# Central Visual Field Defects in Patients with Distinct Glaucomatous Optic Disc Phenotypes

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• PURPOSE: To investigate central visual field (VF) defects among 4 phenotypes of glaucomatous optic discs.
• DESIGN: Cross-sectional study.
• METHODS: Optic disc phenotypes were determined in eyes with definite or suspected glaucoma that had a 24-2 VF with mean deviation (MD) better than −12 dB and a 10-2 VF. 10-2 VFs were classified as abnormal based on a cluster criterion. Additionally, the average of the total deviation values at each 10-2 test point was compared by optic disc phenotype.
• RESULTS: The following 4 glaucomatous optic disc phenotypes were identified in 448 eyes of 309 patients: focal ischemic (FI) (n = 121); generalized cup enlargement (GE) (n = 109); myopic glaucoma (MY) (n = 66); and senile sclerotic (SS) (n = 152). Although 24-2 VF MD values were similar among optic disc phenotypes, GE eyes had higher 10-2 VF MD ($P = .004$), as well as lower 24-2 VF pattern standard deviations (PSD) ($P < .001$) and VF 10-2 PSD ($P < .001$) than the other phenotypes. The prevalence of an abnormal VF 10-2 was highest in FI eyes (78.5%) and lowest in GE eyes (50.5%) ($P < .001$). In glaucoma suspects, the prevalence of an abnormal 10-2 VF was highest in the MY eyes (31.2%) and FI eyes (23.5%) and lowest in GE eyes (8.6%). In mild glaucoma, the prevalence of abnormal 10-2 VF test results was highest in FI eyes (79.2%) and lowest in GE eyes (44.4%) ($P = .013$).
• CONCLUSIONS: The severity and prevalence of central VF loss varied among different glaucomatous optic disc phenotypes. Glaucomatous eyes with FI and MY optic disc phenotypes are more likely to have 10-2 VF loss, particularly in early disease, and especially may benefit from testing with both 10-2 and 24-2 VF tests. (Am J Ophthalmol 2021;223:229–240. © 2020 Elsevier Inc. All rights reserved.)

EARLY DETECTION AND INTERVENTION IS VITAL TO reduce the progression and minimize loss of vision of glaucoma.[1] It has been suggested that different patterns of glaucomatous optic disc injury are related to distinctive pathophysiologic mechanisms. Nicolela and Drance[2] and Broadway and associates[3] divided glaucomatous eyes into the following 4 optic disc phenotypes based on their appearance: focal ischemic (FI), generalized cup enlargement (GE), myopic glaucomatous (MY), and senile sclerotic (SS). Each phenotype is associated with several distinctive clinical features. For instance, although optic discs with generalized enlargement are associated with elevated levels of intraocular pressure (IOP), optic discs with focal notches are associated with localized visual field (VF) loss.[3–5]

Detection of central VF loss in patients with glaucoma is important as the loss may affect more tasks such as reading, watching, recognizing faces, walking, and driving than peripheral VFs.[6] When used to evaluate the central VF, the 10-2 test pattern is often used because it has denser and more test points within the central 10-degrees of the VF than the 24-2 VF test pattern. Moreover, glaucomatous VF defects can be detected close to fixation even with early disease. Several studies suggest that these central VF changes detected by 10-2 VFs may be missed by 24-2 or 30-2 VFs.[7–10] Other studies suggest that, using pattern standard deviation (PSD) or cluster criteria, a similar number of eyes are identified with central VF damage by 24-2 VF and 10-2 VF testing; both tests can miss some central VF damage that the other test identifies.[11,12]

Although the patterns of glaucomatous VF defects have been reported to be different among the four optic disc phenotypes,[2,5] those results were derived from analyses of solely 24-2 VF results and the central VFs were not fully evaluated. The present authors hypothesized that each glaucomatous optic disc phenotype represented a unique degree and pattern of central VF defect. The present study investigated central VF damage detected on 10-2 VF tests in 4 optic disc phenotypes of glaucoma. Moreover, regional VF defect patterns were compared with severity of central VF damage shown on 10-2 tests in definite and suspected

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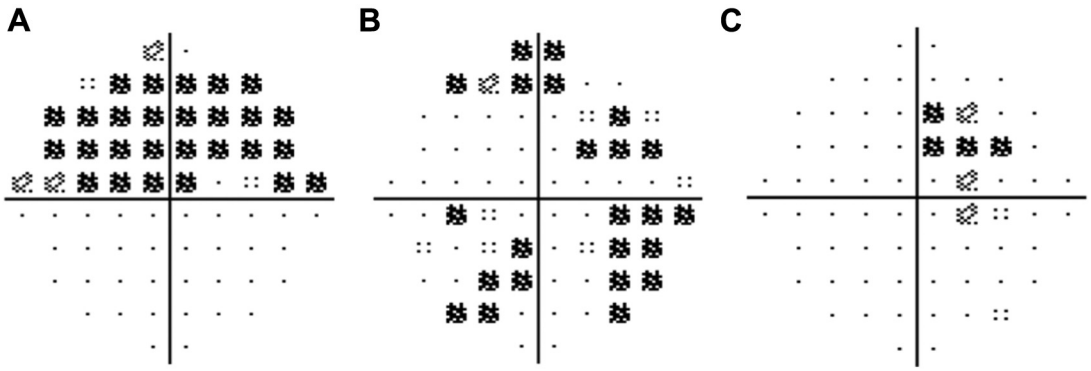


**FIGURE 1. Examples of 10-2 visual field (VF) categories. All VFs are presented from the right-eye view. Graphs show VFs with loss consistent with an arcuate-like pattern (A). VF with diffuse loss (B) and VFs with temporal loss are classified as other (C).**

glaucoma among different glaucomatous optic disc phenotypes.

## METHODS

GLAUCOMA PATIENTS AND HEALTHY SUBJECTS WERE recruited from the longitudinal University of California San Diego (UCSD)-based DIGS (Diagnostic Innovations in Glaucoma Study) and multicenter ADAGES (African Descent and Glaucoma Evaluation Study). The ADAGES is a collaboration of the UCSD Hamilton Glaucoma Center, Columbia University Irving Medical Center Edward S. Harkness Eye Institute (New York, New York, USA) and the University of Alabama at Birmingham, Department of Ophthalmology (Birmingham, Alabama, USA). That report is a cross-sectional analysis. The institutional review boards at all sites approved the study methodology, which adheres to the tenets of the Declaration of Helsinki for research involving human subjects and to the Health Insurance Portability and Accountability Act. Informed consent was obtained from all participants.

