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Influence of Glaucomatous Visual Field Loss on Health-Related Quality of Life

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We examined the influence of glaucomatous visual field defects on vision-targeted and generic health-related quality of life. Vision-targeted and generic health status were assessed across 5 glaucoma treatment categories and a normal reference group from 5 tertiary care ophthalmology practices during regularly scheduled eye care visits. The sample consisted of 147 patients who were members of specific glaucoma treatment categories and 44 reference group patients. For patients with glaucoma, eligibility included a diagnosis of glaucoma at least 1 year prior to enrollment and no evidence of other eye disease. Participants completed 2 vision-targeted surveys, the National Eye Institute Visual Functioning Questionnaire and the VF-14, and a generic health-related quality of life measure, the Medical Outcomes Study 36-Item Short Form. Data from automated perimetry (Humphrey Field Analyzer 24-2, Humphrey Instruments, San Leandro, Calif) were used to generate Advanced Glaucoma Intervention Study scores for all participants. The Medical Outcomes Study 36-Item Short Form scores from glaucoma and reference group participants collected on a random half of the sample were similar. However, comparisons of the vision-targeted surveys demonstrated significant mean differences on 7 of 11 National Eye Institute Visual Functioning Questionnaire scales, and a trend toward significant differences for the VF-14 (P<.07 by linear regression). Greater visual field defects in the better eye were significantly associated with poorer National Eye Institute Visual Functioning Questionnaire scores (P<.05), as well as with worse VF-14 scores. These findings were most dramatic for patients with the most severe field loss in the better eye. Vision-targeted questionnaires were more sensitive than a generic health-related quality of life measure to differences between glaucoma and normal reference participants. Our findings indicate that self-reports of vision-targeted health-related quality of life are sensitive to visual field loss and may be useful in tandem with the clinical examination to fully understand outcomes of treatment for glaucoma.

There is growing recognition of the importance of assessing a broad array of outcomes such as physical and social functioning and other dimensions of health-related quality of life (HRQOL) when examining the influence of ophthalmic conditions on patients’ functioning and well-being. However, until recently, the measurement of vision-targeted functioning and HRQOL have rarely been incorporated into clinical studies of patients with glaucoma. For conditions such as glaucoma that are unlikely to influence central vision until late in the disease process, it is possible that surveys designed to measure multidimensional vision-targeted functioning may provide a more comprehensive assessment of visual disability because of early visual field loss.
PATIENTS, MATERIALS, AND METHODS

STUDY DESIGN AND POPULATION

A prospective sample of glaucoma and reference group participants who met eligibility criteria were enrolled from five tertiary care ophthalmology practices between June 1, 1995, and January 31, 1996. Patients were approached at the time of regularly scheduled visits. Eligibility criteria included an age of at least 30 years, English-speaking, and no cognitive or hearing impairments. Cognitive status was assessed with an abbreviated form of the Folstein Mini-Mental Status Examination. The interviewers used their judgment to determine whether the patient had adequate hearing to provide informed consent and participate in the interview. The research protocol was approved by all appropriate institutional review boards and participants gave written informed consent prior to enrollment.

We enrolled patients between the ages of 30 and 90 years with onset of glaucoma after 18 years of age and at least 1-year duration. Patients whose conditions were diagnosed as primary open-angle glaucoma, pigmentary glaucoma, exfoliation syndrome, or chronic angle-closure glaucoma were eligible to participate. Patients with other eye diseases were excluded. However, because of the high prevalence of early, nonvisually significant cataracts among patients with glaucoma, patients with a cataract Lens Opacities Classification System II (LOCS II)13 grade of 1 or less were eligible for inclusion. Additionally, patients with pseudophakia in 1 or both eyes were also eligible.

