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Vision-Related Quality of Life in Patients with Ocular Graft-versus-Host Disease

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Purpose: To assess the vision-related quality of life (QOL) in a cohort of patients with ocular graft-versus-host disease (GVHD).

Design: Prospective study.

Participants: Eighty-four patients diagnosed with chronic ocular GVHD.

Methods: We assessed the vision-related QOL with the 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25). The symptoms of ocular GVHD were assessed using the Ocular Surface Disease Index (OSDI) and Symptom Assessment in Dry Eye (SANDE) questionnaires.

Main Outcome Measures: We assessed vision-related QOL with the NEI-VFQ-25 and compared the scores obtained from patients with ocular GVHD with those from a healthy population. In the ocular GVHD population, we also evaluated the associations between the NEI-VFQ-25 and the dry eye symptoms measured by the OSDI and SANDE questionnaires, age, duration of disease, best-corrected visual acuity (BCVA), corneal fluorescein staining (CFS), tear break-up time, and Schirmer test.

Results: The mean composite NEI-VFQ-25 score in patients with ocular GVHD was 76.5±17. Compared with healthy subjects, patients with ocular GVHD reported reduced scores on all NEI-VFQ-25 subscales (each $P < 0.001$) with the exception of color vision ($P = 0.11$). The NEI-VFQ-25 composite scores significantly correlated with OSDI ($R = -0.81$, $P < 0.001$), SANDE ($R = -0.56$, $P < 0.001$), CFS ($R = -0.36$, $P = 0.001$), and BCVA ($R = -0.30$, $P = 0.004$).

Conclusions: Patients with ocular GVHD experience measurable impairment of vision-related QOL. This study highlights the impact of ocular GVHD on the vision-related QOL, and thus the importance of comprehensive diagnosis and treatment of this condition. *Ophthalmology 2015;122:1669-1674 © 2015 by the American Academy of Ophthalmology.*

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Allogeneic hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for various malignant and nonmalignant hematologic disorders. Medical advances have increased the frequency of transplants and survival rates,[1,2] and long-term complications after HSCT have consequently become key determinants of the overall quality of life (QOL) in these patients. Graft-versus-host disease (GVHD), a condition occurring after allogeneic HSCT when donor-derived immune cells recognize and attack the recipient tissues,[3] is a major cause of morbidity that compromises patients' QOL.[4] Manifestations of GVHD can be seen in various organs, including skin, gastrointestinal tract, liver, lungs, oral mucosa, and eyes.[5]

Ocular involvement presents in 40% to 60% of patients undergoing allogeneic HSCT.[6] Ocular GVHD generally manifests as dry eye disease with symptoms of ocular discomfort, pain, redness, grittiness, and blurred vision. The clinical signs include conjunctival hyperemia, corneal epitheliopathy, meibomian gland dysfunction, conjunctival and corneal scarring, stromal ulceration, and symblepheron.[7,8] Dry eye disease has been shown to affect QOL in other settings, but there is limited information regarding the impact of manifestations of ocular GVHD on vision-related QOL.[9–12]

The 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) is used to assess patients' perceptions of their visual function and the impact of an eye disease on their QOL.[13] The NEI-VFQ-25 has been used to assess vision-related QOL in various eye diseases, such as cataract, macular degeneration, glaucoma, ocular chemical burns, diabetic retinopathy, uveitis, dry eye disease, and low vision.[11,14–18] The purpose of this study was to evaluate vision-related QOL in a large cohort of patients with a diagnosis of ocular GVHD using the NEI-VFQ-25. In addition, we evaluated the association between the measured QOL and the signs and symptoms of ocular GVHD.

Methods

A total of 100 consecutive patients with ocular GVHD examined at the Cornea Service, Massachusetts Eye and Ear Infirmary, Boston,

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Massachusetts, were included in this prospective study. The study was approved by the institutional review board and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients. The inclusion criteria required patients to have a diagnosis of chronic ocular GVHD confirmed by an ophthalmologist, to be older than 18 years of age, and to comprehend the English language. All the patients satisfied the National Institutes of Health criteria for diagnosis of ocular GVHD, which require a distinctive affectation of chronic GVHD in an organ different from the eye accompanied by 1 of the following ocular manifestations: (1) new ocular sicca documented with a bilateral Schirmer test averaging ≤5 mm or (2) a new onset of ocular sicca by slit-lamp examination with a bilateral Schirmer test averaging 6 to 10 mm.[5]

All the participants self-responded to the NEI-VFQ-25 questionnaire once the basic instructions were provided by the research staff.[13] This questionnaire consists of 25 vision-targeted questions representing 11 subscales that include general vision, difficulty with near vision activities, difficulty with distance vision activities, ocular pain, limitations in social functioning due to vision, role limitations due to vision, dependency on others due to vision, mental health symptoms due to vision, driving difficulties, limitations with peripheral vision, and color vision. In addition, the NEI-VFQ-25 includes 1 question that assesses the patient's general health. The overall composite score for the NEI-VFQ-25 is calculated by averaging the scores of all the subscales with the exception of the general health question. The score of each subscale is represented by the average of the responses to questions answered in each subscale section. Both the composite and subscale scores range from 0 to 100, where higher scores indicate better QOL.

