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*Mult Scler* 2000; 6: 382

DOI: 10.1177/135245850000600604

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Self-reported visual dysfunction in multiple sclerosis: results from the 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25)

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Visual impairment is one of the most common clinical manifestations of Multiple Sclerosis (MS), and is strongly related to overall health-related quality of life (HRQOL) in MS and other disorders. However, the assessment of vision-specific HRQOL in patients with MS has been limited. The purpose of this study was to examine self-reported visual dysfunction in a clinically heterogeneous MS cohort using the 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25). The VFQ-25 was administered by telephone interview to a subset of participants in a follow-up study to a phase III trial of interferon beta-1a for relapsing–remitting MS. Mean VFQ-25 composite scores and selected sub-scale scores were significantly lower (worse) among patients in our MS cohort (n=35) compared with a published reference group of patients with no history of chronic eye disease (n=118). These differences were observed despite a relatively younger age and tighter distribution of binocular visual acuities in the MS cohort. Patients with MS in this study thus demonstrated a greater degree of self-reported visual dysfunction, as measured by the VFQ-25, compared with an eye disease-free reference group. The VFQ-25 is a potentially useful measure of vision-specific HRQOL in patients with MS. Multiple Sclerosis (2000) 6, 382–385

Keywords: vision; health-related quality of life; multiple sclerosis; MS; VFQ-25; NEI-VFQ

Introduction

Visual loss is one of the most common clinical manifestations of Multiple Sclerosis (MS).1–2 Visual impairment occurs at some time in 80% of patients with MS, and up to 50% experience visual loss as an initial presenting symptom.3,4 “The most commonly reported symptoms of visual dysfunction in MS include blurring and distortion.”5 Such visual loss is often difficult for patients to characterize, and is frequently described as a sense that the vision is ‘not right’, or ‘washed-out’.6 Even patients with visual acuities of 20/20 or better in both eyes may note these symptoms. Visual dysfunction in MS may occur on the basis of involvement of the optic nerves or other structures in the afferent visual pathways, or may reflect disease in the ocular motor system.1–3 Although visual symptoms in MS may precede, occur simultaneously with, or follow the development of other neurologic manifestations, they may represent the most prominent symptoms of MS from the patient’s point of view.7

Visual function and self-perceived visual impairment are therefore important aspects of health-related quality of life (HRQOL) in patients with MS.8,9 Measures of HRQOL, such as the Multiple Sclerosis Quality of Life Index (MSQLI), have become increasingly important in the assessment of patient outcomes for clinical trials and other research.10 A five-item subscale to assess self-perceived visual function has been included in the MSQLI.11 Independent of the development of the MSQLI, the 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25) has been demonstrated to be reliable and valid (Mangione et al, submitted 1999) as a measure of vision-specific HRQOL.12

The VFQ-25, and the 51-item questionnaire from which it was derived (the 51-Item NEI-VFQ), have been widely used to demonstrate self-perceived visual impairment in patients with a variety of ocular disorders, including glaucoma, age-related macular degeneration, and many others.8,12–14 More recently, the 51-Item NEI-VFQ was administered to patients in the Optic Neuritis Treatment Trial (ONTT) cohort.8 Even at 5–8 years following the initial episode of acute optic neuritis, patients in the ONTT demonstrated a significant degree of self-reported visual dysfunction. Results were shown to be similar when items from the short-form version (VFQ-25) only were used for analysis.8 Importantly, self-perceived visual dysfunction was more common among those patients from the ONTT who had developed clinically-definite
MS. This relation was observed even though neurologic impairment in these patients was generally mild (70% of the 134 patients with MS had EDSS scores ≤2.5, indicating minimal disability and unassisted ambulation).

The purpose of the current study was to examine vision-specific HRQOL and self-reported visual dysfunction using the VFQ-25 in a clinically heterogeneous cohort of patients with clinically-definite MS. We also sought to compare mean VFQ-25 composite scores and selected sub-scale scores from our MS cohort with those of a published reference group of eye disease-free patients. We hypothesized that patients in the MS cohort would demonstrate a greater degree of self-reported visual dysfunction.

**Patients and methods**

**Selection of patients**

Patients who were participants in a follow-up study to a phase III trial of interferon β-1a for MS were invited to participate in this investigation. At the time of entry into the phase III trial, patients had a mean disease duration of 6.5 years, a mean age of 37 years, and a mean EDSS score of 2.3. Written informed consent for the present study was obtained from each patient at the time of entry into the follow-up study (mean follow-up from randomization in the phase III trial was 8.1 years). Patients were seen in the clinic for the primary goals of the follow-up study, and were subsequently invited to participate in this sub-study of vision-specific HRQOL. Study protocols were approved by Institutional Review Boards at the University of Pennsylvania and at both patient recruitment sites (Cleveland Clinic and University of Buffalo). Written informed consent was obtained from each participant.

