Relationships Between Stereoscopic Non-Mydriatic Retinal Camera, Nerve Fiber Layer and Visual Field Parameters in Different Stages of Glaucoma

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ABSTRACT

Purpose: To investigate the relationships between stereoscopic non-mydriatic retinal camera (NMRC), retinal nerve fiber layer thickness (RNFLT), and visual field (VF) parameters in different stages of glaucoma.

Materials and Methods: This retrospective study included 112 eyes from 112 patients with glaucoma which were grouped according to the disc damage likelihood scale (DDLS) obtained by the NMRC: DDLS stage 1 (group 1, n=11), DDLS stage 2 (group 2, n=48), and DDLS stage 3 (group 3, n=53). Data of NMRC, RNFLT, and VF were compared and correlated.

Results: All RNFLT measurements revealed that the group 3 had significantly lower values in all sections ($p<0.05$ for all). The VF measurements revealed that although the mean deviation (MD) values were higher in the group 3, this difference was not statistically significant ($p=0.08$). However, Hodapp-Anderson-Parrish (HAP) score was significantly higher in the group 3 ($p<0.01$). The DDLS stage was significantly correlated with MD ($p<0.01$, $r=0.30$), HAP score ($p<0.01$, $r=0.35$), and all RNFLT measurements ($p<0.05$ for all, r between -0.22 and -0.36). The vertical cup to disc (C/D) ratio was also significantly correlated with MD ($p<0.01$, $r=0.38$), HAP score ($p<0.01$, $r=0.36$), and all RNFLT measurements ($p<0.05$ for all, r between -0.30 and -0.48).

Conclusion: All the NMRC, RNFLT, and the VF measurements are comparable and discriminative devices in staging glaucoma. The DDLS stage and vertical C/D obtained by NMRC are useful parameters in the monitoring glaucoma.

Key Words: Glaucoma, non-mydriatic retinal camera, retinal nerve fiber layer thickness, visual field.

INTRODUCTION

Glaucoma is a progressive optic neuropathy characterized by loss of retinal ganglion cells, thinning of retinal nerve fiber layer thickness (RNFLT), and defects in visual field (VF).[1,2] Evaluation, diagnosis, and prevention of glaucoma is important because glaucoma is the second most common cause of blindness worldwide and the injury caused by glaucoma is irreversible.[1,3]

Glaucoma diagnosis is based on the measurement of intraocular pressure (IOP), the VF test, and examination of the optic nerve head (ONH).[4] Assessment of a patient's ONH morphology is an essential part of the correct diagnosis and evaluation of glaucoma because structural changes in the ONH precede the VF defects.[5-7] When the ONH is assessed with ophthalmoscope or a color fundus photographs, the ONH cupping and the severity of glaucoma may be underestimated because of the difficulty in stereoscopic viewing.[8] The main limitations of subjective examination are its high intra- and inter-observer variability in interpreting the ONH, even among glaucoma specialists.[4,9-11] The use of advanced equipment may make a detailed, repeatable, and reliable assessment of ONH morphology. Spectral domain optical coherence tomography (SD-OCT) is a high-resolution, cross-sectional imaging technique that allows in vivo measurement of tissue thickness and an objective, noninvasive, and noncontact imaging technique has gained large acceptance among ophthalmologists.[4,5,12,13] Previous reports have shown that the RNFLT measurement by OCT has a high sensitivity and specificity for diagnosing glaucoma, and has a good correlation with the VF.[1, 14] Over the past decade, stereoscopic non-mydriatic retinal camera

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(NMRC) has also gained widespread use for the diagnosis and follow-up of patients with glaucoma and those at risk for glaucoma.[15] The NMRC provides a software algorithm that automatically displays disc damage likelihood scale (DDLS) in its final report output. The DDLS has been reported to provide a more accurate assessment of ONH than the conventional cup to disc (C/D) ratio measurement, and a high correlation has been found between the DDLS and various indices obtained from OCT in patients with glaucoma.[4,7,16] The VF provides functional sequences of glaucoma and it is widely used for the diagnosis and follow-up for glaucoma.[1] However, perimeter can remain within normal limits until there is 25–50% loss of retinal ganglion cells.[1,17]

The purpose of the present study was to determine comparisons of the NMRC, RNFLT, and VF parameters in different stages of glaucoma.

MATERIALS AND METHODS

Medical records of 112 eyes with glaucoma were enrolled retrospectively in this study. The study was conducted in accordance with the tenets of the Helsinki Declaration, and approval of the institutional ethics review board was obtained.

