Optic Disc Area Asymmetry May Also Play a Significant Role in Glaucoma When Evaluating Patients With Macro-Disc Optic Nerves

Conley, E.J., OD, Baltimore VA Medical Center

Abstract

Purpose: To evaluate and compare optic nerve parameters of patients suspected of having glaucoma, specifically, those considered to have enlarged or "macro" optic discs defined as an overall area greater than 2.82 mm^2.

Methods: Retrospective evaluation of 245 patients subjected to confocal scanning laser ophthalmoscopy by the Heidelberg Retinal Tomograph (Heidelberg Engineering, Dossenheim, Germany) presenting for consultative evaluation were analyzed. Of these 245 patients, 44 (18%) were designated as having at least one optic disc greater than 2.82 mm^2 Of the 44 macro-disc patients available, 20 patients also performed reliable Humphrey visual field perimetry testing to differentiate between normal and glaucomatous eyes.

Results: Of the 20 macro-disc glaucoma suspect patients analyzed, six patients (30%) demonstrated visual field loss, in at least one eye. Further delineation among optic nerve characteristics, including disc area, rim area, cup/disc area ratio, rim/disc area ratio, cup volume, rim volume, mean RNFL thickness, horizontal cup/disk ratio and vertical cup/disk ratio as derived by HRT, was performed. Of the six glaucoma patients, a statistically significant difference (p=0.021) occurred in the measurement of optic disc area with a mean value of 3.12 mm^2 (sd: 0.413) in glaucomatous eyes and 2.48 mm^2 (sd: 0.389) in non-glaucomatous eyes. Additionally, the vertical C/D parameter was also statistically significant (p=0.003) within this glaucoma group, with an average vertical C/D of 0.850 in eyes with VF loss and 0.562 in fellow non-glaucomatous eyes. Complete C/D ratios between these 12 eyes demonstrated a mean value 0.566 (sd: 0.247) in glaucomatous loss eyes and 0.308 (sd: 0.157) in fellow non-loss eyes, p=0.056, which is narrowly outside of statistical significance. Examination of data among 14 patients with macro-discs and *no apparent visual field loss* in either nerve was also analyzed; notably, no statistical difference existed between right and left eyes in any parameters, and specifically not in disc area. The calculated mean disc area for this group was 3.04 mm^2 (sd: 0.495) and 2.95 mm^2 (sd: 0.403), which were not statistically significant. Additionally, vertical and overall C/D ratios between these eyes demonstrated no significant difference between eyes, as vertical C/D was 0.668 (sd:0.236) and 0.691 (sd:0.086); and complete C/D 0.563 (sd: 0.085) and 0.507 (sd: 0.188).

Conclusions: Patients demonstrating enlarged optic disc areas, or macro-discs, who present to ophthalmic care should be evaluated for overall optic disc area asymmetry between eyes, in addition to C/D and vertical C/D asymmetry. This cohort, although reduced in sample size, suggests significant differences in visual field outcomes when patients with suspicious appearing, enlarged optic nerves present with asymmetry in overall disc area. The detection of cup-to-disc asymmetry has long been a critical diagnostic finding in glaucoma patients; however, optic disc area asymmetry may also be significant factor when evaluating patients with macro-disc optic nerves.

INTRODUCTION

The diagnosis and management of glaucoma presents many challenges to eyecare practitioners. Diagnosis of glaucoma upon initial presentation has proven very difficult especially when in its earliest stages. Furthermore, distinction between normal physiologic cupping and early glaucomatous damage becomes uniquely difficult when optic nerves are larger than average. Clinically, glaucomatous injury more often causes concentric enlargement of the cup to disc ratio as ganglion axons are damaged, rather than the easily detected and visualized "notching" of the NRR.[1] Concurrently, concentric cupping is also apparent in normal physiological cupping, only serving to complicate the diagnostic process. Clinical studies demonstrate that less support exists from glial cells and astrocytes in the inferior and superior regions of the optic nerve.[2] Accordingly, nasal and arcuate fibers derived from those regions are therefore primarily affected by concentric enlargement leading to arcuate and nasal step visual field defects. Currently, an enlarged macro optic disc, often defined as megalopapilla syndrome, is viewed as a large optic nerve appearing abnormal, with increased cupping, but associated with a normal rim volume, normal visual field and normal IOP.[3-4] In essence, these megalopapilla nerves, have been considered unlikely to have glaucomatous damage. However, because larger nerves with significant cupping often appear glaucomatous, a need still exists to distinguish

potentially damaged optic nerves from larger, normal physiological discs. The aim of the current study was to investigate whether certain optic nerve characteristics, if any, are unique toward the development of glaucomatous damage in the macro-disc population.

