

## REVIEW

# Psychological implications of Graves' orbitopathy

I Coulter, S Frewin, G E Krassas<sup>1</sup> and P Perros

Endocrine Unit, Level 6, Freeman Hospital, Newcastle upon Tyne, NE7 7DN, UK and <sup>1</sup>Department of Endocrinology and Metabolism, 'Panagia' General Hospital, Thessaloniki 55132, Greece

(Correspondence should be addressed to P Perros; Email: petros.perros@ncl.ac.uk)

## Abstract

Patients with thyroid eye disease, Graves' orbitopathy (GO), often appear distressed and it is likely that features of the condition such as disturbances in visual function, orbital discomfort and alterations in facial appearance can impart significant psychological morbidity upon the patient, which in turn can be detrimental to their quality of life. When considering the psychological impact of GO, two elements of the disease are important. The disfiguring changes to the eyes and face can have a direct effect upon psychological health, while physical aspects of the disease such as altered visual acuity, diplopia, orbital pain and lacrimation may influence psychological function as a secondary phenomenon, due to interference with daily living. Evidence appears to confirm the anecdotal impression of many clinicians dealing with GO patients that the prevalence of psychological morbidity in this patient group is high. A 'biopsychosocial' approach to care that addresses biological and psychosocial functioning as major determinants of health is an appropriate strategy when treating patients with GO.

*European Journal of Endocrinology* 157 127–131

## Introduction

Patients with Graves' orbitopathy (GO) often appear distressed, particularly in the early days after the diagnosis of the disease. It is probable that several factors contribute to their psychological state, but the predominant components are disturbances in visual function, orbital discomfort, alterations in facial appearance and the uncertainty of the future.

Psychological aspects of GO are important determinants of quality of life (QOL), which is a major outcome of disease management (1), and therefore of interest to clinicians treating these patients.

The impact of GO on QOL has been the subject of several recent studies (2–10), and a disease-specific-validated QOL questionnaire is now available for clinical use (11–13). However, psychological aspects of GO – including responses to medical or surgical therapies on psychological function – have not been studied systematically, and we are not aware of any psychological interventional studies in this disease.

## Psychological impact of GO

Several studies have examined the prevalence of psychological symptoms in patients with GO. Gerding *et al.* (2) studied 70 newly referred patients with GO at a tertiary centre. All patients were euthyroid at the time of the study. The Medical Outcomes Study-24 questionnaire (MOS-24) was used to assess general mood,

depression, anxiety and psychological well-being. The GO group of patients scored significantly worse than controls or other groups of patients with chronic diseases (heart failure, diabetes and emphysema). Studies by Kahaly *et al.* (6, 9) showed that 45% of 102 consecutive patients with GO suffered anxiety or depression, and as a group GO patients scored significantly lower than controls on 'emotional role' limitation (extent of limitation in work or daily activities due to emotional strain) and on 'mental health' using the Short Form-36 questionnaire. When compared with control and diabetic groups, psychosocial scales were substantially reduced in patients with GO. Emotional distress was common in patients with GO and associated with poor QOL. Anxiety and depression were present in 40 and 23% of patients, with GO respectively.

Another study (14) confirmed high levels of anxiety and depression in a population of GO patients. Furthermore, the degree of depression and anxiety was related to both visual changes and disfigurement of the eye. However, levels of anxiety and depression were not significantly different from an age- and sex-matched control group of patients with Graves' disease without GO. A recent evaluation of the National Eye Institute Visual Function Questionnaire 25 by Bradley *et al.* (15) found that patients with GO were especially impaired on the Mental Health subscale. These findings have been corroborated by Farid *et al.* (16) who utilised the Profile of Mood States survey to study mood disturbances in 48 patients with GO. Patients categorised as having moderate to severe GO exhibited significantly greater

emotional distress than a comparable group with mild GO. Yeatts (10) analysed the responses of 53 consecutive patients with GO to a battery of questionnaires and found that patients with GO reported greater impairment in both physical and mental health when compared with control groups. Disturbances in sleep, social functioning and work functioning were also found to be more common in GO patients than controls.