Details of the DIGS and ADAGES protocols and eligibility have been described previously.[13] Briefly, all patients underwent an annual comprehensive ophthalmologic examination, including review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, IOP measurements using Goldmann applanation tonometry, gonioscopy, dilated fundus examination, stereoscopic optic disc photography (3Dx stereo camera; Nidek, Palo Alto, California, USA) after maximal pupil dilation, and ultrasound pachymetry for central corneal thickness measurements in both eyes. The semiannual examination included IOP, spectral domain optical coherence tomography, and both 24-2 and 10-2 VF testing.

Glaucoma patients in this study were defined as individuals in whom glaucomatous optic neuropathy was present (defined as excavation, the presence of focal thinning, notching of neuroretinal rim, or localized or diffuse atrophy of the retinal nerve fiber layer on the basis of masked grading of optic disc photographs by 2 graders or clinical examination by a glaucoma specialist, and with (definite glaucoma) or without (glaucoma suspect) reliable (fixation losses ≤33%, false negatives <33%, and false positives ≤ 15%) and repeatably abnormal 24-2 VF tests. Inclusion criteria for this study were older than 18 years of age, demonstrated open angles with gonioscopy, had best-corrected visual acuity of 20/40 or better, and had refraction less than ±5.0 diopters (D) of sphere and 3.0 D of cylinder. Participants with a history of intraocular surgery (except for uncomplicated cataract surgery or uncomplicated glaucoma surgery), retinal pathologies including diabetic retinopathy and hypertensive retinopathy, nonglaucomatous optic neuropathy, uveitis, ocular trauma, Parkinson disease, Alzheimer disease, or stroke affecting VF were excluded. Those with unreliable VFs were also excluded from this report.

Participants who underwent automated VF testing using the 24-2 and 10-2 VF patterns on the Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, California, USA) within 6 months of imaging were enrolled. Although the 10-2 tests were not used at baseline to define the diagnostic groups, they had to meet the same reliability criteria as the 24-2 tests.

The quality of VF test results were reviewed by the Visual Field Assessment Center staff to identify and exclude VFs with evidence of inattention, inappropriate fixation, artifacts such as eyelid and lens rim artifacts, fatigue effects, macular pathology, and abnormal results caused by diseases other than glaucoma. Only those patients who had at least 2 reliable 10-2 VF results were included. Glaucoma severity was classified based on the 24-2 test only into glaucoma suspects, mild (MD ≥ −6 dB) and moderate (−12 ≤ MD < −6 dB) glaucomatous defects. Severity of glaucoma was restricted from early to moderate with MD ≥ −12 dB to avoid central field defects due to severe glaucoma.

• **CLASSIFYING 10-2 VISUAL FIELD TEST RESULTS:** For 10-2 VF tests, the same reliability criteria were required. The

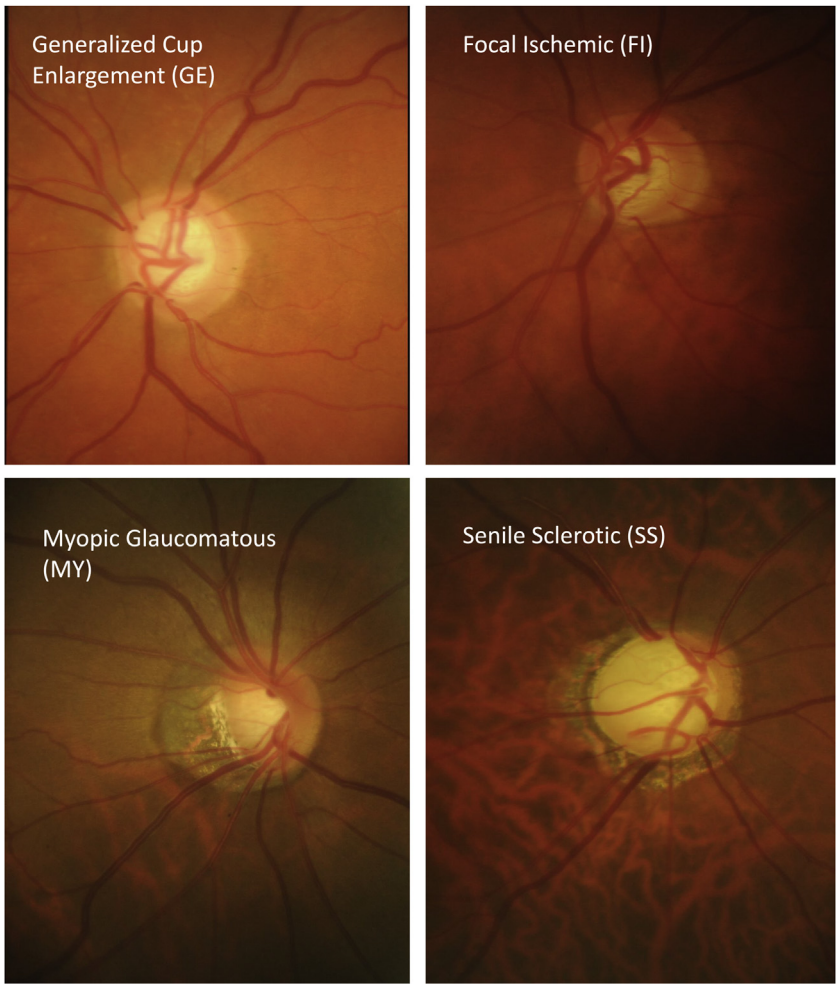


**FIGURE 2. Glaucomatous optic disc types divided into 4 groups as described by Nicolela and Drance.[2] FI = focal ischemic; GE = generalized cup enlargement; MY = myopic glaucomatous; SS = senile sclerotic disc.**

10-2 VF test result was considered abnormal if the hemifield on the total deviation or pattern deviation plot was abnormal on 2 consecutive visits. Hemifields were classified as abnormal if there was a cluster of 3 contiguous points (5%, 5% and 1% or 5%, 2%, and 2%) within a hemifield on either total deviation or pattern deviation plot.[14] The specificity of this cluster criteria has been reported to be approximately 95%.[14] The VF hemifields that were abnormal by this cluster test were divided into the following 3 categories based on the pattern and shape of abnormal points: 1) arcuate-like, 2) diffuse, and 3) other (Figure 1). The arcuate-like category included arcuate, a continuous, dense defect that involved both quadrants; partial arcuate, a continuous defect that involved both quadrants but was less dense than an arcuate; and nasal, a defect restricted largely to the nasal quadrant.[14,15] The diffuse category was defined as a loss in all 4 quadrants on total deviation and pattern deviation plots that did not appear arcuate-like. Abnormal hemifields that did not fall into either of those categories were classified as other, which were predominately scattered across the whole field or predominately located in the temporal quadrants.[14] Moreover, the average of the total deviation values at each 10-2 test point were compared by optic disc phenotype.

