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Health-related Quality of Life in Behçet Patients with Ocular Involvement

Nilgün Tanrıverdi*, İbrahim Taşkıntuna†,
Çağay Dürü*, Pınar Özdal†, Serap Ortaç† and Esin Fırat†

*Department of Psychiatry, Başkent University, Ankara, Turkey; †SSK Ankara Eye Center and Eye Bank, Ankara, Turkey

Purpose: Health-related quality of life (HRQOL) is an important outcome factor in chronic diseases such as Behçet syndrome. We aimed to investigate the relation of HRQOL to the duration of illness, mental state, and visual acuity of patients with Behçet syndrome.

Methods: We conducted a cross-sectional clinical trial of 45 consecutive Behçet patients with ocular involvement. The control group consisted of an age-, sex-, and education-matched group of 45 healthy individuals. All patients and the controls had been given a complete ophthalmic examination. In addition, they completed a questionnaire comprising the SF-36 Health Survey, Beck Depression Inventory, and Beck Anxiety Inventory. Eight multiple regression analyses were carried out in the patient group to determine whether total anxiety scores, total depression scores, duration of the disease, and visual acuity predicted the dependent variable SF-36 subscales.

Results: Using the analysis of variance statistical method, comparisons of the patient and the control groups for depression, anxiety, and the subscales of the SF-36 Health Survey indicated a statistical significance for this battery of tests.

Conclusions: Behçet patients with ocular involvement are susceptible to anxiety and depression when compared to age and sex matched controls. It is important for the ophthalmologist to know that changes in the mental state of his patient may trigger a new ocular attack, and to be aware that these changes may play a critical role in the management and preventive measures for Behçet syndrome. **Jpn J Ophthalmol 2003;47:85–92** © 2003 Japanese Ophthalmological Society

Key Words: Behçet syndrome, health-related quality of life, mental state.

Introduction

Behçet syndrome is a generalized occlusive vasculitis of unknown etiology described by the Turkish physician Hulusi Behçet in 1937.[1] It is characterized by three components: iridocyclitis (historically with hypopyon), aphthous lesions in the mouth, and ulceration of the genitalia. It is more common in some geographic areas (Japan, eastern Mediterranean, the Middle East) with higher prevalence rates. The disease occurs most frequently in younger adults. Behçet syndrome is a chronic disorder that may lead to blindness if ischemic optic neuropathy and retinopathy are not adequately treated. Central nervous system symptoms such as stroke, palsy, and a confused state may develop in 10–49% of patients, and are the first symptoms of the disease in 5% of patients. A variety of other signs including polyarthritis, vascular conditions (blood vessel occlusions and aneurysms), epididymis, gastrointestinal, pulmonary and heart lesions may also occur.[2,3]

Chronic diseases such as Behçet syndrome may lead to temporary or permanent functional disabilities and may cause some psychiatric disorders. In their earlier paper, Wells and associates[4] described the prevalence of psychiatric disorders in persons with or without chronic medical conditions. In their

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Correspondence and reprint requests to: Nilgün TANRIVERDİ, MD, Boğaz Sokak 30/5, 06700 GOP-Ankara, Turkey. Telephone: +90 (312) 212-1821; e-mail:taskintuna@superposta.com

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study they found that 1) there was a strong overall association between psychiatric disorders and chronic medical conditions, and 2) that persons with any recent chronic medical condition had a high prevalence, relative to those without any chronic medical condition, of lifetime substance use disorders and recent mood and anxiety disorders.[4] On the other hand, research on the psychiatric aspects of Behçet syndrome, and health-related quality of life has been surprisingly limited in the literature; the psychiatric aspects of Behçet syndrome have been peripherally mentioned in many reviews and case reports, but few papers deal with this aspect exclusively. According to previous studies, patients with Behçet syndrome usually relate to others in a "passive and overtly compliant manner," and are characterized by a dependent life style, intermittent periods of overt mood disorder, poor psychosexual adjustment, and marked somatization.[5–8] In the Koptagel et al study,[9] the psychiatric investigation of 55 patients with Behçet syndrome through a psychoanalytically oriented interview and the application of the Rorschach test revealed that psychosocial stress factors were predominant prior to the onset of the disease. The personality structures of the patients, according to the Rorschach findings, were pathological with a weak ego, regressive tendencies, disturbed body image, high anxiety, difficulties in social adaptation and in evaluation of realities, as well as inadequate expression of and difficulty in coping with emotions. Orsucci[10] maintained that psychosomatic patterns of thinking might be paramount in these patients, but indicated that psychosocial events may play an interesting and complex role in the chronicity of the syndrome. He showed that the relapsing cycle of the syndrome had some interesting connections with important life events, important changes in emotion, and modifications in patterns of thinking.

