Vision- and Health-Related Quality of Life in Patients With Behçet Uveitis

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Objective: To investigate vision- and health-related quality of life in patients with Behçet disease.

Methods: Fifty-one consecutive patients with Behçet uveitis were enrolled in the study from January 1 through June 30, 2008. The National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25) and the 36-Item Short Form Health Survey (SF-36) were administered. Sociodemographic and clinical data were also collected. Main outcome measures were comparison of the NEI-VFQ-25 and SF-36 subscale item scores among subgroups and multivariate analysis of the NEI-VFQ-25 and SF-36 subscale item scores.

Results: Patients rated the general health subscale score of the NEI-VFQ-25 and all subscale item scores of the SF-36 lower than the NEI-VFQ-25 subscales related to vision. The NEI-VFQ-25 subscale item scores showed significant differences with respect to age, educational level, Behçet uveitis activity and severity, and visual acuity in the better and worse eyes. The SF-36 subscale item scores revealed significant differences according to sex, educational level, and the systemic treatment used. In the best model of linear regression, independent variables accounted for 57.0% of the variance in the NEI-VFQ-25 subscale item (color vision subscale; adjusted $R^2 = 0.57$, $P < .001$) and for only 23.0% of the variance in the SF-36 subscale item score (role limitation owing to emotional problems subscale; adjusted $R^2 = 0.23$, $P = .004$).

Conclusions: General health is more affected than visual functioning in patients with Behçet uveitis. Sociodemographic and clinical variables had a significant effect on vision- and health-related quality of life. Multivariate analysis of the NEI-VFQ-25 and SF-36 subscales revealed that each subscale item score is affected by additional factor(s) other than those analyzed here.

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BEHÇET DISEASE (BD), FIRST DESCRIBED by Hulusi Behçet in 1937, is a chronic multisystem disorder characterized by relapsing inflammation of unknown origin.[1] The underlying condition in BD is an obliterative and necrotizing vasculitis that affects arteries and veins in all organ systems. Ocular involvement in patients with BD is 70.0%. The typical form of ocular involvement is characterized by bilateral uveitis mostly affecting the posterior segment of the eye as panuveitis and retinal vasculitis and has a relapsing-remitting course. Despite treatment, visual loss associated with uveitis is progressive in 15.0% of eyes with Behçet uveitis, and recurrent episodes of intraocular inflammation may eventually lead to blindness.[2] Because of its effect on vision, uveitis related to BD is expected to reduce vision-related quality of life (VR-QOL). Behçet uveitis involving the posterior segment requires systemic treatment with immunosuppressive or biologic agents that can lead to adverse events and hence a reduction in health-related quality of life (HR-QOL). Systemic manifestations of BD, including oral ulceration, genital ulceration, skin lesions, thrombophlebitis, and arthritis, are also expected to affect HR-QOL.

When evaluating patients, ophthalmologists increasingly recognize the importance of assessing a broad array of outcomes, such as physical function, social function, and overall health, in addition to standard clinical variables. To understand the effect of a disease on patients' quality of life and to evaluate disease from the patients' perspective, questionnaires that assess VR-QOL and HR-QOL may be used.

We herein report VR-QOL and HR-QOL in a population of patients with Behçet uveitis using the National Eye Institute Vision Function Questionnaire (NEI-VFQ-25) and the 36-Item Short Form Health Survey (SF-36) instruments. To the best of our knowledge, this is the first study to measure VR-QOL and HR-QOL in patients with Behçet uveitis.

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METHODS

PATIENT SELECTION

This prospective study enrolled consecutive patients with Behçet uveitis who were scheduled for vision care at the Uveitis Service of the Department of Ophthalmology, Marmara University School of Medicine, from January 1 through June 30, 2008. Eligibility criteria were having at least 6 months of follow-up, having no other systemic or ocular disease that could potentially affect vision, and being aged 16 years or older. All patients were white and of Turkish descent. The study was approved by the ethics committee of the medical school (approval MR-YC-2008-0128) and conducted according to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients.

DATA COLLECTION

The NEI-VFQ-25 and SF-36 instruments were administered by 1 of the authors (F.S.). The questionnaires were completed before the ophthalmic examination to reduce the influence of the clinical encounter on patient responses.

