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24-2 Visual Fields Miss Central Defects Shown on 10-2 Tests in Glaucoma Suspects, Ocular Hypertensives, and Early Glaucoma

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Purpose: To investigate the prevalence of visual field defects in glaucomatous eyes, glaucoma suspects, and ocular hypertensives with 24-2 and 10-2 visual fields.

Design: Prospective, cross-sectional study.

Participants: Patients with or suspected glaucoma tested with 24-2 and 10-2. Patients were classified into 3 groups on the basis of the presence of glaucomatous optic neuropathy (GON) and 24-2 visual field abnormalities: early glaucoma (GON and abnormal visual field, mean deviation >-6 decibels [dB]), glaucoma suspects (GON and normal visual field), and ocular hypertensives (normal disc, normal visual field, and intraocular pressure >22 mmHg). For the classification of visual field abnormalities, 24-2 and 10-2 tests performed on the same visit were analyzed.

Main Outcome Measures: Comparison of the prevalence of abnormal 24-2 versus 10-2 visual field results based on cluster criteria in each diagnostic group.

Results: A total of 775 eyes (497 patients) were evaluated. A total of 364 eyes had early glaucoma, 303 eyes were glaucoma suspects, and 108 eyes were ocular hypertensives. In the glaucoma group, 16 of the 26 eyes (61.5%) classified as normal based on cluster criteria on 24-2 tests were classified as abnormal on 10-2 visual fields. In eyes with suspected glaucoma, 79 of the 200 eyes (39.5%) classified as normal on the 24-2 test were classified as abnormal on 10-2 visual fields. In ocular hypertensive eyes, 28 of the 79 eyes (35.4%) classified as normal on the 24-2 were classified as abnormal on the 10-2. Patients of African descent were more likely to have an abnormal 10-2 result (67.3 vs. 56.8%, $P = 0.009$).

Conclusions: Central visual field damage seen on the 10-2 test is often missed with the 24-2 strategy in all groups. This finding has implications for the diagnosis of glaucoma and classification of severity. *Ophthalmology 2017;■:1–8 © 2017 by the American Academy of Ophthalmology*

There is compelling structural and functional evidence that glaucomatous damage to the macula occurs even in early stages of the disease.[1] For example, since Drance[2] first pointed out that the central visual field could be affected even in early glaucoma, evidence has been mounting that macular damage, as seen with standard automated perimetry (SAP), is common.[1,3–7] This information is clinically important because the macula (herewith defined as the central 8 degrees around the fovea) includes approximately 30% of all retinal ganglion cells (RGCs)[8] and supplies the information for 55% to 60% of the primary visual cortex.[9] Given this high density of RGCs in the macula and their overwhelming representation in the visual cortex, it is not surprising that damage to the macula can substantially affect health-related quality of life (HRQoL).[10] Glaucoma affects patients' HRQoL in multiple ways, including driving,[11] walking and falls,[12] and reading.[13] Moreover, central vision, which correlates with macular function, is important when performing activities of daily life. The psychologic burden increases as vision decreases, along with a growing fear of blindness, social withdrawal from impaired vision, and depression.[14] Therefore, glaucoma care aims to preserve patients' HRQoL by maintaining visual function without causing untoward effects from treatment.[15]

However, glaucomatous damage to the macula will be missed in clinical practice if only 24-2 visual fields and peripapillary optical coherence tomography (OCT) scans are performed,[16,17] as is often the case. In particular, studies have shown that macular damage is prevalent among patients with early glaucoma if one uses the appropriate tools to assess it, namely, 10-2 visual fields[4–6,16] and OCT cube scans of the macula.[1,17–19]

Traynis et al[4] have shown that as much as 16% of eyes with a normal 24-2 visual field result have significant abnormalities on 10-2 in this sample of patients with early glaucomatous functional loss. This number is striking because many of the so-called glaucoma suspects or those with pre-perimetric glaucoma may in fact have central damage, which now classifies them with "severe glaucoma"

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according to the clinical classification system currently widely used.[20] This information comes from a prospective, cross-sectional database in which patients underwent 24-2, 10-2, and spectral-domain (SD) OCT testing irrespective of their clinical status to minimize selection bias, as long as they had signs of glaucomatous optic neuropathy (GON) and their visual fields were not severely affected (i.e., 24-2 visual field mean deviation [MD] >−6 decibels [dB]).[4] However, a limitation of that study is that all patients had GON, which by itself limits the generalizability of our conclusions. Likewise, Park et al[5] found that 74% of eyes had a parafoveal scotoma detected on the 10-2 visual field test in a population with GON and abnormal 24-2 visual fields with MD better than −6 dB. In a population including those with primary open-angle glaucoma (mild, moderate, and severe), ocular hypertensives, and glaucoma suspects, Sullivan-Mee et al[6] reported that 6% of eyes without 24-2 field loss exhibited a 10-2 defect. However, the breakdown of the prevalence of 10-2 abnormalities among ocular hypertensives and glaucoma suspects was not reported, because the group "without 24-2 field loss" represented pooled information from all 3 groups (i.e., including patients with so-called glaucoma with no loss on the 24-2).