Before the practice session, staff in each office reviewed the medical records of all patients who were scheduled for eye examinations to identify potential candidates who were members of 1 of 5 glaucoma treatment groups: (1) those on medications only who were using systemic and binocular topical medications, including β-blockers, miotics, and carbonic anhydrase inhibitors; (2) a laser-only group treated with argon laser trabeculoplasty or laser iridotomy in both eyes with no current topical or systemic medication use; (3) an incisional surgery-only group previously treated with surgery who were not using medications; (4) a laser and medications group who had argon laser trabeculoplasty or laser iridotomy in 1 or both eyes in the past and were using medications in at least 1 eye; and (5) an incisional surgery and medications group with surgery in 1 or both eyes and topical medication use in at least 1 eye. Patients who had received laser and incisional surgery were counted under the incisional surgery categories. Because of the small number of patients (n = 2) who had laser-only treatment, for the purposes of adjusting for treatment effects in the multivariate models, these 2 cases were combined with the surgery-only group. Efforts were also made to have balanced representation by sex and race.

Patients in the reference group who had no underlying vision problems except for correctable refractive error were enrolled from the same practices as the patients with glaucoma. Initially, reference participants were eligible if their age was within 5 years of the mean age of the previous 3 enrolled patients with glaucoma for that site. However, because some sites had difficulty recruiting older patients with no known eye diseases, the criterion was relaxed to include patients the same age as, or older than, the mean age of the 3 youngest patients with glaucoma enrolled at that site.

DATA COLLECTION

All of the patients completed both vision-targeted questionnaires, while a random half of the sample completed the Medical Outcomes Study 36-Item Short Form (SF-36). Therefore, all analyses involving the SF-36 measurement will consist of approximately half of the total study sample. Each participant also completed a 16-item medical comorbidity checklist obtained from the Medical Outcomes Study.14 Multivariate analyses were adjusted for the unweighted sum of medical comorbidities. To avoid a possible bias from information learned during their clinical examination, patients completed the questionnaires prior to seeing the ophthalmologist.

HEALTH STATUS MEASUREMENTS

Participants were asked to complete self-administered versions of the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ).18-19 VF-14,20 and SF-36. Subjects were given verbal instructions prior to filling out the questionnaires. If a patient asked for help, the research interviewer was instructed to read each question verbatim and to record the responses. Approximately 30% of the patients with glaucoma and none of the reference group participants required assistance in filling out the surveys. To avoid a response-order bias, surveys were randomly ordered in each enrollment packet.

Participants completed the 51-item NEI-VFQ field test version, which generates subscales for the following dimensions of vision-targeted HRQOL: overall health, overall vision, difficulty with near vision activities, difficulty with distance vision activities, limitations in social functioning due to vision, role limitations due to vision, dependency due to vision, mental health symptoms due to vision, future expectations for vision, driving difficulties, limitations with peripheral and color vision, and pain or discomfort in or around the eyes (Table 1). Subscales are scored on a 0 to 100-point scale in which 100 indicates the best possible score on the measure and 0 indicates the worst.18,19

The NEI-VFQ is a vision-targeted survey that assesses the influence of visual disability on HRQOL. The content of the NEI-VFQ field test version was derived from condition-specific focus groups. The conditions represented in the focus groups include age-related cataract, age-related macular degeneration, glaucoma, diabetic retinopathy, and cytomegalovirus retinitis. The test version consists of 51 items and takes 15 minutes, on average, to administer in the interviewer format. Research is underway to determine the psychometric properties of the NEI-VFQ.

Participants also completed the VF-14, which measures difficulty with 14 vision-targeted activities ranging from reading prints of various sizes to driving.20 Each item has 5 response options ranging from "no difficulty" to "unable to do this activity." Items are scored from 0 (unable to do activity) to 5 (no visual field loss, but also from the effects of treatment. And while a variety of methods for quantifying visual field loss exists, there is little information about how visual field loss relates to patient-reported functioning or HRQOL.
difficulty), and an average score is generated from the answered items. This score is then transformed to a 0- to 100-point scale, with 0 indicating an inability to do any of the activities and 100 indicating no difficulty on all activities.

