AMERICAN ACADEMY OF OPHTHALMOLOGY®
In partnership with the AMERICAN GLAUCOMA SOCIETY

Distribution and Rates of Visual Field Loss across Different Disease Stages in Primary Open-Angle Glaucoma

Siamak Yousefi, PhD,[1] *Golnoush Sadat Mahmoudi Nezhad, MD,*[1] *Saeedeh Pourahmad, PhD,*[2] *Koenraad A. Vermeer, PhD,*[3] *Hans G. Lemij, MD*[3]

Purpose: To identify patterns and rates of visual field (VF) loss in primary open-angle glaucoma (POAG) across different levels of severity.

Design: Retrospective, observational case series.

Participants: Visual fields of 278 eyes of 139 patients with POAG (9 years of follow-up with ~17 visits) from the Rotterdam Eye Hospital in The Netherlands were analyzed to identify patterns and rates of VF loss.

Main Outcome Measures: Rate of VF decline for the entire VF, each region, and test point. Hemifield asymmetric rate if VF decline for each region and test point.

Methods: Total deviation (TD) values were extracted from the Humphrey VF Analyzer (Carl Zeiss Meditec, Dublin, CA). Eyes were stratified into 3 glaucoma stages by means of the mean deviation (MD): better than −6 decibels (dB), worse than −6 dB and better than −12 dB, and worse than −12 dB. Each hemifield was divided into 5 regions according to the Glaucoma Hemifield Test (GHT): central, paracentral, nasal, and peripheral arcuates 1 and 2. Point-wise and region-wise asymmetric patterns of VF loss and rate of VF loss were identified by comparing the values in the superior hemifield and the inferior hemifield at each severity level using a generalized estimating equation.

Results: The mean age of the patients was 60.2±10.3 years (mean ± standard deviation [SD]). The rate of MD loss, for all eyes taken together, was −0.11 dB/year. In the cross-sectional analysis, in eyes in the early and moderate stages, central and peripheral arcuate 2 regions in the superior hemifield were worse than their inferior counterpart, whereas in the advanced stage all GHT regions in the superior hemifield were significantly worse than the corresponding regions in the inferior hemifield ($P \leq 0.05$). In the longitudinal analysis, there was no significant difference in the rate of VF loss between the GHT regions in the superior and inferior hemifields.

Conclusions: Our findings suggest that in POAG, VF damage is worse in the superior hemifield than in the inferior hemifield. *Ophthalmology Glaucoma 2018;1:52-60 © 2018 by the American Academy of Ophthalmology*

Glaucoma is the second leading cause of blindness worldwide after cataract.[1–3] Primary open-angle glaucoma (POAG) constitutes the largest proportion of patients with glaucoma, although it is the most underdiagnosed glaucoma condition.[4] Visual damage due to glaucoma significantly compromises patients' quality of life.[5] Damage to the retinal nerve fiber layer in glaucoma is irreversible, which makes early diagnosis important for preventing advanced visual impairment later on in life.[6] Different studies have shown different spatial patterns of visual field (VF) loss and structural properties of the optic disc among POAG and primary angle-closure glaucoma phenotypes.[7–10] These patterns of VF loss have been partially explained by differences in pathogenesis, including pressure-dependent and pressure-independent hypotheses. However, the observed variation in VF loss patterns has not been fully explained.[11,12] Although intraocular pressure (IOP) contributes to the onset and progression of disease,[12] a direct correlation between IOP and the pattern of VF loss is not fully understood in POAG.[13] It is believed that the IOP plays an important role in the extent of VF loss, and, consequently, patterns of VF loss are different between normal-tension glaucoma (NTG) and high-tension glaucoma (HTG). For instance, it has been reported that VF loss in NTG is typically more localized and closer to the fixation point.[14,15] However, NTG studies could be biased because patients with NTG are typically selected on the basis of suspicious discs and not elevated IOP. In addition, patients with NTG with more peripherally located VF defects are likely to stay asymptomatic longer than those with more centrally located scotomas; because the eye pressures are normal in all, NTG with more peripheral VF defects is more likely to pass unnoticed by community optometrists and opticians. By contrast, however, some found no significant difference in the patterns of VF loss between those with NTG and those with HTG.[16] Although pathophysiologic factors affect the VF loss in patients with POAG,[7–9] the differences in reported patterns of VF loss could be due to

https://doi.org/10.1016/j.ogla.2018.05.005
ISSN 2589-4196/18

the differences in the number of eyes included, different definitions for disease, inconsistent stratification approaches, and differences in the analyses.

Identifying the spatial characteristics of VF loss in glaucoma may provide a better understanding of the distribution of the damage, which is associated with vision-related quality of life of the patients knowing that VF loss in the superior hemifield is less likely to affect a patient's quality life than VF loss in the inferior hemifield.[17] This study sought to identify cross-sectional patterns of VF loss and longitudinal rates of VF loss in different VF test locations, in VF regions, and in global VF of eyes with POAG over a long-term course of follow-up.

