

# Association Between Rates of Binocular Visual Field Loss and Vision-Related Quality of Life in Patients With Glaucoma

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**Importance:** It is reasonable to hypothesize that for 2 patients with similar degrees of integrated binocular visual field (BVF) loss, the patient with a history of faster disease progression will report worse vision-related quality of life (VRQOL) than the patient with slowly progressing damage. However, to our knowledge, this hypothesis has not been investigated in the literature.

**Objective:** To evaluate the association between binocular rates of visual field change and VRQOL in patients with glaucoma.

**Design:** Observational cohort study.

**Setting:** Patients were recruited from the Diagnostic Innovations in Glaucoma Study and the African Descent and Glaucoma Evaluation Study.

**Participants:** The study included 796 eyes of 398 patients with diagnosed or suspected glaucoma followed up from October 1, 1998, until January 31, 2012, for a mean (SD) of 7.3 (2.0) years.

**Main Outcome Measures:** The VRQOL was evaluated using the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) at the last follow-up visit. The NEI VFQ-25 was completed for all patients during the period extending from December 1, 2009, through

January 31, 2012. Integrated BVFs were calculated from the monocular fields of each patient. Linear regression of mean deviation values was used to evaluate rates of BVF change during the follow-up period. Logistic regression models were used to investigate the association between abnormal VRQOL and rates of BVF change, while adjusting for potentially confounding socioeconomic and demographic variables.

**Results:** Thirty-two patients (8.0%) had abnormal VRQOL as determined by the results of the NEI VFQ-25. Patients with abnormal VRQOL had significantly faster rates of BVF change than those with normal VRQOL ( $-0.18$  vs  $-0.06$  dB/y;  $P < .001$ ). Rates of BVF change were significantly associated with abnormality in VRQOL (odds ratio = 1.31 per 0.1 dB/y faster;  $P = .04$ ), after adjustment for confounding variables.

**Conclusions and Relevance:** Patients with faster rates of BVF change were at higher risk of reporting abnormal VRQOL. Assessment of rates of BVF change may provide useful information in determining risk of functional impairment in glaucoma.

*JAMA Ophthalmol.* 2013;131(4):486-494.

Published online February 28, 2013.

doi:10.1001/jamaophthalmol.2013.2602

**G**LAUCOMA IS A PROGRESSIVE optic neuropathy that may result in significant visual impairment. The loss of vision affects quality of life and also has economic consequences for the patient and society.<sup>1</sup> The effect of glaucoma on vision-related quality of life (VRQOL) has frequently been investigated using questionnaire-based, self-reported assessments, such as the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25).<sup>2-5</sup> Previous studies<sup>2,5</sup> have found a significant association between the severity of visual field defects on stan-

dard automated perimetry (SAP) and the results on the NEI VFQ-25, with more severe defects associated with worse scores. Patients with visual field loss in both eyes tend to have worse scores on the NEI VFQ-25 than those with unilateral defects. For patients with asymmetric degrees of damage, visual field assessment of the less affected eye frequently shows a stronger association with questionnaire results than the more affected eye. Such an association is understandable because one eye may compensate for the loss of vision of the other eye. For this reason, it has been suggested that binocular visual field (BVF) tests may represent the best

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way to gauge the effect of field losses on quality of life. In the absence of “true” binocular vision tests, one can approximate the BVF by integrating the results of monocular visual fields.<sup>6</sup> These integration methods have been found to agree closely with the “true” BVF, thus offering a practical way for studying rates of BVF change.

Previous studies<sup>2,5</sup> investigating the association between BVF results and NEI VFQ-25 have been conducted using cross-sectional data and have only considered the visual field status at the time of questionnaire administration. This approach ignores the rate at which the patients develop visual field defects. Although significant associations have been reported between BVF and NEI VFQ-25, the strength of the association has been far less than perfect. One reason for the imperfect association between the severity of visual field damage and patient-reported VRQOL may be the development of compensatory strategies by affected patients.<sup>7</sup> It is likely that patients with slowly progressing disease will have more time to adapt to their limited functional status by developing compensatory strategies and, therefore, will be less likely to report an abnormal VRQOL. On the other hand, in patients with rapidly progressing disease, the visual field defects may result in substantial impairment in the ability to perform daily activities without time for development of compensatory strategies. This would be more readily recognized by such a patient and more likely to be reported as an abnormal VRQOL. Therefore, it is reasonable to hypothesize that for 2 patients with similar degrees of visual field loss, the patient with a history of faster disease progression will report worse VRQOL status than the patient with slowly progressing damage. However, to our knowledge, this hypothesis has not been investigated in the literature. Our objective was to investigate the association between rates of BVF loss and results of patient-reported VRQOL outcomes in patients with glaucoma, as assessed by the NEI VFQ-25.

## METHODS

### STUDY PATIENTS

This was an observational cohort study. Participants in this study were included in 2 prospective longitudinal studies designed to evaluate optic nerve structure and visual function in glaucoma (the African Descent and Glaucoma Evaluation Study [ADAGES] and the Diagnostic Innovations in Glaucoma Study [DIGS]). The 3-site ADAGES collaboration includes the Hamilton Glaucoma Center at the Department of Ophthalmology, University of California, San Diego (UCSD); the New York Eye and Ear Infirmary; and the Department of Ophthalmology, University of Alabama at Birmingham. Although DIGS includes only patients recruited at UCSD, the protocol of the 2 studies is identical. Methodologic details have been described previously.<sup>8</sup> The UCSD Human Subjects Committee approved all protocols, and methods adhered to the Declaration of Helsinki.