**Data collection**

The 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25) was administered by telephone interview. Standard instructions for administration of the VFQ-25 were followed; patients were instructed to answer all VFQ-25 items as though they were wearing their usual glasses or contact lenses for the activity specified. The VFQ-25 is a short-form version of the 51-Item NEI-VFQ, a vision-specific HRQOL instrument derived from a multi-condition focus group process. Psychometric properties of the VFQ-25, including reliability and validity, are comparable to those of the NEI-VFQ (Mangione et al, in press). The VFQ-25 contains 12 sub-scales (Table 1), and requires 10 min to complete in an interviewer-administered format.

**Data analysis**

Statistical analyses were performed jointly by investigators at the University of Pennsylvania and the AMC Cancer Research Center in Denver, Colorado. Stata 5.0 and SAS statistical software were used for all analyses and calculations.

Table 1 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25)

<table>
<thead>
<tr>
<th>VFQ-25 sub-scale</th>
<th># Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>General health</td>
<td>1</td>
</tr>
<tr>
<td>General vision</td>
<td>1</td>
</tr>
<tr>
<td>Ocular pain</td>
<td>2</td>
</tr>
<tr>
<td>Near activities</td>
<td>3</td>
</tr>
<tr>
<td>Distance activities</td>
<td>3</td>
</tr>
<tr>
<td>Vision-specific social functioning</td>
<td>2</td>
</tr>
<tr>
<td>mental health</td>
<td>4</td>
</tr>
<tr>
<td>role difficulties</td>
<td>2</td>
</tr>
<tr>
<td>dependency</td>
<td>3</td>
</tr>
<tr>
<td>Driving</td>
<td>2</td>
</tr>
<tr>
<td>Color vision</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral vision</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral vision</td>
<td>1</td>
</tr>
<tr>
<td>Composite score</td>
<td>24</td>
</tr>
</tbody>
</table>

*: Indicates sub-scale included in analysis for this study. **As recommended by Mangione et al. (in press), the VFQ-25 composite score is calculated as an unweighted average of responses to all items except for the general health sub-scale (one item).

The VFQ-25 was scored according to the VFQ-25 Scoring Algorithm. Using this algorithm, VFQ-25 sub-scales (Table 1) are scored on a scale from 0 to 100, with 100 indicating the highest level of function. As specified by Mangione et al. (in press), the VFQ-25 composite score was calculated as the unweighted average of all items excluding the general health sub-scale (one item).

Mean scores and standard deviations were calculated for each VFQ-25 sub-scale and for the composite score. Four VFQ-25 sub-scales (general health, general vision, distance activities, and color vision) were selected for further statistical analyses since patients with MS often note difficulties with distance vision despite proper refraction, and frequently state that their vision is ‘not right’ in general. Mean scores for each of the four selected sub-scales and the composite score were compared with those from a published reference group of eye disease-free patients using a two-tailed t-test for independent samples. As recommended by Mangione et al. (submitted 1999), statistical comparison of mean scores from the four selected sub-scales was performed only after it was determined that the mean composite scores for the MS and reference groups were significantly different. A type-I error of \( P < 0.05 \) was considered significant for all statistical tests.

**Results**

**MS cohort and reference group**

Thirty-five patients with clinically-definite MS participated in this study. The mean age for the MS cohort at the time of the present study was 35 years (Table 2); 68% were women. The median binocular visual acuity was 20/25 (range 20/16–20/64). Mean disease dura-
tion for the MS group at the time of the study was 14 years (range 9–27). Expanded Disability Status Scale (EDSS) scores ranged from 0–8.0 (median 4.5).

The reference group for the VFQ-25, described by Mangione et al includes 118 patients with no history of chronic eye disease who were evaluated for comprehensive ophthalmologic examinations or correction of refractive error. Data from this group were obtained as part of the evaluation of psychometric properties for the 51-Item NEI-VFQ (longer questionnaire from which the VFQ-25 items were derived). The mean age for patients in the reference group was 64 years (Table 2); 60% were women. The median binocular visual acuity for the reference group was 20/20 (range 20/10–20/125).