The SF-36 is a generic HRQOL measure designed for chronically ill medical patients. The SF-36 includes 8 subscales: general health, physical function, role limitations due to physical and mental disability, mental health, social function, vitality, and bodily pain. Each of the subscales is scored on a 0 to 100 scale, in which 100 indicates the best possible score on a specific subscale and 0 indicates the worst function. Our reported scores are based on a published algorithm for the SF-36. The SF-36 has been tested extensively with many different populations and is one of the most widely used measures in health services research.

OPHTHALMOLOGIC EXAMINATION

All participants completed a comprehensive dilated ophthalmologic examination that included an assessment of current eye diseases and previous history of ophthalmic surgical procedures. Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity was measured for each eye while patients were wearing their current, or "walking about," correction. Patients with visual acuity so poor that they could not read any of the largest letters at 4 m were tested for light perception. Patients with no light perception were included in the study. The presence and severity of cataracts were graded during a slit-lamp examination using the LOCS II reference standards.

VISUAL FIELD

Data from automated perimetry (Humphrey Field Analyzer, 24-2 or 30-2; Humphrey Instruments) were obtained within 6 months of the study participation. Participants with other diseases that cause visual field loss, such as optic neuritis, were excluded. Only "reliable" visual fields, defined by false-positive results, false-negative results, or fixation losses not exceeding 33%, were used.

Advanced Glaucoma Intervention Study (AGIS) scores were calculated for each eye based on the main deviation plot from the automated perimetry visual fields. Advanced Glaucoma Intervention Study scores represent the number and depth of depressed visual field sites found in less than 5% of normal values and an index for quantifying visual field defects for the entire eye. Advanced Glaucoma Intervention Study scores can range from 0, indicating no defects, to 20, indicating near or complete visual field loss. Advanced Glaucoma Intervention Study scores are calculated from points awarded to 3 areas: the upper field, the lower field, and the nasal area. A maximum of 9 points can be awarded to the upper and lower fields, while the nasal area can be awarded a maximum of 2 points. For our study, an AGIS score was calculated for each participant's better and worse eye.

STATISTICAL ANALYSES

The distribution of age, sex, race, and number of medical comorbidities was compared for patients with glaucoma and the reference group using the Student t and χ² tests. As a test of between-group validity, we compared mean SF-36, NEI-VFQ, and VF-14 scores for patients with glaucoma with those who were in the reference group. For these comparisons, we used regression analyses to adjust for between-group factors known to influence HRQOL scores, such as age, sex, race, and number of medical comorbidities. Models were also adjusted for cataract and prior cataract surgery in 1 or both eyes. Although cataract with a LOCS II grading of 2 or greater was an exclusion for this study, a small number of patients (n=9) were enrolled who had a cataract with a LOCS II grading of 2 or in at least 1 eye. We included these participants because, in all adjusted models, cataract was a nonsignificant variable.

Since patients with monocular vision can perform most visual activities with ease, we expected NEI-VFQ and VF-14 scores to be significantly correlated with visual acuity and measured visual field in the better eye. To test the significance of this association in our study, Spearman rank correlation coefficients were calculated between mean NEI-VFQ scores and VF-14 scores and visual acuity and visual field in the better and worse eye.

To determine whether patients with greater field loss reported poorer vision-targeted HRQOL, linear regression models were used to compare adjusted NEI-VFQ and VF-14 scores by AGIS score in the better eye. To ensure that any differences were owing to glaucoma and not other patient characteristics, all models were adjusted for the influence of age, sex, race, medical comorbidities, prior cataract surgery, and cataract. Additionally, all models were adjusted for AGIS score in the worse eye: NEI-VFQ score = β₀ + β₁ (AGIS better eye) + β₂ (AGIS worse eye) + β₃ (age) + β₄ (sex) + β₅ (medical comorbidities) + β₆ (race) + β₇ (LOCS II grade) + β₈ (pseudophakia) + error.

