Treatment and Vision-Related Quality of Life in the Early Manifest Glaucoma Trial

*Leslie G. Hyman, PhD,[1] Eugene Komaroff, PhD,[1] Anders Heijl, MD, PhD,[2] Bo Bengtsson, MD, PhD,[2] M. Cristina Leske, MD, MPH,[1] for the Early Manifest Glaucoma Trial Group**

Purpose: To evaluate the effect of treatment, visual function, and other factors on vision-targeted health-related quality of life (HRQOL) of patients with early glaucoma.

Design: Randomized clinical trial.

Participants: Two hundred fifty-five patients with newly detected open-angle glaucoma and repeatable early visual field (VF) defects, 50 to 80 years old (66% female).

Methods: Patients were randomized to receive either betaxolol plus laser trabeculoplasty in eligible eye(s) or no initial treatment and had ophthalmologic examinations every 3 months. A Swedish translation of the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) was self-administered at 2 follow-up visits (3 and 6 years after randomization).

Main Outcome: Multiple linear regression analyses determined the effect of treatment and other factors on (1) VFQ-25 composite scores at the first administration and (2) change in scores between administrations.

Results: Two hundred thirty-three patients had 1 NEI VFQ-25 administration and 167 patients had 2 administrations. Internal consistency reliability was high for the composite VFQ-25 score (Cronbach $\alpha = 0.88$) and satisfactory ($\alpha \geq 0.76$) for most subscale scores. At the first administration, the composite score was high (88.8 ± 11.7). Mean subscale scores were also generally high (98.0–58.3) and were similar for each study group when analyzed separately. Most lower subscale scores were modestly but significantly related to worse visual acuity (VA) or mean deviation (MD) (better eye, $r = 0.15$–0.35). Composite scores were similar for treated and untreated patients. Lower composite scores were associated with low VA in the better eye (worse than 0.70) and worse perimetric MD (<4.16 decibels) and nuclear lens opacities (Lens Opacities Classification System II grade ≥ 2), but not with age, gender, VF progression, intraocular pressure, cardiovascular disease, or hypertension. Between VFQ-25 administrations, larger decreases in the composite score were associated with larger decreases in VA ($P<0.05$), female gender ($P = 0.001$), and older age at first administration ($P = 0.006$). Treatment (assigned at randomization or later in the study) was not associated with change in HRQOL.

Conclusions: Results suggest that absence or delay of treatment did not influence vision-targeted HRQOL in these newly diagnosed glaucoma patients. However, visual function affected vision-targeted quality of life up to 6 years after Early Manifest Glaucoma Trial enrollment. *Ophthalmology 2005;112:1505–1513 © 2005 by the American Academy of Ophthalmology.*

Open-angle glaucoma (OAG) is a leading cause of visual impairment worldwide. The visual disability caused by glaucoma can affect quality of life and functional ability, particularly in patients with advanced disease. Clinical measures such as perimetry, commonly used to evaluate glaucoma severity and progression, do not necessarily reflect the impact of disease on overall functioning status or on vision-targeted health-related quality of life (HRQOL). There is a growing body of literature that addresses this issue based on questionnaires that examine self-perceived HRQOL and visual function among glaucoma patients.[1–16] Most of these studies have focused on patients with moderate to advanced disease, emphasizing comparisons to persons without glaucoma, but little is known about the role of immediate treatment of early glaucoma on HRQOL. A recent Scandanavian study indicated that >80% of glaucoma patients reported negative feelings (anxiety, fear of blindness, depression) at the time of their diagnosis.[15] The impact on HRQOL of receiving treatment or remaining untreated at the time of diagnosis remains unclear. The Early Manifest

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[1] Department of Preventive Medicine, School of Medicine, Stony Brook University, Stony Brook, New York.

[2] Department of Ophthalmology, Malmö University Hospital, Malmö, Sweden.

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Correspondence and reprint requests to Leslie G. Hyman, PhD, Department of Preventive Medicine, School of Medicine, Stony Brook University, Health Sciences Center, Level 3, Room 086, Stony Brook, NY 11794-8036.

*Members of the Group are listed in Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120:1268–79.

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Glaucoma Trial (EMGT), as the only glaucoma clinical trial to include an untreated arm and evaluate vision-targeted HRQOL, provides a unique opportunity to address this issue.

