Assessment of Quality of Life and Depression in Korean Patients with Graves’ Ophthalmopathy

Hun Lee, Hyun Seok Roh, Jin Sook Yoon, Sang Yeul Lee
Department of Ophthalmology, Institute of Vision Research, Yonsei University College of Medicine, Seoul, Korea.

Purpose: To assess quality of life and depressive status in Korean patients with Graves’ ophthalmopathy.

Methods: A cross-sectional study of 49 patients (mean age, 41 years; sex ratio, M:F=11:38) with Graves’ ophthalmopathy (referred to as the Graves’ group) and 48 age-matched and sex-matched controls (mean age, 40.2 years; sex ratio, M:F=11:37) was performed using the Korean version of the 36-item Short-Form General Health Survey (SF-36) questionnaire and the Beck Depression Inventory (BDI). Survey data was compared among patients with mild, moderately severe, and sight-threatening Graves’ ophthalmopathy and between patients with low (0 or 1) or high (2 or 3) Gorman scores.

Results: Those in the Graves’ group scored significantly lower on all categories of the SF-36, as compared to the control group (p<0.05). The 4 patients with sight-threatening Graves’ had significantly lower scores for physical functioning, role limitations due to physical health, and the physical component summary of the SF-36, when compared with the 28 patients with mild Graves’ and the 17 patients with moderately severe Graves’ (p<0.05). The 17 patients in the high Gorman score group had lower physical component summary scores than the 32 patients in the low Gorman score group (p=0.03). The 16 patients with BDI scores ≥16 had significantly lower scores on the SF-36 and higher clinical activity scores, as compared to the 33 patients with BDI scores <16 (p<0.05).

Conclusions: Patients with Graves’ ophthalmopathy had reduced health-related quality of life and were more likely to be depressed, especially those with a sight threatening condition or significant diplopia. It is important to identify these patients to provide the necessary psychological support.

Key Words: Depression, Graves ophthalmopathy, Quality of life

Graves’ ophthalmopathy is a potentially disfiguring and sight-threatening disease occurring in 25% to 50% of patients with Graves’ thyroid disease [1]. Clinical signs include lid retraction, disfiguring proptosis, extraocular muscle dysfunction, eyelid edema, conjunctival injection, chemosis, and optic neuropathy [2]; symptoms include pain, swelling of the eyelid, a gritty sensation in the eyes, diplopia, and visual impairment, which profoundly impair the health-related quality of life of affected individuals [2-11].

Both Graves’ disease and Graves’ ophthalmopathy contribute to worsened quality of life, particularly with regards to physical functioning, physical and emotional role functioning, vitality, social functioning, and mental health [3-6]. In several reports, general health-related quality of life in patients with Graves’ ophthalmopathy was markedly lower compared to both the general population and patients with other chronic diseases [4,7]. In fact, the impact of Graves’ ophthalmopathy on quality of life has been a popular subject of study in Western countries, and a disease-specific validated quality of life questionnaire has been developed for clinical use. However, there has never been a health-related quality of life study using a generic questionnaire in Korean Graves’ ophthalmopathy patients, nor has there been a study using a disease-specific questionnaire which is validated and translated into the Korean language. In addition, in patients with cosmetic disfigurement or functional impairment caused by inflammatory symptoms, diplopia and visual dysfunction may be associated with emotional problems, such as depression. Therefore, in this study, we used the Medical Outcomes.
Graves' ophthalmopathy was defined as lid retraction score 1) or no diplopia (Gorman score 0). Moderately severe involvement, exophthalmos < 21 mm, or transient (Gorman defined as minor lid retraction (< 2 mm), mild soft tissue involvement) [12]. Mild Graves' ophthalmopathy was the European Group on Graves' Orbitopathy (EUGOGO) classification system [12]. Mild Graves' ophthalmopathy was defined as minor lid retraction (< 2 mm), mild soft tissue involvement, exophthalmos < 21 mm, or transient (Gorman score 1) or no diplopia (Gorman score 0). Moderately severe Graves' ophthalmopathy was defined as lid retraction ≥ 2 mm, moderate or severe soft tissue involvement, exophthalmos ≥ 21 mm, or constant diplopia (Gorman score 2) or constant diplopia (Gorman score 3). Very severe, sight-threatening Graves' ophthalmopathy was defined as dysthyroid optic neuropathy or corneal breakdown. Patients with a history of optic neuropathy but who were without optic neuropathy at the time of the survey were included in the moderately severe group. Optic neuropathy was defined as the presence of disc swelling or pallor, a visual field defect, or relative afferent pupillary defect, or if visual acuity less than 0.3 in the absence of other reasons for sight loss [12]. Inflammation activity was determined using a clinical activity score based on seven signs of inflammation of the orbit, with each scored as absent (0) or present (1), with a maximum possible score of 7 [12].