Demographic data collected included age, sex, duration of BD and Behçet uveitis, follow-up period, and educational level (determined by self-report). Clinical data collected were those related to systemic involvement of BD and those related to Behçet uveitis. Occurrence of extraocular findings was questioned for the occurrence of any finding at any time and at the time of the evaluation. On the basis of the occurrence of extraocular findings at any time, the severity of BD was grouped according to the criteria described by Krause and colleagues.[3]

All patients underwent a complete ophthalmologic examination, including best-corrected visual acuity, slitlamp biomicroscopy, tonometry, and indirect ophthalmoscopy. Visual acuity was measured by a retroilluminated Early Treatment Diabetic Retinopathy Study (ETDRS) chart at 3.2 m. Standard protocols for the ETDRS charts and equipment that yielded each patient's best refractive correction were used. Visual acuity testing was performed for each eye separately. The ETDRS charts were scored letter by letter. The eyes of each patient with involvement were designated as better or worse on the basis of his or her logMAR visual acuity scores. For those with bilateral involvement, worse eyes were defined as those with a 0.1 logMAR unit or worse logMAR visual acuity score than that of the contralateral eye. If both eyes of a patient had identical logMAR visual acuities, then both eyes were designated as better eyes for purposes of analyses. In patients with unilateral involvement, the visual acuity of the eye with involvement was grouped under worse eyes unless the eye without uveitis had lower visual acuity owing to other reasons, such as amblyopia. Patients with legal blindness (having a logMAR visual acuity worse than 1.0 for the better-seeing eye) and eyes with loss of vision (logMAR visual acuity of 0.4 or worse according to Standardization of Uveitis Nomenclature [SUN] criteria)[4] were also identified.

The ocular clinical data collected included location of inflammation (anterior, posterior, or panuveitis), laterality (unilateral or bilateral involvement), uveitis activity (active, inactive, or in remission), and uveitis severity (mild, moderate, or severe according to preset criteria before the initiation of the study). Treatment used at the time of the evaluation was grouped as follows: (1) immunosuppressive agents (antimetabolites, T-cell signal inhibitors, or alkylating agents) and (2) biologic agents (interferon alfa-2a or anti–tumor necrosis factor). In our uveitis routine, patients with posterior segment involvement of BD are prescribed immunosuppressive therapy on diagnosis as recommended.[5] Flare-up of uveitis is managed by the use of corticosteroids (periocular, oral, or pulse). The aim of the management course is having patients obtain inactivity of uveitis while not taking corticosteroids but instead taking immunosuppressive or biologic agents. Oral corticosteroids are tapered to 10 mg/d or less of prednisone equivalent or, ideally, their use is discontinued when control of intraocular inflammation is achieved. In refractory cases, immunosuppression is altered using a stepladder approach, starting from lower potential agents and increasing the potency. Cases refractory to lower potential immunosuppressive agents, such as azathioprine and/or cyclosporine, are prescribed biologic agents. Patients unresponsive to biologic agents are prescribed alkylating agents.

Uveitis activity reporting was performed as described by the SUN working group[4] and as in Foster and Vitale's *Diagnosis and Treatment of Uveitis*.[6] Inactive anterior uveitis was defined as rare cells or less.[4] Vitritis, evidenced by the presence of cells, not haze, was graded from 0 to 4 and considered inactive when there were 0.5 cells or fewer.[6] Inflammation of the posterior segment was documented by the presence of retinal vasculitis, retinitis, cystoid macular edema, and papillitis. According to the former descriptions, a patient's condition was defined as being *active* or *inactive* based on the location of inflammation. For example, inactivity of the the anterior chamber and vitreous inflammation along with the absence of posterior segment intraocular inflammatory signs was defined as inactive panuveitis. On the basis of the recommendations of the SUN working group, *remission* was defined as inactive disease for at least 3 months after discontinuation of treatment of uveitis.[4]

Uveitis severity was defined as being *mild* if there was unilateral or bilateral anterior uveitis and absence of loss of vision of the involved eye. It was defined as *moderate* if there was unilateral posterior or panuveitis or the presence of unilateral loss of vision, and as *severe* if there was bilateral posterior or panuveitis or legal blindness or the occurrence of complications such as optic atrophy, end-stage fundus appearance, macular scar, or phthisis bulbi.

QUALITY-OF-LIFE ASSESSMENT

The VR-QOL was assessed using the NEI-VFQ-25, which measures visual level in 12 dimensions. It consists of 25 items presented in Likert scale format in which patients are asked to rate the level of severity of particular visual symptoms or difficulty of activities, such as driving or reading ordinary print in newspapers. It generates subscales for the following 12 dimensions of VR-QOL: general health, general vision, ocular pain, near activities, distance activities, vision-specific social functioning, vision-specific mental health, vision-specific role difficulties, vision-specific dependency, driving, color vision, and peripheral vision. Finally, an overall composite score is calculated that serves as an average of all subscales excluding the general health subscale. Scores range from 0 to 100, with higher scores indicating better quality of life.[7]

To examine overall aspects of HR-QOL, the SF-36, the most widely used generic HR-QOL measure, was administered. The SF-36 is a short-form questionnaire with 36 items that measure 8 HR-QOL domains: physical functioning, social functioning, role limitation owing to physical problems, role limitation owing to emotional problems, mental health, energy and vitality, bodily pain, and general perception of health. For each quality-of-life domain tested, item scores are coded, summed, and transformed into a scale from 0 (worst) to 100 (best) using the standard SF-36 scoring algorithms. Physical and mental component summary scores are also calculated using an algorithm described by the developers.[8] The NEI-VFQ-25 and SF-36 have been translated into the Turkish language, and their reliability and validity have been established.[9,10]

STATISTICAL ANALYSIS

Univariate Analysis

SPSS statistical software, version 16.0 (SPSS Inc, Chicago, Illinois), was used for the statistical analysis. The Mann-Whitney and Kruskal-Wallis tests were used to test for differences in the NEI-VFQ-25 and SF-36 subscale item scores between the subgroups. The Dunn test was used as a multiple comparison post hoc test. Categorical data were analyzed with the χ^2 test.