Health-related quality of life (HRQOL) is an important outcome factor in chronic diseases such as Behçet syndrome. HRQOL may decline due to the prolonged duration of the illness, medication, and disability, or because of the depressive mood state in chronic diseases.[11,12] We were not able to locate any HRQOL studies on the ocular involvement of Behçet syndrome through our computer-based search in PubMed. In this study our objective was to investigate the relation of HRQOL with duration of illness, mental state, and the visual acuity of patients having the ocular findings of Behçet syndrome.

Materials and Methods

Subjects

The study group consisted of 45 consecutive patients with Behçet syndrome seen at the Uveitis and Behçet Syndrome Clinic at SSK Ankara Eye Center and Eye Bank, between December 2000 and June 2001. All patients had Behçet syndrome with ocular involvement and their vision was affected to some degree by their illness. The diagnoses of the patients were made in accordance with the diagnostic criteria of the "International Study Group for Behçet Disease." Nine women (20%) and 36 men (80%) were included in the study. The mean age was 33.68 ± 9.19 years (range, 18–65 years). The control group consisted of 45 individuals known to be healthy physically and matched for age, sex, and education. All patients and control subjects provided an informed consent and the study was approved by the Ethics Committee of the SSK Ankara Eye Center and Eye Bank. The characteristics of the patients and the controls are summarized in Table 1.

Instruments

Beck Depression Inventory. Beck Depression Inventory is a 21-item self-report inventory. The items consist of symptoms of depression. Some items are related to physical concerns such as sleep distur-

Table 1. Baseline Characteristics of the Patient and Control Groups

Characteristic	Patient Group (n = 45)	Control Group (n = 45)	*P*-value
Male/female	36/9	36/9	<.01
Mean age in years (median; range)	33.68 (33; 18–65)	33.04 (32; 18–62)	NS
Mean BCVA* (median; range)	0.62 (0.9; 0.001–1.0)	1.0 (1.0; 1.0–1.0)	<.01
Mean duration (months) of disease (median; range)	63.04 (48; 1–180)	–	
Mean duration (months) of ocular involvement (median; range)	50.08 (48; 1–180)	–	

BCVA: best corrected visual acuity.

bances and loss of weight. Other items refer to the emotional (hopelessness, sorrow), motivational (willingness to work), and cognitive aspects (concentration, self-evaluation). For each symptom category there are four sentences and the subject chooses one of them according to his/her experience during the previous week. Each sentence is scored as 0, 1, 2, or 3. Test scores higher than 17 indicate a high level of depression. This test was developed by Beck and associates in 1961 and then revised by Beck in 1979.[13,14] The 1979 version of the Beck Depression Inventory was adapted to Turkish by Hisli in 1988 and 1989.[15,16]

Beck Anxiety Inventory

The Beck Anxiety Inventory is a 21-item self-report inventory. It is designed to measure the level of anxiety. The items consist of symptoms of anxiety. Information is obtained about the physical (feeling shaky, butterflies in the stomach), cognitive (being afraid that something terrible will happen, fear of losing control) and emotional aspects (being tense, angry). Subjects are asked how much they experienced each symptom during the previous week on a 4-point preference type scale ranging from 0 to 3. Higher total scores indicate higher levels of anxiety. This anxiety inventory was developed by Beck and associates in 1988 and adapted to Turkish by Ulusoy.[17,18]