The EMGT is a randomized clinical trial that evaluated whether initial treatment to reduce intraocular pressure (IOP), versus no or delayed treatment, slows progression in patients with early, newly detected OAG. The EMGT's results showed that initial treatment significantly reduced glaucoma progression, as measured by visual field (VF) and optic disc outcomes.[17] To evaluate the effect of treatment on the HRQOL of EMGT patients, the study used the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25).[18] This instrument was developed to assess the impact of various eye conditions on self-perceived visual function and has been validated and used in numerous studies worldwide.[18–20] Specifically, this article aims to (1) report the development of a Swedish translation of the NEI VFQ-25 and its use in EMGT patients, including an evaluation of its internal consistency and reliability in this population; (2) describe HRQOL among EMGT patients at the time of the first VFQ-25 administration; (3) evaluate the relationship of HRQOL to early or delayed treatment and other factors such as age, gender, visual acuity (VA), perimetric mean deviation (MD), glaucoma progression, IOP, lens opacities, and comorbidities (i.e., cardiovascular disease and hypertension); and 4) evaluate whether these factors also are related to change in HRQOL over time.

Materials and Methods

Study Population

The EMGT design has been described in detail elsewhere.[17,21,22] The study enrolled 255 patients between January 1993 and April 1997 at a clinical center in Malmö and a satellite center in Helsingborg, Sweden. Eligibility criteria required patients between 50 and 80 years old to have newly detected, previously untreated, manifest OAG (including chronic simple glaucoma, normal-tension glaucoma, and exfoliative glaucoma) with repeatable early glaucoma VF defects in at least one eye by Humphrey threshold perimetry. Patients were excluded with (1) advanced VF defects; (2) VA$<$0.5; (3) mean IOP $>$ 30 mmHg or any IOP $>$ 35 mmHg in at least one eye; or (4) lens opacities or any condition precluding reliable VFs or disc photography, use of study treatments, or 4-year follow-up. Randomized patients received betaxolol twice daily plus laser trabeculoplasty in eligible eye(s) (n = 129) or no initial treatment (n = 126). The study outcome was EMGT progression determined by perimetric or optic disc assessment based on standardized independent criteria. Perimetric progression was defined as significant changes from baseline in at least 3 of the same progressing points in 3 consecutive VFs, assessed by glaucoma change probability maps based on pattern deviation. This criterion has been shown to be a sensitive measure of VF deterioration and is associated with an average worsening of MD by -1.93 decibels (dB).[23] Optic disc progression was based on photographic criteria that required clear change on an optic disc follow-up photograph, as detected by flicker chronoscopy, and was confirmed by side-by-side gradings in 2 consecutive visits. Patients were considered to have progressed when one eye had progressed. All patients were observed in their original allocation arms. When significant EMGT progression occurred, control patients were given the option of treatment.

Development of the Swedish Version of the 25-Item National Eye Institute Visual Function Questionnaire

Early Manifest Glaucoma Trial investigators developed a Swedish translation from the original English version of the NEI VFQ-25, which became available in 1996, about 3 years after the beginning of the trial. An initial Swedish version was (1) pilot tested in 10 patients, (2) backtranslated into English, (3) compared with the original English version, and (4) retranslated into Swedish.

Data Collection

Follow-up visits were held every 3 months, with data collected by trained and certified EMGT examiners, following a standardized protocol. Visits included ophthalmologic examinations with Humphrey Full Threshold 30-2 VF tests (Carl Zeiss Meditec, Inc., Dublin, CA), Goldmann applanation tonometry, and VA measured by Monoyer–Granström standard decimal charts after subjective refraction. Data on systemic and ocular conditions were collected at each visit. Lens opacities were graded by type at the slit lamp using Lens Opacities Classification System II[24] and were defined by a Lens Opacities Classification System II nuclear, cortical, or posterior subcapsular grade of $\geq$2.

The NEI VFQ-25 questionnaire was self-administered once at a median of 3 years after randomization and again at a median of 6 years after randomization.

Data Analyses

All analyses were conducted using SAS 8.2 (SAS Institute Inc., Cary, NC). The NEI VFQ-25 was grouped into 12 subscales and an overall composite scale. The scoring algorithm developed by Mangione et al[18] was followed. The Cronbach coefficient α was used to determine reliability for each subscale and for the composite score. Correlations of each subscale and the composite score to VA and MD based on better and worse eyes were assessed by Spearman correlation coefficients.

Measures for VA, MD, and IOP were based on the better eye at first VFQ administration in all further analyses, regardless of eye eligibility status for the trial. Alternative analyses considered the worse eye, with no substantive change in conclusions.