• **OPTIC DISC PHENOTYPE ASSESSMENT:** Disc types of glaucomatous and suspect eyes were divided into 4 groups as described by Nicolela and Drance[2] or as mixed or unclassified phenotypes[5] (Figure 2). In the FI phenotype, the optic disc had focal loss in the neuroretinal rim while other areas were normal. In the GE phenotype, there was a large and deep concentric circular cup without a localized defect of the neuroretinal rim. In the MY phenotype, there was temporal parapapillary atrophy with temporal cupping and a slightly tilted and ellipsoid optic disc. In the SS phenotype, there was an atrophic halo (chorioretinal atrophy) around the optic disc, saucerized and shallow cupping, and a "moth-eaten" and pale neuroretinal rim. For combination optic disc phenotypes, the optic disc was classified as

**TABLE 1.** Patient and Eye Characteristics in the Study Groups

| Patient Characteristics | Classification | | |
|---|---|---|---|
| | Glaucoma Suspect (n = 41; eyes = 94) | Glaucoma (n = 268; eye = 354) | *P* Value |
| Mean (95% CI) age | 69.8 (66.8-72.9) | 73.0 (71.6-74.4) | 0.133 |
| Females | 30 (73.2) | 131 (48.9) | 0.021 |
| Males | 11 (26.8) | 137 (51.1) | |
| African descent | 12 (29.3) | 108 (40.3) | 0.016 |
| European descent/other | 29 (70.7) | 160 (59.7%) | |
| Eye characteristics | | | |
| Mean (95% CI) IOP | 15.8 (14.6-17.0) | 14.1 (13.5-14.7) | 0.008 |
| Mean (95% CI) AL | 24.1 (23.9-24.2) | 24.1 (24.0-24.2) | 0.743 |
| Mean (95% CI) SE | −0.31 (−0.69 to 0.06) | −0.44 (−0.63 to −0.24) | 0.836 |
| Mean (95% CI) BMO Area | 2.09 (1.96-2.22) | 2.16 (2.09-2.23) | 0.512 |
| Mean (95% CI) VF 24-2 MD | −1.38 (−1.87 to −0.89) | −9.65 (−10.59 to −8.72) | <0.001 |
| Mean (95% CI) VF 24-2 PSD | 1.97 (1.74-2.20) | 7.39 (6.97-7.81) | <0.001 |
| Mean (95% CI) VF 10-2 MD | −0.84 (−1.28 to −0.40) | −8.82 (−9.73 to −7.91) | <0.001 |
| Mean (95% CI) VF 10-2 PSD | 1.55 (1.30-1.79) | 7.23 (6.69-7.78) | <0.001 |
| Phenotype | | | |
| FI | 17 (18.1) | 104 (29.4) | |
| GE | 35 (37.2) | 74 (20.9) | |
| MY | 16 (17.0) | 50 (14.1) | |
| SS | 26 (27.7) | 126 (35.6) | |

AL = axial length; BMO = Bruch's membrane opening; FI = focal ischemic; GE = generalized cup enlargement; IOP = intraocular pressure; MD = mean deviation; MY = myopic glaucomatous; PSD = pattern standard deviation; SE = spherical equivalent; SS = senile sclerotic disc; VF = visual field.

Continuous data are mean (95% confidence interval [CI]) and categorical data are n (%). Significance was determined by ANOVA and $\chi^2$ tests for patient-level continuous and categorical data and by generalized estimating equation (GEE) models for eye-level data.

mixed and unclassified. Two glaucoma specialists (E.E. and S.M.), who were masked as to the participant's identity, diagnostic status, race, and other results, classified the disc types independently. If initial classifications did not agree, consensus was obtained after the photographs were reviewed again. Any optic disc in which consensus could not be reached was categorized as unclassified. Mixed and unclassified eyes (n = 80) were not included in the statistical analysis.

• **STATISTICAL ANALYSIS:** Descriptive statistics were calculated as the mean (95% confidence interval [CI]) for continuous variables and count (percentage) for categorical variables. The statistical significance of continuous and categorical patient-level variables were compared among different phenotypes using analysis of variance (-ANOVA) and $\chi^2$ tests, respectively. Eye-level continuous characteristics were compared across groups using generalized estimating equation models, assuming an exchangeable working correlation matrix to account for within-patient clustering. Similarly, logistic generalized estimating equation models were used to assess the rates of abnormal 10-2 VF defect results among the optic disc phenotypes, with and without additional effects for age and 24-2 VF MD in the model. *P* values less than .05 were considered statistically significant. All analyses were performed using R software version 3.6.1 (R Project, Vienna, Austria).

## RESULTS

A TOTAL OF 448 EYES OF 309 GLAUCOMA PATIENTS WERE included in the analysis; 94 eyes were glaucoma suspects and 354 eyes had definite glaucoma. The interexaminer agreement for classification of eyes into FI, GE, MY, SE, or mixed/unclassified disc appearance types was good with a Kappa value of 0.83 (95% CI: 0.81-0.84).

Demographic and ocular characteristics of the study population are presented in Table 1. There were no significant differences in age, axial length, spherical equivalent, and Bruch's membrane opening area between glaucoma suspects and definite glaucoma groups. The definite glaucoma group had a higher proportion of males and African Americans, lower VF 10-2 MD, lower VF 24-2 MD, greater VF 10-2 PSD, and greater VF 24-2 PSD than the glaucoma suspects.

Among 448 glaucomatous (definite or suspect) eyes, the optic discs of 121 eyes (27%) were classified as FI; 109 eyes (24%) as GE; 66 eyes (15%) as MY; and 152 eyes (34%) as