At an outpatient clinic visit, patients completed a questionnaire on demographics and duration and previous treatments of Graves' ophthalmopathy and Graves' thyroid disease. Quality of life was assessed by the SF-36, and depressive status was evaluated by the BDI. Patients who could not fill out the survey themselves were provided support from those conducting the research. Patients were asked to provide any missing information at the outpatient clinic.

**Materials and Methods**

**Study design and recruitment of participants**

This cross-sectional study included 49 patients with Graves' ophthalmopathy who were followed at the Department of Ophthalmology, Yonsei University College of Medicine between July 2008 and December 2008 (referred to as the Graves' group). We excluded patients who were not biochemically euthyroid to eliminate the possible effect of dysthyroidism on quality of life. The control group was composed of healthy volunteers who were age- and sex-matched to the study group. Written informed consent was obtained from all participants after gaining approval from the Institutional Review Board at Yonsei University College of Medicine.

Graves' ophthalmopathy was defined as the presence of typical eye symptoms and signs in a patient with autoimmune Graves' disease. A complete ophthalmic investigation was performed, and an assessment of the severity and activity of Graves' ophthalmopathy was performed [12]. Proptosis and eye muscle involvement were assessed using a Hertel exophthalmometer and the Gorman diplopia scale [13]. A Gorman score of 0-1 was considered low; a score of 2-3 was considered high.

Severity of Graves' ophthalmopathy was scored according to the European Group on Graves' Orbitopathy (EUGOGO) classification system [12]. Mild Graves' ophthalmopathy was defined as minor lid retraction (< 2 mm), mild soft tissue involvement, exophthalmos < 21 mm, or transient (Gorman score 1) or no diplopia (Gorman score 0). Moderately severe Graves' ophthalmopathy was defined as lid retraction ≥ 2 mm, moderate or severe soft tissue involvement, exophthalmos ≥ 21 mm, or constant diplopia (Gorman score 2) or constant diplopia (Gorman score 3). Very severe, sight-threatening Graves' ophthalmopathy was defined as dysthyroid optic neuropathy or corneal breakdown. Patients with a history of

**Survey instruments**

1) **Medical outcome study SF-36**

The Korean version of the SF-36 was used to evaluate the health-related quality of life of the study participants. The SF-36 has been previously shown to be a credible and reliable instrument to measure the quality of life in study groups [14]. The SF-36 contains eight itemized categories and 36 questions. The eight categories are: 1) physical functioning (walking, lifting); 2) role function-physical (limitations in ability to perform usual activities); 3) bodily pain (level of bodily pain or discomfort); 4) general health perceptions (global evaluation of health); 5) vitality (energy level or fatigue); 6) social functioning (impact of health or emotional problems on social activities); 7) role function-emotional (impact of emotional problems on work or daily activities); and 8) mental health (anxiety, depression, sense of psychological well-being). The first four categories are grouped as the physical component summary, while the last four categories are grouped as the mental component summary. These eight categories and two summaries were converted into scores and evaluated with respect to the sociodemographic and clinical characteristics of the participants.

2) **BDI**

Depression in patients with Graves' ophthalmopathy was evaluated with the BDI, a standardized questionnaire of the cognitive, affective, and somatic symptoms of depression. The BDI was developed to assess the type and severity of depression based on clinical symptoms [15]. The Korean version of the BDI has high reliability, and a score of 16 or higher has been suggested as the optimal cutoff score for the diagnosis of major depression in Korea [16,17].

