1.12 D) and cylindrical measurements (-0.05 ± 0.36 D and -0.00 ± 0.12 D) were similar between two groups (p=0.17, p=0.45 Mann Whitney U test). There was not any significantly difference in mean deviation (MD) and pattern standard deviation (PSD) values between two groups (p=0.65, p=0.36, respectively Mann Whitney U test).

The mean CMT of the group 1 was similar to the second group (246.55 ± 22.73mm and 245.85 ± 18.19mm respectively, p=0.1 Mann Whitney U test). The mean and four quadrants (superior, nasal, inferior, temporal) of peripapillary RNFLT values are represented in table 1.

The mean and six quadrants (superior, temporal inferior, temporal superior, inferior, nasal inferior, nasal superior) of the macular GCA measurements are demonstrated and compared between two groups in table 2.

Table 1. *Comparison of the mean and four quadrants of peripapillary RNFLT values of the eyes in both groups.*

Peripapillary RNFLT Measurements (mm)*	Group 1 (n=86)	Group 2 (n=88)	P**
Average	93.00	99.00	**0.001**
Superior quadrant	118.00	125.50	**0.019**
Nasal quadrant	72.00	72.00	0.28
İnferior quadrant	119.00	130.50	**<0.001**
Temporal quadrant	63.00	66.00	**0.003**

*Median values, **Statistical analysis was calculated by Mann-Whitney U test, RNFLT: Retinal Nerve Fiber Layer Thickness

Table 2: *Comparison of the mean and six quadrants of macular GCA values of the eyes in both groups.*

Ganglion cell analysis (mm)	Group 1	Group 2	P**
GCA Average	83.50	84.00	0.40
GCA_S	84.50	85.00	0.93
GCA_Ti	82.50	86.00	**0.03**
GCA_Ts	82.00	83.50	0.35
GCA_I	82.00	85.00	0.09
GCA_Ni	84.00	85.00	0.35
GCA_Ns	85.00	85.00	0.82

*Mean Rank values, **Statistical analysis was calculated by Mann-Whitney U test, GCA: Ganglion cell analysis, GCA_S: Ganglion cell analysis in superior, GCA_Ti: Ganglion cell analysis in temporal-inferior GCA_Ts: Ganglion cell analysis in temporal-superior, GCA_I: Ganglion cell analysis in inferior, GCA_Ni: Ganglion cell analysis in nasal-inferior, GCA_Ns: Ganglion cell analysis in nasal-superior.

In the correlation analysis, the CDR showed statistically significant negative correlation with the neuroretinal rim thickness and mean and three quadrants of the peripapillary RNFLT except nasal quadrant and only with inferotemporal quadrant of macular GCLT (Table 3).

Table 3: *The correlation between CDR and SD-OCT parameters.*

Correlation with	Rho (r) constant	P
Neureretinal rim thickness	-0.737	**<0.001**
Mean peripapillary RNFLT	-0.258	**0.001**
Superior quadrant of peripapillary RNFLT	-0.178	**0.019**
Inferior quadrant of peripapillary RNFLT	-0.302	**<0.001**
Temporal quadrant of peripapillary RNFLT	-0.207	**0.006**
Inferotemporal quadrant of macular GCA	-0.161	**0.034**

CDR; cup to disc ratio, SD-OCT; spectral domain optic coherence tomography, RNFLT; retinal nerve fiber layer thickness, GCA; ganglion cell analysis.

DISCUSSION

Although there is no definitive statement about the prevalence of physiological high cup to disc ratio, the rate was reported as 6% in a previous glaucoma meeting[7]. It is important to remember that the relation between the size of the optic disc and the size of the optic cup. For example, a normal large disc will have a large cup and a normal small disc will have a small cup. Thus, in current study we took into account the ratio of cup area to disc area to avoid inaccurate measurements.

Glaucoma is characterized by loss of RGCs results with thinning of the neuroretinal rim thickness, enlarging of the CDR[8,9], visual field defects and decreasing the measurements of RNFLT[4,5]. Snydacker[10] and Armaly[11] demonstrated that the CDR, is a useful parameter to suspect from the glaucomatous damage. However, the optic nerve has lots of variations and these variations can cause misdiagnose. The term of large physiological cupping, without any glaucomatous damage, was first introduced by Jonas et al.[3] And it is not shown whether eyes with large physiological cupping has the same morphological characteristics as small-cupped eyes[12].

Previous studies reported the association of large cupping and the severity of the glaucoma and the localized RNFL defects as a good parameter to show early glaucomatous damage[13,14]. And some studies demonstrated that the measurements of GCA can identify the structural changes of the optic nerve and diagnose glaucoma with a similar sensitivity as the measurements of RNFL and VF analysis[15,16].

Prata et al[17]. demonstrated that the measurement of GCA and RNFLT decrease in glaucomatous patients. However they evaluated GCA in only mean, superior and inferior quadrant. They classified the groups according to vertical cup to disc ratio which higher or lower than 0.6[17]. They compared patients with glaucoma and glaucoma suspect and the number of patients were less than current study.

In this study both of the groups are healthy with no glaucoma or glaucoma suspect. Even so, this study shows significant difference in peripapillary RNFLT measurements except nasal quadrant between two groups and also detects negative correlation between CDR and peripapillary RNFLT measurements. However there is no difference in macular GCA measurements between two groups except inferotemporal quadrant. These results demonstrate that the large physiological cupping decrease the measurements of the RNFLT by thinning the neuroretinal rim thickness, while it does not change the measurements of the GCA. However, in a previous study showed that there was not any correlation between optic cupping and RNFLT in children[18]. So that these results can be considered that age may be associated with RNFLT in healthy population with or without optic cupping.

CONCLUSION

In the clinical practise, the measurements of the RNFLT can mislead the clinician when diagnosing the early glaucomatous damage due to have a changing potential in physiological conditions, too. So that, the measurements of GCA should be thought more valuable parameter than RNFLT to evaluate the glaucomatous damage. To best of our knowledge, the measurements of RNFLT and GCA have not demonstrated in healthy individuals with large physiological cupping before.

Future studies to investigate the OCT parameters in individuals with large physiological cupping will provide better enlightenment on this subject.

Acknowledgement

The authors have no conflict of interest with any companies.

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