Multiple linear regression was used to model the factors associated with (1) the VFQ composite score at the first administration and (2) the change in the composite score between the 2 administrations. For the first set of analyses, a multiple linear regression model was built to determine whether the VFQ composite score was independently associated with glaucoma treatment before the first administration (whether assigned by randomization at baseline to the treated group or received by controls during follow-up, after EMGT progression or IOP $>$ 35 mmHg as per protocol). The model included VA (4 categories: 1.0, 0.9, 0.8, and $\leq$0.7), MD and IOP (based on quartiles of the distribution), and age ($\leq$73/$>$73 years; median based), all at time of first administration. Other variables considered were gender, EMGT progression before first administration, history of cardiovascular disease (cardiac incompensation, myocardial infarction, arrhythmia/bradycardia, or stroke), hypertension (systolic $>$ 160 mmHg, diastolic $>$ 95 mmHg, or history of hypertension medication use), and lens opacities (nuclear, cortical, or posterior subcapsular) before or at the first administration. All variables were entered in the initial model simultaneously. The final (reduced) model was obtained by

manually deleting one variable at a time (other than age and gender, which were considered, a priori, as potentially confounding variables) based on the least significant *P* value (type III sums of squares) at each step until all *P* values were <0.05. Adjusted means were derived from the model and Tukey–Kramer adjusted *P* values were determined (least squares means).

The change in composite VFQ scores between first and second administrations was calculated for the 167 patients who received the second VFQ administration. Using a similar multiple regression modeling approach as described for the first administration, the second set of models evaluated the relationship between change in VFQ composite score and glaucoma treatment received before the second administration. These models accounted for previously associated factors, as well as the VFQ score at the first administration. The latter was included to account for the potential nonequivalence of subgroups with initial VFQ scores. Because the VFQ change analysis is based on a nonrandom subset of EMGT patients, the inclusion of the first VFQ score ensured that regression to the mean would be operating equally in all subgroups. The following variables were also evaluated: change in VA in the better eye at first administration (4 categories: −0.70 to −0.21, −0.20 to −0.11, −0.10 to −0.01, and ≥0.00 [no change/improvement]), change in MD in the better eye from the first administration (4 quartile-based categories: −11.53 to −1.98, −1.97 to −0.65, −0.64 to 0.12, and 0.13–4.32 dB), EMGT progression before the second administration, gender, and age (≤73/>73 years). The final model, built using the manual backward elimination procedure, included only those factors that were found to be significantly associated ($P<0.05$) with change in VFQ composite score.

Results

Two hundred thirty-three EMGT patients (treated group, n = 116; control group, n = 117) had the NEI VFQ-25 administered once, and 167 (treated group, n = 84; control group, n = 83) had it administered twice (Fig 1, Table 1). The baseline characteristics of patients with 1 NEI VFQ-25 administration and those with 2 administrations were similar to those of the entire EMGT population and to each other (Table 1). For all 3 groups, the mean baseline age was approximately 68 years, and approximately two thirds were female. Visual impairment was mild, the frequency of cardiovascular disease history was low, and about 40% had hypertension (Table 1). The similarity of these comparisons suggests that the findings concerning VFQ scores should be representative of all EMGT patients.

First Administration

For this Swedish NEI VFQ-25 translation, internal consistency reliability was high (Cronbach α, 0.88) for the composite score and adequate ($\alpha \geq 0.76$) for all subscales, except social functioning ($\alpha = 0.64$) and driving ($\alpha = 0.27$), with the latter result being based on a smaller sample size (Table 2). At the first administration, mean VFQ scores ranged from low scores of 58.3 and 78.6 for subscales of general health and general vision, respectively, to high scores of 98.0 for (lack of) dependency on others, 95.0 for color vision, and 94.8 for social functioning (Table 2). Visual Function Questionnaire scores were similar for each study group when analyzed separately (Fig 2).

In this cross-sectional analysis, VFQ scores were modestly but significantly correlated to VA and MD for the composite score and for most subscales. Results were similar when based on better or worse eyes, indicating that lower VFQ scores were generally correlated with worse visual function. Visual acuity was most highly correlated with general vision ($r = 0.35$ in the better eye, $r = 0.47$ in the worse eye), near activities ($r = 0.32$ in the better eye, $r = 0.35$ in the worse eye), and the composite VFQ scores ($r = 0.31$ in the better eye, $r = 0.38$ in the worse eye) and least correlated with ocular pain and general health scores. Similar patterns were observed for MD. Separate analyses in each study group found similar and consistent results for the Spearman correlations of VFQ composite scores to VA and MD. For example, correlations between the composite VFQ score and VA in the better eye were 0.35 in the treated group ($P = 0.0001$) and 0.28 in the control group ($P = 0.0023$); correlations between the composite VFQ score and MD in the better eye were 0.34 in the treated group (0.0002) and 0.28 in the control group ($P = 0.002$).