**Statistical analysis**

All measures of the SF-36 were compared between the
Graves’ and control groups using independent two-sample t-tests. Quality of life (by SF-36 scores) and depressive status (by BDI scores) were compared among patients with mild, moderately severe, and sight-threatening Graves’ ophthalmopathy using one-way analysis of variance (ANOVA) and the Pearson chi-square test for continuous and categorical variables, respectively. SF-36 and BDI scores were also compared between the high and low Gorman score groups using the same statistical methods.

Characteristics, including age, sex, duration of Graves’ disease and Graves’ ophthalmopathy, Hertel exophthalmos values, current activity score, and severity stage by EUGOGO classification were compared between the patients with high (≥16) and low (<16) BDI scores, using the independent two-sample t-test and the Pearson chi-square test for continuous and categorical variables, respectively. The relationship between the BDI and SF-36 scores and age, sex, duration of Graves’ disease and Graves’ ophthalmopathy, Gorman score, severity, and activity were examined by the Pearson correlation or Spearman rank correlation test.

A p-value <0.05 was considered statistically significant in all analyses. Data were entered twice into a special computer program to minimize typing errors. Data were analyzed with SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA).

Results

Demographic details and clinical characteristics of the patient population are shown in Table 1. The 49 patients included 38 women (77.6%) and 11 men (22.4%), with a mean age of 41.4 years and an average duration of Graves’ ophthalmopathy of 12 months. Nine patients (18.4%) had a history of optic neuropathy, and four patients (8.1%) had optic neuropathy at the time of the survey. The patients were asked “What is the main cause of emotional distress now?” with three possible answers: disfiguring change, functional impairment, or both equally distressful. Twenty patients (40.8%) responded with disfiguring change, 14 patients (28.6%) responded with functional impairment, and 15 patients (30.6%) reported both. The control group included 48 individuals ages 23 to 76 years (mean age, 40.2 years sex ratio, M:F=11:37). As shown in Fig. 1, the Graves’ group scored lower on all categories of the SF-36, as compared to the control group (p<0.05).

In comparing the SF-36 and BDI scores among the mild,

| Table 1. General characteristics of patients with Graves’ ophthalmopathy at the time of survey (n=49) |
|---|---|
| Characteristics | Values |
| Age (yr), mean±SD | 41.4±13.4 |
| Sex (F / M) | 38 (77.6) / 11 (22.4) |
| Duration of GO (mon) | 12 (1–120) |
| Duration of GD (mon) | 24 (1–250) |
| Bilateral : Unilateral manifestation (n) | 35:14 |
| Best corrected visual acuity | |
| Right eye | 20/20 (20/100–20/20) |
| Left eye | 20/20 (20/50–20/20) |
| Upper lid retraction above limbus (n) | 38 |
| Exophthalmometry (mm) | |
| Right eye | 18 (12–26) |
| Left eye | 18 (12–26) |
| Current Gorman score of diplopia | 28 (57.1) / 4 (8.2) / 9 (18.4) / 8 (16.3) |
| Past history of optic neuropathy | 9 (18.4) |
| Current state of optic neuropathy | 4 (8.1) |
| Current clinical activity score | 1 (1–6) |
| Score 0 / 1 / 3 / ≥ 4 | 18 (36.7) / 27 (55.1) / 4 (8.2) |
| Current severity by EUGOGO classification | |
| Mild / Moderately severe / Sight-threatening | 28 (57.1) / 17 (34.7) / 4 (8.2) |
| Previous treatment (n) | |
| Prednisone | 22 |
| Radiotherapy | 1 |
| Decompression | 11 |
| Eye muscle surgery | 4 |
| Eye lid surgery | 7 |

Values are presented as median (range) or number (%) unless otherwise indicated. EUGOGO=European Group on Graves’ Orbitopathy; GO=Graves’ ophthalmopathy; GD=Graves’ thyroid disease. *2 of 11 eyes without retraction had previous surgeries for lid retraction.*
Fig. 1. Comparison between quality of life in patients with Graves’ ophthalmopathy (GO) (n=49) and normal individuals (n=48). All the subscales of Medical Outcomes Study Short-Form 36 (SF-36) were significantly lower in patients with GO than in normal individuals.

moderately severe, and sight-threatening Graves’ groups (Table 2), the four patients with sight-threatening Graves’ ophthalmopathy had significantly lower scores for physical functioning, role function-physical, and the physical component summary than the 28 patients with mild and 17 patients with moderately severe Graves’ ophthalmopathy (p<0.05). Patients with mild and moderately severe Graves’ ophthalmopathy had similar scores for most SF-36 items. A higher BDI score was observed in patients with sight-threatening Graves’ ophthalmopathy, as compared to patients with mild or moderately severe Graves’ ophthalmopathy, and a higher proportion of patients with sight-threatening Graves’ had depression (BDI score ≥16) than did patients with mild and moderately severe Graves’ (although this difference was not statistically significant).