At each visit during follow-up, patients underwent a comprehensive ophthalmic examination, including review of medical history, best-corrected visual acuity, slitlamp biomicroscopy, intraocular pressure measurement using Goldmann applanation tonometry, gonioscopy, dilated funduscopy examination using a 78-diopter (D) lens, stereoscopic optic disc photography, and SAP with 24-2 Swedish Interactive Thresh-

old Algorithm (Carl Zeiss Meditec, Inc). To be included, patients had to have best-corrected visual acuity of 20/40 or better, spherical refraction less than  $\pm 5.0$  D, cylinder correction less than 3.0 D, and open angle with gonioscopy. Patients with coexisting retinal disease, uveitis, or nonglaucomatous optic disc neuropathy were excluded from the study.

We included 796 eyes of 398 patients with diagnosed or suspected glaucoma at the baseline visit. Eyes were classified as having glaucoma based on repeatable abnormal visual field test results at baseline, defined as a pattern standard deviation with  $P < .05$ , and/or glaucoma hemifield test results outside normal limits, regardless of the appearance of the optic disc. Patients suspected of having glaucoma were defined as those with eyes with abnormal-appearing optic discs (presence of neuroretinal rim thinning or localized or diffuse retinal nerve fiber layer defects indicative of glaucoma, ie, glaucomatous optic neuropathy) by masked stereophotographic assessment without repeatable abnormal SAP results. Patients suspected of having glaucoma also included patients with eyes with intraocular pressure greater than 22 mm Hg but with healthy-appearing optic discs and without repeatable abnormal SAP results.

Each patient was required to have a minimum of 5-paired (ie, visual field tests of both eyes on the same day) SAPs during a minimum of 5 years of follow-up before completion of the NEI VFQ-25. The period of follow-up for the study started on October 1, 1998, and extended until January 31, 2012; however, patients entered and exited the study at different dates. The NEI VFQ-25 was completed for all patients during the period extending from December 1, 2009, through January 31, 2012. For each patient, only SAPs obtained before the NEI VFQ-25 were included.

### MONOCULAR AND BINOCULAR VISUAL FIELDS

Monocular SAP was performed using the 24-2 Swedish Interactive Threshold Algorithm at all visits during the follow-up period. Only reliable tests ( $\leq 33\%$  fixation losses and false-negative results and  $\leq 15\%$  false-positive results) were included. In addition, all visual fields were evaluated by the UCSD Visual Field Assessment Center.<sup>9</sup> Visual fields were reviewed and excluded in the presence of artifacts, such as eyelid or rim artifacts, fatigue effects, inattention, or inappropriate fixation. Visual fields were also reviewed for the presence of abnormalities that could indicate diseases other than glaucoma, such as homonymous hemianopia.

For calculation of the estimated pointwise sensitivities of the BVF, the monocular SAP threshold sensitivities of the right and left eyes were used. The 24-2 stimulus presentation pattern consists of 54 points within the central  $24^\circ$  in a  $6^\circ$  grid bracketing the horizontal and vertical meridians. The 2 points corresponding to the blind spot and the 2 most nasal points of each eye were excluded for the calculations of the BVF. This was necessary because these points do not have a spatial correspondent in the visual field of the fellow eye. Therefore, each individual BVF had a total of 48 overlapping points, as shown in **Figure 1**.

The sensitivity for each point of the BVF was estimated using the binocular summation model described by Nelson-Quigg et al.<sup>6</sup> According to this model, the binocular sensitivity can be estimated using the following formula:

$$\text{Binocular Sensitivity} = \sqrt{Sr^2 + Sl^2}$$

where  $Sr$  and  $Sl$  are the monocular threshold sensitivities for corresponding visual field locations of the right and left eyes, respectively. To calculate the binocular sensitivity from this formula, light sensitivity had to be converted to a linear scale (apo-

stilbs) and then converted back to logarithmic scale (decibels).

Evaluation of rates of visual field change during follow-up was performed using the mean deviation (MD). For calculation of monocular and BVF MD, we applied the formula described by Anderson<sup>10</sup>:

$$MD = \frac{\frac{1}{L} \sum_{i=1}^L \frac{TD_i}{Si^2}}{\frac{1}{L} \sum_{i=1}^L \frac{1}{Si^2}}$$

where  $L$  is the total number of locations,  $TD_i$  is the total deviation in decibels of the normal age-matched population at location  $i$ , and  $Si^2$  is the variance of the  $i$  point in the same normal age-matched population. We used data from 102 paired visual fields of age-matched patients from the DIGS and ADAGES cohorts to calculate the  $TD_i$  and the  $Si^2$  of monocular and binocular visual fields.