The selection of the independent clinical variables in the multivariate models requires some discussion. The decision to test the association between better-eye AGIS values and scale scores comes from evidence that a person's visual acuity in the better eye is a stronger predictor of self-reported functioning than is visual acuity in the weaker eye. Because it is uncertain whether the better visual field will be a stronger predictor of self-reported functioning, we have adopted a conservative approach that adjusts all models for severity of field loss in the worse eye. To determine whether the adjustment for field loss in the worse eye influenced our interpretation of the models, the same better-eye AGIS models were fitted on all vision-targeted scales without adjusting for worse-eye values. The tests of significance and the partial squared correlation coefficients were unchanged when the worse-eye adjustment was omitted. Inclusion of treatment variables representing specific medication and type of surgery, and visual acuity in the better and worse eye, also did not change the significance of the observed associations between field loss in the better eye and vision-targeted HRQOL.

To determine whether the NEI-VFQ, VF-14, and SF-36 were reliable when administered to patients with glaucoma, we calculated Cronbach's α as a measure of internal consistency for each of the multi-item subscales. Whereas generic HRQOL questionnaires allow for comparisons across disease groups, disease-targeted surveys are more sensitive to the particular clinical features of that disease. Studies that have included generic and vi-
vision-targeted HRQOL questionnaires to assess outcomes after cataract surgery have found greater positive change for vision-targeted surveys. While there may be similarities in the way cataract and glaucoma influence patient functioning, because cataracts are a reversible condition that can be addressed by surgery and glaucoma is a chronic progressive condition with much uncertainty for future functioning, we would expect that these differences alone would influence a person’s perception of vision-targeted functioning and HRQOL. For this reason, it is not clear that surveys designed for use among patients with cataracts will capture adequately the influence of glaucoma on vision-targeted HRQOL.

To assess the validity and reliability of health status questionnaires when used in glaucoma, we determined whether generic and vision-targeted surveys of HRQOL could discriminate between patients with and without glaucoma. Additionally, we examined the influence of glaucomatous visual field defects on reported decrements in vision-targeted and generic HRQOL.

**RESULTS**

**PATIENT POPULATION**

Among the group with glaucoma and the reference group, 60% of the participants were women. Fewer blacks were enrolled in the group with glaucoma compared with the reference group (30% vs 50% [P<.05]). Additionally, those with glaucoma were, on average, 15 years older than reference group participants (P<.01). Patients with glaucoma had similar levels of medical comorbidity as those in the reference group (P<.21). As would be expected, those with glaucoma also had significantly poorer visual acuity (P<.01) and greater visual field deficits in the better and worse eye compared with the reference group participants (Table 2).

**COMPARISON OF SF-36 SCORES FOR PATIENTS WITH AND WITHOUT GLAUCOMA**

The demographic and clinical characteristics of the random half of the sample who completed the SF-36 were not significantly different from the group overall (P<.05). When compared with reference group participants, the adjusted scores for those with glaucoma had a trend toward lower scores on all 8 SF-36 subscales. However, only 1 scale, social functioning, approached significance (P<.07) (Figure 1). Although 5- to 10-point differences in SF-36 scores are likely to be clinically relevant, these observed differences were not statistically significant in our small sample size. Because of limited statistical power owing to sample size, examination of the relationship between SF-36 scores and severity of field loss was unexplored.

**COMPARISON OF NEI-VFQ AND VF-14 SCORES FOR PATIENTS WITH AND WITHOUT GLAUCOMA**

When compared with the reference group, patients with glaucoma had significantly poorer adjusted mean scores on 7 of 11 NEI-VFQ subscales (Figure 2). These scales included general vision, discomfort or pain in and around the eyes, difficulty with near vision, difficulty with distance vision activities, difficulty with driving, decreased well-being due to vision, and role limitations attributable to vision. Additionally, there was a trend toward worse adjusted VF-14 scores for those with glaucoma relative to the reference group (P=.07).