**TABLE 2.** Patient And Eye Characteristics Across Different Glaucoma Phenotypes

| | Phenotype | | | | |
|---|---|---|---|---|---|
| | FI (n = 89; eye = 121) | GE (n = 72; eye = 109) | MY (n = 41; eye = 66) | SS (n = 107; eye = 152) | *P* Value |
| Patient characteristics | | | | | |
| Mean (95% CI) age | 70.2 (67.8, 72.6) | 69.6 (66.8, 72.5) | 71.9 (68.9, 74.9) | 76.7 (74.8, 78.7) | <0.001 |
| Females | 48 (53.9) | 38 (52.8) | 21 (51.2) | 54 (50.5) | 0.967 |
| Males | 41 (46.1) | 34 (47.2) | 20 (48.8) | 53 (49.5) | |
| African descent | 39 (43.8) | 38 (52.8) | 16 (39.0) | 27 (25.2) | 0.002 |
| European descent/other | 50 (56.2) | 34 (47.2) | 25 (61.0) | 80 (74.8) | |
| Eye characteristics | | | | | |
| Mean (95% CI) IOP | 14.6 (13.7-15.5) | 15.0 (13.9-16.1) | 14.2 (12.4-16.0) | 14.0 (13.1-15.0) | 0.557 |
| Mean (95% CI) AL | 23.9 (23.8-24.1) | 24.0 (23.9-24.2) | 24.3 (24.0-24.5) | 24.2 (24.0-24.4) | 0.002 |
| Mean (95% CI) SE | −0.38 (−0.69 to −0.08) | −0.25 (−0.52 to 0.01) | −0.82 (−1.31 to −0.32) | −0.38 (−0.70 to −0.07) | 0.212 |
| Mean (95% CI) BMO area | 2.11 (2.02-2.21) | 2.18 (2.08-2.28) | 2.01 (1.88-2.13) | 2.21 (2.10-2.33) | 0.041 |
| Mean (95% CI) VF 24-2 MD | −7.65 (−8.84 to −6.46) | −6.90 (−8.51 to −5.28) | −8.82 (−10.91 to −6.73) | −8.80 (−10.26 to −7.34) | 0.260 |
| Mean (95% CI) VF 24-2 PSD | 7.20 (6.46-7.94) | 4.90 (4.23-5.58) | 6.45 (5.38-7.52) | 6.48 (5.78-7.18) | <0.001 |
| Mean (95% CI) VF 10-2 MD | −7.60 (−8.83 to −6.37) | −5.07 (−6.47 to −3.67) | −8.05 (−10.31 to −5.78) | −8.18 (−9.64 to −6.73) | 0.004 |
| Mean (95% CI) VF 10-2 PSD | 7.76 (6.78 to 8.74) | 4.47 (3.68 to 5.27) | 5.79 (4.60 to 6.97) | 6.02 (5.24 to 6.81) | <0.001 |

AL, axial length; BMO = Bruch's membrane opening; FI = focal ischemic; GE = generalized cup enlargement; IOP = intraocular pressure; MD = mean deviation; MY = myopic glaucomatous; PSD = pattern standard deviation; SE = spherical equivalent; SS = senile sclerotic disc; VF = visual field.

Continuous data mean (95% confidence interval [CI]), and categorical data are n (%)). Significance was determined by ANOVA and $\chi^2$ tests for patient-level continuous and categorical data and by generalized estimating equation (GEE) models for eye-level data.

**TABLE 3.** Visual Field Characteristics Of Different Optic Disc Glaucoma Phenotype Across Disease Severity

| | FI | GE | MY | SS | *P* Value |
|---|---|---|---|---|---|
| Glaucoma suspect eyes | n = 17 | n = 35 | n = 16 | n = 26 | |
| Mean (95% CI) VF 24-2 MD | −0.59 (−1.14 to −0.05) | −0.18 (−0.60 to 0.24) | −1.31 (−2.20 to −0.42) | −0.64 (−1.28 to −0.00) | 0.097 |
| Mean (95% CI) VF 24-2 PSD | 1.91 (1.64-2.18) | 1.85 (1.51-2.19) | 1.91 (1.53-2.30) | 2.00 (1.64-2.35) | 0.950 |
| Mean (95% CI) VF 10-2 MD | 0.13 (−0.35 to 0.60) | −0.04 (−0.60 to 0.53) | −1.00 (−1.82 to −0.19) | −0.53 (−1.29 to 0.23) | 0.068 |
| Mean (95% CI) VF 10-2 PSD | 1.27 (1.15-1.39) | 1.39 (1.31-1.47) | 1.42 (1.18-1.67) | 1.43 (0.97-1.88) | 0.337 |
| Mean (95% CI) VF 10-2 foveal sensitivity | 36.4 (35.3-37.4) | 35.8 (35-36.6) | 35.3 (33.7-36.8) | 34.5 (33.6-35.4) | 0.319 |
| Glaucoma eyes | n = 104 | n = 74 | n = 50 | n = 126 | |
| Mean (95% CI) VF 24-2 MD | −8.44 (−9.75 to −7.14) | −9.36 (−11.47 to −7.25) | −11.02 (−13.38 to −8.66) | −10.51 (−12.07 to −8.96) | 0.109 |
| Mean (95% CI) VF 24-2 PSD | 7.94 (7.23-8.64) | 6.11 (5.31-6.91) | 7.83 (6.79-8.88) | 7.51 (6.80-8.22) | 0.004 |
| Mean (95% CI) VF 10-2 MD | −8.42 (−9.72 to −7.12) | −6.98 (−8.83 to −5.14) | −10.23 (−12.87 to −7.58) | −9.78 (−11.34 to −8.22) | 0.079 |
| Mean (95% CI) VF 10-2 PSD | 8.55 (7.58-9.52) | 5.59 (4.55-6.62) | 7.12 (5.84-8.40) | 7.11 (6.28-7.94) | <0.001 |
| Mean (95% CI) VF 10-2 foveal sensitivity | 35 (34.3-35.7) | 34.4 (33.5-35.4) | 34.3 (33.2-35.3) | 33 (32.2-33.8) | 0.2928 |
| Mild glaucoma | n = 48 | n = 36 | n = 21 | n = 46 | |
| Mean (95% CI) VF 24-2 MD | −2.97 (−3.47 to −2.48) | −2.81 (−3.25 to −2.38) | −3.12 (−3.94 to −2.30) | −3.18 (−3.66 to −2.69) | 0.711 |
| Mean (95% CI) VF 24-2 PSD | 5.20 (4.37-6.02) | 3.84 (3.14-4.54) | 4.98 (3.94-6.03) | 3.86 (3.36-4.35) | 0.013 |
| Mean (95% CI) VF 10-2 MD | −3.97 (−5.02 to −2.92) | −1.95 (−2.46 to −1.44) | −2.63 (−4.00 to −1.25) | −3.41 (−4.38 to −2.45) | <0.001 |
| Mean (95% CI) VF 10-2 PSD | 5.81 (4.45-7.16) | 2.58 (1.87-3.28) | 3.96 (2.43-5.49) | 3.96 (2.96-4.97) | <0.001 |
| Mean (95% CI) VF 10-2 foveal sensitivity | 35.7 (35.1-36.3) | 34.7 (33.5-35.9) | 35 (33.5-36.4) | 33.1 (32.2-34.1) | 0.065 |
| Moderate glaucoma | n = 32 | n = 13 | n = 10 | n = 30 | |
| Mean (95% CI) VF 24-2 MD | −8.35 (−8.89 to −7.80) | −8.17 (−9.09 to −7.24) | −8.42 (−9.21 to −7.64) | −8.45 (−8.99 to −7.91) | 0.961 |
| Mean (95% CI) VF 24-2 PSD | 9.41 (8.39-10.43) | 7.08 (5.86-8.29) | 7.42 (6.62-8.23) | 8.89 (7.66-10.11) | 0.002 |
| Mean (95% CI) VF 10-2 MD | −8.75 (−12.30 to −5.19) | −5.44 (−9.61 to −1.28) | −5.20 (−14.46 to 4.06) | −8.61 (−11.87 to −5.35) | 0.567 |
| Mean (95% CI) VF 10-2 PSD | 9.90 (8.36 to 11.43) | 5.65 (4.07-7.22) | 6.83 (4.92-8.73) | 7.60 (6.03-9.17) | <0.001 |
| Mean (95% CI) VF 10-2 foveal sensitivity | 34 (32.6-35.3) | 33.6 (31.8-35.3) | 32.9 (31.7-34.1) | 32.9 (31.7-34.1) | 0.475 |