Multivariate Analysis

Linear regression models were constructed for multivariate analysis of the NEI-VFQ-25 and SF-36 subscale item scores. They were obtained by using factor(s) identified to be significant in univariate analysis.

RESULTS

DEMOGRAPHIC AND CLINICAL FEATURES

Fifty-one patients were included in the study. No eligible patient refused to participate. Demographic features and BD characteristics of the patients are given in **Table 1**. The mean (SD) age of the patients was 36.2 (10.7) years (range, 18.0-59.0 years). Of the patients, 32 (62.7%) were men and 19 (37.3%) were women. The mean (SD) durations of BD and Behçet uveitis were 7.0 (6.1) and 5.9 (4.7) years, respectively. Of the patients, 9 (17.6%) graduated from a university. Of the remaining, 38 (74.5%) graduated from at least primary school and 4 (7.9%) were illiterate. Comparison of educational level between female and male patients revealed a significant difference (χ^2=12.54, *P*=.01). Although all illiterate patients were female, male patients had a higher educational level than female patients.

Ocular clinical features are also provided in Table 1. Fourteen patients (27.5%) had unilateral and 37 patients (72.5%) had bilateral involvement. Of 88 eyes with Behçet uveitis, 11 (12.5%) had anterior uveitis, 4 (4.5%) had posterior uveitis, and 73 (83.0%) had panuveitis. At the time of evaluation, uveitis activity was as follows: 8 patients (15.7%) were active, 25 patients (49.0%) were inactive, and 18 patients (35.3%) were in remission. Uveitis severity was classified as being mild in 5 (9.8%), moderate in 15 (29.4%), and severe in 31 (60.8%). None of the patients was legally blind, and 13 eyes (14.7%) were identified to have loss of vision. At the time of evaluation, 26 patients (51%) were undergoing conventional immunosuppressive or biologic therapy, and the remaining 25 patients (49.0%) were receiving colchicine or were not taking any systemic medication.

QUALITY-OF-LIFE ASSESSMENT

In general, patients rated the general health subscale score of the NEI-VFQ-25 and all subscale item scores of the SF-36 lower than that of the NEI-VFQ-25 subscales related to vision (**Table 2**). The NEI-VFQ-25 subscale item scores were compared with respect to age, sex, duration of uveitis, educational level, laterality of uveitis, uveitis activity and severity, systemic treatment used, and visual acuity in the bet-

Table 1. Demographic Information and Clinical Features of Patients With Behçet Disease and Behçet Uveitis[a]

Feature	No. (%)
Sex	
Female	19 (37.3)
Male	32 (62.7)
Behçet Uveitis	
Duration, y	
1-2	11 (21.6)
3-5	23 (45.1)
6-10	9 (17.6)
≥11	8 (15.7)
Laterality	
Unilateral	14 (27.5)
Bilateral	37 (72.5)
Anatomical localization	
Anterior	11 (12.5)
Posterior	4 (4.5)
Panuveitis	73 (83.0)
Activity status	
Active	8 (15.7)
Inactive	25 (49.0)
Remission	18 (35.3)
Severity	
Mild	5 (9.8)
Moderate	15 (29.4)
Severe	31 (60.8)
Systemic treatment	
Colchicine[b,c]	9 (17.6)
Antimetabolites[d]	10 (19.6)
Interferon alfa-2a	15 (29.4)
Etanercept	1 (2.01)
None	16 (31.4)
Behçet Disease	
Duration, y	
1-2	11 (21.6)
3-5	17 (33.3)
6-10	13 (25.4)
≥11	10 (19.6)
Educational level,[a,b]	
Male	
Illiterate	0
Primary school	9 (28.1)
Junior high school	3 (9.43)
High school	12 (37.5)
University	8 (25.0)
Female	
Illiterate	4 (21.0)
Primary school	9 (47.3)
Junior high school	2 (10.5)
High school	3 (15.8)
University	1 (5.3)
Severity	
Mild	0
Moderate	8 (15.7)
Severe	43 (84.3)
logMAR visual acuity, median (SEM) [range]	
Better eyes (n=75)	0 (0.01) [−0.3 to 0.8]
Worse eyes (n=27)	0.2 (0.1) [−0.4 to 3.0]

[a] Data are presented as number (percentage) of patients unless otherwise indicated. Percentages may not total 100 because of rounding.
[b] Determined by self-report. χ^2=12.54, *P*=.01.
[c] Prescribed by rheumatologists for extraocular manifestations of Behçet disease.
[d] Nine patients were taking azathioprine and 1 was receiving mycophenolate mofetil therapy.