Symptoms of ocular surface disease were assessed with the following 2 questionnaires: Ocular Surface Disease Index (OSDI) and Symptom Assessment in Dry Eye (SANDE).[19,20] The OSDI questionnaire consists of 12 questions measuring the frequency of dry eye symptoms, visual impact of dry eye, and triggers; each question was graded on a scale from 0 ("none of the time") to 4 ("all of the time"). The total OSDI score was calculated according to the questionnaire's algorithm with a total score ranging from 0 to 100, where higher scores indicate greater disability.[20] The SANDE questionnaire comprises 2 questions measuring the frequency and severity of dry eye symptoms; each of these 2 items was assessed on a 100-mm visual analog scale and scored from 0 to 100. The total SANDE score was calculated as the square root of the product of the 2 item scores, and ranges from 0 to 100 with higher scores indicating greater disability.[19] In addition, we recorded the time of HSCT, duration of ocular GVHD, and assessed the following clinical parameters at the same visit when the questionnaires were administered: Snellen best-corrected visual acuity (BCVA), Schirmer I test with anesthesia, tear break-up time (TBUT), and corneal fluorescein staining (CFS) (National Eye Institute grading system).[21] We excluded 16 patients who had other ocular comorbidities unrelated to ocular GVHD that could affect visual function, such as cataract with BCVA of ≤20/30 (8 patients), glaucoma (1), macular or retinal disorders (4), amblyopia (1), hemianopia (1), and intraocular surgery within 1 month (1). There were no patients with any history of refractive surgery.

Data are presented as the mean ± standard deviation (SD) and range for continuous variables, and percentages for categoric variables. The NEI-VFQ-25 composite and subscale scores were computed according to the published algorithms.[22] The NEI-VFQ-25 subscale mean scores from patients with ocular GVHD were compared with the mean scores of 122 healthy subjects from the original NEI-VFQ-25 developmental work using the Welch's unpaired *t* test.[13] The healthy control population included 75 women (62%) and 47 men (38%) aged more than 21 years (mean, 59±14 years), with no evidence of underlying eye disease other than refractive errors correctable to ≥20/25 in the worse eye. The median visual acuity in the better eye was 20/20 (range, 20/13−20/100).[13,16] We evaluated the association of the QOL scores with patients' age, dry eye symptoms, and duration of ocular GVHD, and with the average of both eyes for BCVA, CFS, TBUT, and Schirmer test using the Spearman's coefficient of correlation. Visual acuities were measured with a standardized Snellen chart and converted to logarithm of the minimum angle of resolution (logMAR) values at the time of the analysis. A 2-sided *P* value <0.05 was considered statistically significant.

Results

The final analysis included 84 patients (56 men and 28 women) with a mean age of 56±12 years (range, 22−74 years). The patients' transplant characteristics are shown in Table 1. The mean BCVA, average of both eyes, was 0.08±0.13 logMAR (Snellen equivalent, 20/24; median, 20/22; range, 20/20−20/150), and the mean BCVA in the better eye was 0.04±0.09 logMAR (Snellen, 20/22; median, 20/20; range, 20/20−20/60). The mean dry eye clinical signs were Schirmer test 4.5±3.6 mm (range, 0−12.5), TBUT 2.6±2.3 seconds (range, 0−9.5), and CFS 6.3±4.4 (range, 0−15). The mean OSDI score was 42.5±24.1 (range, 0−94), and the mean SANDE score was 52.2±24.2 (range, 0−95). The mean NEI-VFQ-25 composite and subscale scores are shown in Table 2. The mean composite score was 76.5±17 (18−98). The comparison between the mean subscales' scores in patients with ocular GVHD and the healthy population of reference is shown in Figure 1. The mean age between the studied GVHD population (56±12) and the reference population (59±14) was comparable ($P = 0.11$). With the exception of color vision, the patients with ocular GVHD presented with significantly lower scores on all NEI-VFQ-25 subscales when compared with the reference population ($P < 0.001$). The subscales that scored particularly low (less QOL) with a difference of more than 10 points compared with the healthy subjects were ocular pain, vision-specific role limitations, vision-specific mental health symptoms, difficulty with near vision, distance vision, general vision activities, vision-specific dependency, peripheral vision, and general health.

Table 1. Characteristics of the Study Population

Characteristic	
Age, mean ± SD yrs	56±12
Gender (%)	
Male	56 (67)
Female	28 (33)
Primary disorder (%)	
Acute myeloid leukemia	33 (39)
Acute lymphoid leukemia	6 (7)
Chronic myeloid leukemia	5 (6)
Chronic lymphoid leukemia	10 (12)
Myelodysplastic syndrome	11 (13)
Non-Hodgkin lymphoma	13 (16)
Hodgkin lymphoma	1 (1)
Multiple myeloma	3 (4)
Others	2 (2)
Duration since HSCT in days, mean ± SD	1348±1002
Duration since diagnosis of ocular GVHD in days, mean ± SD	873±955

GVHD = graft-versus-host disease; HSCT = hematopoietic stem cell transplantation; SD = standard deviation.