36-item Short Form-36 Health Survey

The 36-item short-form (SF-36) was constructed to survey health status in the Medical Outcomes Study in the United States. The SF-36 was designed for use in clinical practice and research, health policy evaluations, and in a general population survey. The test has been developed in an attempt "to develop a general health survey that is comprehensive and psychometrically sound, yet short enough to be practical for use in large-scale studies of patients in practice settings."[19] The SF-36 includes one multi-item scale that assesses eight health concepts: 1) limitations in physical activities (physical functioning) because of health problems (assessment of limitations on daily activities, eg, pulling a table, lifting the goods after shopping, climbing stairs, walking a couple of blocks, as a result of bad health); 2) limitations in social activities because of physical or emotional problems (social functioning; assessment of social activities, eg, visiting friends, relatives, as a result of physical health or emotional problems); 3) limitations in usual role activities because of physical health problems (role limitations due to physical health; assessment of deterioration in work or other daily activities, eg, limitations in working hours); 4) bodily pain (assessment of severity of pain and how it affects one's working ability); 5) general mental health (psychological distress and well-being; assessment of one's level of anger, sadness, happiness); 6) limitations in usual role activities because of emotional problems (role limitations due to emotional problems; questions to detect if one has problems with his work or daily activities as a result of emotional problems, eg, depression or anxiety; 7) vitality (energy and fatigue; questions about one's assessment of his energy level, tiredness); and 8) general health perceptions (how one feels about his own health). The survey was constructed for self-administration by persons 14 years of age and older, and for administration by a trained interviewer in person by telephone. SF-36 was developed by Ware and associates in 1992 and adapted to Turkish by Koçyiğit et al in 1999.[19,20] The SF-36 is an instrument for measuring health perception in a general population. It is easy to use, acceptable to patients, and fulfills the stringent criteria of reliability and validity.

Each subscale has a standard formula represented by [(raw score − lowest raw score)/possible raw score] × 100. Each subscale score varies between 0 and 100, and the higher the score the better the health condition.

Procedure

All patients and the controls had a complete ophthalmic examination including best-corrected visual acuity, slit-lamp examination, applanation tonometry, and fundus examination with 20 D and 78 D lenses through a dilated pupil. For statistical purposes best-corrected visual acuity was calculated as follows: Perception (P) + projection (P) + = 0.001; hand motion (HM) = 0.005; counting fingers (CF) at 1 m = 0.01; and CF at 5 m = 0.05. Visual acuity was evaluated individually for the better eye; this was because the patient was able to see through his better eye even if the other eye had no vision. The patients and the controls were given a questionnaire composed of the SF-36 Health Survey, Beck Depression Inventory, and Beck Anxiety Inventory.

Statistical Analysis

Statistical analyses were carried out with SPSS version 10.0. The analysis of variance test (ANOVA) was used for the comparison of the patients and the controls for depression, anxiety, and the subscales of the SF-36 Health Survey. A P value of $< .05$ was set

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for statistical significance. We tested the mean values of the patient and the control groups with ANOVA. In ANOVA, an *F*-ratio is obtained by dividing the between-group estimate (between-group estimate is a statistic showing the difference between groups) by the within-group estimate (within-group estimate is an indicator of differences within groups because of individual differences, uncontrolled variables in the study; actually, if the groups are compared, we would like the within-group estimate to be small). The *P* value represents the confidence interval chosen. In ANOVA analysis, the results are given as: $F(1,89) = 4.47$, $P < .05$. The numbers in parentheses are the degrees of freedom of the analysis. Degrees of freedom represent the number of values that are free to vary after certain restrictions are placed on the data. Degrees of freedom are calculated both between groups (the first number in the parentheses) and within groups (the second number in the parentheses). The number after the equal sign is the *F*-ratio and *P* denotes the confidence interval. Linear regression analyses were carried out for the patient group to see whether total anxiety scores, total depression scores, duration of the disease, and visual acuity predicted the dependent variables of SF-36 subscales (physical functioning, social functioning, pain, role limitations due to emotional problems, role limitations due to physical health, general health, mental health, and energy/fatigue). The Student *t*-test was carried out for comparisons of men and women for all variables. Linear regression analysis is used to determine the relationship between a dependent variable (dependent in the sense that it can be predicted from a set of independent variables; eg, physical functioning in this research) and a set of independent variables (independent in the sense that we are not interested in what is influencing these variables, anxiety, depression, in this study). The dependent variable is "predicted" by a set of independent variables; the correlation between dependent and independent variables is calculated. After they are corrected statistically, they are denoted by the β symbol. Each independent variable thus has a β value, and the βs act as correlation coefficients. Correlation coefficients indicate the relationship between variables. These coefficients vary between −1 and +1. Coefficients approaching −1 indicate a negative relationship, meaning that if one variable increases, the other one decreases (eg, if the level of depression increases, the level of motor activity decreases). Those values approaching +1 indicate that both variables vary in the same way: they increase or decrease together. Those values around 0 indicate that there is no consistent relationship between the variables. In regression analysis, to check if βs are statistically significant (ie, the results are not due to chance), they are tested with the Student *t*-test. This test is similar to ANOVA, and tests the difference between the means of the groups. In testing βs, we compare them with a 0 correlation; if the β is big enough in a confidence interval to yield a significant result ($P < .05$ in this study), then, the results are statistically significant and the variable is a good predictor of the dependent variable.