All subjects had undergone complete ophthalmic examination including visual acuity, medical, ophthalmic, and family history, IOP measurement using Goldmann applanation tonometry, central corneal thickness, slit lamp microscopy, gonioscopy, non-dilated fundoscopy, VF (SITA Standard 24–2, size III stimulus, Humphrey Field Analyzer, Carl Zeiss Meditec Inc., Dublin, CA), RNFLT measurements (SD-OCT; Heidelberg Engineering, Version 1.7.1.0, Germany), and stereoscopic NMRC (Nonmyd WX; Kowa Optimed Inc., VK-2 WX Analysis Software). Glaucoma was defined by complete analysis of all examinations by a glaucoma specialist. Participants were grouped according to the DDLS stage obtained from NMRC device as DDLS stage 1 (group 1), DDLS stage 2 (group 2), and DDLS stage 3 (group 3). Adult patients ≥18 years old with a diagnosis of primary open angle glaucoma, low-tension glaucoma, or pseudoexfoliation glaucoma were admitted to the study. Patients whose records were lacking, myopia-hyperopia greater than -5.00 diopters, any corneal, retinal (e.g., diabetic retinopathy), optic nerve pathologies other than glaucoma, or neurologic pathology associated with VF or RNFLT defects were excluded from the study.

The NMRC recorded both right and left parallactic images simultaneously through a single optical system handling light paths in 2 directions.[13] Candidate contour dots were automatically extracted for disc or cup through the optic disc analysis dialog box. After the automatic extraction, contour dots were edited by one of the authors (D.A.) for disc and cup and results were taken. The contour of the disc was delineated by the inner margin of Elschnig's scleral ring, and the contour of the cup was delineated by the outer margin of the cup, which was indicated by the bending of the ONH vessels at the rim. Parameters of the NMRC in this study included vertical C/D ratio and the DDLS stage. The DDLS stage is a diagnostic parameter reported by the disc size and the rim disc ratio; which was previously suggested by Bayer et al.[7]

The SD-OCT was used to measure RNFLT. The scan circle diameter was set at 3.4 mm around the ONH for the measurements. The RNFLT print-out included the sectors of superior temporal, temporal, inferior temporal, inferior nasal, nasal, superior nasal, and global average.

Parameters of the VF included mean deviation (MD) and Hodapp-Anderson-Parrish (HAP) scores.[18] Unreliable VF tests (fixation losses of more than 20% and a false-positive and false-negative rate of more than 15%) were excluded.

The SPSS 17.0 software package was used in data analysis. For the descriptive statistics, discontinuous variables were shown as numbers and percentages (%); continuous variables were shown as mean values. Normality of the data was evaluated with the Kolmogorov Smirnov test. For the comparison of measurements; ANOVA test was used for continuous variables that distributed normally, post-hoc Tukey test was used for subgroup comparisons. Kruskal Wallis test was used for continuous variables that did not distribute normally, if significant difference was found, post-hoc Banforoni corrected Mann Whithney U test was used for subgroup comparisons. Chi Square test was used for categorical values. For the correlation of measurements; Pearson test was used for continuous variables that distributed normally and Spearman test was used for continuous variables that did not distribute normally. A P value of 0.05 or less was considered as significant.

RESULTS

A total of 112 eyes were evaluated. Sixty seven (59.8%) were male and 45 (40.2%) were female. The mean age was 60.59±14.49 (21–94) years. The mean age was 52.55±11.34 years in the group 1, 57.29±15.59 years in the group 2, and 65.25±12.57 years in the group 3 ($p<0.01$). Eleven (9.8%) eyes had DDLS stage 1, 48 (42.9%) eyes had DDLS stage 2, and 53 (47.3%) eyes had DDLS stage 3. The NMRC measurements revealed that the vertical C/D ratio was 0.54±0.14 in the group 1, 0.64±0.09 in the group 2, and 0.74±0.09 in the group 3.

The RNFLT measurements (Table 1) revealed that the global RNFLT was 90.91±8.55 microns in the group 1, 88.63±15.92 microns in the group 2, and 73.04±23.18 microns in the group 3 (p<0.01). The group 3 had also significantly lower values for temporal (p<0.01), superior temporal (p<0.01), superior nasal (p<0.01), nasal (p=0.015), inferior nasal (p<0.01), and inferior temporal (p<0.01) sectors.

The VF measurements (Table 2) revealed that the average MD were -2.49±2.25 dB in the group 1, -2.97±4.65 dB in the group 2, and -7.55±9.09 in the group 3; the average MD values were higher in the group 3 but this difference was not statistically significant among the groups (p=0.08). However, HAP score was significantly higher in the group 3 (p<0.01).