METHOD

Retrospective evaluation of 245 patients subjected to confocal scanning laser ophthalmoscopy by the Heidelberg Retinal Tomographer (Heidelberg Engineering, Dossenheim, Germany) was performed. The accuracy of the HRT for intraocular measurements had been established previously by Jonas, et al., demonstrating that values represented are accurate diameters, areas and volumes with strong correlations to in vivo dimensions with quality reproducibility and accuracy.[5-6] Parameters investigated included disc area, rim area, cup/disc area ratio, rim/disc area ratio, cup volume, rim volume, mean RNFL thickness, horizontal cup/disk ratio and vertical cup/disk ratio as available in the HRT software. Optic nerve parameters of patients suspected of glaucoma with enlarged or "macro" optic discs (defined as a disc area greater than 2.82 mm^2) were targeted. The selection of the 2.82mm^2 macro disc limit was established upon three key factors: (1) the understanding that the size of the optic disc is independent of axial length, age, or refractive error, even though high myopia occasionally tends toward larger disc areas;[7] (2) previous research done separately by Jonas, Britton, and Capriolli have established 2.8 to 2.9 mm^2 area values as the upper limit for normal populations -- designating values above as statistically "abnormal" and (3), an area of 2.82mm^2 was likewise considered outside "normal range" according to Heidelberg Engineering statistical analysis models. Patients were analyzed and disqualified for any optic nerve enlargement and/or visual field loss relating to any possible non-glaucomatous etiologies such as pseudotumor cerebri, ischemic optic neuropathy, etc. Qualification rendering patients displaying an actual "visual field defect" was based on the *LTG-P Cluster Criteria*,[8] which has been designated as three (3) contiguous points (touching rows or clusters) using all points on 24-2 SITA and all non-edge points on 30-2 SITA test results of the Pattern Deviation Plot; the criteria requires at least one point significantly depressed P<1% or worse on Pattern Deviation Plot combined with two (2) additional points significantly depressed P<5% or worse on the Pattern Deviation Plot. This method is known to provide excellent sensitivity, correctly identifying glaucoma in 95% of test subjects. Patients with demonstrated glaucomatous visual field loss were then compared to their non-glaucoma cohort. Due to the retrospective nature of the study, all appropriate ethical and regulatory standards were met as all clinical data was reviewed and evaluated independent of treatment decisions. Moreover, no patient was subjected to any period of physical or emotional harm due to delayed or non-treatment at any time during the study.

RESULTS

Of the 245 patients evaluated, 44 (18%) were designated as having at least one optic disc greater than 2.82 mm^2. Of the 44 macro-disc patients available, 20 patients also performed reliable Humphrey visual field perimetry testing to differentiate between normal and glaucomatous eyes. Of the 20 macro-disc glaucoma suspect patients analyzed, six patients (30%) demonstrated visual field loss in at least one eye. Further delineation among optic nerve characteristics, including disc area, rim area, cup/disc area ratio, rim/disc area ratio, cup volume, rim volume, mean RNFL thickness, horizontal cup/disk ratio and vertical cup/disk ratio as derived by HRT, was performed. Of the six glaucoma patients, a statistically significant (p=0.021) difference, based on Student's *t*-test, occurred in the measurement of optic disc area with a mean value of 3.12 mm^2 (sd: 0.413) in glaucomatous eyes and 2.48 mm^2 (sd: 0.389) in opposite non-glaucomatous eyes (see Figure 1). Additionally, the vertical C/D parameter was also statistically significant (p=0.003) within this glaucoma group, with mean vrtical C/D of 0.850 in eyes with VF loss and 0.562 in fellow non-glaucomatous eyes (see Figure 2). Overall C/D ratios between these 12 eyes demonstrated a mean value 0.566 (sd: 0.247) in glaucomatous loss eyes and 0.308 (sd: 0.157) in fellow non-loss eyes, p=0.056, which is narrowly outside of statistical significance. Examination of data among 14 patients with macro-discs and *no*

apparent visual field loss in either nerve were also analyzed; notably, no statistical difference existed, between right and left eyes in any parameters, and specifically not in disc area. The calculated mean disc area for this group was 3.04 mm^2 (sd: 0.495) and 2.95 mm^2 (sd: 0.403), statistically insignificant. Additionally, vertical and overall C/D ratios between these eyes demonstrated no significant difference between eyes as vertical C/D was 0.668 (sd:0.236) and 0.691 (sd:0.086); and overall C/D 0.563 (sd: 0.085) and 0.507 (sd: 0.188).