The unadjusted and adjusted mean composite VFQ scores for the factors found to be associated with lower composite VFQ scores in the multiple regression model are presented in Table 3. The lowest composite VFQ scores were found among patients in the lowest categories of VA (≤0.70 in the better eye) and MD (≤−4.16 dB in the better eye). Among the VA categories, the largest difference in composite scores was between the lowest and highest categories (adjusted difference between mean scores of 8.7 [$P = 0.001$]). Among the MD categories, differences in composite

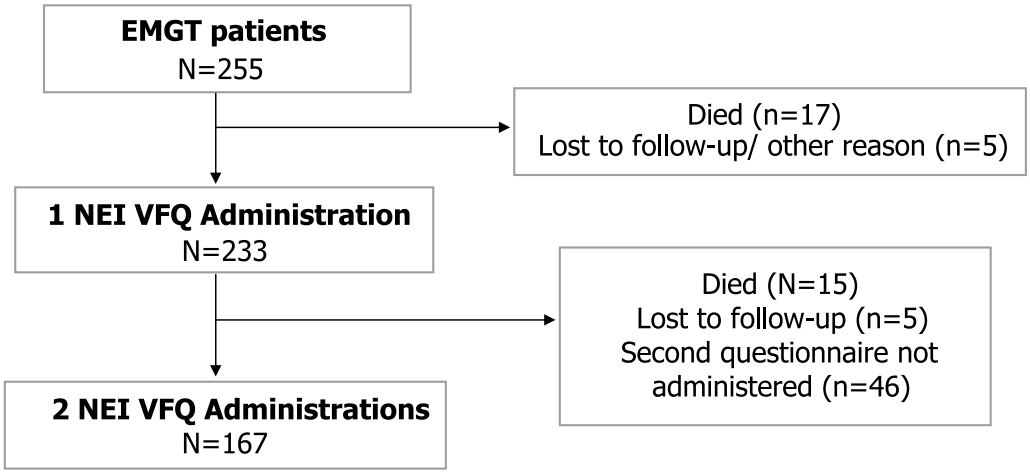

Figure 1. Early Manifest Glaucoma Trial (EMGT) patients with National Eye Institute Visual Function Questionnaire (NEI VFQ) administration.

Table 1. Baseline Characteristics of All Early Manifest Glaucoma Trial (EMGT) Patients and Patients with 1 and 2 Visual Function Questionnaire (VFQ) Administrations

Characteristic	All EMGT Patients (N = 255) (Mean ± SD)	1 VFQ Administration (N = 233) (Mean ± SD)	2 VFQ Administrations (N = 167) (Mean ± SD)
Age (yrs)	68±4.9	68.0±5.0	67.9±5.0
Gender			
Male	34%	32%	31%
Female	66%	68%	69%
Randomization assignment			
Treatment group	51%	50%	50%
Control group	49%	50%	50%
Cardiovascular disease history	12%	12%	14%
Hypertension*	38%	38%	41%
Visual acuity			
Better eye			
1.0	79%	80%	80%
0.9	11%	10%	10%
0.8	8%	8%	8%
0.7	2%	2%	1%
	1.0±0.1	1.0±0.1	1.0±0.1
Worse eye			
1.0	60%	62%	67%
0.9	18%	18%	14%
0.8	13%	12%	11%
0.7	7%	6%	5%
0.6	2%	2%	2%
0.5	0%	0%	1%
	0.9±0.1	0.9±0.1	0.9±0.1
Mean deviation (decibels)			
Better eye	−1.5±2.5	−1.4±2.5	−1.1±2.4
Worse eye	−4.9±3.7	−4.7±3.5	−4.5±3.6
Intraocular pressure (mmHg)			
Better eye	19.1±3.6	19.1±3.5	18.9±3.7
Worse eye	21.2±4.1	21.2±4.1	21.1±4.3

SD = standard deviation.
*Systolic pressure > 160 mmHg or diastolic pressure > 95 mmHg, or history of hypertension medication.

scores between the lowest category and the others ranged from 5.7 to 6.5 (P value ranging from 0.07 to 0.009). Nuclear lens opacities (Lens Opacities Classification System II score ≥ 2) were also associated with lower composite VFQ scores ($P = 0.002$), regardless of the inclusion of age or gender in the model (Table 3). Because the composite VFQ score was not significantly associated with variables excluded from the full model (treatment assigned at randomization or received later, history of cardiovascular disease or hypertension, and IOP, all with $P \geq 0.05$), these factors accounted for very little of the variance (<2%) in this score. Although not statistically significant, age and gender were retained in the final model, and there was no evidence of interaction (effect modification) among any of the retained variables. Thus, worse VA, worse MD, and the presence of nuclear lens opacities were independently associated with lower self-perceived vision-targeted HRQOL.

Change in Visual Function Questionnaire Scores

There was a small but significant decrease in the composite VFQ scores (mean ± standard deviation, −2.6±8.4; $P<0.0001$) between the first and second administrations. Scores in all VFQ subscales other than ocular pain also worsened between the 2 administrations, with the mean change in scores ranging from 1.2±12.6 points for color vision to 4.0±14.0 for distance activities and 4.0±16.1 for peripheral vision. The change was statistically significant ($P<0.05$) for all subscales except ocular pain, role difficulties, driving, and color vision. Compared with patients randomized to treatment, controls tended to have larger decreases in the composite and subscale scores (except general health), but these differences were small and not statistically significant (data not presented).