Table 2. NEI-VFQ-25 and SF-36 Subscale Item Scores in Patients With Behçet Uveitis

Item	Median (SEM) Score [Range]
NEI-VFQ-25	
General health	55.0 (2.2) [18.0-83.0]
General vision	65.0 (2.1) [5.0-85.0]
Ocular pain	62.5 (3.1) [25.0-100.0]
Near activities	80.0 (3.2) [4.0-100.0]
Distance activities	85.0 (3.1) [8.0-100.0]
Vision specific	
Social functioning	100 (2.7) [17.0-100.0]
Mental health	65.0 (3.9) [0-100.0]
Role difficulties	75.0 (3.3) [0-100.0]
Dependency	87.5 (3.7) [6.0-100.0]
Driving	91.6 (3.7) [42.0-100.0]
Color vision	100.0 (2.6) [0-100.0]
Peripheral vision	100.0 (2.9) [25.0-100.0]
Overall, composite score	81.1 (2.6) [13.4-97.7]
SF-36	
Physical functioning	80.0 (3.0) [30.0-100.0]
Social functioning	55.5 (2.7) [11.1-88.8]
Role limitations owing to	
Physical problems	50.0 (5.3) [0-100.0]
Emotional problems	66.6 (5.9) [0-100.0]
Mental health	60.0 (2.9) [8.0-92.0]
Energy and vitality	55.0 (2.8) [5.0-95.0]
Bodily pain	66.6 (3.4) [0-100.0]
General perception of health	50.0 (1.6) [20.0-70.0]
Physical component summary score	57.3 (2.5) [19.0-88.0]
Mental component summary score	55.8 (2.5) [21.1-87.2]

Abbreviations: NEI-VFQ-25, National Eye Institute Visual Functioning Questionnaire; SF-36, 36-Item Short Form Health Survey.

ter and worse eyes. The NEI-VFQ-25 subscale item scores showed statistically significant differences according to age, educational level, Behçet uveitis activity and severity, and visual acuity in the better and worse eyes (**Table 3**). Patients older than 30 years had significantly lower near and distance vision than those younger than 30 years. Patients with a lower educational level had significantly lower general vision, ocular pain scores (indicating more pain), near vision, vision-specific social functioning, and vision-specific mental health and overall composite scores than patients with a higher educational level. Patients with a low educational level also had lower role difficulty and dependency scores, indicating more role difficulty and dependency. Patients with active uveitis were identified to have significantly lower mental health when compared with those with inactive uveitis and those whose uveitis was in remission. Severe Behçet uveitis was associated with significantly lower mental health and significantly higher dependency compared with scores for milder uveitis. Patients with low visual acuity (logMAR acuity of 0.4 or worse) in the better eye had significantly lower general vision, near and far vision, social functioning, color vision, and overall scores than those with higher vision in the better eye. They also had lower role difficulty and dependency scores. Patients with better visual acuity (logMAR acuity of 0.3 or better) in the worse eye had significantly better near and far vision, social functioning, and overall scores.

The SF-36 subscale item scores were compared with respect to age, sex, duration of BD, educational level, severity of BD, and systemic treatment used. The SF-36 subscale item scores revealed statistically significant differences according to sex, educational level, and the treatment used (**Table 4**). Female patients had significantly lower role limitation owing to emotional problems scores (indicating more role limitation) compared with male patients. Lower educational level was associated with significantly lower physical and social functioning. Those with a low educational level also had significantly lower role limitation owing to physical and emotional problems scores, indicating more role limitation and significantly lower mental component summary scores. Patients taking conventional immunosuppressive agents had significantly lower general perception of health than those who were taking colchicine and biologic agents and those who were not taking any systemic medication.

Linear regression models constructed for multivariate analysis of the NEI-VFQ-25 and SF-36 subscale item scores by using factor(s) identified to be significant in univariate analysis are given in **Table 5**. In the best model of linear regression for the NEI-VFQ-25 subscales, independent variables accounted for 57.0% of the variance in the NEI-VFQ-25 subscale item (color vision subscale; adjusted $R^2=0.57$, $P<.001$). On the other hand, in the best model of linear regression for SF-36 subscales, independent variables accounted for only 23.0% of the variance in the SF-36 subscale item score (role limitation owing to emotional problems subscale; adjusted $R^2=0.23$, $P=.004$).