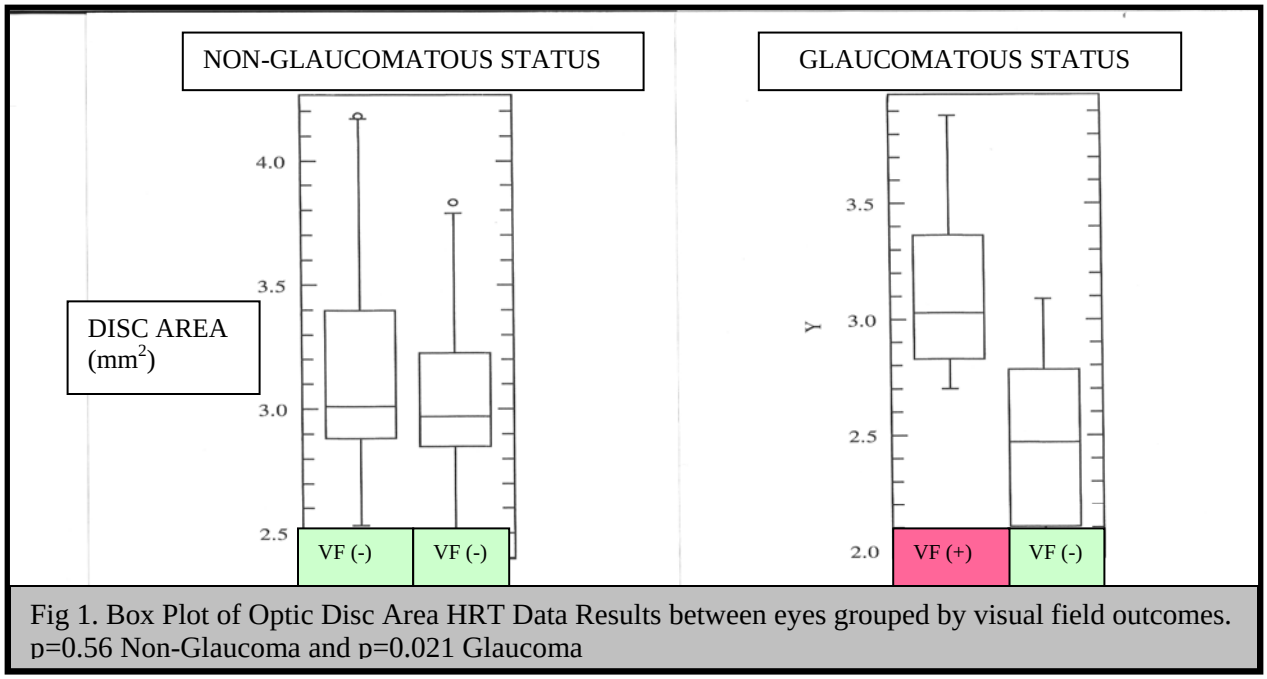

Fig 1. Box Plot of Optic Disc Area HRT Data Results between eyes grouped by visual field outcomes. p=0.56 Non-Glaucoma and p=0.021 Glaucoma