Nine patients who were previously diagnosed with optic neuropathy but recovered after orbital decompression surgery or high-dose steroid treatment were included in the moderately severe group. No significant difference in SF-36 and BDI scores were observed between the 9 patients with previously diagnosed optic neuropathy and the remaining 8 patients in the moderately severe category (data not shown).

The 17 patients with a high Gorman score had a significantly lower physical component summary score on the SF-36 than the 32 patients with a low Gorman score (p=0.035) (Table 3). Compared to the low Gorman score group, the high Gorman score group also had lower subscale scores on the SF-36 for all measures but vitality, the mental component summary score, and mean BDI score (albeit without statistical significance).

Sixteen patients (32.7%) had BDI scores ≥16 (indicative of clinical depression). These patients had significantly lower scores on the eight subscales and two summary scores of the SF-36, as well as higher clinical activity scores, as compared to the 33 patients with low BDI scores (p<0.05) (Table 4). No significant differences were observed between the high and low BDI score groups with respect to age, sex, duration of Graves’ disease or Graves’ ophthalmopathy, or Hertel exophthalmos values. There were no significant differences between patients with high and low BDI scores in terms of current severity stage by EUGOGO classification, main cause of distress, or history of optic neuropathy (p>0.05). Although not statistically significant, it is interesting that 50% of patients in the depressed group (BDI≥16) reported that both functional impairment and facial disfigurement equally affected their emotional distress, whereas only 18.2% of patients in the non-depressed group (BDI<16) reported that both parameters were equally distressing (p=0.058) (Table 4). In addition, no significant correlation was observed between BDI score and age (r=0.025, p=0.863), sex (r=0.090, p=0.538), duration of Graves’ disease (r=0.113, p=0.441), duration of Graves’ ophthalmopathy (r=0.863, p=0.556), Gorman score (r=0.203, p=0.163), severity (r=0.209, p=0.150), or disease activity (r=0.201, p=0.166). However,

| Table 2. SF-36 subscales and BDI for the mild, moderately severe, and sight-threatening group |
|-----------------------------------------------|
| SF-36 | Mild (n=28) | Moderately severe (n=17) | Sight-threatening (n=4) | p-value |
|-----------------------------------------------|
| Physical functioning | 81.6±18.6 | 78.8±17.0 | 53.7±11.0 | 0.018* |
| Role limitations due to physical health | 62.5±36.3 | 58.8±34.2 | 6.3±12.5 | 0.014* |
| Bodily pain | 61.3±27.7 | 62.6±22.9 | 47.3±21.6 | 0.555 |
| General health perceptions | 48.3±18.1 | 43.8±13.6 | 41.0±14.1 | 0.667 |
| Vitality | 43.4±22.8 | 42.9±14.6 | 40.3±17.5 | 0.956 |
| Social functioning | 68.3±24.9 | 69.9±14.7 | 56.3±7.7 | 0.505 |
| Role limitations due to mental health | 65.5±41.1 | 60.8±41.2 | 53.4±38.5 | 0.349 |
| Mental health | 57.6±21.6 | 53.6±14.9 | 51.0±20.8 | 0.404 |
| Physical component summary | 45.5±7.9 | 44.9±7.2 | 34.6±7.6 | 0.035* |
| Mental component summary | 41.2±11.0 | 40.0±7.4 | 40.8±6.1 | 0.922 |
| BDI score | 11.3±7.3 | 13.6±7.0 | 15.5±10.0 | 0.412 |
| 16 or more, n (%) | 7 (25.0) | 7 (41.2) | 2 (50.0) | 0.418 |