To address this issue, in the present article we analyzed an independent database that includes subjects with and without GON, including eyes with early glaucoma field loss, glaucoma suspects, and ocular hypertensives. Participants of the African Descent and Glaucoma Evaluation Study (ADAGES),[21] a multicenter, prospective, longitudinal study including the entire spectrum of glaucomatous damage, were included. In the ADAGES, all participants underwent a standardized frequency of visits and testing, including 24-2 and 10-2 visual field testing. Moreover, all participants had extensive experience with perimetry, which minimized the undesired effects of unreliable test results and learning effects. In this group of patients, we tested the hypothesis that central, 10-2 visual field defects often are missed on 24-2 tests not only in eyes with established glaucoma but also in glaucoma suspects and ocular hypertensives.

Methods

The 3-site ADAGES collaboration includes the Hamilton Glaucoma Center at the Department of Ophthalmology, University of California-San Diego (data coordinating center), Edward S. Harkness Eye Institute at Columbia University Medical Center (site formerly located at New York Eye and Ear Infirmary), and the Department of Ophthalmology, University of Alabama-Birmingham. The institutional review boards at all sites approved the study methodology, which adheres to the tenets of the Declaration of Helsinki and to the Health Insurance Portability and Accountability Act. All participants gave written informed consent. Enrollment in ADAGES began in January 2003 and ended in July 2006, and follow-up continued until 2016.

Participants

Participants were asked to identify their race by self-report using the National Eye Institute inclusion/enrollment system describing ethnicity and race (http://orwh.od.nih.gov/pubs/outreach.pdf [pages 120−121]). Information regarding a family history of glaucoma (biological mother, father, sibling, aunt, uncle, and grandparent) also was obtained. Normal and patient participants were recruited from the glaucoma clinics and ophthalmic practices at each of the 3 recruiting sites by advertisement and community presentations, and referral from other ophthalmologists and optometrists in the community.

The ocular testing completed for ADAGES has been described.[21] In brief, participants underwent a comprehensive ophthalmic examination, including annual review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure, dilated fundoscopy examination, pachymetry, simultaneous stereoscopic optic disc photography, and SAP with 24-2 and 10-2 Swedish interactive threshold algorithm (Carl Zeiss Meditec, Inc, Dublin, CA). Both 24-2 and 10-2 visual fields were repeated every 6 months, and optic disc photographs were performed every 12 months.

Inclusion Criteria at Baseline

All participants had open angles, a best-corrected visual acuity ≥20/40, and a refractive error <5.0 diopters sphere and <3.0 diopters cylinder. At least 1 high-quality stereophotograph and 2 reliable SAP Humphrey 24-2 field test results at baseline were required, defined as <33% false-positives, false-negatives, and fixation losses. 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. Both eyes were included, except in patients in whom only 1 eye met the study criteria. All participants were aged more than 18 years. Diabetic participants without evidence of retinopathy were included.

Exclusion Criteria

Participants were excluded if they had a history of intraocular surgery (except for uncomplicated cataract surgery or glaucoma surgery); secondary causes of glaucoma (e.g., iridocyclitis, trauma); other systemic or ocular diseases known to affect the visual field (e.g., pituitary lesions, demyelinating diseases); significant cognitive impairment; history of stroke, Alzheimer disease, or dementia; problems other than glaucoma affecting color vision; an inability to perform visual field examinations reliably; or a life-threatening disease that precluded retention in the study.

Evaluation of the Optic Nerve Complex

All data were processed through the ADAGES Coordinating Center, the Visual Field Assessment Center, and the Imaging Data Evaluation and Analysis (IDEA) Center housed at the Hamilton Glaucoma Center, University of California-San Diego. The IDEA Center processed and reviewed the quality of all simultaneous stereophotographs. These reading centers also handled all data from Diagnostic Innovations in Glaucoma Study (DIGS) and other National Eye Institute or industry-sponsored trials. Both centers are responsible for certifying visual field and imaging technicians and photo graders, processing any data-related queries to and from each site, and requesting that tests be repeated when needed.

All color simultaneous stereophotographs were taken using a Nidek Stereo Camera Model 3-DX (Nidek Inc, Palo Alto, CA) after maximal pupil dilation. All photograph evaluations were performed using a simultaneous stereoscopic viewer (Asahi Pentax Stereo Viewer II; Pentax, Tokyo, Japan) with a standard fluorescent light bulb. Certified photograph graders evaluated all photographs. To be certified, individuals were trained and then tested on separate standardized sets of stereophotographs depicting (1) glaucomatous and healthy eyes and (2) progressing and