Results

Mean duration of the Behçet syndrome was 63.04 ± 47.48 months (range, 1–180 months); and mean duration of ocular involvement was 50.09 ± 37.94 (range, 1–180 months) for the patient group. None of the patients had a psychiatric disorder or was taking medicine for a psychiatric illness at the time of the study. Mean best corrected visual acuity was 0.62 ± 0.43 (range, 0.001–1) for the better eye of the patients and 1.00 (range, 1.0–1.0) for the controls. None of the patients had a history of corticosteroid use for the last 4 months prior to their testing. Sixteen (35.6%) patients were using cyclosporine-A alone; 7 (15.6%) were using cyclosporine-A plus colchicine; 10 (22.2%) were using colchicine alone; 3 (6.7%) were using cyclosporine-A plus azathioprine; 1 (2.2%) patient was using azathioprine alone; and 8 (17.7%) were using nothing at the time of the study (Table 2). It was confirmed by magnetic resonance that none of the patients had central nervous system involvement of Behçet syndrome.

Comparisons of the patient and the control groups for depression, anxiety, and sub-scales of the SF-36 Health Survey using the ANOVA test revealed statistical significance for these batteries of tests. The results are summarized in Table 3. Mean Beck depression scores were 20.08 ± 12.96 for the patient group and 11.44 ± 9.71 for controls [$F(1,89) = 12.83$; $P < .01$]. Mean Beck anxiety scores were 22.09 ±

Table 2. Medication Being Taken by Patients

Medication	Patient Group* (n = 45)	Control Group (n = 45)
Cyclosporine-A	16 (35.6)	–
Cyclosporine-A +colchicine	7 (15.6)	–
Colchicine	10 (22.2)	–
Cyclosporin-A +azathioprine	3 (6.7)	–
Azathioprine	1 (2.2)	–
No systemic treatment	8 (17.7)	–

*Values in parentheses are percentages.

14.52 for the patient group and 8.69 ± 8.17 for controls [$F(1,89) = 29.110$; $P < .01$]. Mean scores of subscales of the SF-36 Health Survey were 59.33 ± 28.50 and 90.11 ± 16.90 for physical functioning [$F(1,89) = 38.829$; $P < .01$]; 51.93 ± 28.29 and 73.53 ± 22.69 for social functioning [$F(1,89) = 15.964$; $P < .01$]; 45.60 ± 26.46 and 78.17 ± 20.24 for pain [$F(1,89) = 43.039$; $P < .01$]; 23.68 ± 30.73 and 65.24 ± 38.92 for role limitations due to emotional problems [$F(1,89) = 31.596$; $P < .01$]; 31.66 ± 37.84 and 77.78 ± 32.08 for role limitations due to physical health [$F(1,89) = 38.881$; $P < .01$]; 33.20 ± 21.41 and 60.38 ± 15.85 for general health [$F(1,89) = 46.845$; $P < .01$]; 47.73 ± 21.43 and 58.49 ± 20.45 for mental health [$F(1,89) = 5.932$; $P = .02$]; 42.63 ± 22.68 and 55.44 ± 21.29 for energy/fatigue for the study group and for controls [$F(1,89) = 7.594$; $P < .01$], respectively. Patients with Behçet syndrome were more prone to mood and anxiety disorders, and their health-related quality of life was inferior compared to their healthy counterparts.