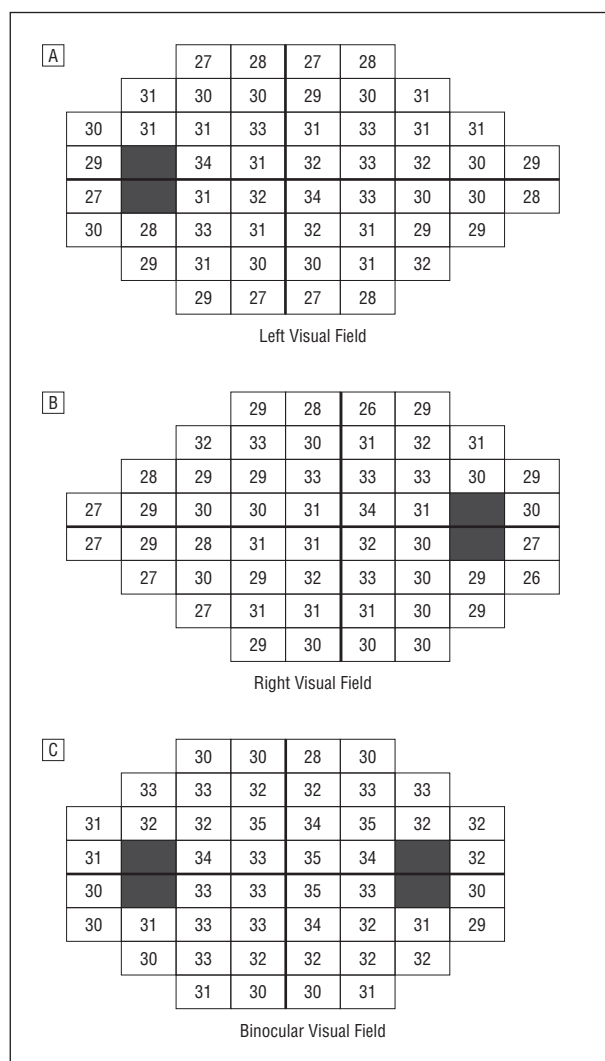
## NATIONAL EYE INSTITUTE VISUAL FUNCTION QUESTIONNAIRE

The VRQOL was evaluated using the NEI VFQ-25. This questionnaire was designed to assess the dimensions of self-reported vision-target health status that are relevant for patients with chronic eye diseases.<sup>11,12</sup> The NEI VFQ-25 consists of a base set of 25 vision-targeted questions that represent 11 vision-related constructs, plus an additional single-item general health rating question. The vision-related scales are as follows: general vision, near- and distance-vision activities, ocular pain, vision-related social function, vision-related role function, vision-related mental health, vision-related dependency, driving difficulties, color vision, and peripheral vision. Each subscale consists of a minimum of 1 item and a maximum of 4 items. The standard algorithm used to score the results has a scale ranging from 0 to 100, with higher scores representing better visual functioning and well-being. In this format, scores represent the achieved percentage of the total possible score (eg, a score of 50 represents 50% of the highest possible score). Thirty-six patients did not answer questions related to driving difficulties because they were not active drivers. Missing data were imputed using multivariable linear regression with information from the other NEI VFQ-25 variables.

We defined abnormal VRQOL as the presence of a score less than 50 on any 1 of the 10 vision-related subscales of the NEI VFQ-25, excluding the subscale related to ocular pain. This corresponds to approximately 2 SDs below the scores previously described for a normal reference population.<sup>12</sup>

## DEMOGRAPHIC, CLINICAL, AND SOCIOECONOMIC VARIABLES

Socioeconomic and clinical questionnaires were also administered to patients at the time of the NEI VFQ-25. These questionnaires contained a survey about demographics, history of ocular and medical conditions, marital status, health insurance coverage, educational level, and income. Because these variables could potentially affect patient perceptions about VRQOL, they were included as potentially confounding factors in the analysis of the association between BVF change and NEI VFQ-25 results. These variables were categorized for inclusion in the multivariable models as marital status (married [yes/no]), presence of health insurance (yes/no), educational level (at least high school degree [yes/no]), and income (<\$25 000 per year [yes/no]). Seventy-eight patients refused



**Figure 1.** Schematic representation of the binocular visual field using the summation method to integrate the sensitivities of the right and left visual fields.

to provide income information. Missing data were imputed based on a multivariable logistic regression using data from the other socioeconomic variables. For comorbidities, we investigated the presence or history of the following conditions: arthritis, asthma, cancers, depression, diabetes mellitus, heart disease, hypertension, and stroke. A simple summation score was used to create a comorbidity index.<sup>13</sup> Visual acuity was measured using an Early Treatment Diabetic Retinopathy chart, and logMAR measurements were used in the analyses. Diagnostic categorization at baseline (glaucoma [yes/no]) was also included in the analyses because glaucomatous patients and those suspected of having glaucoma could have different perceptions about VRQOL.

During follow-up, patients were treated at the discretion of the attending ophthalmologist. History of topical antiglaucomatous treatment during follow-up was also included as a potentially confounding variable in multivariable analysis.