FI = focal ischemic; GE = generalized cup enlargement; MD = mean deviation; MY = myopic glaucomatous; PSD = pattern standard deviation; SS = senile sclerotic disc; VF = visual field. Values are mean (95% confidence interval [CI]).

**TABLE 4.** Prevalence of Abnormal VF 10-2 by Phenotype, Stratified by Severity Group

| | Phenotype | | | | |
|---|---|---|---|---|---|
| | FI | GE | MY | SS | *P* Value |
| Glaucoma suspect | n = 17 | n = 35 | n = 16 | n = 26 | |
| Abnormal VF 10-2 | 4 (23.5) | 3 (8.6) | 5 (31.2) | 3 (11.5) | |
| Mild glaucoma | n = 48 | n = 36 | n = 21 | n = 46 | 0.013 (0.014) |
| Abnormal VF 10-2 | 38 (79.2) | 16 (44.4) | 13 (61.9) | 31 (67.4) | |
| Moderate glaucoma | n = 32 | n = 13 | n = 10 | n = 30 | |
| Abnormal VF 10-2 | 29 (90.6) | 11 (84.6) | 10 (100.0) | 30 (100.0) | |
| Total (Definite and suspected glaucoma) | n = 121 | n = 109 | n = 66 | n = 152 | <0.001 (0.005) |
| Abnormal VF 10-2 | 95 (78.5) | 55 (50.5) | 47 (71.2) | 113 (74.3) | |

FI = focal ischemic; GE = generalized cup enlargement; GON = glaucomatous optic neuropathy; GVFD = glaucomatous visual field defect; MD = mean deviation; MY = myopic glaucomatous; SS = senile sclerotic disc; VF = visual field; VF = visual field.

Significance was determined by a binomial generalized estimating equation model (assuming an exchangeable working correlation matrix). *P* values in parenthesis are adjusted for VF 24-2 MD and age. Due to sparsity, no *P* value was reported for GON-only eyes or moderate glaucoma eyes.

SS (Table 2). SS eye participants were significantly older ($P < .001$) than participants with the other optic disc phenotypes. Race distribution differed among the phenotypes, and the GE group had more patients of African descent than the other groups ($P = .002$). Axial length was the highest ($P = .002$) and Bruch's membrane opening area was the lowest ($P = .041$) in MY eyes. There were no significant differences in sex, IOP, or spherical equivalent, among different optic disc phenotypes. Although VF 24-2 MD were comparable among glaucomatous optic disc phenotypes ($P = .260$), GE eyes had the greatest VF 10-2 MD ($P = .004$), the lowest VF 24-2 PSD ($P < .001$), and the lowest VF 10-2 PSD ($P < .001$).

No significant differences in VF 10-2 and VF 24-2 global indices were found among optic disc phenotypes in the glaucoma suspects. In the glaucoma group, VF 24-2 MD results were comparable among the phenotypes. However, VF 24-2 PSD ($P = .004$) and VF 10-2 PSD ($P < .001$) were the lowest in the GE eyes (6.11; 95% CI: 5.31-6.91 dB and 5.59; 95% CI: 4.55- 6.62 dB; respectively) and highest in the FI eyes (7.94; 95% CI: 7.23-8.64 dB and 8.55; 95% CI: 7.58-9.52 dB, respectively). In mild glaucoma, although there were no significant group differences in VF 24-2 MD among optic disc phenotypes, VF 10-2 MD results ($P < .001$) were the lowest and VF 10-2 PSD results ($P < .001$) were the highest in the FI eyes. In moderate glaucomatous eyes, no significant group differences in VF 24-2 MD and VF 10-2 MD results were found. However, VF 24-2 PSD ($P = .002$) and VF 10-2 PSD ($P < .001$) were the lowest in GE eyes and highest in FI eyes in those eyes (Table 3).

The prevalence of abnormal VF 10-2 clusters in the all-glaucoma (definite and suspected) eyes was highest in the FI eyes (78.5%) ($P < .001$) and lowest in the GE eyes (50.5%). In glaucoma suspects, the MY (31.2%) and FI (23.5%) groups had the highest and GE (8.6%) group had the lowest 10-2 abnormality. The prevalence of abnormal VF 10-2 test results in mild glaucoma was the lowest in GE eyes (44.4%) and highest in FI eyes (79.2%) ($P = .013$) (Table 4).

• **CLASSIFICATION OF 10-2 VISUAL FIELDS:** Results of the 10-2 hemifield classification are shown in Table 5. In all-glaucomatous eyes (definite and suspected), the superior hemifield of VF 10-2 was affected more often than the inferior hemifield in all optic disc phenotypes, and the arcuate-like pattern was the most common pattern of 10-2 VF defects. In mild glaucoma, similarly, the superior hemifield was affected more prominently in all optic disc phenotypes, and the arcuate-like pattern was the most common pattern of the 10-2 VF defect in superior and inferior hemifield in all glaucomatous optic disc phenotypes. Of note, the superior hemifield was more preferentially affected in the MY and FI groups.

