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The Impact of Location of Progressive Visual Field Loss on Longitudinal Changes in Quality of Life of Patients with Glaucoma

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Purpose: To evaluate the association between rates of progressive loss in different regions of the visual field and longitudinal changes in quality of life (QoL).

Design: Prospective, observational cohort study.

Participants: The study included 236 patients with glaucomatous visual field loss followed for an average of 4.3±1.5 years.

Methods: All subjects had the 25-item National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) performed annually and standard automated perimetry (SAP) at 6-month intervals. Subjects were included if they had a minimum of 2 NEI VFQ-25 and 5 SAP tests during follow-up. Evaluation of rates of visual field change was performed using 4 different regions (central inferior, central superior, peripheral inferior, and peripheral superior) of the integrated binocular visual field. The association between change in NEI VFQ-25 Rasch-calibrated scores and change in different regions of the visual field was investigated with a joint multivariable longitudinal linear mixed model.

Main Outcome Measures: The relationship between change in QoL scores and change of mean sensitivity in different regions of the visual field.

Results: There was a significant correlation between change in the NEI VFQ-25 Rasch scores during follow-up and change in different regions of the visual field. Each 1 decibel (dB)/year change in binocular mean sensitivity of the central inferior area was associated with a decline of 2.6 units/year in the NEI VFQ-25 scores ($R^2 = 35\%$; $P < 0.001$). Corresponding associations with change in QoL scores for the peripheral inferior, central superior, and peripheral superior areas of the visual field had R^2 values of 30%, 24%, and 19%, respectively. The association for the central inferior visual field area was statistically significantly stronger than those of the central superior area ($P = 0.011$) and peripheral superior area ($P = 0.001$), but not the peripheral inferior area ($P = 0.171$). Greater declines in NEI VFQ-25 scores were also seen in patients who had worse visual field sensitivity at baseline.

Conclusions: Progressive decline in sensitivity in the central inferior area of the visual field had the strongest association with longitudinal decline in QoL of patients with glaucoma. *Ophthalmology 2015;■:1–6 © 2015 by the American Academy of Ophthalmology.*

Glaucoma is the leading cause of irreversible blindness and visual impairment worldwide.[1] Its treatment involves lowering the intraocular pressure to slow down or halt progressive retinal ganglion cell damage and prevent vision loss.[2] Current therapeutic options are not without side effects. Therefore, it is important to consider the rate of visual function loss and decline in quality of life (QoL) before initiating or modifying therapy.[3]

Visual function in glaucoma is measured by standard automated perimetry (SAP). The impact of this functional loss on QoL is measured by patient-reported outcomes, such as the 25-item National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25).[4–6] In recent longitudinal studies, we evaluated how rates of change in SAP were associated with decline in QoL in patients with glaucoma.[3,7] These studies have included only global measures of visual field loss, such as the integrated binocular mean sensitivity. However, an investigation of the impact that change in different regions of the visual field has on QoL also may be important. For example, it is possible that loss of sensitivity in central areas of the visual field may carry a larger impact on QoL than loss of sensitivity in peripheral areas.[8] Likewise, loss in the inferior visual field may have more impact than loss in the superior field.[9]

Prior studies have investigated the relationship between location of visual field damage and QoL in patients with glaucoma; however, all these have used cross-sectional designs that do not permit assessment of progressive changes in visual field and the impact on QoL. Cross-sectional studies are further limited by the individual variability in perceptions of QoL and long-term compensatory mechanisms to visual loss.[3,10] Patients with glaucomatous damage adapt to visual function loss on activities of daily living. These compensatory mechanisms may depend on the

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velocity and location of damage over long periods of time, none of which can be measured in a cross-sectional study.

The purpose of this study was to evaluate and quantify the association between rates of change in different regions of the visual field and progressive changes in QoL of patients with glaucoma, as assessed by NEI VFQ-25s acquired over time.

Methods

Subjects included in this study were selected from a prospective longitudinal study designed to evaluate functional impairment in glaucoma conducted at the Visual Performance Laboratory, Department of Ophthalmology, University of California San Diego. Written informed consent was obtained from all participants. This study received institutional review board approval, and the methodology adhered to the tenets of the Declaration of Helsinki and to the Health Insurance Portability and Accountability Act.

At each visit during follow-up, subjects underwent a comprehensive ophthalmic examination, including review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure measurement using Goldmann applanation tonometry, gonioscopy, dilated ophthalmoscopic examination using a 78-diopter lens, and stereoscopic photographs of the optic nerves. Only patients with open angles on gonioscopy were included. Subjects with coexisting retinal disease, uveitis, or nonglaucomatous optic disc neuropathy were excluded from the study.