COMMENT

This study included patients with Behçet uveitis who showed demographic and clinical characteristics that were in concordance with previously published data[2]; hence, our data are representative. Fifty-one patients with a mean age of 36.2 years, most of whom had bilateral uveitis in the form of posterior or panuveitis, were included. The male to female ratio was 1.7:1. Mean duration of Behçet uveitis was 5.9 years; the patients were followed up for a mean (SD) duration of 6.5 (5.1) years (range, 1.0-25.0 years). Behçet uveitis severity was determined according to a criteria set developed by 2 of the authors (S.O. and H.K.). According to those criteria, uveitis severity was moderate or severe in 90.2% of patients. The BD severity was determined to be moderate or severe in all patients using criteria described by Krause and associates.[3] According to the classification system, ocular involvement, involving the anterior or posterior segment, results in scores that are classified as moderate or severe.[3]

None of the patients were legally blind, and 14.7% of eyes with Behçet uveitis were identified to have loss of vision. The relatively good visual acuity despite severity of Behçet uveitis may be explained by the disease activity at the time of evaluation and the treatment used during follow-up. Indeed, only 15.7% of the patients had had active uveitis at the time of evaluation; the remaining were inactive or in remission. We also reviewed the previous treatment of the patients and recognized that only 27.5%

Table 3. Comparison of NEI-VFQ-25 Subscale Item Scores Between Subgroups

Characteristic	Median (SEM) Score[a]												
	GH	GV	OP	NA	DA	VSSF	VSMH	VSRD	VSD	D	CV	PV	Index
Age, y													
16-30 (n=22)	60 (3.8)	70 (2.7)	68.7 (4.6)	88.7 (3.4)	95.8 (3.8)	91.6 (2.4)	70 (5.5)	75 (4.2)	90.6 (3.9)	100.0 (3.2)	100.0 (1.8)	100.0 (3.5)	84.1 (2.7)
≥31 (n=29)	50 (2.6)	65 (3.0)	62.5 (4.2)	75.0 (4.8)[b]	79.1 (4.5)[b]	100.0 (4.5)	60 (5.4)	68.7 (5.0)	81.2 (5.6)	87.5 (6.9)	100.0 (4.3)	75.0 (4.3)	77.5 (4.0)
Educational level													
Illiterate (n=4)	42.5 (2.5)	57.5 (6.8)	50.0 (5.1)	60.0 (14.7)	56.2 (14.4)	62.5 (17.5)	35.0 (17.7)	40.6 (15.8)	37.5 (23.4)	. . .	75.0 (14.4)	75.0 (10.2)	52.3 (12.9)
Primary school (n=18)	48.7 (4.1)	55.0 (2.9)	50.0 (4.8)	69.7 (5.0)	75.4 (4.8)	87.5 (3.9)	45.0 (6.3)	59.3 (4.9)	65.6 (5.0)	83.3 (11.6)	100.0 (3.0)	75.0 (5.1)	72.2 (3.4)
Junior high school (n=5)	55.0 (4.2)	70.0 (2.9)	50.0 (7.2)	79.1 (7.4)	95.8 (4.5)	100.0 (1.6)	65.0 (7.6)	68.7 (6.9)	100.0 (10.0)	75.0 . . .	100.0 (5.0)	100.0 (5.0)	83.8 (4.0)
High school (n=15)	60.0 (3.6)	70.0 (4.7)	75.0 (5.2)	95.8 (6.9)	91.6 (6.7)	100.0 (5.7)	80.0 (5.7)	81.2 (6.8)	100.0 (6.3)	95.8 (4.4)	100.0 (6.8)	100.0 (6.3)	85.9 (5.4)
University (n=9)	60.0 (5.7)	70.0 (5.5)[b]	87.5 (8.8)[b]	95.8 (4.3)[c]	100.0 (5.1)	100.0 (2.8)[b]	95.0 (8.9)[b]	100. 0 (6.1)[b]	100.0 (5.4)[b]	100.0 (4.5)	100.0 (0.1)	100.0 (3.6)	95.7 (4.5)[d]
Uveitis activity													
Active (n=8)	57.5 (5.1)	62.5 (3.8)	56.2 (8.3)	75.0 (5.7)	75.0 (6.0)	95.8 (9.0)	52.5 (5.8)	62.5 (5.4)	65.6 (9.8)	83.3 (4.8)	100.0 (6.2)	100.0 (4.5)	75.9 (5.3)
Inactive (n=25)	50.0 (3.4)	65.0 (3.3)	62.5 (4.2)	75.0 (4.8)	85.0 (5.1)	91.6 (4.1)	65.0 (5.9)	68.7 (5.2)	87.5 (5.1)	87.5 (7.1)	100.0 (4.5)	75.0 (4.9)	76.3 (4.0)
Remission (n=18)	60.0 (3.2)	70.0 (3.2)	75.0 (5.2)	93.7 (5.7)	100.0 (4.5)	100.0 (3.6)	87.5 (5.9)[c]	81.2 (5.2)	100.0 (6.1)	100.0 (3.1)	100.0 (3.2)	100.0 (3.5)	90.2 (4.0)
Uveitis severity													
Mild (n=15)	47.5 (7.8)	65.0 (7.3)	62.5 (6.8)	79.2 (5.6)	85.0 (3.8)	100.0 (1.6)	85.0 (11.3)	68.7 (8.2)	100.0 (5.0)	100.0 . . .	100.0 (0.1)	100.0 (10.0)	85.6 (4.8)
Moderate (n=15)	55.0 (3.5)	70.0 (3.1)	62.5 (5.4)	90.0 (5.6)	95.8 (4.5)	100.0 (4.1)	85.0 (6.5)	75.0 (4.8)	100.0 (7.2)	91.6 (3.2)	100.0 (3.8)	100.0 (4.7)	83.8 (4.0)
Severe (n=31)	60.0 (3.0)	65.0 (2.9)	62.5 (4.3)	79.1 (4.5)	75.0 (4.4)	91.6 (4.0)	45.0 (4.9)[b]	62.5 (4.6)	75.0 (4.6)[c]	91.6 (6.7)	100.0 (3.9)	100.0 (4.0)	74.3 (3.6)
Visual acuity, best eye													
≥0.3 (n=72)	60.0 (2.1)	67.5 (1.6)	62.5 (3.0)	87.5 (2.4)	86.2 (2.3)	100.0 (1.6)	67.5 (3.7)	75.0 (2.8)	90.6 (2.7)	95.8 (3.8)	100.0 (1.0)	100.0 (2.4)	84.9 (1.9)
≤0.4 (n=3)	42.5 (4.4)	40.0 (12.5)[d]	50.0 (4.1)	29.1 (11.8)[d]	37.5 (12.3)[d]	25.0 (15.4)[d]	25.0 (6.6)	31.2 (14.5)[c]	12.5 (24)[b]	. . .	50.0 (22.0)[d]	75.0 (16.6)	38.5 (12.5)[c]
Visual acuity, worse eye													
≥0.3 (n=17)	60.0 (4.1)	65.0 (3.0)	62.5 (5.7)	79.1 (4.1)	83.3 (4.5)	100.0 (2.6)	65.0 (5.4)	75.0 (4.0)	87.5 (4.9)	95.8 (6.6)	100.0 (2.0)	100.0 (4.7)	81.1 (3.1)
≤0.4 (n=10)	45.0 (4.5)	50.0 (6.4)	50.0 (5.0)	51.6 (9.2)[b]	47.9 (8.0)[c]	66.6 (9.2)[c]	45.0 (10.0)	46.8 (9.6)	68.7 (12.1)	83.3 (0)	87.5 (10.8)	75.0 (8.3)	61.4 (7.9)[b]

