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

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Abstract

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 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.

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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 1dB/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 central superior (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 those 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 glaucoma patients.

INTRODUCTION

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) prior to 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 glaucoma patients.[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 may also 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] Similarly, 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 glaucoma patients; however, all these have employed 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 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 glaucoma patients, as assessed by NEI VFQ-25 questionnaires 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 non-glaucomatous optic disc neuropathy were excluded from the study.

This study enrolled a cohort of glaucoma patients diagnosed based on the presence of repeatable glaucomatous visual field defects at baseline. An abnormal visual field was determined by the presence of pattern standard deviation with $P < 0.05$, and/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.

NEI VFQ-25 questionnaires 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-25 questionnaires 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 (less than 33% fixation losses and less than 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 one of these regions by averaging the antilogs of the individual sensitivity thresholds and then recalculating the logarithm.

Rasch Analysis of the NEI-VFQ-25 Questionnaire

QoL was assessed by the NEI VFQ-25 questionnaire.[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 plus 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.

We have previously published the details of the Rasch modeling procedure in this population.[3] In brief, 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 elsewhere.[16–18,19,20] 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. As multiple longitudinal measures were evaluated resulting in a very large number of random effects, the pairwise fitting approach of Fieuws and Verbeke was used for joint modeling of the multivariate longitudinal profiles.[21]

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

RESULTS

The study included 236 glaucoma patients followed for an average of 4.3 ± 1.5 years. Table 1 summarizes 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 (IQR: 6 to 12) SAP tests and 3 (IQR: 2 to 4) NEI VFQ-25 questionnaires. 83 patients had 2, 89 patients had 3, 53 patients had 4, 10 patients had 5 and 1 patient had 6 NEI VFQ-25 questionnaires. Mean ± standard deviation (SD) of the SAP mean deviation at baseline of worse and better eyes were −5.4 ± 5.8 and −2.2 ± 3.5 dB, respectively. There was a wide range of mean deviation values at baseline in the eyes included in the study, ranging from −28.9 to 2.5 dB. The mean sensitivity was calculated as the average of the binocular visual field threshold sensitivities for the integrated field. Average binocular mean sensitivity at baseline was 28.7 ± 3.3 dB.

Table 2 reports the associations between change in NEI VFQ-25 scores and progressive change in mean sensitivity, according to the region of the binocular visual field. Progressive decline in sensitivity in the central inferior area of the visual field had the strongest association with decline in NEI VFQ-25 scores. Each 1dB/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 NEI VFQ-25 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 (Table 2). Loss of vision in the central inferior region corresponded to the greatest impact on NEI VFQ-25 scores when compared to both the central superior and peripheral superior areas (P=0.011 and

P=0.001, respectively). There was not statistically significant difference between the central and peripheral inferior areas (*P*=0.171). Figure 2 shows scatterplots of change in mean sensitivity versus change in NEI VFQ-25 for the different regions of the visual field.

Figure 3 shows a grayscale map illustrating R^2 values for the relationship between change in sensitivity at each visual field location and change in NEI VQ-25 scores. Lighter areas correspond to stronger associations. In agreement with the regional results presented above, the points with strongest association with change in NEI VFQ-25 scores were those located in the central area, particularly the central inferior zone.

Change in NEI VFQ-25 scores was also associated with the severity of visual field loss at baseline (Table 2). Greater declines in NEI VFQ-25 scores were seen in those patients who had worse visual field sensitivity at baseline, with stronger association for the inferior areas compared to superior ones. For the central inferior visual field, each 1dB lower mean sensitivity at baseline was associated with a 0.15-unit/year greater decline in NEI VFQ-25 scores (R^2= 18%; *P*<0.001).

DISCUSSION

In the current study we demonstrate that progressive decline in sensitivity in the central inferior area of the visual field has the strongest association with decline in QoL of glaucoma patients, as measured by the NEI VFQ-25. To our knowledge this is the first study to evaluate the relationship between rates of change in regional visual field sensitivity and patient-reported outcomes in glaucoma. By determining which areas of the visual field carry greater impact on QoL, our findings may have significant clinical implications for monitoring functional damage in patients with glaucoma and for determining aggressiveness of therapy according to the pattern of visual field loss over time.

The relationship between progressive field loss and change in NEI VFQ-25 scores was almost two times stronger for the central inferior (R^2 = 35%) as compared to the peripheral superior (R^2 = 19%) region of the visual field. This is not surprising, as it is likely that loss of vision in the inferior area would carry a greater impact on the ability to perform daily activities such as reading, walking down stairs or seeing objects off to the side while walking.[22] The fact that defects in the central inferior region are likely to coexist with defects in the peripheral inferior region of the visual field of the same patient might explain why changes in mean sensitivity for the peripheral inferior region and change in NEI VFQ-25 scores (R^2 = 30%) was not significantly different than that for the central inferior region (R^2 = 35%) (*P*=0.171).