Between administrations, there were also small but significant ($P<0.0001$) decreases in VA (means, 0.1 and 0.09 for better and worse eyes, respectively) and decreases in MD (means, −1.2 and −1.7 dB for better and worse eyes, respectively). These decreases did not significantly differ for those randomized to treatment versus controls.

Because the assessment of visual function was patient based and involved both eyes for these analyses, subsequent analyses of changes in VA and MD between the 2 VFQ administrations considered the difference between the better eyes at each visit. Based on Spearman correlations, the change in VA was modestly but positively and significantly correlated ($P<0.05$) with the change in VFQ scores for general vision ($r = 0.16$) and role difficulties ($r = 0.16$). Change in MD was correlated ($P<0.05$) with a decrease in the composite VFQ score ($r = 0.17$) and general vision ($r = 0.19$), role difficulties ($r = 0.16$), and dependency ($r = 0.17$).

The same factors evaluated for a possible association with VFQ scores at the first administration were included in multiple regression models as covariates to evaluate their associations with decreases in the composite VFQ scores (Table 4). No associations with change in VFQ composite scores between the 2 administra-

Table 2. Internal Consistency Reliability, Mean Visual Function Questionnaire (VFQ) Score, and Spearman Correlation* between VFQ Score and Visual Acuity (VA) and Mean Deviation (MD) for Each Subscale at First VFQ Administration†

Subscale	K	Cronbach α	VFQ Score (Mean ± SD) (*Median*)	Spearman Correlation (*r*) VA		Spearman Correlation (*r*) MD	
				Better Eye	*Worse Eye*	*Better Eye*	*Worse Eye*
General health	1	NA	58.3±25.0 *50.0*	**0.20**	**0.20**	**0.15**	0.12
General vision	1	NA	78.6±14.1 *80.0*	**0.35**	**0.47**	**0.33**	**0.26**
Ocular pain	2	0.79	87.4±17.6 *100.0*	0.08	**0.17**	0.10	0.12
Near activities	3	0.78	83.9±17.7 *91.7*	**0.32**	**0.35**	**0.30**	**0.22**
Distance activities	3	0.81	85.9±18.0 *91.7*	**0.28**	**0.33**	**0.24**	**0.18**
Social functioning	2	0.64	94.8±10.7 *100.0*	**0.29**	**0.33**	**0.19**	**0.19**
Mental health	4	0.76	89.3±13.2 *93.8*	**0.25**	**0.29**	**0.27**	**0.18**
Role difficulties	2	0.84	88.1±18.8 *100.0*	**0.24**	**0.23**	**0.24**	**0.19**
Dependency	3	0.84	98.0±7.4 *100.0*	**0.31**	**0.30**	**0.26**	**0.18**
Driving	2	0.27	81.6±27.3 *87.5*	**0.24**	**0.30**	**0.20**	0.15
Color vision	1	NA	95.0±12.4 *100.0*	**0.20**	**0.21**	**0.16**	**0.13**
Peripheral vision	1	NA	87.3±19.2 *100.0*	**0.23**	**0.26**	**0.22**	**0.19**
Composite‡		0.88	88.4±11.7 *92.4*	***0.31***	***0.38***	***0.31***	***0.22***

K = no. of items; NA = not available; SD = standard deviation.
*Bolded correlations indicate $P < 0.05$.
†N = 233, except social functioning and color vision (N = 232) and driving (N = 123).
‡Does not include driving subscale.

tions were found for treatment assigned or received during follow-up, change in MD, EMGT progression, incident lens opacities, and incident cardiovascular disease. Consistent with the first administration results, patients with a decrease in VA worse than 0.20 had the largest decrease in mean composite VFQ score, with score differences between the largest and smallest decreases or no change/improvement ranging from 4.8 to 5.8 points (*P* values ranging from 0.27 to 0.05). Female gender ($P = 0.001$) and age > 73 years ($P = 0.006$) also were associated with larger decreases in the VFQ composite scores (Table 4).

Discussion

The EMGT is the first study to evaluate the effect of early treatment versus no initial treatment on vision-targeted HRQOL in patients with early glaucoma (i.e., mild or moderate VF defects). The EMGT clinical trial results showed that initial treatment significantly slowed glaucoma progression based on a clinical sensitive measure of VF change. Nonetheless, the current analyses show that EMGT treatment, whether assigned by randomization or received during follow-up, was not related to vision-targeted HRQOL within 6 years after study enrollment. These results suggest that early treatment did not affect vision-related quality of life throughout this period.