Abbreviations: CV, color vision; D, driving; DA, distance activities; ellipses, not applicable; GH, general health; GV, general vision; index, overall composite score; NA, near activities; NEI-VFQ-25, National Eye Institute Visual Functioning Questionnaire; OP, ocular pain; PV, peripheral vision; SEM, standard error of the mean; VSD, vision-specific dependency; VSMH, vision-specific mental health; VSRD, vision-specific role difficulties; VSSF, vision-specific social functioning.

[a] Post hoc analyses, which were significant at the level of $P<0.5$, revealed the following: for educational level, with illiterate designated as 1; primary school, 2; junior high school, 3; high school, 4; and university, 5; 1<3, 1<4, 1<5, 2<3, 2<4, 2<5 for GV, 1<4, 1<5, 2<4, 2<5 for OP, 1<4, 1<5, 2<4, 2<5 for NA, 1<3, 1<4, 1<5, 2<3, 2<5 for VSSF, 1<3, 1<4, 1<5, 2<3, 2<4, 2<5 for VSMH, 1<3, 1<4, 1<5, 2<5 for VSRD, 1<3, 1<4, 1<5, 2<3, 2<4, 2<5 for VSD, and 1<3, 1<4, 1<5, 2<3, 2<4, 2<5 for index; for uveitis activity, with active designated as 1; inactive, 2; and remission, 3; 1<2, 1<3 for VSMH; and for uveitis severity, with mild designated as 1; moderate, 2; and severe, 3; 3<1 for VSMH and VSD.

[b] $P<.05$.

[c] $P\leq.01$.

[d] $P\leq.001$.

never received any immunosuppressive or biologic therapy in the past. Our treatment approach in patients with Behçet uveitis has been described in the "Methods" section. Of the patients, 35.3% were in remission, meaning that they used immunosuppressive or biologic therapy and their uveitis was inactive for at least 3 months after discontinuation. Another important issue is the high percentage of patients (29.4%) receiving interferon alfa-2a at the time of evaluation. In our uveitis routine, interferon alfa-2a is used in patients refractory to azathioprine and/or cyclosporine.