## STATISTICAL ANALYSIS

Descriptive statistics included mean (SD) for normally distributed variables and median and interquartile range for nonnormally distributed variables. The association between changes

**Table 1. Baseline Clinical and Demographic Characteristics of Patients With Normal and Abnormal Vision-Related Quality of Life**

Characteristic	Vision-Related Quality of Life <sup>a</sup>		P Value
	Normal (n = 366)	Abnormal (n = 32)	
Rates of change of the binocular visual field, dB/y	−0.06 (0.17)	−0.18 (0.33)	<.001
BVF MD, dB	−0.79 (3.02)	−2.15 (4.04)	.009
logMAR visual acuity	0.08 (0.15)	0.12 (0.13)	.29
Age, y	66.11 (11.25)	61.53 (14.53)	.03
Educational level of at least a high school degree, %	59.8	75.0	.09
Income <\$25 000, %	17.5	43.8	<.001
Married, %	54.9	34.4	.03
Comorbidity index	1.18 (1.03)	1.53 (1.26)	.07
Baseline diagnosis of glaucoma, %	49.7	59.4	.30
African American ancestry, %	41.0	53.1	.18
Female sex, %	41.5	37.5	.66
Treatment during follow-up, %	72.1	71.9	.98
Insurance, %	92.1	87.5	.37
Follow-up time, y	7.4 (2.0)	6.8 (1.8)	.13

Abbreviations: BVF, binocular visual field; MD, mean deviation.

<sup>a</sup>Data are presented as mean (SD) unless otherwise indicated.

in BVF MD and abnormality in VRQOL was initially investigated using a random-intercept, random-slope, linear-mixed model with a *t*-distribution for random effects.<sup>14-20</sup> In these models, the mean evolution of a specific response is described using some function of time, and patient-specific deviations from this mean evolution are introduced by random intercepts and random slopes, allowing for different baseline values and different rates of change for each eye. In the linear mixed model, BVF MD values were considered the dependent variable. The presence of abnormality in VRQOL was included as a fixed-effect covariate with a value of 1 if the patient had an abnormal VRQOL as determined by the NEI VFQ-25 and a value of 0 if the patient had a normal VRQOL. Time was included as a continuous predictor. The 2-way interaction between time and VRQOL was included in the model to evaluate whether there was a significant difference in longitudinal BVF MD over time between those with normal and abnormal VRQOL. Rates of change were calculated for the BVF and for monocular visual field examinations. For each patient, eyes with faster (more negative slope) and slower rates of change (more positive slope) were identified as the worse and better eyes, respectively.

We were interested in whether rates of BVF change were predictive of abnormality in VRQOL. For this analysis, we investigated the association between VRQOL (dependent variable) and rates of BVF change using a multivariable logistic model, after adjusting for the described potentially confounding demographic, clinical, and socioeconomic variables. We also adjusted for the BVF MD value closest to the NEI VFQ-25 to determine whether rates of BVF change could provide statistically independent information besides that provided by the most recent BVF in predicting abnormality in VRQOL.

All statistical analyses were performed with commercially available software (STATA, version 11; StataCorp LP). The  $\alpha$  level (type I error) was set at .05.

**Table 2. Results of the National Eye Institute Visual Function Questionnaire in Patients With Normal and Abnormal Vision-Related Quality of Life**

Variable	Vision-Related Quality of Life, Mean (SD) <sup>a</sup>	
	Normal (n = 366)	Abnormal (n = 32)
General health	68.2 (21.4)	48.4 (24.5)
General vision	81.5 (12.3)	59.4 (23.5)
Near vision	89.2 (12.2)	62.5 (21.4)
Distance vision	91.8 (10.0)	72.5 (18.5)
Vision-specific social functioning	98.0 (6.2)	87.9 (16.9)
Vision-specific mental health	91.8 (8.8)	58.4 (19.0)
Vision-specific role difficulties	94.6 (11.8)	57.0 (29.4)
Vision-specific dependency	99.0 (4.4)	82.0 (25.8)
Driving	89.6 (11.7)	65.1 (18.9)
Color vision	98.3 (6.8)	89.8 (19.9)
Peripheral vision	93.6 (13.0)	68.0 (27.8)
Composite score	92.7 (6.2)	70.3 (14.2)

<sup>a</sup>*P* < .001 for all variables.

## RESULTS

This study included 3678 calculated BVFs of 398 patients followed up for a mean (SD) of 7.3 (2.0) years before the completion of the NEI VFQ-25. Mean (SD) age at the questionnaire visit was 65.7 (11.6) years. Two hundred twenty-two (55.8%) patients were white, 167 (42.0%) were African American, and 9 (2.2%) were of other race/ethnicity. Two hundred thirty-four (58.8%) were female, and 164 (41.2%) were male. The mean (SD) number of visits during follow-up was 9.2 (3.2).

Thirty-two patients (8.0%) had abnormal VRQOL as determined by the results of the NEI VFQ-25. **Table 1** lists the baseline clinical and demographic characteristics for patients with normal and abnormal VRQOL. Patients with abnormal VRQOL had significantly faster rates of BVF change than those without normal VRQOL (−0.18 vs −0.06 dB/y; *P* < .001). The follow-up time was similar between groups (7.4 [2.0] vs 6.8 [1.8]; *P* = .13). **Table 2** lists the results of the NEI VFQ-25 component scores in patients who had normal VRQOL vs those who had abnormal VRQOL. Statistically significant differences were found for all vision-related subscales.