• **PATTERN OF GLAUCOMATOUS VF DAMAGE:** In mild glaucoma, the proportion of eyes with at least 1 abnormal point depressed <1% in the most central 16 points, and most central 4 points of the 10-2 VF pattern deviation plot were lower in GE eyes (7; 19.4% and 12; 25.0%, respectively) than in FI eyes (30; 62.5%, and 12; 25.0%, respectively), MY eyes (12; 57.1%, and 7; 33.3%, respectively), and SS eyes (27; 58.7%, and 14; 30.4%, respectively; $P = 0.002$ and $P = 0.183$, respectively). The pattern of glaucomatous VF damage in the macula in different optic disc phenotypes is presented in Figure 3, using pseudocolors. In mild glaucoma (Figure 3, First row), FI eyes and MY eyes were more severely affected. Furthermore, in those optic disc phenotypes, the deepest defects (yellow and red) were close to fixation in the superior VF and the superior papillomacular region (blue rectangles) and inferior hemifield were less affected. In all glaucoma cases (Figure 3, second row), a similar pattern was found with FI and MY phenotypes demonstrating predominant involvement of the superior

**TABLE 5.** 10-2 Visual Field Defect Location and Pattern in Eyes With Glaucoma

| | Optic Disc Phenotype | | | |
|---|---|---|---|---|
| | FI | GE | MY | SS |
| Mild glaucoma | (n = 48) | (n = 36) | (n = 21) | (n = 46) |
| Defect location | | | | |
| None | 10 (20.8) | 20 (55.6) | 8 (38.1) | 15 (32.6) |
| Inferior only | 10 (20.8) | 5 (13.9) | 2 (9.5) | 7 (15.2) |
| Superior only | 21 (43.8) | 7 (19.4) | 9 (42.9) | 10 (21.7) |
| Both | 7 (14.6) | 4 (11.1) | 2 (9.5) | 14 (30.4) |
| Superior pattern | | | | |
| None | 20 (41.7) | 25 (69.4) | 10 (47.6) | 22 (47.8) |
| Arcuate-like | 25 (52.1) | 10 (27.8) | 9 (42.9) | 20 (43.5) |
| Diffuse | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Other | 3 (6.2) | 1 (2.8) | 2 (9.5) | 4 (8.7) |
| Inferior pattern | | | | |
| None | 31 (64.6) | 27 (75.0) | 17 (81.0) | 25 (54.3) |
| Arcuate-like | 14 (29.2) | 9 (25.0) | 3 (14.3) | 16 (34.8) |
| Diffuse | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Other | 3 (6.2) | 0 (0.0) | 1 (4.8) | 5 (10.9) |
| Total (definite and suspected glaucoma) | (n = 121) | (n = 109) | (n = 66) | (n = 152) |
| Defect location | | | | |
| None | 26 (21.5) | 54 (49.5) | 19 (28.8) | 39 (25.7) |
| Inferior only | 21 (17.4) | 8 (7.3) | 6 (9.1) | 16 (10.5) |
| Superior only | 34 (28.1) | 14 (12.8) | 15 (22.7) | 19 (12.5) |
| Both | 40 (33.1) | 33 (30.3) | 26 (39.4) | 78 (51.3) |
| Superior pattern | | | | |
| None | 47 (38.8) | 62 (56.9) | 25 (37.9) | 55 (36.2) |
| Arcuate-like | 70 (57.9) | 44 (40.4) | 33 (50.0) | 80 (52.6) |
| Widespread | 0 (0.0) | 0 (0.0) | 1 (1.5) | 6 (3.9) |
| Other | 4 (3.3) | 3 (2.8) | 7 (10.6) | 11 (7.2) |
| Inferior pattern | | | | |
| None | 60 (49.6) | 68 (62.4) | 34 (51.5) | 58 (38.2) |
| Arcuate-like | 51 (42.1) | 37 (33.9) | 27 (40.9) | 74 (48.7) |
| Widespread | 0 (0.0) | 0 (0.0) | 1 (1.5) | 6 (3.9) |
| Other | 10 (8.3) | 4 (3.7) | 4 (6.1) | 14 (9.2) |

FI = focal ischemic; GE = generalized cup enlargement; GON = glaucomatous optic neuropathy; GVFD = glaucomatous visual field defect; MD = mean deviation; MY = myopic glaucomatous; SS = senile sclerotic disc; SS = senile sclerotic disc; VF = visual field; VF = visual field. Values are n (%).

VF. Although the 10-2 VF was affected more diffusely in SS and GE phenotypes, still, superior VF defects close to fixation and inferior defects were at the nasal edge of the inferior field. Likewise, superior papillomacular region and inferior hemifield were less affected. Figure 4 shows the average total deviation values for the 24-2 visual field. Similarly, the most central 12- and most central 4-most inner points were more affected in eyes with FI and MY phenotypes.

## DISCUSSION

THESE RESULTS SHOW THAT CENTRAL VF DAMAGE WAS less common in eyes with the GE phenotype. In eyes classified as glaucoma suspects or mild glaucoma (MD better than −6 dB in 24-2 tests), abnormal 10-2 VFs were more common in FI and MY phenotypes, despite no significant differences between the 24-2 VFs. Abnormal central VFs were found in up to one-fourth and three-fourths of eyes with FI phenotypes in glaucoma suspects and mild glaucoma, respectively. This information may help the clinicians to better understand the role of 10-2 VF tests in glaucoma standard care and provides clinical clues to predict the presence of parafoveal scotoma.

Different optic disc phenotypes have been found associated with distinct clinical characteristics that may be involved in glaucoma pathogenesis.[2,3] FI eyes in which there is a markedly focal change of the optic disc have highly characteristic VF changes.[4] Discs of this type are