Formerly, Schiffman and colleagues[11] had reported on visual functioning and general health level in patients with uveitis. Their results showed that those patients had poorer visual functioning and general health level than healthy people. Patients with more severe uveitis had worse visual functioning and general health than those with milder disease.

Although there are limited reports, the NEI-VFQ-25 and SF-36 subscale item scores in patients with Behçet uveitis are lower than that reported in the healthy Turkish population, confirming that Behçet uveitis has a significant effect on visual functioning and general health status.[12,13] The present study also showed that the general health status was more affected than visual functioning because the patients with Behçet uveitis rated their HR-QOL less than that of VR-QOL.

Significant reductions in some aspects of visual functioning were observed in relation to age, educational level, Behçet uveitis activity and severity, and visual acuity in the better and worse eyes. Although no significant difference was observed with respect to

Table 4. Comparison of SF-36 Subscale Item Scores Among Subgroups

Characteristic	Median (SEM) Score[a]									
	PF	SF	RP	RE	MH	VT	BP	GH	PCS	MCS
Sex										
Male (n=32)	85.0 (3.7)	61.1 (3.5)	50.0 (6.6)	66.6 (7.2)	64.0 (3.4)	57.5 (3.2)	66.6 (3.7)	50.0 (2.0)	59.1 (2.9)	60.3 (3.0)
Female (n=19)	65.0 (5.1)	55.5 (4.2)	25.0 (8.6)	33.3 (9.2)[b]	48.0 (5.3)	55.0 (5.3)	55.5 (6.4)	50.0 (2.8)	54.1 (4.3)	42.1 (4.2)
Educational level										
Illiterate (n=4)	60.0 (11.3)	38.8 (7.8)	0 (6.2)	0	42.0 (6.2)	47.5 (3.2)	55.5 (9.6)	55.0 (2.8)	43.6 (4.7)	33.7 (1.6)
Primary school (n=18)	65.0 (5.4)	55.5 (3.5)	25.0 (8.6)	33.3 (9.7)	62.0 (4.6)	57.5 (4.4)	61.1 (6.7)	45.0 (3.1)	53.4 (4.6)	48.0 (3.8)
Junior high school (n=5)	85.0 (9.2)	44.4 (4.9)	50.0 (9.3)	0 (20.0)	64.0 (11.2)	50.0 (9.8)	55.5 (5.4)	40.0 (5.8)	54.1 (2.1)	40.4 (7.4)
High school (n=15)	80.0 (5.0)	66.6 (4.6)	50.0 (9.7)	66.6 (8.0)	56.0 (4.8)	55.0 (4.3)	66.6 (5.6)	55.0 (2.5)	59.1 (4.1)	59.9 (3.6)
University (n=9)	100.0 (4.4)[b]	88.8 (8.5)[b]	100.0 (12.8)[b]	100.0 (12.1)[d]	84.0 (7.3)	85.0 (9.0)	88.8 (7.8)	55.0 (3.4)	84.7 (5.8)	81.1 (6.9)[c]
Systemic treatment										
Colchicine (n=9)	65.0 (6.9)	55.5 (5.4)	25.0 (14.5)	33.3 (15.7)	48.0 (7.7)	55.0 (8.6)	55.5 (8.6)	55.0 (2.8)	54.1 (6.2)	51.8 (7.4)
Antimetabolites (n=10)	72.5 (7.1)	55.5 (5.2)	50.0 (12.2)	33.3 (13.3)	544.0 (7.5)	57.5 (5.8)	61.1 (9.3)	35.0 (2.6)	43.1 (6.3)	41.8 (5.3)
Biologic agents (n=16)	85.0 (6.0)	55.5 (5.1)	62.5 (10.0)	66.6 (10.0)	58.0 (4.9)	55.0 (5.1)	66.6 (5.5)	55.0 (2.3)	57.7 (4.5)	59.8 (4.1)
None (n=16)	80.0 (5.1)	55.5 (5.8)	50.0 (8.6)	66.6 (10.9)	64.0 (4.9)	57.5 (4.6)	66.6 (5.7)	52.5 (2.6)[d]	59.3 (4.0)	61.2 (4.7)

Abbreviations: BP, bodily pain; GH, general perception of health; MCS, mental component summary score; MH, mental health; PCS, physical component summary score; PF, physical functioning; RE, role limitation owing to emotional problems; RP, role limitation owing to physical problems; SEM, standard error of the mean; SF, social functioning; SF-36, 36-Item Short Form Health Survey; VT, energy and vitality.