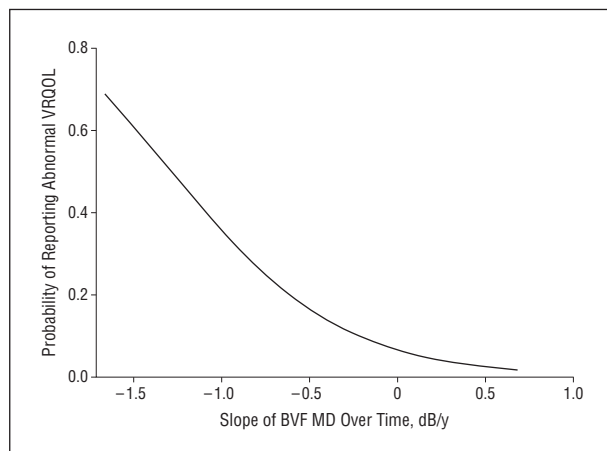
We investigated whether rates of BVF change were indicative of abnormality in VRQOL, after adjusting for BVF MD closest to the NEI VFQ-25 and other demographic, clinical, and socioeconomic variables in a logistic regression model. **Table 3** lists the results of the univariable and multivariable logistic regression analyses. In univariable regressions, the rate of BVF change (odds ratio [OR] = 1.23 per 0.1 dB/y faster; *P* = .001), lower BVF MD closest to the questionnaire visit (OR = 1.10 per 1 dB lower; *P* = .03), younger age (OR = 1.39 per decade younger; *P* = .008), and lower income (OR = 3.67; *P* < .001) were significantly associated with abnormality in VRQOL. Being married at the time of the VRQOL questionnaire was associated with a decrease in the odds of having abnormal VRQOL (OR = 0.43; *P* = .03). Higher educational level (OR = 2.01; *P* = .10), longer follow-up



**Table 3. Results of the Univariable and Multivariable Logistic Regression Models for Prediction of Abnormality in Vision-Related Quality of Life**

Variable	Univariable Model		Multivariable Model	
	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)	P Value
Rate of change in the BVF per 0.1 dB/y faster	1.23 (1.08-1.40)	.001	1.31 (1.01-1.68)	.04
BVF MD per 1 dB lower	1.10 (1.01-1.20)	.03	0.95 (0.80-1.12)	.53
Age per decade younger	1.39 (1.03-1.88)	.03	1.62 (1.14-2.31)	.008
Educational level of at least a high school degree	2.01 (0.88-4.60)	.10	1.49 (0.59-3.76)	.40
Income <\$25 000	3.67 (1.74-7.76)	<.001	2.87 (1.22-6.71)	.02
Married	0.43 (0.20-0.92)	.03	0.57 (0.24-1.33)	.19
Follow-up time per 1 y longer	0.85 (0.69-1.05)	.13	0.94 (0.73-1.20)	.60
Comorbidity index	1.34 (0.97-1.86)	.07	1.52 (1.06-2.18)	.02
African American ancestry	1.63 (0.79-3.67)	.18	0.79 (0.32-1.89)	.58
Baseline diagnosis of glaucoma	1.48 (0.71-3.08)	.30		
logMAR per 0.1 dB/y higher	3.26 (0.37-28.80)	.29		
Female sex	1.18 (0.56-2.49)	.66		
Treatment during follow-up	0.99 (0.44-2.20)	.98		
Insurance	0.60 (0.20-1.84)	.37		

Abbreviations: BVF, binocular visual field; MD, mean deviation.



**Figure 2.** Probability of reporting abnormal vision-related quality of life (VRQOL) according to the slope of the binocular visual field (BVF) mean deviation (MD) over time. Patients with faster rates of BVF change had a higher probability of reporting abnormal VRQOL.

period (OR = 0.85 per year longer;  $P = .13$ ), higher comorbidity index (OR = 1.34 per additional comorbidity;  $P = .07$ ), and African American ancestry (OR = 1.63;  $P = .18$ ) tended to be associated with abnormal VRQOL, but the association did not reach statistical significance. All other variables had univariable associations with  $P > .20$ . All variables with  $P < .20$  were entered in the multivariable model as indicated in Table 3. Rate of BVF change was still significantly associated with abnormality in VRQOL even after adjustment for degree of BVF loss (MD at the visit closest to questionnaire administration) and other confounding variables (OR = 1.31 per 0.1 dB/y faster;  $P = .04$ ). Each 0.1-dB/y faster slope of BVF change was associated with a 31% increase in the odds of abnormality in VRQOL. Age (OR = 1.62 per decade younger;  $P = .008$ ) and income (OR = 2.87;  $P = .02$ ) were also significantly associated with abnormal VRQOL in the multivariable logistic model. **Figure 2** shows the probability of reporting abnormal VRQOL according to the slope of BVF MD over time. Patients with faster rates of

BVF change had a higher chance of reporting abnormality in VRQOL.