Overall, vision-targeted HRQOL was generally good in EMGT patients for all subscales other than general health and was related to visual function (VA and MD), based on better and worse eyes. A lower self-perceived visual function (composite score) was associated with poorer VA, worse MD, and nuclear opacities at a median of 3 years after randomization. The overall VFQ score was 8.7 points higher for patients with good (0.91–1.0) versus poor (0.20–0.70) VA and was 6.5 points higher for patients with better (>−1. 27 dB) versus worse (<−4.16 dB) MD. Decreases in the composite VFQ scores over time were associated with decreases in VA > 0.20, female gender, and age > 73 years. Early Manifest Glaucoma Trial progression, cardiovascular disease history, hypertension, and IOP were not associated with VFQ scores at either administration or with change in scores.

Results are based on 2 administrations of a Swedish version of the NEI VFQ-25, adapted for use in the EMGT according to a rigorous process involving backtranslation. This version demonstrated good to excellent internal consistency reliability for all subscales other than driving. However, only about half of EMGT patients were drivers. The correlation of VFQ scores with visual function, a result also found by other studies,[13,18] supports the validity of this translation and its usefulness for other research requiring the evaluation of vision-targeted HRQOL in Swedish populations.

The NEI VFQ-25 was added to the EMGT protocol during the follow-up period, rather than included at baseline, because this instrument was not available when the EMGT began. Furthermore, the Swedish translation had

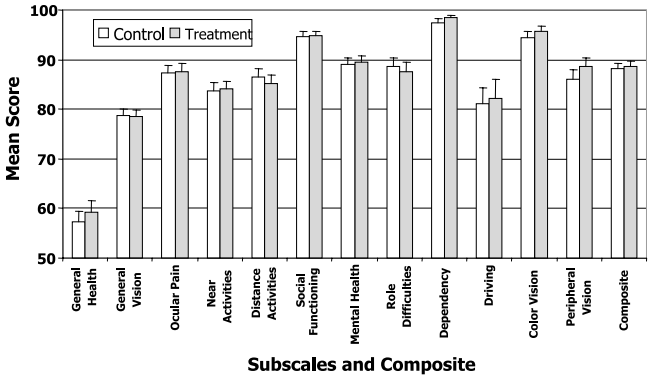

Figure 2. Mean (standard error) 25-item National Eye Institute Visual Function Questionnaire scores at first administration by randomization assignment.

Table 3. Multiple Regression Model: Unadjusted and Adjusted Composite Visual Function Questionnaire Scores at First Administration

	N	Unadjusted		Adjusted	
		Mean	*SD*	*Mean**	P *Value*†
Visual acuity (better eye)					
0.91–1.00	125	91.6	8.0	89.3	0.001
0.81–0.90	36	88.3	11.7	86.6	0.066
0.71–0.80	28	89.3	8.6	88.8	0.007
0.20–0.70	44	78.9	16.3	80.6	‡
Mean deviation (decibels)					
0.22–2.87	57	91.9	8.0	88.4	0.009
−1.27 to 0.21	58	91.9	7.7	88.4	0.007
−4.15 to −1.28	59	88.8	11.2	86.6	0.072
−19.08 to −4.16	59	81.3	14.9	81.9	‡
Nuclear opacities (LOCS score)					
≥2	50	81.1	15.9	83.5	0.002
<2	183	90.4	9.3	89.2	‡
Gender					
Male	74	90.7	10.7	87.2	0.239
Female	159	87.4	11.9	85.4	‡
Age (yrs)					
≤73	117	89.3	10.4	85.7	‡
>73	116	87.5	12.8	87.0	0.388

LOCS = Lens Opacities Classification System; SD = standard deviation.
*Least squares means with other covariates in the model set equal to their mean values.
†Adjusted for multiple comparisons with the Tukey–Kramer procedure.
‡Reference category.

to be developed before the NEI VFQ-25 could be incorporated into the EMGT protocol. Marked changes in HRQOL between baseline and the first NEI VFQ-25 administration seem unlikely, because glaucoma progresses slowly and EMGT patients had early disease. The similarity in VFQ scores between treatment groups at approximately 3 years suggests that the 2 groups were also similar at baseline.