Values are presented as mean±SD unless otherwise indicated.
BDI=Beck Depression Inventory; SF-36=Medical Outcomes Study Short-Form 36.
p<0.05.
### Table 3. SF-36 subscales and BDI for the higher and lower Gorman score groups

|                        | Gorman score 0,1 (n=32) | Gorman score 2,3 (n=17) | p-value |
|------------------------|-------------------------|-------------------------|---------|
| Physical functioning   | 81.9±17.8               | 71.8±19.6               | 0.086   |
| Role limitations due to physical health | 61.7±35.3               | 47.1±39.4               | 0.209   |
| Bodily pain            | 64.6±25.2               | 53.1±25.3               | 0.141   |
| General health perceptions | 49.3±16.7               | 41.8±14.6               | 0.115   |
| Vitality               | 42.9±21.3               | 44.4±16.5               | 0.794   |
| Social functioning     | 68.4±21.5               | 66.9±20.2               | 0.817   |
| Role limitations due to mental health | 63.5±40.9               | 56.9±42.1               | 0.598   |
| Mental health          | 56.6±20.7               | 55.3±16.4               | 0.807   |
| Physical component summary | 46.2±7.5               | 40.9±8.2               | 0.035   |
| Mental component summary | 40.5±9.9               | 41.3±8.7               | 0.773   |
| BDI score              | 10.9±5.9               | 15.2±9.1               | 0.054   |
| 16 or more, n (%)      | 8 (25.0)               | 8 (47.0)               | 0.117   |

Values are presented as mean± SD unless otherwise indicated.

BDI=Beck Depression Inventory; SF-36=Medical Outcomes Study Short-Form 36.

* p<0.05.

### Table 4. Comparison of the characteristics of depressed and non-depressed patients with Graves’ ophthalmopathy

| Characteristics                              | BDI <16 (n=33) | BDI ≥16 (n=16) | p-value |
|----------------------------------------------|----------------|----------------|---------|
| Age (yr)                                     | 40.2±13.6      | 43.8±12.9      | 0.390   |
| Sex                                          |                |                |         |
| Female                                       | 26 (78.8)      | 12 (75.0)      | 0.766   |
| Duration of GD (mon)                         | 33.2±36.9      | 48.4±62.46     | 0.380   |
| Duration of GO (mon)                         | 19.1±19.9      | 22.2±31.1      | 0.717   |
| Exophthalmometry (mm)                        |                |                |         |
| Right                                        | 17.8±3.1       | 18.7±3.6       | 0.439   |
| Left                                         | 17.7±3.2       | 19.2±3.2       | 0.134   |
| Current severity by EUGOGO classification    |                |                |         |
| Mild / Moderately severe / Sight-threatening | 21 / 10 / 2    | 7 / 7 / 2      | 0.396   |
| Current activity score                       | 1.0±1.3        | 2.3±1.7        | 0.009   |
| 4 or more                                    | 2 (6.0)        | 2 (12.5)       |         |
| Main cause of emotional distress             |                |                |         |
| Disfiguring change                           | 10 (30.3)      | 4 (25.0)       | 0.058   |
| Functional impairment                        | 17 (51.5)      | 4 (25.0)       |         |
| Both equally distressful                     | 6 (18.2)       | 8 (50.0)       |         |
| Past history of optic neuropathy             | 4 (12.1)       | 5 (31.3)       | 0.130   |
| SF-36                                        |                |                |         |
| Physical functioning                         | 84.1±16.5      | 66.6±18.3      | 0.003   |
| Role limitations due to physical health      | 69.7±32.9      | 29.7±30.6      | <0.001  |
| Bodily pain                                  | 67.9±25.7      | 45.4±17.9      | 0.001   |
| General health perceptions                   | 51.6±14.8      | 36.6±14.7      | 0.002   |
| Vitality                                     | 47.1±20.3      | 35.9±15.9      | 0.043   |
| Social functioning                           | 73.1±21.2      | 57.0±15.8      | 0.005   |
| Role limitations due to mental health        | 71.7±39.2      | 39.6±36.9      | 0.009   |
| Mental health                                | 61.8±18.8      | 44.5±14.4      | 0.001   |
| Physical component summary                  | 47.2±6.8       | 38.7±7.8       | 0.001   |
| Mental component summary                    | 43.3±9.5       | 35.5±6.9       | 0.002   |

Values are presented as mean±SD or number (%).

