

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

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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

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Study 36-Item Short Form Health Survey (SF-36) and Beck Depression Inventory (BDI) questionnaires, both of which are available in Korean versions which have been shown to be validated and reliable in other quality of life studies, to evaluate Korean patients with Graves' ophthalmopathy of varying degrees of disease activity and severity. The SF-36 items and scales are constructed using the Likert method of summated ratings. These ratings are summed to produce raw scale scores for each health concept and are transformed to a 0 to 100 scale, with 100 indicating the best possible score. The BDI has 21 items scored on a 4-point Likert scale (0 to 3). The converted scores from the questionnaires were evaluated with respect to the sociodemographic and clinical characteristics of the participants. These objective evaluations will aid in the identification of patients with Graves' ophthalmopathy who are more likely to need further physical and mental support.

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 \geq 2 mm, moderate or severe soft tissue involvement, exophthalmos \geq 21 mm, or inconstant (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.

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 \pm SD	41.4 \pm 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	
Score 0 / 1 / 2 / 3	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.

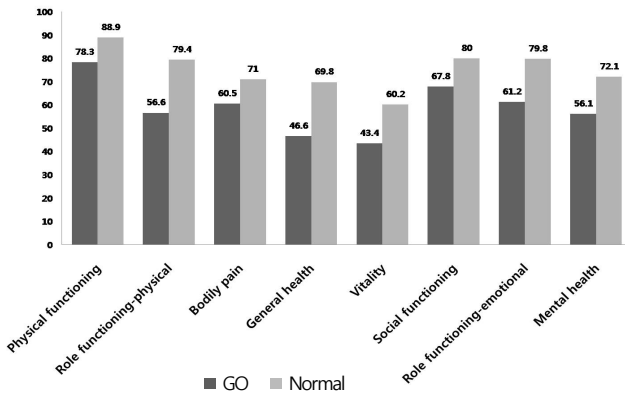


Fig. 1. Comparison between quality of life in patients with Graves' ophthalmopathy (GO) (n=49) and normal individuals (n=48). All the subscales of Medical Outcomes Study Short-Form 36 (SF-36) were significantly lower in patients with GO than in normal individuals.

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 now 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±7.2	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

SF-36	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.

* $p < 0.05$.

the BDI scores had significant negative correlations with all subscale scores on the SF-36 (data not shown, $p < 0.05$).

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.

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