The DDLS was significantly correlated with age (p<0.01, r=0.32), MD (p<0.01, r=0.30), HAP score (p<0.01, r=0.35), superior temporal RNFLT (p=0.01, r=-0.32), temporal RNFLT (p=0.09, r=-0.25), inferior temporal RNFLT (p<0.01, r=-0.41), inferior nasal RNFLT (p=0.03, r=-0.28), nasal RNFL (p=0.02, r=-0.22), superior nasal RNFLT (p<0.01, r=-0.35), and global RNFLT (p<0.01, r=-0.36).

The vertical C/D ratio was significantly correlated with age (p<0.01, r=0.39), MD (p<0.01, r=0.38), HAP score (p<0.01, r=0.36), superior temporal RNFLT (p=0.01, r=-0.44), temporal RNFLT (p=0.01, r=-0.30), inferior temporal RNFLT (p<0.01, r=-0.48), inferior nasal RNFLT (p<01, r=-0.36), nasal RNFLT (p<01, r=-0.38), superior nasal RNFLT (p<0.01, r=-0.39), and global RNFLT (p<0.01, r=-0.47).

DISCUSSION

This study compared and correlated the NMRC, RNFLT, and VF parameters in different glaucoma stages. In summary, the NMRC, RNFLT, and VF measurements were well-matched devices in monitoring glaucoma. The DDLS and vertical C/D ratio of the NMRC parameters in this study were highly comparable and significantly correlated with the RNFLT and VF. The automatic calculation of the DDLS together with vertical C/D ratio obtained by the NMRC showed good predictability in the different stages

Table 1. *Comparisons of retinal nerve fiber layer thicknessses between different disc damage likelihood scales (DDLS)*

	Group 1 (DDLS 1)	Group 2 (DDLS 2)	Group 3 (DDLS 3)	P value
Global (μ)	90.91	88.63	73.03	<0.01**
Superior temporal (μ)	128.82	117.83	98.85	<0.01**
Temporal (μ)	66.09	68.21	58.40	<0.01*
Inferior temporal (μ)	131.82	123.69	93.13	<0.01**
Inferior nasal (μ)	97.36	97.54	80.70	<0.01*
Nasal (μ)	65.73	68.90	57.81	0.015*
Superior nasal (μ)	105.63	95.50	79.20	<0.01**

*Anova test, **Kruskal Wallis Test

Table 2. *Comparison of visual field measurements between different disc damage likelihood scales (DDLS)*

	Group 1 (DDLS 1)	Group 2 (DDLS 2)	Group 3 (DDLS 3)	P value
Mean Deviation (dB)	-2.49	-2.97	-7.54	0.08*
HAP Score	1.09	1.17	1.70	<0.01**

*Kruskal Wallis Test, **Chi Square Test

Table 3. *Comparison of visual field measurements between different disc damage likelihood scales (DDLS)*

	Group 1 (DDLS 1)	Group 2 (DDLS 2)	Group 3 (DDLS 3)	P value
Mean Deviation (dB)	-2.49	-2.97	-7.54	0.08*
HAP Score	1.09	1.17	1.70	<0.01**

*Kruskal Wallis Test, **Chi Square Test

of glaucoma. These results also showed that the NMRC is feasible in discriminating different glaucoma stages.

Fundus cameras have given the opportunity to introduce computer assisted analysis of the ONH. One of the latest devices, the NMRC, can produce stereoscopic images with its built-in software and optional polarized filters. The device enables to provide highly consistent and objective results in evaluating the ONH.[5] Although ophthalmoscopic examination offers the advantages of immediate information utilizing inexpensive equipment, it has several shortcomings. The value of ophthalmoscopy is strongly affected by the skill of the examiner and the understanding of the examiner about how glaucoma affects the ONH and retina.[19,20] Previous studies reported that observers are more consistent with their own repeat evaluations than with each other both with regard to vertical C/D ratio and recognizing glaucomatous damage.[10,21,22] Higher inter-observer variability and lower reproducibility is also reported.[16]

To overcome this problem, the NMRC takes both right and left parallactic images simultaneously through a single optical system without pupil dilation to automatically determine stereo image from two different shoot points. When the two images are overlaid, there is a horizontal shift and disparity in the position of the photographed object which correlates with depth. The calculated values are then used to generate the depth distribution of the ONH.[13,23] The high consistency of the ONH parameters is previously reported and attributed mainly to determination of the border between the rim and the cup.[13]