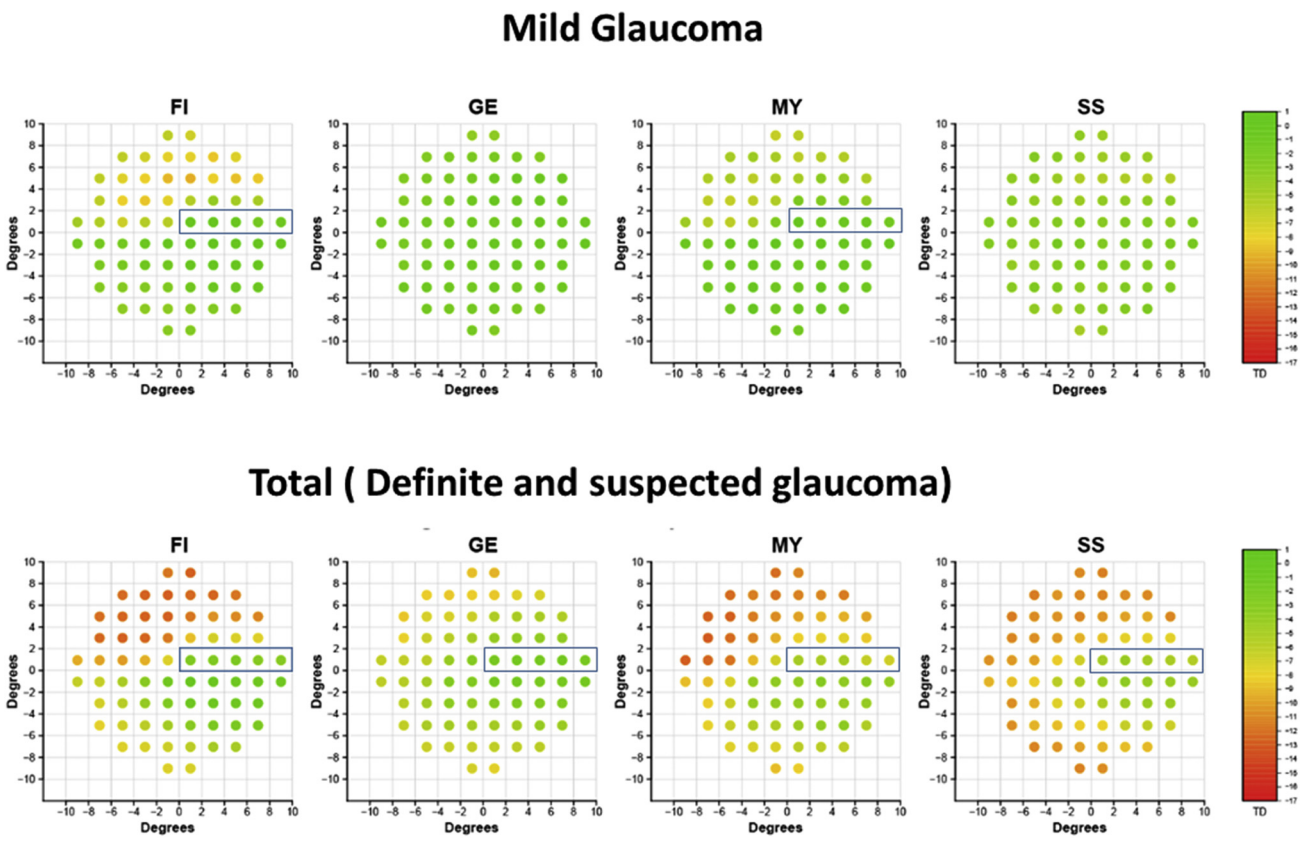


**FIGURE 3. Pseudocolor map for average total deviation values at each 10-2 location in mild glaucoma (top) and all glaucoma (bottom). The blue rectangle corresponds to the papillomacular region, which is preserved in the superior hemifield. Both maps are from the right-eye view. FI = focal ischemic; GE = generalized cup enlargement; MY = myopic glaucomatous; SS = senile sclerotic disc.**

characterized by localized neuroretinal rim tissue loss primarily at the inferior or superior pole of the optic nerve head (just temporal to the midline) and less frequent involvement of the temporal or nasal disc.[3] The age of subjects with the FI phenotype is slightly younger than the mean age of all primary open-angle glaucoma patients, and women are more likely to be affected than men.[2] It was found that the GE group had proportionately more patients of African descent than the other groups, despite similar axial lengths and refractive errors in the African and European descent groups. A previous study showed that there are structural differences within the optic nerve complex between these groups and that eyes in patients of African descent were less likely to have focal damage than the eyes of patients of European descent.[16] In the present study, the FI phenotype in definite glaucoma occurred more frequently than in cases of suspected glaucoma. This agrees with previous investigations that showed glaucomatous eyes with the FI phenotype had more rapid neuroretinal rim loss and VF progression than the other phenotypes.[4]

Different pathophysiologic mechanisms may be involved in producing the 4 types of optic disc phenotypes.[2,3] For example, mechanical distortion of the lamina cribrosa with impingement on the retinal ganglion cell axons may result in diffuse damage.[17] Similarly, generalized compromise of optic nerve head blood flow also may result in diffuse damage.[18] Localized damage may be related to a focal area of weakness in the lamina or localized vascular event such as one heralded by a disc hemorrhage or focal loss of choriocapillaris.[16,19,20] Localized optic disc change associated with glaucomatous paracentral scotomas lie closer to the papillomacular bundle than that due to peripheral VF loss.[21] As another example, Sawada and associates[22] reported that the severity of lamina cribrosa defects in myopic glaucoma usually correlated with the extent of disc tilting, and the location of lamina cribrosa defects usually were observed at the temporal region of the optic disc. With these observations, they suggest reasons why the central scotomas appear in the early stage in myopic glaucoma.

Early glaucomatous damage often involves the macula. Even in glaucoma suspect eyes, abnormal central VF defects were observed in as many as one-third of FI and MY eyes. This finding is similar to that in the study by Grillo and associates which demonstrated that abnormal central VF were prevalent in 35% and 39% of ocular hypertensive and glaucoma suspect eyes, respectively, whereas 21.5% and 24.8% classified as normal based on 10-2 were classified as abnormal by the 24-2.[23] In another study, Traynis and associates[10] showed that as many as 16% of eyes with a