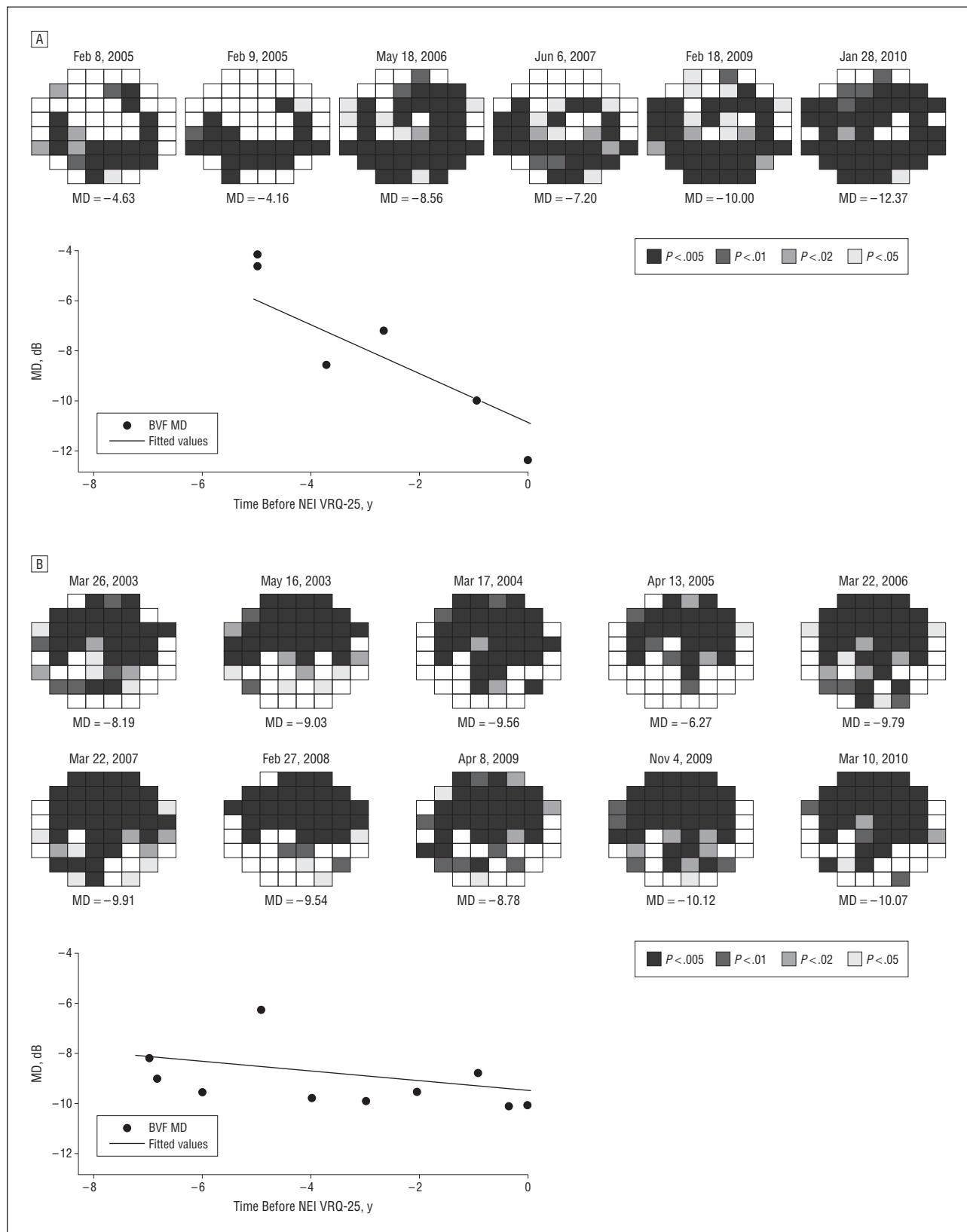
We also evaluated whether the rate of visual field change of the worse and the better eyes was independently associated with abnormal VRQOL, after adjusting for the MD and for the same demographic, clinical, and socioeconomic variables specified previously. Rates of visual field change for the worse (OR = 1.12 per 0.1 dB/y faster;  $P = .10$ ) and better eyes (OR = 1.14 per 0.1 dB/y faster;  $P = .10$ ) were not statistically associated with abnormal VRQOL.

**Figure 3** shows visual field test results of 2 patients included in the study who had similar BVF damage at the time corresponding to the questionnaire visit. Patient A had an abnormal VRQOL, whereas patient B had a normal VRQOL. During the follow-up period before the questionnaire administration, patient A had a rate of change of  $-1.29$  dB/y and clearly showed progression in the BVF. Conversely, patient B had a much slower rate of change of  $-0.22$  dB/y during follow-up.

#### COMMENT

In the present study, we demonstrated that progressive loss in BVF sensitivity was associated with self-reported abnormal VRQOL, measured by the NEI VFQ-25. Information provided by rates of BVF change was statistically predictive of abnormality in VRQOL even after adjustment for the degree of BVF loss at the time of questionnaire administration and other demographic and clinical potential confounders. Rates of BVF change also provided more information than monocular rates of change and cross-sectional visual field information for predicting VRQOL. To the best of our knowledge, this is the first study to relate rates of progressive BVF damage to self-reported VRQOL outcomes in glaucoma. These results may have significant implications for evaluation of the risk for developing functional impairment in glaucoma.

Each 0.1-dB/y faster rate of BVF change was associated with a 31% increase in the odds of reporting abnormal



**Figure 3.** Example of binocular visual field (BVF) results of 2 patients included in the study who had similar visual field damage at the time of the questionnaire. A, Patient who reported an abnormal vision-related quality of life (VRQOL) on the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) and clearly showed progression during the follow-up period of 5 years, with a mean rate of change of  $-1.29$  dB/y. B, Patient with normal VRQOL and slower rate of visual field loss of  $-0.22$  dB/y during the follow-up period of 7 years. MD indicates mean deviation.

VRQOL. When we investigated the association between monocular rates of visual field change (better and worse eyes) and abnormality in VRQOL, we observed that the predictive abilities were inferior to that of the BVF. Moreover, the association between monocular rates of visual field change and abnormality in VRQOL did not reach statistical significance. These results indicate that longitudinal assessment of the integrated BVF seems to provide more information for detecting patients at risk of presenting functional impairment than assessment of monocular visual fields separately. This finding can be explained by the fact that the BVF combines the sensitivities of both visual fields and, therefore, is likely to be a better representation of the patient's experience of the external world.