Methods

Participants and Visual Fields

In this retrospective cohort study, patients' records were acquired from the Rotterdam Eye Hospital in The Netherlands. Informed consent was obtained through study officials from all subjects, and the design of this study was reviewed and approved by the Institutional Review Board of the Rotterdam Eye Hospital.[18] Glaucoma diagnosis was based on 2 of the following conditions: pattern standard deviation significant at the 5% level, abnormal hemifield test result, or cluster of $\geq$3 points depressed at the $P = 0.05$ level or 1 point at the $P = 0.01$ level. Also, VF defects had to be reproducible on at least 1 occasion. Both eyes of each participant were included if they were both glaucomatous. All eyes with secondary glaucoma or evidence of VF abnormality consistent with other disease were excluded; eyes were also excluded for further analysis if their best-corrected visual acuity was worse than 0.3 (logarithm of the minimum angle of resolution), their refractive error fell outside the -10.0 to $+5.0$ diopters range (spherical equivalent), or they had undergone cataract surgery in the previous 12 months. Eyes were also excluded if they had a history of refractive or vitreoretinal surgery. Any evidence of diabetic retinopathy, including diabetic macular edema, was also a reason for exclusion.

Visits were scheduled every 6 months; during every visit, standard clinical ophthalmic examinations including visual acuity, intraocular pressure, gonioscopy, and ophthalmoscopy were performed. Also, standard automated perimetry was done. Visual fields were carried out on a Humphrey Visual Field Analyzer (Carl Zeiss Meditec, Dublin, CA) with a standard white-on-white 24-2 field with the full threshold program. Demographic information was recorded, including age, gender, IOP, mean deviation (MD), and total deviation (TD). Patients' therapies could be adjusted as deemed necessary by their managing glaucoma specialists.

Stratification and Region Computation

Eyes were stratified into 3 groups by the severity of their VF loss at baseline: early glaucoma (MD ≥ -6 decibels [dB]), moderate glaucoma (MD < -6 dB and > -12 dB), and advanced glaucoma (MD ≤ -12 dB).[19,20] Then, the entire VF was divided into 10 regions: a central, a paracentral, a nasal and peripheral arcuate 1 and arcuate 2 in each of superior and inferior hemifields, derived from the Glaucoma Hemifield Test (GHT) and also following previous studies (Fig 1).[7,21] The average of TD values in each of these 10 GHT regions was calculated, as well as the average TD values in the entire superior and inferior hemifields. Asymmetric patterns of VF loss were calculated by comparing the point-wise and region-wise TD values in the superior hemifield and inferior hemifield of eyes in each group. Likewise, any asymmetries in the rate of VF loss were calculated by comparing the rate of VF loss in both the individual test points and the GHT regions of the superior hemifield and inferior hemifield of eyes in each group.

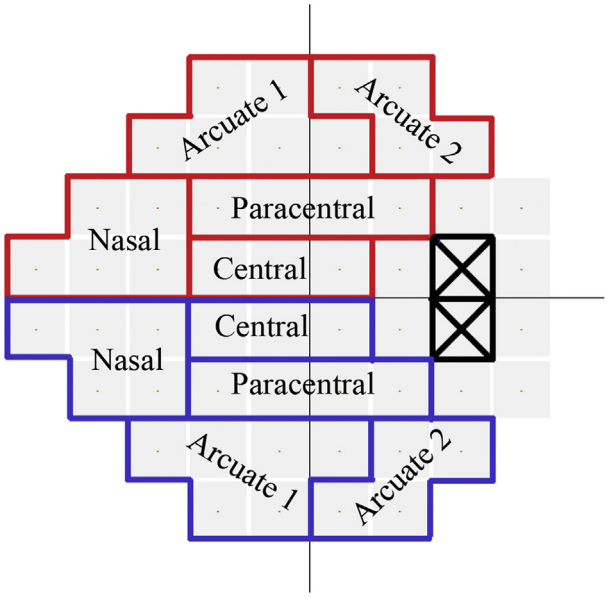

Figure 1. Glaucoma Hemifield Test (GHT) regions in the superior and inferior hemifields.

Analysis

The first VF test of each eye was excluded from the analysis because of the learning effect. For the point-wise cross-sectional analysis, each VF test location in the superior hemifield was compared with its mirrored counterpart test location in the inferior hemifield (across the horizontal midline). Likewise, for region-wise, cross-sectional analysis, the average TD values for every GHT region in the superior hemifield was compared with its counterpart in the inferior hemifield at each severity level. The asymmetric patterns of VF loss were identified in VF test points or regions by using a generalized estimating equation (GEE) method at the significance level of 0.05.

To compute the rate of loss, the slopes of TD values in 52 VF test points, in 10 GHT regions, in the entire superior and inferior hemifields, and in global MD were computed. Similar to cross-sectional analysis, rates of VF loss in VF test points, GHT regions, and entire superior and inferior hemifields were compared across the horizontal midline to identify any asymmetries in rates of VF loss across all eyes. The rates of VF loss were calculated in 2 different manners: rate of VF loss based on VF sequences with all available visits for each eye and rate of VF loss based on VF sequences of 5 to 15 visits (Fig 2). Then, similar to the cross-sectional analysis, a GEE model was used to compare the rates of VF loss at each VF point and at each region in the superior and inferior hemifields. The outcome variables were compared for the VF sequences of all visits and VF sequences of 5 to 15 visits in the GEE model separately. The asymmetric rates of VF loss were identified in VF test points or regions with a significance level of 0.05.

We also excluded eyes with high IOP (IOP at baseline for cross-sectional analysis and maximum IOP across all visits for longitudinal analysis; the threshold of 21 mmHg) and repeated the analyses to identify any IOP-dependent rates of VF loss. We used a GEE model with a Gaussian link function for continuous variables