BDI=Beck Depression Inventory; SF-36=Medical Outcomes Study Short-Form 36; GD=Graves’ thyroid disease; GO=Graves’ ophthalmopathy.

* p<0.05.
Discussion

Because the goal of the treatment of Graves’ ophthalmopathy is to improve functioning and make patients look and feel better, the functional capacity and quality of life should be evaluated. The impact of Graves’ ophthalmopathy on quality of life has been the subject of several studies. The first article on quality of life in patients with Graves’ ophthalmopathy was published by Gerding et al [14], using a general quality of life questionnaire. In that study, the patient group was found to have lower score compared to a large reference group; however, the correlations between scores on general quality of life questionnaires and duration, severity, or activity of Graves’ ophthalmopathy were low [14]. An Australian group conducted a cross-sectional study using a modified instrument to measure quality of life in patients with Graves’ ophthalmopathy [15], finding a significant relationship between impaired quality of life and severity of ophthalmopathy, as measured by NOSPECS [5]. Yeatts [18] found a reduction in quality of life for both physical and mental health in patients with Graves’ ophthalmopathy using National Eye Institute visual functioning questionnaires (NEI-VFQ). Bradley et al. [19] used the NEI-VFQ to evaluate patients with Graves’ ophthalmopathy and found that these patients were especially impaired on the mental health subscale. Farid et al. [20] used the Profile of Mood State Survey in 48 patients with Graves’ ophthalmopathy and reported that patients with moderate to severe Graves’ ophthalmopathy exhibited significantly greater emotional distress than did patients with mild Graves’ ophthalmopathy.

To our knowledge, this is the first study that assesses both quality of life and the frequency and severity of depressive symptoms in Korean patients with Graves’ ophthalmopathy, although we did not use a Graves’ ophthalmopathy-specific questionnaire. The results show that patients with Graves’ ophthalmopathy had significantly lower quality of life scores than individuals in the age-and sex-matched control group, and that these scores were comparable to those of patients with other chronic diseases [21-23].

The prevalence of depression in this study was 32.7%, much higher than the 10% prevalence in the general population [24]. This is higher than the prevalence of depression found in patients with retinitis pigmentosa [20] and similar to patients with diabetes [25], cancer [26], or myocardial infarction [27]. Studies by Kahaly et al. [28] showed that 45% of patients with Graves’ ophthalmopathy have anxiety or depression, and patients with Graves’ ophthalmopathy score significantly lower than controls on measures of emotional role limitation and mental health. We assumed that both cosmetic disfigurement and functional impairment play key roles in causing emotional distress (including depression) in patients with Graves’ ophthalmopathy. Recently, Paik and Yang [29] showed that patients with moderate to severe ophthalmopathy reported significantly greater emotional distress than patients with mild ophthalmopathy, according to the Korean Profile of Mood States survey. In particular, patients whose disfiguring signs were predominantly due to proptosis had significantly greater emotional stress, as compared to patients in whom diplopia was predominant. In our study, however, no differences in Hertel exophthalmos values were observed between the high and low BDI score groups. As cosmetic disfigurement is acknowledged differently between patients and because there are other determinants of cosmetic disfigurement beyond proptosis (such as lid retraction, lid swelling, and conjunctival injection), we surveyed results from somewhat subjective self-questionnaires regarding the main cause of distress. More patients in the depressed group (BDI ≥16, 50%) reported that both functional impairment and facial disfigurement equally contribute to their emotional distress than did those in the non-depressed group (BDI <16, 18.2%) with borderline significance (p=0.058). Results from the current study are not consistent with the recent report by Paik and Yang [29] possibly because of different survey instruments and methods of analysis. We found that patients with Graves’ ophthalmopathy with depression had significantly lower quality of life (with lower SF-36 scores for all subscales), as compared to those without depression. Additionally, the BDI scores in patients with Graves’ ophthalmopathy were negatively correlated with the SF-36 score. Interestingly, patients with Graves’ ophthalmopathy and depression had significantly higher clinical activity scores, as compared with those without depression, indicating that the severity of depression is associated with current inflammatory symptoms, such as pain, swelling, and chemosis (p<0.05).