**Comparison of mean VFQ-25 scores: MS vs reference group**
Mean VFQ-25 composite and selected sub-scale scores (with the exception of the color vision sub-scale) were significantly lower (worse) in the MS cohort compared with the eye disease-free reference group (Table 2). These differences were observed despite the lower mean age (35 vs 64 years) and narrower range of binocular visual acuities among the MS patients. As specified by Mangione et al (in press), the VFQ-25 composite score does not include the general health sub-scale (one item). The difference in mean composite scores between the MS and reference groups, therefore, does not merely reflect a difference in responses to the general health question (Table 2). The three selected vision sub-scale scores did correlate significantly with the VFQ-25 composite score (general vision \( r_s=0.62, P=0.0004 \); distance activities \( r_s=0.73, P<0.0001 \); color vision \( r_s=0.57, P=0.001 \)). Mean VFQ-25 composite and selected sub-scale scores were also consistently lower (worse) among patients with EDSS scores \( \geq 3 \) (vs those with scores <3), but these differences did not reach statistical significance.

**Table 2** Comparison of mean VFQ-25 scores (+standard deviation) for MS cohort vs eye disease-free reference group

<table>
<thead>
<tr>
<th>VFQ-25 sub-scale</th>
<th>MS group ((n=35))</th>
<th>Reference group ((n=118))</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>General health</td>
<td>54 ± 22</td>
<td>69 ± 24</td>
<td>*P=0.001</td>
</tr>
<tr>
<td>General vision</td>
<td>77 ± 16</td>
<td>83 ± 14</td>
<td>*P=0.03</td>
</tr>
<tr>
<td>Distance activities</td>
<td>87 ± 16</td>
<td>94 ± 11</td>
<td>*P=0.02</td>
</tr>
<tr>
<td>Color vision</td>
<td>94 ± 14</td>
<td>98 ± 8</td>
<td>*P=0.11</td>
</tr>
<tr>
<td>Composite score(^b)</td>
<td>88 ± 5</td>
<td>92 ± 7</td>
<td>*P=0.0003</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>35</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Median VA (range)</td>
<td>20/25</td>
<td>20/20</td>
<td></td>
</tr>
<tr>
<td>(20/16–)</td>
<td>(20/10–)</td>
<td>(20/64–)</td>
<td></td>
</tr>
</tbody>
</table>

VA=visual acuity (binocular). *Significant differences were noted for the composite score and for the general health, general vision, and distance activities sub-scale scores (t-test for independent samples). \(^b\)VFQ-25 composite score does not include the general health sub-scale score; differences in composite score therefore reflect vision-specific quality of life sub-scales only.

**Discussion**
In this study, patients with MS demonstrated a greater degree of self-perceived visual dysfunction, as measured by the VFQ-25, compared with a reference group of patients with no history of chronic eye disease. Such differences were observed despite the relatively younger age of our MS cohort, and despite the wider range of binocular visual acuities among the reference group patients. However, since expectations of visual function may also differ among age groups, future studies of vision-specific HRQOL in MS will involve the comparison of age-matched populations.

The assessment of self-reported visual dysfunction in patients with MS, using established scales with known psychometric properties (including the VFQ-25), has thus far been limited. Previous studies have provided evidence that vision is strongly related to HRQOL in MS, and have indicated that the impact of ‘blurred vision’ on HRQOL may be even greater than that of other serious health conditions. Cole et al demonstrated that patients in the Optic Neuritis Treatment Trial (ONTT) cohort had lower (worse) scores on the 51-item NEI-VFQ compared with the eye disease-free reference group. Among the 244 patients examined 5–8 years following the initial episode of acute optic neuritis, self-reported visual impairment was greater among the 110 patients who had developed clinically-definite MS during the follow-up period. This was observed despite the fact that neurologic impairment among patients with MS in the ONTT cohort was generally mild (85% had EDSS scores \( \leq 2.5 \)). Mean VFQ-25 sub-scale scores from our MS group were comparable to 51-item NEI-VFQ scores from the ONTT cohort, with the exception of ONTT patients with EDSS scores \( \geq 3 \); these patients \((n=16)\) had lower scores compared with our MS cohort. Compared with other ocular disorders, mean VFQ-25 composite and sub-scale scores from our MS group were most similar to those for patients with glaucoma and cytomegalovirus (CMV) retinitis, and were higher than those for age-related macular degeneration and low vision.

Our results provide important evidence that the assessment of vision-specific HRQOL is an important aspect of MS outcomes assessment, and that the VFQ-25 is a potentially useful measure of self-reported visual impairment in MS. Future investigations are needed to: (1) determine which aspects of vision-specific HRQOL are valued most by patients with MS, and which aspects differ most from age-matched eye disease-free patients; (2) examine the relation of vision-specific HRQOL to visual impairment in MS, as assessed by clinical visual outcome measures; and (3) examine the relation of visual function and vision-specific HRQOL to overall neurologic impairment in patients with MS. The development of MS-specific items (to potentially supplement the VFQ-25) and
questionnaires that assess visual symptoms and self-reported visual dysfunction will represent an important next step in the study of vision in MS populations.

Acknowledgments
This work was supported by NIH grant EY00351 (to LJ Balcer).

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