Even though the reported associations found in our study may not be seen as surprising, their magnitudes had not been previously quantified. We demonstrated that each 1dB/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. However, it is important to note that the decline in NEI VFQ-25 scores was also associated with baseline disease severity. For the central inferior visual field, for example, each 1dB lower mean sensitivity at baseline was associated with 0.15-unit/year greater decline in NEI VFQ-25 scores. This is again an

expected result as the same amount of visual field loss over time is likely to have greater impact in the ability to perform daily activities for patients who start off with worse visual fields.

Previous studies have shown that visual field defects in glaucoma tend to progress by deepening, expansion of an existing scotoma, or through a combination of both.[23, 24] Therefore patients with greater inferior and/or central visual field defects in both eyes at baseline are likely to need more close monitoring and to be candidates for more aggressive treatment. It is possible that certain specific tasks or items evaluated by the NEI VFQ-25 could have different associations with damage to different regions of the visual field.[8, 22, 25] However, the validity of using subscales separately has been questioned in the literature.[26, 27] Therefore, we have avoided the use of subscales in our work.

This study has limitations. Previous studies have reported that central visual field areas may have less variability than peripheral ones.[28] Therefore, the stronger association with QoL found for changes in the central area could perhaps be due to more precision in the estimation of slopes of central field loss compared to peripheral ones. However, our conclusions would still be applicable in the context of how visual field measurements are routinely assessed in clinical practice. Another limitation is that a large number of patients included in the study had only a few NEI VFQ-25 questionnaires during follow-up. As responses to the questionnaires are subject to variability, this would limit the ability to obtain precise estimates of individual change in NEI VFQ-25 scores. However, inferences obtained from sample averages for comparisons of the relationships with different visual field locations, as conducted in our study, should still be valid. Another possible limitation of the study is that changes in visual field sensitivity and QoL could be caused by cataract or other media opacities.[29] However, it is unlikely that media opacities would explain the regional differences found in the relationship with changes in QoL, as found in our study.

In conclusion, the results of this study demonstrate that progressive sensitivity loss occurring in the central and inferior regions of the visual field have the strongest association with decline of QoL in patients with glaucoma. By providing guidance on which patterns of visual field loss may put patients at greater risk for loss in vision-related QoL, our results may provide useful information for guiding therapeutic decisions in glaucoma.

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Abbreviations

QoL	Quality of life
NEI VFQ-25	National Eye Institute Visual Functioning Questionnaire
SAP	Standard automated perimetry

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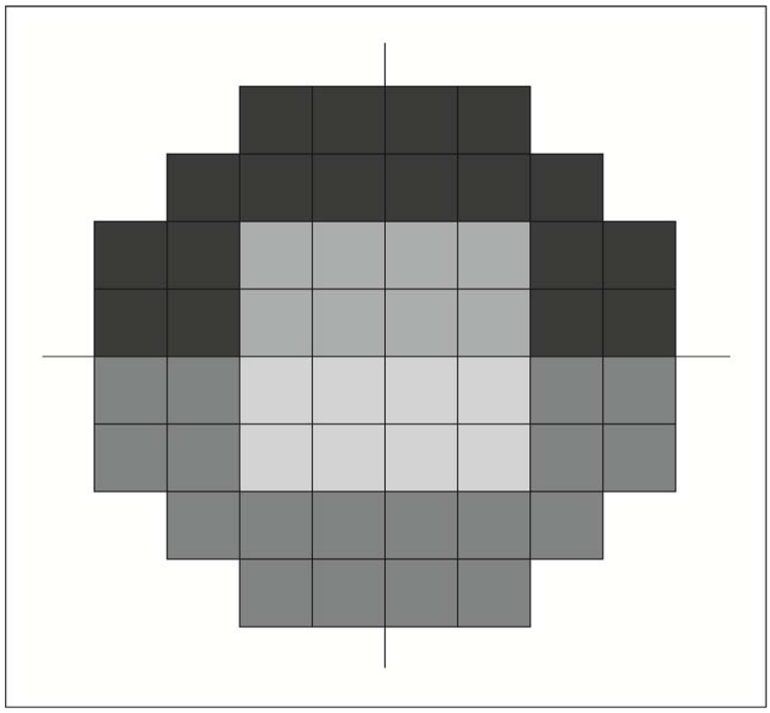

Figure 1.
Binocular summation thresholds points divided into 4 regions: central inferior, central superior, peripheral inferior, and peripheral superior.