Quality of life in glaucoma patients has been evaluated using both generic instruments (e.g., Medical Outcomes Study,[2,6,16] Symptom and Health Problem Checklist,[10] Swedish Health-Related Quality of Life Survey[14]) and instruments that target vision functioning (e.g., Activities of Daily Vision Scale,[3] 14-item Visual Function Index,[2,6] Visual Activities Questionnaire,[5,10] NEI VFQ-51 questionnaire[2,6]). To the best of our knowledge, only 2 studies other than the EMGT have

Table 4. Final Multiple Linear Regression Model: Unadjusted and Adjusted Change in Composite Visual Function Questionnaire (VFQ) Scores between First and Second Administrations

	N	Unadjusted		Adjusted	
		Mean	*SD*	*Mean**	P *Values*†
Change in visual acuity					
≥0.0 (no change/improve)	75	−2.0	7.3	−1.7	0.046
−0.10 to −0.01	36	−1.9	9.5	−0.7	0.027
−0.20 to −0.11	30	−1.9	7.5	−1.0	0.051
−0.70 to −0.21	26	−6.1	10.3	−6.5	‡
Gender					
Male	52	−0.3	4.9	−0.2	0.001
Female	115	−3.6	9.5	−4.8	‡
Age (yrs)					
≤73	102	−1.5	7.9	−0.6	‡
>73	65	−4.3	8.9	−4.3	0.006
Composite at first VFQ administration	167	−0.19 (β)	0.07 (SE)		0.020

SD = standard deviation; SE = standard error.
*Least squares means with other covariates in the model set equal to their mean values.
†Adjusted for multiple comparison with the Tukey–Kramer procedure.
‡Reference category.

used the NEI VFQ-25[13,18] in glaucoma patients. Most investigations have reported cross-sectional analyses that have contrasted HRQOL of patients with and without glaucoma, with disease stage ranging from moderate to severe. Because these studies have used different instruments and different measures of VF loss, their direct comparison to EMGT results is limited. Despite the differences among studies, there is general agreement that glaucoma patients with good vision and better MD also have good general HRQOL[2] and that a decrease in VA or MD is correlated with decreases in vision-targeted HRQOL.[2,5,6] Early Manifest Glaucoma Trial results support these observations.

Two other studies in Scandinavia investigated HRQOL in glaucoma patients with mostly mild to moderate VF damage. One study[14] involved 270 glaucoma patients (mean age, 75 years; 54% with simplex glaucoma) from 2 departments of ophthalmology in different parts of Sweden and used a generic HRQOL instrument adapted from the Medical Outcomes Study. Health-related quality of life was generally good in these glaucoma patients, who had scores on all scales similar to those of age- and gender-matched controls from a standard population sample. The other study was conducted in Norway[15] and included 589 glaucoma patients who answered a questionnaire concerning their feelings and experiences of living with glaucoma at home. It found a modest association between visual function and subjective vision-related HRQOL. Although these Scandinavian studies used different study designs and different HRQOL instruments and the classification of glaucoma was not specified, their results were similar to those of the EMGT. However, the EMGT is the only study, in Scandinavia and elsewhere, that allows a comparison of HRQOL between treated and untreated patients. Although the study conducted in Norway found that glaucoma patients expressed negative feelings about their diagnosis, it was unable to examine whether receiving treatment affected their HRQOL. In the EMGT, responses to the question "How much of the time do you worry about your eyesight?" were similar in untreated controls and in patients who received treatment at randomization or during follow-up (median score, 75 in each group; $P = 0.245$ based on the Kruskal–Wallis test). This observation, based on results at the first NEI VFQ-25 administration, suggests that patients' concerns about their eyesight, a median of 3 years after a glaucoma diagnosis, are similar whether or not they receive treatment for the disease.

Comparisons with Other Studies Based on the 25-Item National Eye Institute Visual Function Questionnaire

The EMGT VFQ scores from the first administration were compared to those from 3 other studies (Fig 3). A recent study in France was based on 173 persons with self-reported glaucoma or ocular hypertension identified through a population-based mail survey.[13] The study used a French translation of the NEI VFQ-25[19] and found high levels of vision-targeted HRQOL, similar to those observed in the EMGT in these persons with glaucoma, who had a mean age of 70 years and reported a mean disease duration of 9.4 years. Another study was based on 77 glaucoma clinic patients selected for evaluation of the NEI VFQ.[18] As might be expected, the VFQ scores of EMGT patients with early glaucoma were higher than those of the clinic-based glaucoma patients in all subscales, other than general health. The last comparison is with a population-based prevalence study of eye disease in 5287 Latinos 40 years and older (Los Angeles Latino Eye Study [LALES][25]) (Fig 3). The LALES population was younger than that of the EMGT (55 vs. 68), 6.3% had visual impairment (defined as 20/40 or worse), and 3% had a history of glaucoma. Early Manifest Glaucoma Trial patients had higher VFQ scores for the composite and subscales of