Cross-sectional information provided by the BVF MD was statistically associated with abnormality in VRQOL in the univariable logistic model. This result is in agreement with previous studies<sup>2,5,21</sup> that have evaluated the association between BVF damage and VRQOL. However, cross-sectional information was not statistically associated with abnormality in VRQOL after adjustment for longitudinal information provided by the rate of BVF change and other clinical and demographic characteristics. This finding may be explained by the fact that having a sequence of visual field tests is likely to provide a more robust evaluation of the visual field status than a single test, which is subject to much more variability and may not always reflect the true existing impairment.<sup>22,23</sup> Our findings indicate the importance of calculating rates of BVF change instead of relying only on the information provided by a single visual field examination to estimate risks of functional impairment.

Our results are not surprising if one considers that patients progressing at a faster rate in the BVF would most likely have less time to adapt to losses in quality of vision, resulting in a significantly greater effect in their daily activities. Previous studies<sup>7,24</sup> have demonstrated that individuals with macular degeneration, for example, develop perceptual plasticity that may help them adapt to central visual field damage. It is reasonable to consider that a similar process may occur after glaucomatous visual field losses. Experimental studies<sup>25-27</sup> suggest that these mechanisms are not immediate and that long-term neuronal reorganization of the visual cortex is necessary. Similarly, the development of other compensatory mechanisms, which would enable patients to cope better with losses of visual function, are likely to occur relatively slowly. Therefore, patients with fast progressive disease may not have enough time to develop those compensatory mechanisms and would be the ones most likely to report worse VRQOL scores. However, potential compensatory mechanisms that follow visual field damage in glaucoma are not completely clear. In fact, previous studies<sup>28-31</sup> have suggested that patients with peripheral visual field loss tend to ignore the region with scotoma rather than making more eye movements to compensate for the loss. Further studies should attempt to evaluate compensatory mechanisms developed by glaucoma patients in the context of their ability to perform everyday activities and the effect of disease on quality of life.

We used estimated BVFs from monocular visual fields instead of "true" BVFs. Although "true" BVFs can be obtained using specific perimetric strategies, they are not routinely performed in clinical practice. Among the several different methods previously proposed for construction of the integrated BVF from monocular fields, we used the summation method because it has been found to have a superior correlation with the "true" BVF examination compared with other approaches.<sup>6</sup> Although the methods used in our study to calculate BVF rates of change require some mathematical calculations, they can be easily implemented into the standard software of visual field instruments to provide clinicians with information about rates of BVF change, which may help determine risk of functional impairment.

The NEI VFQ-25 was used to assess VRQOL. This questionnaire has been previously validated to investigate quality of life in patients with chronic eye diseases and had a better correlation with visual impairment than other questionnaires.<sup>2,5,32</sup> However, no consensus exists on how to classify patients based on the results of the NEI VFQ-25. In our study, we determined that abnormality in VRQOL was present if at least 1 of the 10 vision-related subscores was below 50, excluding the one related to ocular pain. This would represent at least 2 SDs below the scores measured on a reference population.<sup>12</sup> This classification ensured the identification of a subgroup with significant abnormality in VRQOL, as indicated by the significant differences for all subscales listed in Table 2. In addition, the general clinical and socioeconomic variables associated with abnormal VRQOL in our analyses are in agreement with previous studies.<sup>33</sup>

Our study has limitations. We did not have longitudinal data on the NEI VFQ-25, and the incidence of VRQOL could not be established in our cohort. Therefore, a causal association between rates of visual field loss and loss in VRQOL could not be established. However, the design of our study is similar to those that have investigated associations between quality of life and a number of predictive factors in several diseases. Despite their limitations, such investigations can still provide important information about factors associated with a particular response and motivate the conduct of studies with more complex designs. Although the association found in our study was still significant after adjustment for potentially confounding variables, prospective studies determining the time course of development of functional impairment in glaucoma and its associated factors will be paramount. Another limitation of our study is that we assumed a linear rate of BVF change over time. Several studies<sup>34-37</sup> have suggested that functional changes do not follow a linear course during the natural history of the disease, which might be related to the logarithmic scaling (decibel) of visual field sensitivity data. Nevertheless, the assumption of linear change is probably a reasonable one for short and medium follow-up periods, as performed in clinical practice. Another limitation is that the NEI VFQ-25 is an instrument that provides subjective measure of VRQOL. As a consequence, this questionnaire may not reflect the true impairment experienced by patients in daily activities. It is known, for example, that adults with aging-associated cognitive im-

pairment have a tendency to overestimate functional abilities,<sup>38</sup> whereas patients with depression tend to underestimate their abilities.<sup>30,40</sup> The use of more objective tests, such as driving simulators,<sup>41</sup> could potentially provide a more accurate representation of the impairment experienced by glaucomatous patients on daily activities. Future studies should investigate the association between rates of visual field loss and objective measures of functional impairment.

In conclusion, rates of progressive BVF loss were predictive of abnormality in VRQOL and may be helpful in identifying patients at risk for development of functional impairment from glaucoma. Longitudinal information on BVFs was more predictive of VRQOL abnormality than longitudinal monocular information and cross-sectional evaluation of visual field damage.