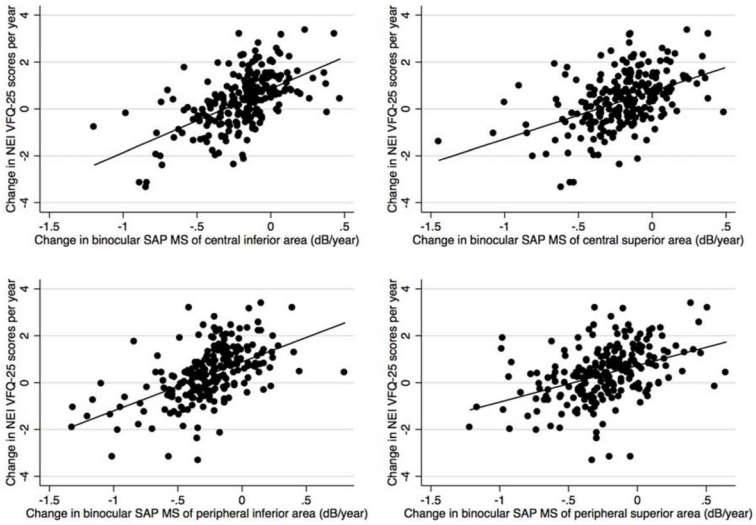

Figure 2.

Scatterplots with fitted regression lines showing the relationship between change in National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) scores and change in binocular mean sensitivity at central inferior, central superior, peripheral inferior, and peripheral superior regions of the visual field. dB = decibel.

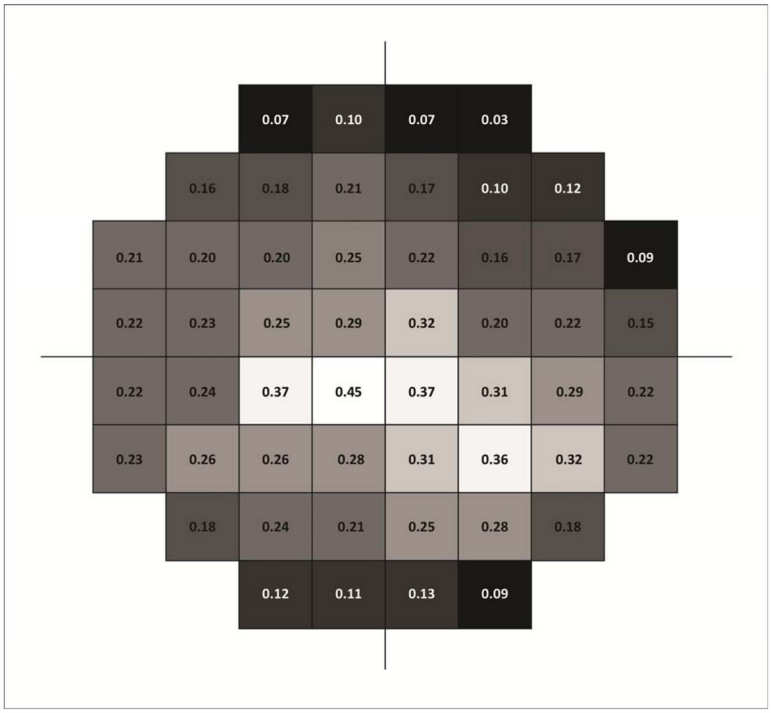

Figure 3.

Grayscale map illustrating R^2 values for the relationship between change in sensitivity at each visual field location and change in National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) scores. Lighter areas correspond to stronger associations. Points with strongest association with change in NEI VFQ-25 score were those located in the central area, particularly the central inferior zone.

Table 1

Baseline Clinical and Demographic Characteristics of Subjects Included in the Study

Characteristic	Value
Age, years	73.1 ± 9.5
Gender, % female	52.5
Race, % caucasian	65.6
% african american	32.2
% asian	2.2
SAP baseline MD (better eye), dB	−2.2 ± 3.5
SAP baseline MD (worse eye), dB	−5.4 ± 5.8
SAP baseline binocular mean sensitivity, dB	28.7 ± 3.3
Baseline NEI VFQ-25 score	68.6. ± 20.4

SAP: standard automated perimetry; MD: mean deviation; dB: decibels
NEI VFQ-25: National Eye Institute Visual Functioning Questionnaire

Table 2

Results of the Univariable Regression Models for Prediction of Rates of Change in National Eye Institute Visual Functioning Questionnaire-25 Scores in different Regions of the Visual Field.

	Slope			Baseline		
	Coefficient	R^2	*P* Value	Coefficient	R^2	*P* Value
Central Inferior	2.62	0.35	<0.001	0.15	0.18	<0.001
Central Superior	1.81	0.24	<0.001	0.08	0.06	<0.001
Peripheral Inferior	2.29	0.30	<0.001	0.14	0.11	<0.001
Peripheral Superior	1.58	0.19	<0.001	0.07	0.05	<0.001