The ONH evaluation using a systematic grading system such as the DDLS increases objectivity and improves diagnostic accuracy for glaucoma.[4] Bayer et al.[7] previously reported the DDLS. The DDLS is a staging scheme for glaucomatous ONH damage based upon the narrowest radial width of rim and vertical disk diameter.[4,7] The two major advantages of the DDLS are, firstly, that it considers disc size and, secondly, that it focuses attention on how much neuroretinal rim tissue is present.[2] Conversely, the two principal limitations of the C/D ratio system are the fact that the system does not account for disc size and that focal narrowing of the neuroretinal rim is not adequately highlighted.[20] The C/D ratio may be especially misleading when the loss of rim is limited to a single sector.[19] The DDLS method requires some effort to learn and is best carried out with the table of stages at hand during slit lamp evaluation of the fundus.[2] Majid et al.[16] reported that the DDLS was a useful index for the diagnosis of glaucoma and was highly correlated with indices measured by the VF, C/D ratio, and the OCT. Han et al.[4] measured the DDLS by the NMRC and showed excellent diagnostic predictability for glaucoma which was almost equal to that of the glaucoma specialist. The DDLS has high inter-observer reproducibility and correlates strongly with the degree of glaucomatous VF damage.[7] Likewise these studies, our findings indicate that the automated DDLS calculation showed good agreement with the RNFLT and the VF.

The peripapillary RNFLT have already been demonstrated to be repeatable and reproducible, and have a high degree of diagnostic sensitivity and specificity in discriminating between healthy and glaucomatous eyes.[22] In our study, all RNFLT measurements revealed that the severe glaucoma group had significantly lower values. In addition, both the DDLS stage and the vertical C/D ratio measured by the NMRC was significantly correlated with all RNFLT measurements. The correlations between the DDLS stage, the vertical C/D ratio, and the RNFLT measurements were highest in inferotemporal sector and global RNFLT. It was previously reported that the global and inferior RNFLT are the best parameters for discriminating between healthy and glaucomatous subjects.[24] Glaucomatous neuroretinal rim loss happens in a sequence of sectors. Generally, it begins in the inferotemporal disc region and then progresses to the superotemporal, the temporal horizontal, the inferior nasal, and finally the superior nasal sectors.[25] Pueyo et al.[26] reported that the global RNFLT is the best OCT parameter for discriminating between healthy and glaucomatous subjects, with sensitivity at 66% and specificity more than 90%.

The perimetry is still the most widely used method to measure visual function in glaucoma.[27] In our study, the VF measurements revealed that although MD values were worse in more severe glaucoma group, the difference was insignificant. On the other hand, the HAP score was significantly higher in severe glaucoma group. In addition, both the DDLS stage and the vertical C/D ratio measured by NMRC was significantly correlated with MD and HAP score. MD is known to be relatively non-specific, declining with general sensitivity loss related to cataract and other factors. The perimetry reveals the functional results of glaucoma damage and the test is dependent on the patients compliance and is much more subjective than the NMRC and the RNFLT measurements. It was therefore not surprising that in our study, both the NMRC and the RNFLT outperformed MD. Grewal et al.[22] previously reported that the RNFL measurements obtained with SD-OCT had poor agreement with the assessments of the VF progression. The MD becomes more negative very slowly, especially in the early stages of glaucoma, the initial glaucomatous changes can be best detected by monitoring the optic nerve.[19,28]

This study has some limitations that warrant further investigation. Healthy controls were not included to the study. The results of the present study are based on grouping by the automatically classification of glaucomatous eyes by the NMRC DDLS system which might influence the diagnostic power of the optical disc photos higher than it is.

CONCLUSION

The NMRC, RNFLT, and VF measurements are discriminative devices in staging glaucoma. Both the DDLS and the vertical C/D ratio obtained by NMRC and all RNFLT measurements outperformed MD. Glaucoma diagnosis should not be made from one single diagnostic test but from a comprehensive examinations that includes thorough examinations.

Ethics

Ethics Committee Approval: Medical Sciences University Gulhane Medical Faculty Ethics Committee – Date:12.03.2019, Number:19/60

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Authorship Contributions

Medical Practices: Mehmet Talay Koylu, Dorukcan Akıncıoglu, Concept: Mehmet Talay Koylu, Fatih Mehmet Mutlu, Design: Mehmet Talay Koylu, Dorukcan Akıncıoglu Data Collection or Processing: Dorukcan Akıncıoglu, Mehmet Talay Koylu, Analysis or Interpretation: Mehmet Talay Koylu, Dorukcan Akıncıoglu, Fatih Mehmet Mutlu, Literature Search: Mehmet Talay Koylu, Dorukcan Akıncıoglu. Writing: Mehmet Talay Koylu

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