**CLINICAL VALIDITY OF THE NEI-VFQ AND VF-14 AMONG PATIENTS WITH GLAUCOMA**

We found that 8 of 11 NEI-VFQ subscales were statistically significantly correlated with AGIS scores in the
better and worse eye (−0.28−0.46), while 6 of 11 subscales were statistically significantly correlated with ETDRS scores in the better and worse eye (0.27−0.35) (Table 3). Based on previous research, we expected to find higher correlations between the responses on the surveys and clinical markers of vision in the better eye, compared with those in the poorer eye. However, for patients in our study, the correlations between responses on the NEI-VFQ subscales and clinical indicators of disease severity were statistically significant and of similar magnitude for the better and worse eye (Table 3). Unadjusted correlations between the VF-14 with ETDRS and AGIS scores in the better and worse eyes were also statistically significant and of similar magnitude as those observed with the NEI-VFQ.

ASSOCIATION BETWEEN SEVERITY OF VISUAL FIELD LOSS AND VISION-TARGETED HRQOL AND FUNCTIONING

Patients with greater field loss in the better eye reported poorer NEI-VFQ scores for 7 of 11 subscales (P<.05). These scales included general vision, difficulty with near vision, difficulty with distance vision, difficulty with driving, visual limitations with social functioning, role limitations due to vision, and dependency on others due to vision (Figure 3, A-G). A similar and statistically significant relationship was observed for the VF-14 (Figure 3, H). To determine if there was a “step-off” in vision-targeted HRQOL vs a steady rate of decline, adjusted NEI-VFQ and VF-14 scores were plotted against AGIS scores. These plots suggest that the relationship between visual field loss on HRQOL approximates a steady linear decline (Figure 3, A-H).

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<tr>
<th>Table 3. Spearman Rank Correlation for the National Eye Institute Visual Functioning Questionnaire and the VF-14 With ETDRS and AGIS Scores (N=147)*</th>
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<td><strong>Subscale Name</strong></td>
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<td>General health scale</td>
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<td>VF-14 scale</td>
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*ETDRS indicates Early Treatment Diabetic Retinopathy Study; AGIS, Advanced Glaucoma Intervention Study.
†P<.001.

SENSITIVITY ANALYSIS OF MULTIVARIATE MODELS OF VISION-TARGETED HRQOL

To determine whether the observed relationship between vision-targeted HRQOL and visual field defects was sensitive to our modeling strategy, we also added ETDRS visual acuity in the better and worse eye and variables for specific medications (propranolol, pilocarpine, and others) or previous surgical procedures. Although adding visual acuity to the models increased the overall proportion of variance explained, it did not change the
Figure 3. Predicted health-related quality of life scores by Advanced Glaucoma Intervention Study (AGIS) best-eye value. Error bars indicate the 95% confidence interval (CI) around the mean predicted score. Predicted scores are from linear regression models adjusted for AGIS score in the worse eye, age, sex, medical comorbidities, race, cataract severity, and pseudophakia.
significance of the parameter estimate associated with better-eye AGIS score and each of the NEI-VFQ subscales or the VF-14. Similarly, when variables representing type of treatment were added to the models, the statistical significance of the association between better-eye AGIS values and the NEI-VFQ or VF-14 scores did not change.

RELIABILITY OF THE NEI-VFQ, VF-14, AND SF-36 IN GLAUCOMA

The Cronbach α showed good to excellent reliability for the NEI-VFQ subscales, ranging from .93 for distance vision to .67 for the visual expectations subscale. Nine of 11 NEI-VFQ subscales had reliability estimates above .78, a range that is sufficient for group to group comparisons. The VF-14 also showed excellent reliability at .93. The SF-36 showed similarly high reliability, with 7 of 8 subscales at or above .78.