[a] Post hoc analyses, which were significant at the level of $P<0.5$, revealed the following: for educational level, with illiterate designated as 1; primary school, 2; junior high school, 3; high school, 4; and university, 5; 1< 5, 2<5 for PF, 1<4, 1<5, 3<4, 3<5 for SF, 1<2, 1<3, 1<4, 1<5, 2<3, 2<4, 2<5 for RP, 1<4, 1<5, 3<4, 3<5 for RE, and 1<4, 1<5, 3<5 for MCS; and for systemic treatment, with colchicine designated as 1; antimetabolites, 2; biologic agents, 3; and none, 4; 2<1, 2<3, 2<4 for GH.

[b] $P<.05$.

[c] $P\leq.01$.

[d] $P\leq.001$.

Table 5. Multivariate Analysis of the NEI-VFQ-25 and SF-36 Subscale Item Scores[a]

Item	Adjusted R^2	*P* Value
NEI-VFQ-25		
General vision	0.37	.001
Ocular pain	0.13	.02
Near activities	0.33	.16
Distance activities	0.42	.04
Vision specific		
Social functioning	0.44	.06
Mental health	0.24	.008
Role difficulties	0.27	.006
Dependency	0.22	.008
Color vision	0.57	<.001
Overall, composite score	0.41	<.001
SF-36		
Physical functioning	0.13	.02
Social functioning	0.17	.01
Role limitations owing to		
Physical problems	0.14	.02
Emotional problems	0.23	.004
Mental health	0.20	.005
General perception of health	0.10	.08
Mental component summary score	0.20	.005

Abbreviations: NEI-VFQ-25, National Eye Institute Visual Functioning Questionnaire; SF-36, 36-Item Short Form Health Survey.

[a] Linear regression models were constructed for multivariate analysis of the NEI-VFQ-25 and SF-36 subscale item scores by using factor(s) identified to be significant in univariate analysis. The R^2 is the proportion of the variation in the dependent factor that is explained by all the independent variables in the model.

duration of uveitis, we speculate that lower near and< distance vision among patients older than 30 years may be related to a longer duration of uveitis. A lower educational level was associated with lower general vision, near vision, social functioning, and mental health and overall scores and more pain, role difficulty, and dependency. This observation may be explained by the fact that educated people are more aware of access to earlier and better health care and have better compliance with treatment. Interestingly, active uveitis was associated with decreased mental scores rather than physical scores, indicating the effect of active Behçet uveitis on patients' emotional well-being. The same was also true for severe Behçet uveitis because those patients with severe uveitis had decreased mental health scores in relation to their vision when compared with those patients with milder uveitis. They also reported a higher dependency, as expected. Also, visual acuity was well reflected in the questionnaires because a low visual acuity in the better eye and a better visual acuity in the worse eye had a significant effect on several aspects of visual functioning.

The SF-36 subscale item scores revealed statistically significant differences according to sex, educational level, and the treatment used. Female patients reported more role limitation compared with male patients. This may be related to a significantly lower educational level in the female patients included in this study and the social limitations of female gender in the Turkish culture. Again, because educated people are more aware of access to earlier and better health care, they reported higher physical and social functioning and hence better general health when compared with those with a lower educational level. Interestingly, patients who were taking conventional immunosuppressive agents had significantly lower general perception of health than those who were taking biologic agents. The main biologic agent used in this study population is interferon alfa-2a. We used a low-dose regimen with dose escalation as described previously elsewhere.[14,15] We believe that a

low dose and a dose-escalating regimen has the advantage of avoiding adverse effects that occur with higher doses. This study also showed that interferon alfa-2a use in patients with Behçet uveitis was associated with a better general perception of health when compared with conventional immunosuppressive agents.

In multivariate analysis of visual functioning and general health, sociodemographic and clinical variable(s) identified to be significant in univariate analysis could only explain limited variance in subscale item scores. This finding may be related to more complex emotional and psychological factors that we were not able to capture and analyze here.

The main shortcoming of our present report is the lack of healthy and disease-carrying control groups. We believe that analysis and comparison of VR-QOL and HR-QOL in another uveitis entity with ocular and systemic involvement, such as ankylosing spondylitis, would also be beneficial. We also assume that modest sample sizes in the univariate analysis limited the power to detect significant differences when subgroup analysis was performed.

In conclusion, the present study has shown that visual functioning and general health status are impaired in patients with Behçet uveitis, with the disease having more effect on general health status. Several demographic and clinical variables had a significant influence on VR-QOL and HR-QOL. However, they alone were not enough to explain a high proportion of variance in the aspects of visual functioning and general health status.

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100 Years Ago in the Archives

I found after doing a number of cases that the astigmatism was scarcely ever over one diopter, so to save time I gave up doing a retinoscopy in every case, and gave them the plus lens they preferred, which in almost every case was a plus ten diopter lens. . . . As excessive astigmatism has been alleged to be caused by this operation, it may be well to call special attention to these facts. I have also observed a number of cases in which escape of vitreous has not occurred, and I found that in them also the average astigmatism was one diopter. . . . The total number examined was 98; in no case was any detachment of the retina present.

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