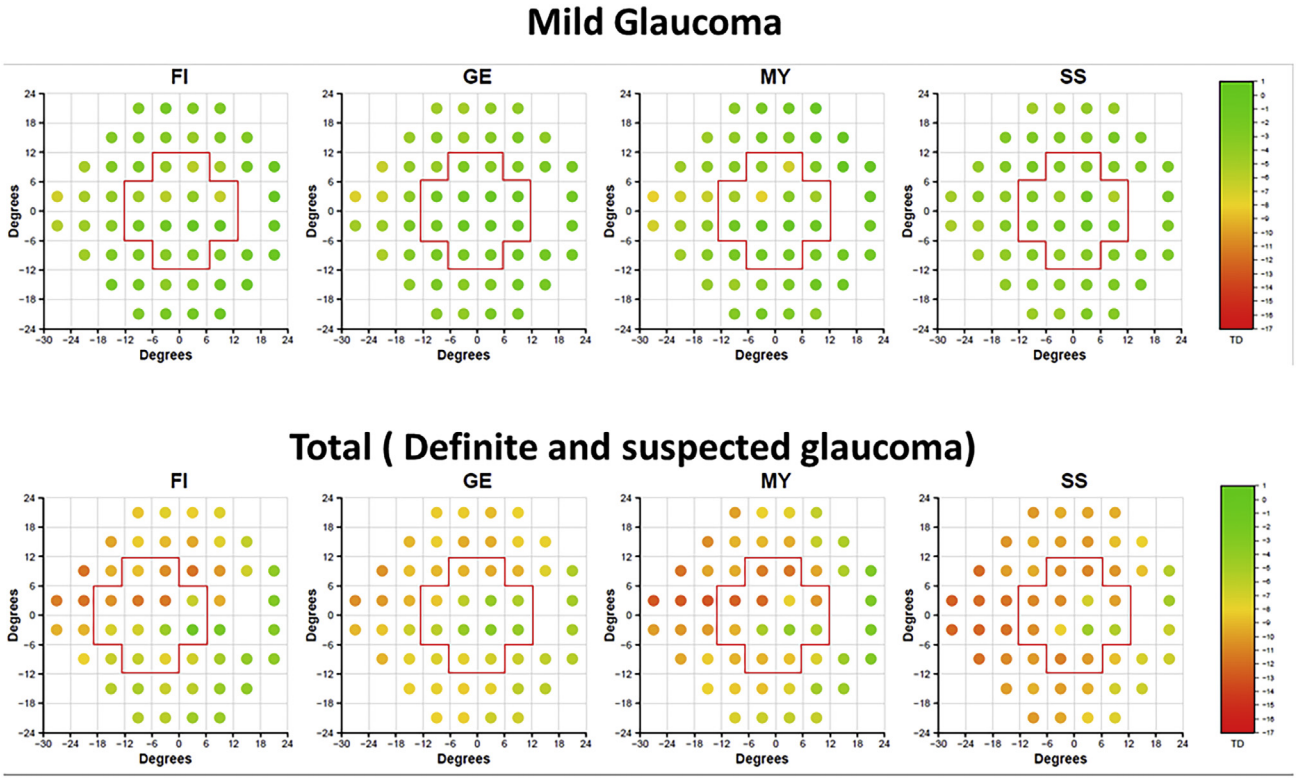


**FIGURE 4. Pseudocolor map for average total deviation values at each 24-2 location in mild glaucoma (top) and all glaucoma (bottom) phenotypes. The red cross area contains central 12 points and corresponds to the central 10-degrees of visual field. Both maps are from the right-eye view. FI = focal ischemic; GE = generalized cup enlargement; MY = myopic glaucomatous; SS = senile sclerotic disc.**

normal 24-2 VF result had significant abnormalities on a 10-2 VF in eyes with early glaucoma. Park and associates[24] found that 74% of eyes had a parafoveal scotoma, detected on the 10-2 VF test results in a population with mild glaucoma. The present study demonstrated that 65% of eyes with mild glaucoma had abnormal 10-2 VF test results and that central VF was more affected in the FI group than in the other glaucomatous optic disc phenotypes. Although the foveal sensitivities were similar among the phenotypes, FI, MY, and SS groups had proportionately more eyes with abnormal points in most central 4 and 16 points of 10-2 VF than in the GE group. Similarly, Nicolela and Drance evaluated 24-2 VF tests in distinct glaucomatous optic disc phenotypes and demonstrated that eyes in the FI and MY groups typically had dense, localized scotomas and that fixation was frequently threatened by these scotomas, particularly in the FI group (81%).[2] The marked predominance of superior scotomas in the FI group corresponded to the great frequency of focal loss in the inferior pole of the disc.[2] These studies were carried out using 24-2 VF and may have underestimated central involvement. Early glaucomatous damage near fixation can be relatively subtle as it involves a loss of only a few dB of sensitivity, very local, or diffuse.[25–27] Patients with glaucoma with VF defects within 5-degrees of fixation are at greater risk of losing visual acuity and global VF,[28,29] and VF defects within 3-degrees of fixation in more than 2 adjacent quadrants may cause reading difficulty.[30] The macula is particularly important for daily functioning, and loss in that region is strongly associated with self-reported diminished quality of life.[31,32] A recent study has shown that the 10-2 VF was abnormal in nearly as many hemifields as was the 24-2 VF, including some with normal 24-2 VF, suggesting that the 24-2 test is not optimal for detecting early damage of the macula. That study recommended 10-2 examinations or their equivalents are necessary to detect central abnormalities and early glaucomatous damage.[33] Other studies have suggested that close examination of the 24-2 VF based on PSD or cluster criteria can detect a similar number of eyes with central VF damage.[11,12]

Present findings have important clinical implications. Patients with central VF damage have functional loss which can affect their quality of life. They also have advanced glaucomatous damage according to many classification systems which consider the presence of central damage a criteria for severe disease.[31,32] Notably, patients in the FI group of the current study were more likely to have central VF abnormalities especially in early stages of

the disease, which underscores the importance of clinically evaluating the optic disc phenotypes.

In contrast to the results found in the FI and MY optic disc phenotypes, only 10% and 40% of eyes with glaucoma suspect and mild glaucoma had central VF damage, respectively, with the GE optic disc phenotype; this was significantly lower than that observed in other optic disc phenotypes. Remarkably, the severity of central functional damage also was lower in GE phenotypes in mild and moderate glaucoma as indicated by significantly better 10-2 MD. Similar findings have been shown by previous investigators.[2] Specifically, in a cross-sectional study diffuse VF loss in 24-2 VF was the only finding in 40% of eyes with GE optic disc phenotype.[2] However, once glaucomatous eyes become moderately damaged, most of the eyes showed central VF defect with 10-2 VF tests. In the current study, the superior hemifield of VF 10-2 was preferentially affected in the MY and GE groups. In both definite and glaucoma suspect eyes, an arcuate-like pattern was the most common pattern of 10-2 VF defect in each of the glaucomatous optic disc phenotypes. This finding agrees with that of Traynis and associates who found that more than two-thirds of abnormal central visual defects were arcuate-like in eyes with early glaucoma.[10] The present results are also supported by the model proposed by Hood and associates.[3] That model assumes that the retinal ganglion cells in the inferior retinal region of the macula largely project to the most vulnerable (inferior) region of the disc and can be damaged early in the glaucoma disease process. The arcuate defects seen in the upper macular VF are associated with arcuate retinal nerve fiber layer defects that are centered primarily in the macular vulnerable zone of the disc. The severity of the damage was also greater in superior central hemifield as observed by heatmap plots, and the superior arcuate VF defect was the most common pattern seen in these groups.

There are some limitations to the current study. First, optic disc phenotypes were based on subjective observations, although the 2 experienced graders in this study had good interobserver agreement in determining the final optic disc phenotype ($\kappa = 0.83$). Second, the differences in some ocular and demographic characteristics among the optic disc phenotype groups may suggest that all factors that might have affected central VF damage were not adequately controlled despite adjusting for confounders in multivariate analysis. Finally, the study was a cross-sectional study that did not evaluate subjects over time, limiting our understanding of the relationship between changes in central VF damage and optic disc phenotypes that a longitudinal study would provide.

In conclusion, macular damage in early glaucoma, as detected with 10-2 VFs, appears more frequently in FI and MY phenotypes than in the GE phenotype despite similar 24-2 results. Central VF damage was less frequent and less severe in eyes in GE glaucomatous optic disc phenotype than in the other groups. The pattern of central VF damage shown in 10-2 tests was mostly arcuate-like in each of the optic disc phenotypes. Assessing the 10-2 VF, particularly in those patients with FI and MY optic disc phenotypes, will enhance glaucoma diagnosis and management.

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