This study enrolled a cohort of patients with glaucoma diagnosed on the basis of the presence of repeatable glaucomatous visual field defects at baseline. An abnormal visual field was determined by the presence of pattern standard deviation with $P < 0.05$ or glaucoma hemifield test result outside normal limits. Subjects were considered to have glaucoma if at least 1 eye had a repeatable glaucomatous visual field defect.

The NEI VFQ-25s were obtained annually, and SAP tests were obtained at 6-month intervals. For inclusion, all subjects were required to have had a minimum of 2 NEI VFQ-25s and at least 5 SAP tests during follow-up.

Perimetric Testing

All patients underwent SAP testing with the Swedish Interactive Threshold Algorithm standard 24-2 strategy using the Humphrey Field Analyzer II (Carl Zeiss Meditec, Inc., Dublin, CA). Only reliable tests were included (<33% fixation losses and <15% false-positives). An integrated binocular field was obtained using the monocular fields for the right and left eyes according to the binocular summation technique described by Nelson-Quigg et al.[11] After the binocular summation thresholds were obtained, the 52 thresholds points were divided into 4 regions, as shown in Figure 1: central inferior, central superior, peripheral inferior, and peripheral superior. The central points were located in the region encompassing approximately the central 10° of the visual field. Mean sensitivity in decibels (dB) was calculated for each of these regions by averaging the antilogs of the individual sensitivity thresholds and then recalculating the logarithm.

Rasch Analysis of the 25-Item National Eye Institute Visual Functioning Questionnaire

Quality of life was assessed by the NEI VFQ-25.[12] This questionnaire consists of 25 questions measuring overall vision, difficulty with near-vision and distance activities, ocular pain, driving difficulties, limitations with peripheral vision and color vision, social functioning, role limitations, dependency and mental health symptoms related to vision, and an additional single-item general health rating question. Rasch analysis was performed to obtain final estimates of "person measures" or Rasch scores, summarizing the NEI-VFQ responses.

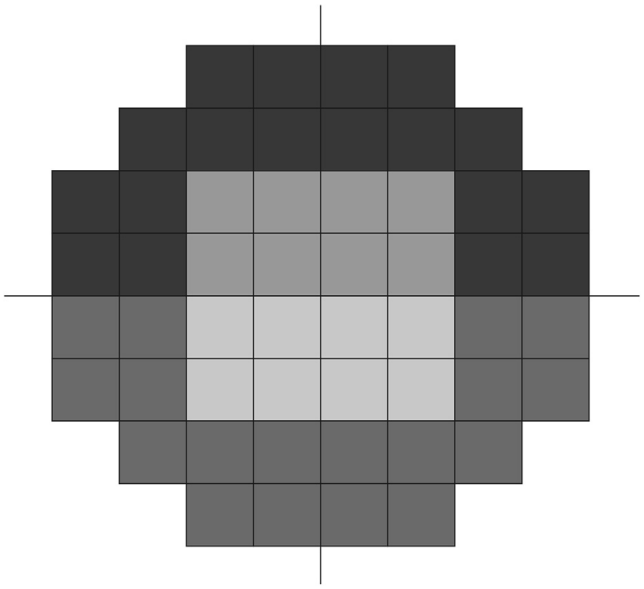

Figure 1. Binocular summation threshold points divided into 4 regions: central inferior, central superior, peripheral inferior, and peripheral superior.

We have previously published the details of the Rasch modeling procedure in this population.[3] Briefly, Rasch scores can be used to express where each respondent falls on a linear scale representing the degree of impairment as measured by the NEI VFQ-25 and can be used for subsequent parametric statistical analyses.[13,14] Person ability scores were rescaled linearly to range from 0 to 100.

Statistical Analysis

The association between change in NEI VFQ-25 scores and change in SAP sensitivity was investigated with a joint multivariable longitudinal linear mixed model.[15] Details about this model have been presented.[16–20] We investigated the relationship between change in NEI VFQ-25 and change in binocular visual field sensitivity according to the different SAP regions defined in Figure 1. The relationship was also investigated for each point in the binocular visual field. Because multiple longitudinal measures were evaluated resulting in a large number of random effects, the pairwise fitting approach of Fieuws and Verbeke[21] was used for joint modeling of the multivariate longitudinal profiles.

Statistical analysis was performed using commercially available software Winsteps version 3.81.0 (Chicago, IL) and Stata version 13 (StataCorp LP, College Station, TX). The alpha level (type I error) was set at 0.05.

Results

The study included 236 patients with glaucoma who were followed for an average of 4.3±1.5 years. Table 1 summarizes the clinical and demographic characteristics of included subjects at baseline. Mean age at baseline was 73.1±9.5 years. Subjects had a median of 8 (interquartile range, 6–12) SAP tests and 3 (interquartile range, 2–4) NEI VFQ-25s. A total of 83 patients

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