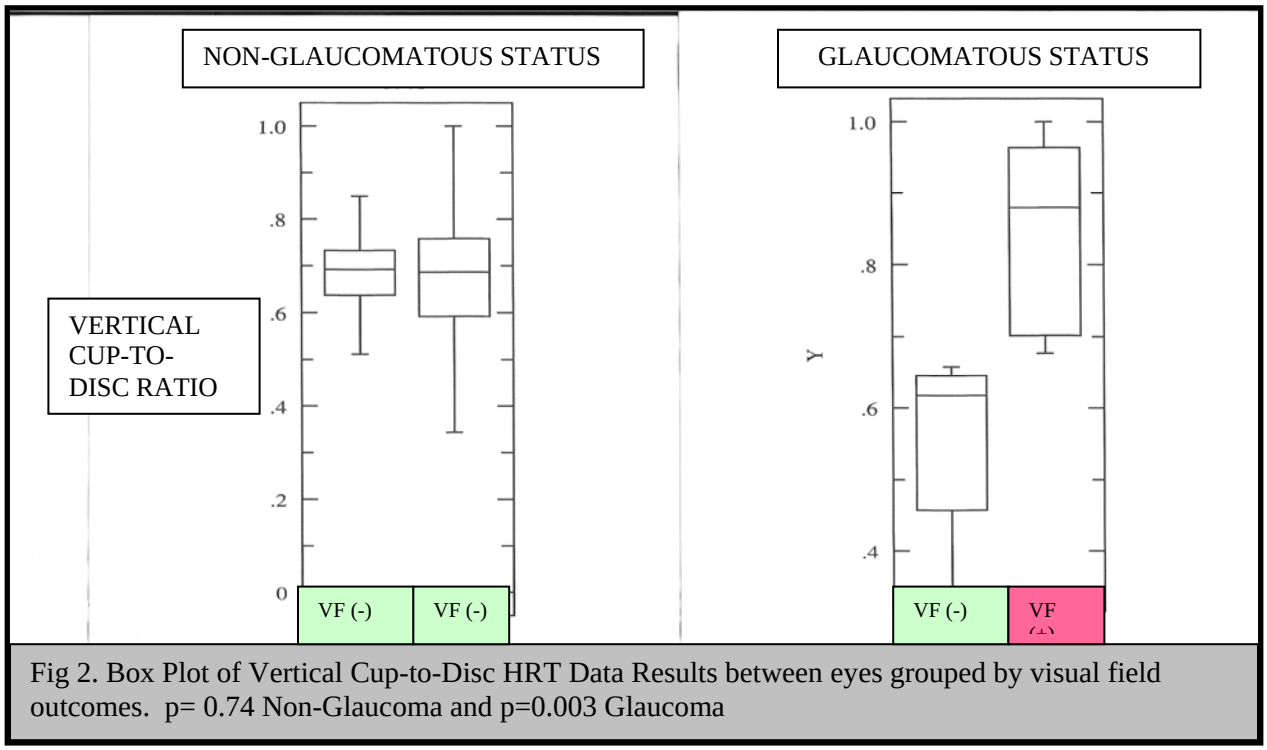

Fig 2. Box Plot of Vertical Cup-to-Disc HRT Data Results between eyes grouped by visual field outcomes. p= 0.74 Non-Glaucoma and p=0.003 Glaucoma

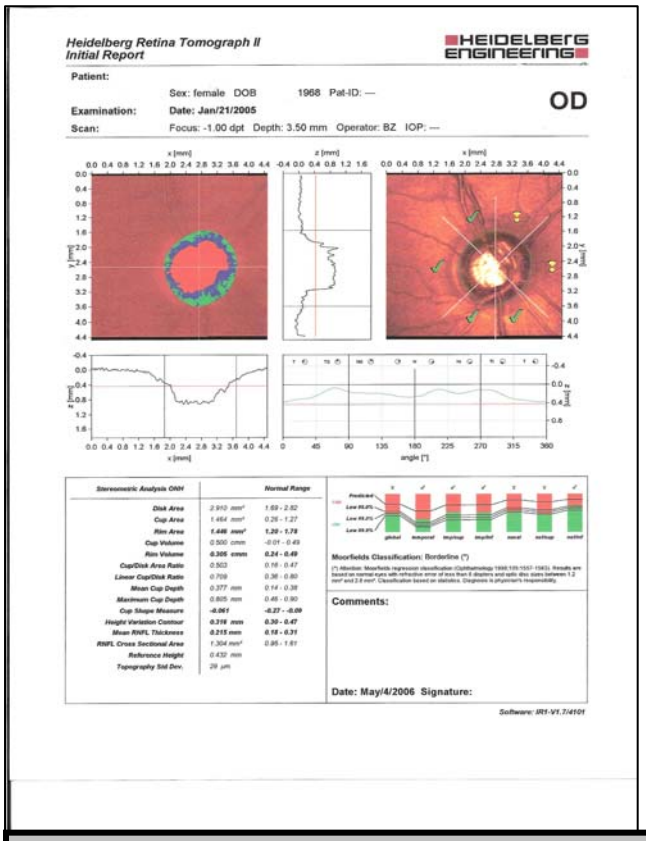

Fig 3. Example Macro-Disc Patient HRT Evaluation demonstrating values presented to clinicians for application in glaucoma diagnosis and management