Eight multiple regression analyses were carried out for the patient group to see whether total anxiety scores, total depression scores, duration of the disease, and visual acuity predicted the dependent variable SF-36 subscales (physical functioning, social functioning, pain, role limitations due to emotional problems, role limitations due to physical health, general health, mental health, and energy/fatigue). Although multiple R was significant [($R = .489$, $F(4,44) = 3.14$, $P < .05$)] when the physical functioning was the dependent variable, none of the independent variables contributed to this significance on its own. When pain was the dependent variable, multiple R was significant [($R = .529$, $F(4,44) = 3.89$, $P < .01$)], but when the independent variables were considered, only total anxiety scores predicted pain [($\beta = -0.53$, $t = -2.47$, $P < .05$)]. When general health was the dependent variable, multiple R was significant [($R = .530$, $F(4,44) = 3.91$, $P < .01$)], but none of the independent variables reached statistical significance alone. When energy/fatigue was the dependent variable, the multiple R was statistically significant [($R = .599$, $F(4,44) = 5.61$, $P < .01$], but none of the independent variables reached statistical significance alone. When social functioning was the dependent variable, multiple R was significant [($R = .513$, $F(4,44) = 3.59$, $P < .05$)], but when the independent variables are considered only visual acuity scores predicted social functioning [($\beta = 0.39$, $t = 2.52$, $P < .05$)]. Mental health as a dependent variable was statistically significant [($R = .538$, $F(4,44) = 4.08$, $P < .01$)], but when the independent variables were considered, only total anxiety scores predicted mental health [($\beta = -0.43$, $t = -2.04$, $P < .05$)]. When role limitations due to emotional problem scores and role limitations due to physical health scores were the dependent variables, multiple R did not reach statistical significance.

The correlation coefficient between anxiety and depression measures in this study was 0.74 ($P < .01$). When comparisons were done for all variables, only total anxiety scores differed between men and women [(mean, for men = 19.06; for women = 34.22; $t(1,43) = 3.06$, $P < .01$]. For the total depression scores, the difference did not reach statistical significance, but there was a trend [(mean, for men = 18.22; for women = 27.55; $t(1,43) = 1.99$, $P = 0.08$).

Discussion

The male to female ratio for Behçet syndrome is even in both northern Europe and Japan but in-

Table 3. Statistical Analysis of BDI, BAI, and SF-36 Test Results*

Test	Patient Group†	Control Group†	ANOVA
BDI	20.08 ± 12.96	11.44 ± 9.71	$F(1,89) = 12.83$; $P < .01$
BAI	22.09 ± 14.52	8.69 ± 8.17	$F(1,89) = 19.11$; $P < .01$
SF-36 Test			
Physical functioning	59.33 ± 28.50	90.11 ± 16.90	$F(1,89) = 38.829$; $P < .01$
Social functioning	51.93 ± 28.29	73.53 ± 22.69	$F(1,89) = 15.964$; $P < .01$
Pain	45.60 ± 26.46	78.17 ± 20.24	$F(1,89) = 43.039$; $P < .01$
Role limitations due to emotional problems	23.68 ± 30.73	65.24 ± 38.92	$F(1,89) = 31.596$; $P < .01$
Role limitations due to physical health	31.66 ± 37.84	77.78 ± 32.08	$F(1,89) = 38.881$; $P < .01$
General health	33.20 ± 21	60.38 ± 15.85	$F(1,89) = 46.845$; $P < .01$
Mental health	47.73 ± 21.43	58.49 ± 20.45	$F(1,89) = 5.932$; $P < .05$
Energy/fatigue	42.63 ± 22.68	55.44 ± 21.29	$F(1,89) = 7.594$; $P < .01$

*BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, SF-36: Short Form-36 Health Survey.
†Values are mean ± SD.

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creases significantly (1.5–5:1) in certain Mediterranean countries and the Middle East.[21] The male to female ratio was 5 to 1 in our patient group; and it reflects the natural distribution of the disease between men and women in our region for Behçet syndrome. When comparisons were done, total anxiety scores differed with statistical significance; there was a trend but the difference did not reach statistical significance for total depression scores between men and women in the patient group. Although it is well known that women are more prone to mood disorders than men,[22] this result may be biased because of the unequal composition (9/36) of the patient group, and it would not be appropriate to draw any conclusion from this result.

These findings reported here broaden our understanding of the relationship of psychiatric disorders and chronic medical conditions. In the current study, comparisons of the patient group with the controls revealed statistically higher depression and anxiety scores using Beck Depression Inventory and Beck Anxiety Inventory. This result is very important in showing that chronic diseases like Behçet syndrome may have a close relation with mood disorders, which in turn may have a deeply negative impact on a patient's daily life. Persons with concurrent psychiatric disorders and chronic medical conditions are of great public health concern because they are likely to have functional limitations and incur higher treatment costs.[23–27]

In a 1989 study, Wells and associates[28] found that persons with each type of the lifetime psychiatric disorder they studied (affective, anxiety, and substance use) had a greater prevalence of multiple lifetime chronic medical conditions than persons without a psychiatric disorder, even after adjusting for sociodemographic factors and the presence of other psychiatric disorders. After adjusting for other factors, they also found that persons with recent anxiety disorders but not other psychiatric disorders showed a greater prevalence of any current chronic medical condition. In his article, Kessler[29] showed that inventories of stressful events predict subsequent depression. A smaller number of controlled comparative studies of people exposed to single major life events provide strong evidence that at least part of this association is due to events causing depression. It is also clear from other studies that this relationship can be reciprocal and that depression can elicit or exacerbate stressful events and difficulties.