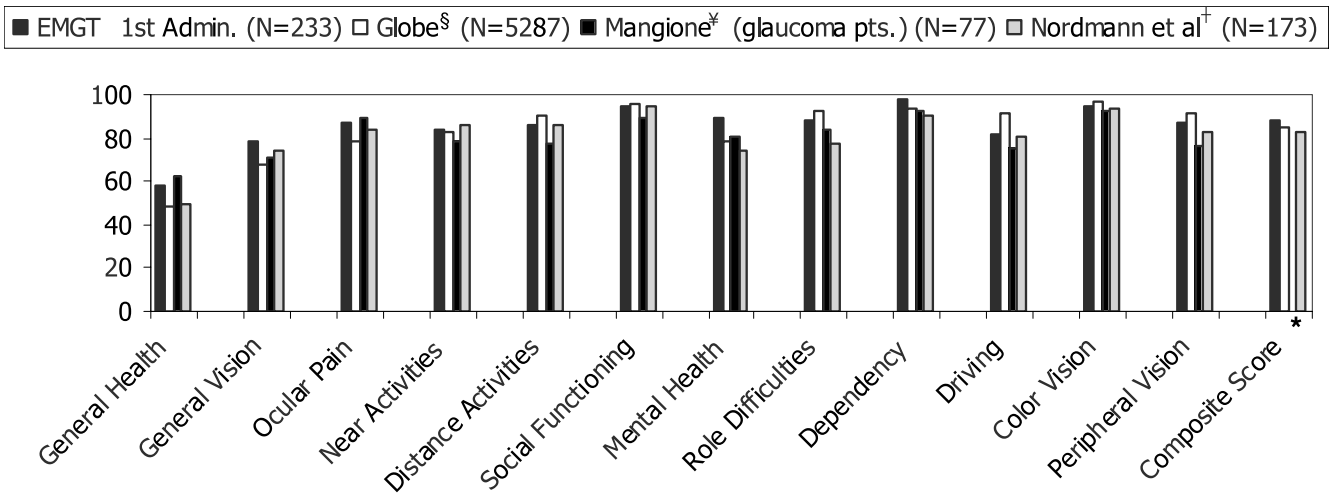

Figure 3. Mean Visual Function Questionnaire scores in 4 populations. Admin. = administration; EMGT = Early Manifest Glaucoma Trial; pts. = patients. *Not included in Mangione et al. §Globe DR, Wu J, Azen SP, Varma R, et al. The impact of visual impairment on self-reported visual functioning in Latinos: the Los Angeles Latino Eye Study. Ophthalmology 2004;111:1141–9. ¥Mangione CM, Lee PP, Gutierrez PR, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 2001;119:1050–8. †Nordmann JP, Auzanneau N, Ricard S, Berdeaux G. Vision related quality of life and topical glaucoma treatment side effects. Health Qual Life Outcomes 2003;1:75.

general health, general vision, ocular pain, near activities, mental health, and dependency, suggesting that EMGT patients have self-perceived overall visual function comparable to or better than that of some general populations. However, EMGT patients had scores for distance activities, social functioning, driving, color, and peripheral vision similar to or lower than those of the LALES population. These results, which are consistent with Parrish et al's observations among clinic-based glaucoma patients,[2] imply that EMGT patients perceive mild deficits in their visual function relative to the LALES population. However, overall these comparisons support the EMGT findings that patients with early glaucoma have good vision-related HRQOL.

Comparisons of Health-Related Quality of Life Results in Other Glaucoma Clinical Trials

The Collaborative Initial Glaucoma Treatment Study (CIGTS), another glaucoma clinical trial, compared HRQOL in 607 newly diagnosed patients with up to 5 years' follow-up who were initially randomized to initial medical therapy or treatment with initial trabeculectomy. The CIGTS used the Visual Activities Questionnaire rather than the NEI VFQ-25 to measure vision-targeted QOL,[10] so the results are not directly comparable to those of the EMGT. These patients were approximately 10 years younger than EMGT patients, which also may influence comparability of results. At baseline, the CIGTS found VF measures to be weakly but significantly associated with patient-reported visual functioning.[5] After 5 years' follow-up, this study found decreases in Visual Activities Questionnaire scores that were related to visual function but were not affected by the type of initial treatment.[10] In addition, the CIGTS found that older patients and females reported more visual symptoms and nonocular comorbidities, results that are consistent with the EMGT.[10]

Although other studies have evaluated the impact of type of glaucoma treatment on HRQOL, the EMGT is the only one to evaluate vision-targeted HRQOL in patients randomized to treatment versus no initial treatment. These results indicate that early treatment of newly diagnosed glaucoma did not affect vision-related quality of life for up to 6 years after EMGT enrollment. The EMGT finding of an association between vision-related quality of life and visual function (VA or MD) is consistent with other reports and suggests that, even at early stages, glaucoma can have a modest effect on vision-targeted HRQOL. Because EMGT patients had early disease and the disease has a protracted clinical course, longer follow-up would be needed to evaluate the long-term effects of initial treatment on HRQOL.

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