Patients in the high Gorman score group had significantly lower physical component summary scores than the patients in the low Gorman score group. Although the patients in the high Gorman score group had a higher mean BDI score than patients in the low Gorman score group, this difference was not statistically significant. Patients with bothersome diplopia are significantly impaired in their social and vocational functions because they cannot establish single binocular vision in primary gaze and create the largest possible field of single binocular vision [30]. Hatt et al. [31] found that median scores on the psychosocial subscale were significantly lower in patients with strabismus, as compared to visually normal adults.Successful treatment of strabismus, although not easy, significantly improves quality of life.

We found that patients with sight-threatening Graves’ ophthalmopathy had lower SF-36 scores and higher BDI scores than those with mild and moderately severe Graves’ ophthalmopathy. The SF-36 and BDI scores were not significantly different between the nine patients who were previously diagnosed with optic neuropathy but had recovered after orbital decompression surgery or high-dose steroid treatment and the others in the moderately severe group.
Although patients may have low quality of life and high depressive status due to sight-threatening severity, prompt and proper treatment will lead to better quality of life and eliminate depression.

Our study has several important limitations. The SF-36 is very broadly based, containing items to measure general aspects of health-related quality of life. It may miss relevant items for a specific disease and may not be able to measure small but clinically important changes for Graves’ ophthalmopathy. Therefore, a Korean version of a disease-specific quality of life questionnaire for patients with Graves’ ophthalmopathy is warranted. We did not diagnose depression using conventional diagnostic criteria, instead measuring symptoms of depression in patients with Graves’ ophthalmopathy using the BDI self-reported questionnaire, as the BDI is a good screening method for depression [32].

This study demonstrates that Graves’ ophthalmopathy can be a risk factor for depression and reduced quality of life. Patients with Graves’ ophthalmopathy that is sight-threatening or associated with significant diplopia showed the greatest impairment in quality of life. In addition, patients with depression were likely to have active inflammation. Our findings suggest the importance of assessing and managing the psychosocial burden and impairments in quality of life in patients with Graves’ ophthalmopathy and suggest that they should be considered part of standard follow-up. Psychological support or treatment is critical in the patient with Graves’ ophthalmopathy to eliminate depression and improve quality of life. Hence, a multidisciplinary approach, including ophthalmology, endocrinology, and psychiatry, is critical for patients with Graves’ ophthalmopathy. Such an integrated approach will help to define the extent of the problem and how patients adapt to living with the disease. In the future, extensive and randomized clinical studies are necessary for the assessment of the clinical effect of this multidisciplinary approach.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

This work was supported by the Yonsei University Research Resettlement Fund in 2008.