**Submitted for Publication:** October 16, 2012; final revision received November 29, 2012; accepted December 3, 2012.

**Published Online:** February 28, 2013. doi:10.1001/jamaophthalmol.2013.2602

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**Conflict of Interest Disclosures:** Dr Zangwill has received research instrument support from Heidelberg Engineering; Carl Zeiss Meditec, Inc; Optovue, Inc; and Topcon, Inc. Dr Weinreb has worked as a consultant for Meditec-Zeiss. Dr Liebmann has worked as a consultant for Alcon Laboratories, Inc; Allergan, Inc; Diopsys, Inc; Optovue, Inc; Glaukos, Inc; Quark, Inc; and Merz Laboratories, Inc, and received research support from Carl Zeiss Meditec, Inc; Diopsys, Inc; Optovue, Inc; Pfizer, Inc; Alcon Laboratories, Inc; Merck, Inc; Allergan, Inc; Topcon Medical Systems, Inc; and Glaukos, Inc. Dr Medeiros has received financial support from Carl-Zeiss Meditec, Inc, and Heidelberg Engineering, GmbH.

**Funding/Support:** This study was supported in part by grants EY021818 (Dr Medeiros), EY11008 (Dr Zangwill), and EY14267 (Dr Zangwill) from the National Institutes of Health/National Eye Institute; CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) grant BEX 1066/11-0; an unrestricted grant from Research to Prevent Blindness; and participant retention incentive grants in the form of glaucoma medication at no cost from Alcon Laboratories, Inc; Allergan, Inc; Pfizer, Inc; Merck, Inc; and Santen, Inc.

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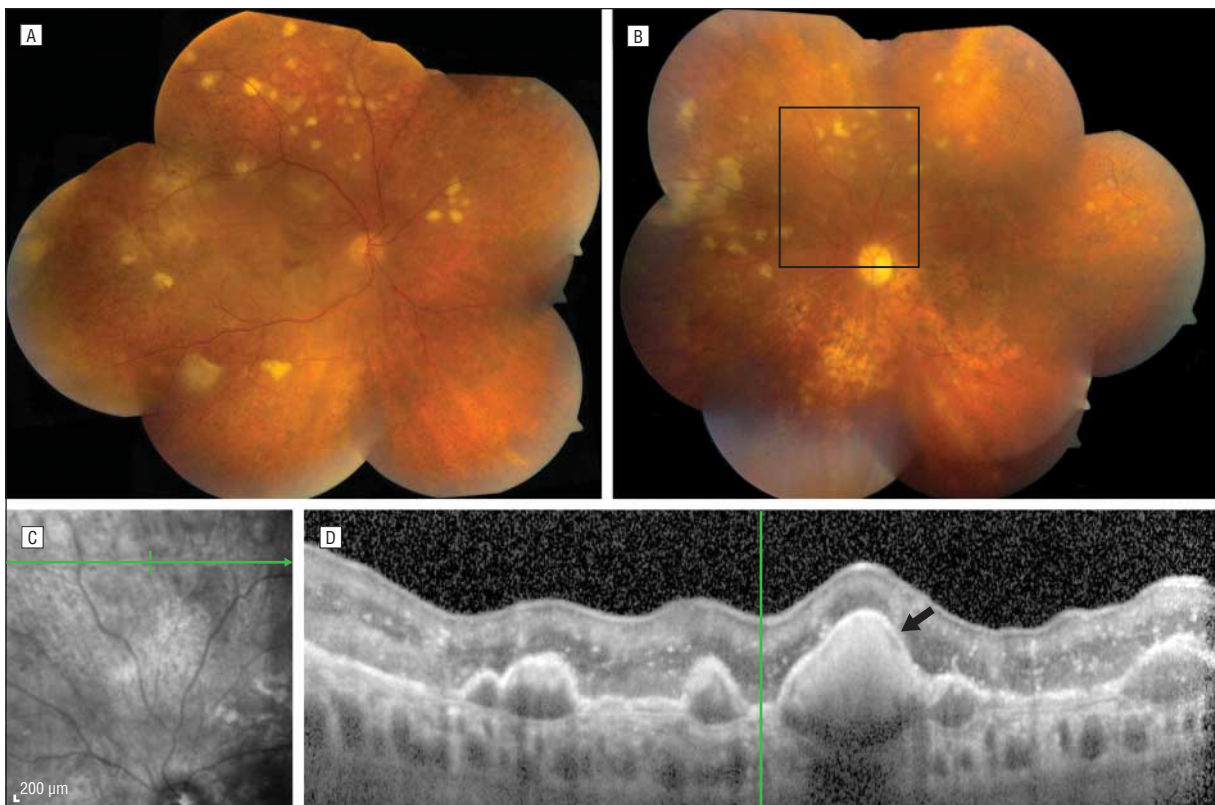
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## Ophthalmic Images

### Primary Central Nervous System Lymphoma With Ocular Involvement

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**Figure.** Fundus photographs of both eyes (A and B) and infrared and optical coherence tomographic images (C and D [Spectralis; Heidelberg Engineering]) of the left eye of a 67-year-old woman with primary central nervous system lymphoma with ocular involvement that was determined by a retinal biopsy. Several yellow nodular lesions with overlying leopard-spot pigmentary changes (A and B) are confirmed to be subretinal pigment epithelial in location (D [arrow]).