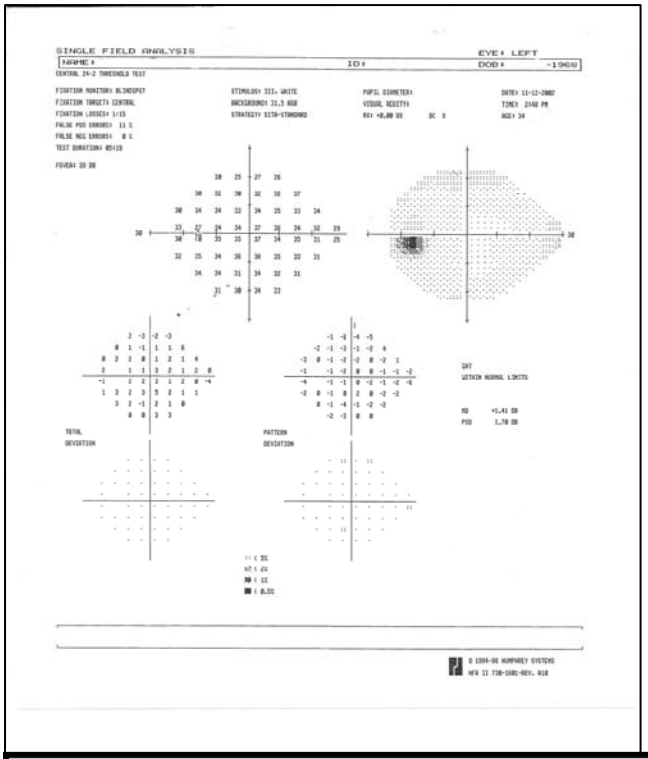

Fig 4. Corresponding Macro-Disc Patient's Humphrey Visual Field 24-2 Sita-Standard Evaluation - demonstrating "normal" visual fields, OS and *OD* (despite its appearance), utilizing the *LTG-P Cluster Criteria*. No point within the nasal cluster on the pattern deviation plot, OD, demonstrated any point at p<1% and was therefore considered WNL; subsequently these subnormal points demonstrated normal "pattern deviation" values in repeat visual field testing in 2004 and 2006 (not shown), representing the usefulness and accuracy of the applied *LTG-P Cluster Criteria.*

CONCLUSIONS

Patients demonstrating asymmetrically enlarged optic disc areas, or macro-discs, as measured by confocal scanning laser ophthalmoscopy and compared with fellow eyes, should be highly suspect of having or developing glaucomatous visual field loss, especially when vertical cup/disc ratios are also dissimilar. Remarkably, the patients with quantifiably *symmetrical* macro-disc areas demonstrated no glaucomatous visual field loss in either nerve at initial presentation. Studies have shown that the diameter of the optic foramen can vary in size from 1000 to 3000 microns.[9] As such, the average opening of the foramen has an area of 1.6mm^2, but varies from 0.68 to 4.42mm^2. The asymmetric variation and subsequent development of glaucoma between eyes suggested in this study requires further investigation. The cohort examined within, although reduced in sample size, suggests significant differences in visual field outcomes when patients with suspicious appearing, enlarged optic nerves, demonstrate asymmetry in overall disc area. The detection of vertical cup-to-disc asymmetry continues to be a critical diagnostic finding in glaucoma patients;however, optic disc area asymmetry may also play a significant role when evaluating patients with macro-disc optic nerves. Future studies need to be performed in order to establish whether or not the overall study results persist in long term evaluation, especially within a larger sample population.

REFERENCES

[1] Litwak, A. Glaucoma Handbook. 2001: p.63-75

[2] Quigley, et al. *Optic nerve damage in human glaucoma. II. The site of injury and susceptibility to damage*. Arch Ophthalmol 1988; 226: 635-49

[3] Swann, PG and Coetzee, J. *Megalopapilla*. Clin Exp Optom. 1999 Sep; 82(5):200-202.

[4] Sampaolesi, R and Sampaolesi JR. *Large optic nerve heads: megalopapilla or megalodiscs*. Int Ophthalmol 2001; 23(4-6):251-7.

[5] Dichtl A, et al. *Comparison between tomographic scanning evaluation of photographic measurements of the neuroretinal rim*. Am J Ophthalmol.1996;121:494-501

[6] Jonas, JB, et al. *Comparison of measurements of neuroretinal rim area between confocal laser scanning tomography and planimetry of photographs*. Br J Ophthalmol.1998;82362-366

[7] Quigley, HA et al. The size and shape of the optic disc in normal human eyes. Arch Ophthalmol. 1990;108:51-7

[8] Katz, Sommer, et al. *Comparison of analytic algorithms for detecting glaucomatous visual field loss*. Arch Ophthalmol. 1991 Dec; 109(12): 1684-9.

[9] Jonas, et al. *Variability of the real dimensions normal human optic discs*. Graefe's Arch Clin Exp Ophthalmol 1988; 226:332-6