COMMENT

For health surveys to be of use in clinical and research settings, they must be able to discriminate between comparable patients with and without a condition, and must also be sensitive to clinically relevant differences in disease severity. Our article demonstrates that 7 of 11 NEI-VFQ subscales, a new vision-targeted survey designed to assess the influence of visual disability on a range of dimensions of HRQOL, are sensitive to the influence of glaucoma and visual field loss. Evidence of clinical validity for the NEI-VFQ is provided by its ability to discriminate between participants without a chronic eye disease from those who have glaucoma. Additionally, for many of the NEI-VFQ subscales, we were able to demonstrate a linear relationship between field loss in the better eye and greater disability on the NEI-VFQ. The internal consistency, as measured by the Cronbach α, indicates that the NEI-VFQ also has adequate reliability to be a useful measure in research and clinical settings for patients with glaucoma.

During this investigation, we also administered the SF-36, a generic measure of HRQOL, to determine whether it could discriminate between patients with glaucoma and patients without chronic eye diseases. If this were the case, then the SF-36 would provide a common metric for evaluating the burden of glaucoma relative to other diseases. Although the differences in SF-36 scores observed for patients with glaucoma were not statistically lower than those observed among reference group participants, the effect size and trend toward significance indicate that a larger sample would have made these differences statistically significant. A useful method for evaluating the clinical significance of an effect size for the SF-36 is to compare the magnitude of the observed differences in mean scores with published scores for patients with specific medical conditions. For example, the results for the participants with glaucoma approximate reported values for patients with a “minor medical” condition comparable with uncomplicated hypertension.

Additionally, we found a trend toward significant differences in VF-14 scores for the group with glaucoma vs the reference group participants in our study (P<.07). The lack of statistical significance may have been because the VF-14 is a shorter survey and, therefore, provides a less precise estimate of visual functioning. As a questionnaire designed for patients with cataract, the VF-14 emphasizes task performance only, an area of functioning that patients with glaucoma are less likely to have problems with until late in the disease process when field loss is severe. The greater sensitivity of the NEI-VFQ to between-group differences may be due to its longer length and emphasis on the effect of visual disability on dimensions of HRQOL other than task performance, such as concern and worry about future visual functioning and perceived limitations in role function due to vision. The progressive nature of glaucoma, vs the reversibility of cataracts, may also explain why we identified a linear relationship between visual field loss and the less physical dimensions of health represented in the NEI-VFQ.

Because the influence of visual field loss on HRQOL should be independent of visual acuity until late in glaucoma, we initially omitted visual acuity from the multivariate models. To determine whether this was the case, we also conducted sensitivity analyses that included visual acuity. These results indicate that visual field loss is largely independent of the influence of visual acuity for vision-targeted HRQOL in glaucoma. However, our results confirm previous findings regarding the importance of visual acuity as an independent predictor of vision-targeted functioning. The lack of association between specific treatments and HRQOL may be because of the heterogeneity of the treatments received by our participants. For example, many patients in our study were receiving multiple medications simultaneously. Whether specific treatments such as medication or surgery have differential influence on HRQOL will be answered by clinical trials that randomize patients to specific therapies.

Our study has several limitations. The first is that this is a selected sample from tertiary care settings, so the observed decrements in HRQOL may not generalize to patients with glaucoma in community-based practices. However, this sampling strategy is unlikely to distract from the observed relationships between field loss and HRQOL. Also, although there is a trend toward significance, because only a random half of our sample received the SF-36, we cannot say definitively that this measure will adequately capture disability from glaucoma.

Our study has demonstrated that detectable decrements in vision-targeted HRQOL are observed for patients with glaucoma who have visual field loss. We also demonstrated that comprehensive vision-targeted HRQOL surveys, such as the NEI-VFQ, and task-oriented surveys, such as the VF-14, are promising tools for monitoring quality and outcomes of care for patients with glaucoma.

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REFERENCES


Correction

Omission. In the landmark article entitled “A Contact Lens,” published in the January ARCHIVES (1997;115:120-121), the original source of the article was inadvertently omitted. The source should be noted as follows: abridged from Arch Ophthalmol Otolaryngol. 1888;17:215-226.