References

1. Bartalena L, Pinchera A, Marcocci C. Management of Graves’ ophthalmopathy: reality and perspectives. Endocr Rev 2000; 21:168-99.
2. Bartley GB, Fatourechi V, Kadrmas EF, et al. Clinical features of Graves’ ophthalmopathy in an incidence cohort. Am J Ophthalmol 1996;121:284-90.
3. Terwee CB, Gerdin MN, Dekker FW, et al. Test-retest reliability of the GO-QOL: a disease-specific quality of life questionnaire for patients with Graves’ ophthalmopathy. J Clin Epidemiol 1999;52:875-84.
4. Gerdin MN, Terwee CB, Dekker FW, et al. Quality of life in patients with Graves’ ophthalmopathy is markedly decreased: measurement by the medical outcomes study instrument. Thyroid 1997;7:885-9.
5. Park JJ, Sullivan TJ, Mortimer RH, et al. Assessing quality of life in Australian patients with Graves’ ophthalmopathy. Br J Ophthalmol 2004;88:75-8.
6. Elberling TV, Rasmussen AK, Feldt-Rasmussen U, et al. Impaired health-related quality of life in Graves’ disease. A prospective study. Eur J Endocrinol 2004;151:549-55.
7. Egle UT, Kahaly GJ, Potrak F, et al. The relevance of physical and psychosocial factors for the quality of life in patients with thyroid-associated orbitopathy (TAO). Exp Clin Endocrinol Diabetes 1999;107(Suppl 5):S168-71.
8. Terwee CB, Dekker FW, Mourits MP, et al. Interpretation and validity of changes in scores on the Graves’ ophthalmopathy quality of life questionnaire (GO-QOL) after different treatments. Clin Endocrinology 2001;54:391-8.
9. Terwee CB, Dekker FW, Prummel MF, et al. Graves’ ophthalmopathy through the eyes of the patient: A state of the art on health-related quality of life assessment. Orbit 2001;20:281-90.
10. Kahaly GJ, Hardt J, Petrak F, Egle UT. Psychosocial factors in subjects with thyroid-associated ophthalmopathy. Thyroid 2002;12:237-9.
11. Terwee C, Wakelkamp I, Tan S, et al. Long-term effects of Graves’ ophthalmopathy on health-related quality of life. Eur J Endocrinol 2002;146:751-7.
12. Bartalena L, Baldeschi L, Dickinson AJ, et al. Consensus statement of the European group on Graves’ orbitopathy (EUGOGO) on management of Graves’ orbitopathy. Thyroid 2008;18:333-46.
13. Gorman CA. The measurement of change in Graves’ ophthalmopathy. Thyroid 1998;8:539-43.
14. Han CW, Lee EJ, Iwaya T, Kohzuki M. Development of the Korean version of Short-Form 36-Item Health Survey: health related QOL of healthy elderly people and elderly patients in Korea. Tohoku J Exp Med 2004;203:189-94.
15. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71.
16. Shin M, Kim Z, Park K. The cut-off score for the Korean version of Beck Depression Inventory. Korean J Clin Psychol 1993;12:71-81.
17. Rhee MK, Lee YH, Park SH, et al. A standardization study of Beck Depression Inventory 1-Korean version (K-BDI); Reliability and factor analysis. Korean J Psychopathol 1995; 4:77-95.
18. Yeatts RP. Quality of life in patients with Graves ophthalmopathy. Trans Am Ophthalmol Soc 2005;103:368-411.
19. Bradley EA, Sloan JA, Novotny PJ, et al. Evaluation of the National Eye Institute visual function questionnaire in Graves' ophthalmopathy. Ophthalmology 2006;113:1450-4.
20. Farid M, Roch-Levecq AC, Levi L, et al. Psychological disturbance in Graves ophthalmopathy. Arch Ophthalmol 2005;123:491-6.
21. Gage H, Hendricks A, Zhang S, Kazis L. The relative health related quality of life of veterans with Parkinson's disease. J Neurol Neurosurg Psychiatry 2003;74:163-9.
22. Wong GL, Law FM, Wong VW, et al. Health-related quality of life in Chinese patients with primary biliary cirrhosis. J Gastroenterol Hepatol 2008;23:592-8.
23. Yun JH, Kang JM, Kim KS, et al. Health-related quality of life in Korean patients with chronic diseases. J Korean
24. Hahm BJ, Shin YW, Shim EJ, et al. Depression and the vision-related quality of life in patients with retinitis pigmentosa. *Br J Ophthalmol* 2008;92:650-4.

25. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24:1069-78.

26. Massie MJ. Prevalence of depression in patients with cancer. *J Natl Cancer Inst Monogr* 2004;32:57–71.

27. Kaptein KI, de Jonge P, van den Brink RH, Korf J. Course of depressive symptoms after myocardial infarction and cardiac prognosis: a latent class analysis. *Psychosom Med* 2006;68:662-8.

28. Kahaly GJ, Hardt J, Petrak F, Egle UT. Psychosocial factors in subjects with thyroid-associated ophthalmopathy. *Thyroid* 2002;12:237-9.

29. Paik JS, Yang SW. Evaluation of mood disturbance in Korean patients with dysthyroid ophthalmopathy. *J Korean Ophthalmol Soc* 2009;50:1301-7.

30. Schotthoefer EO, Wallace DK. Strabismus associated with thyroid eye disease. *Curr Opin Ophthalmol* 2007;18:361-5.

31. Hatt SR, Lesko DA, Bradley EA, et al. Development of a quality of life questionnaire for adults with strabismus. *Ophthalmology* 2009;116:139-44.

32. Bennett DS, Ambrosini PJ, Bianchi M, et al. Relationship of Beck Depression Inventory factors to depression among adolescents. *J Affect Disord* 1997;45:127-34.