There is further evidence that the onset of the initial symptoms of Behçet syndrome and the timing of major relapses occur at emotionally critical periods.[5–9] Data gathered from our study showed that patients with ocular involvement of Behçet syndrome were susceptible to anxiety and depression when compared to their age and sex matched healthy counterparts. These findings are in accordance with other studies on chronic diseases with mood disorders.[23–29] Although any relation between a stressful event that causes depression or anxiety and a subsequent attack of uveitis in the patient group has not been investigated; it is conceivable that this relation may exist in the wake of earlier studies.[23–29] Therefore, it is very important for the ophthalmologist to know that the mood changes of his/her patient may trigger a new attack in the eye; being aware of this phenomenon may play a critical role in the management and preventive measures for Behçet syndrome in the future. Working in close cooperation with a psychiatrist, and treating the patients for their mood changes, may prevent some of the new attacks in the eye, and this may play a major role in the long-term management of Behçet syndrome.

Medical therapy can no longer be evaluated on the grounds of life extension alone. On the basis of a multidimensional concept of quality of life, the study carried out here examined the subjective restrictions and strains for patients whose lives were so dramatically changed by the permanent handicap of their chronic disease. All eight health concepts of the SF-36 Health Survey revealed statistically significant differences between the patients and the controls.

In the current study, pain was related to anxiety; the more anxious a patient was, the more pain he was to experience. This seems quite important; when treating patients with pain, it is reasonable to check on the level of anxiety and treat their anxiety as well. There is extensive research in the literature showing the relationship between mood states and the treatment of pain using antidepressant drugs and psychotherapy.[30–33] General health was predicted best by a *group* of variables, and it turned out that levels of anxiety and depression, duration of the disease, and visual acuity were related to the concept of general health, as well as the physical condition of the patient. This result was quite striking because general health in this study was assessed by questions that did not directly probe the psychological aspects of health. It is conceivable to treat patients not only for their physical illness, but also for the psychological aspects of their illness as well. None of the independent variables reached statistical significance alone when energy/fatigue was the dependent variable, although multiple R was statistically significant. One's energy level was not only a result of her/his physical

condition but was also related to her/his psychological condition, anxiety, and depression. Visual acuity scores predicted social functioning in the current study. Actually, this is quite understandable in our country, Turkey. The physical environment is not well designed for disabled people, and they are mostly confined at home. Only total anxiety scores predicted mental health. This might be a result of the fact that the subscale measuring mental health consisted of items related to depression. It is well known from previous research that anxiety and depression are highly related concepts. When we look at the symptoms of anxiety and depression we see that some of them are overlapping: irritability, agitation/restlessness, concentration difficulties, insomnia, and fatigue.[34] Because of this overlapping, anxiety might have suppressed depression in the regression equation.

The independent variables (total anxiety scores, total depression scores, duration of the disease, visual acuity) seem to predict most of the dependent variables (physical functioning, social functioning, pain, role limitations due to emotional problems, role limitations due to physical health, general health, mental health, energy/fatigue) in the regression analyses as a group, but not alone. If this is true, while we are treating our patients we should take into account all the independent variables. Ignoring one or more of them in our treatment (not paying enough attention to the anxiety or depression levels of the patients, duration of the disease, or visual acuity) might result in the deterioration of the general health of our patients.

It was clearly demonstrated in our study that patients with Behçet syndrome had a poorer quality of life compared to their age and sex matched healthy counterparts. Therefore, the ophthalmologist should help the patient to improve his/her quality of life by means of any available therapeutic and supportive methods. There is considerable room for future research in the area of quality of life in patients with Behçet syndrome. While it is not clear that different levels of quality of life may result from different therapy modalities, determining the extent to which these differences may be caused by the therapy should be the focus of additional research.

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