Bartley *et al.* (17) found that 10 years after the initial presentation to a tertiary centre, 61% of patients with GO reported that the appearance of their eyes remained abnormal and 38% of patients felt unhappy about their appearance.

Terwee *et al.* (7) studied 168 patients with GO approximately 12 years after their initial presentation. The health-related QOL scores (which included questions on psychological health) were considerably better than those of untreated newly diagnosed GO patients but worse than those of controls.

The evidence therefore confirms the anecdotal impression of many clinicians dealing with GO patients that the prevalence of psychological morbidity in this patient group is high. Furthermore, the psychological morbidity may persist and become chronic, although its severity may decline with the passage of time and as a result of treatment.

When considering the psychological impact of GO, several elements of the disease are important. The disfiguring changes to the eyes and face can have a direct effect upon psychological health, while physical aspects of GO such as altered visual acuity, diplopia, orbital pain or discomfort, retro-orbital 'tightness', photophobia, grittiness and excessive lacrimation may impact on psychological function as a secondary phenomenon due to interference with daily living. Separating the objective changes of the eyes of patients with GO from subjective symptoms in appraising the psychological impact of GO is no doubt an artificial distinction. Nonetheless, despite its limitations, such an analysis is worthy as it may impart insight to clinicians as to what aspects of management of this condition may be most appreciated by patients.

### **Prevalence and psychological consequences of different features of GO**

**Impaired vision** The commonest and greatest of fears in patients with eye diseases relate to the risk of blindness and the effect of this would have on their responsibilities and their ability to work and support their families (18). Difficulties with vision have a major impact on QOL (19–21). Although patients with GO are at risk of blindness through optic nerve compression or severe corneal exposure, these complications are now very rare. However, impaired vision in patients with GO is common due to the effects of excessive lacrimation,

photophobia, various degrees of dysmotility and changes in refraction caused by GO. Some of these alterations in visual function (for example, intermittent blurred vision due to excessive lacrimation) evade objective measurement.

The prevalence of impaired vision in patients with GO appears to be relatively high. A cross-sectional study of 101 patients attending our centre revealed that the prevalence of diplopia was 46% and visual acuity was reduced in 9% (22). In an incidence cohort of 120 patients from Olmsted County, Minnesota, 33% of patients complained of diplopia, 21% of excessive lacrimation, 16% of photophobia and 7% of blurred vision. Optic neuropathy was present in 9% of patients (23). In Kahaly *et al.* study of 102 patients with GO, 56% suffered from blurred vision, 41% complained of diplopia and 9% exhibited signs of optic neuropathy (9). Terwee *et al.* (7) reviewed 172 patients with GO who had been treated 10–20 years earlier with immunosuppressive therapies. Fifty-two percent of patients continued to experience double vision and 27% had low visual acuity. A recent study by Park *et al.* (8) studied 128 patients with GO, 72% of whom reported a GO-related impairment in their vision. Visual impairment therefore is common in patients with GO and chronic in a significant proportion of cases.

The impact of impaired vision on psychological parameters was studied by Frewin *et al.* (14). A cohort of 36 patients with GO were asked to complete a number of validated psychometric questionnaires. Ophthalmic assessments were performed within 2 weeks of completion of the questionnaires. Impaired vision (due to diplopia) was strongly associated with anxiety, depression, confusion, fatigue, anger and tension, using the Hospital Anxiety and Depression Scale and the Profile of Mood State. Kahaly *et al.* (6, 9) confirmed that diplopia had a major negative effect on QOL assessed by the SF-36 questionnaire. Bradley *et al.* (15) also found that health-related QOL scores were lower for those with symptoms of diplopia when compared with those without. Terwee *et al.* (4) confirmed in a prospective study of 164 patients with GO that improvement of visual functioning after treatment (orbital decompression, orbital irradiation or eye muscle surgery) led to significant improvements in QOL scores. These findings suggest that visual impairment induced by GO can have a detrimental impact upon a patient's QOL, but this may not be disease-specific. Interestingly, Yeatts (10) reported very little difference in vision-related quality of health between patients with GO and those with diabetic retinopathy or age-related macular degeneration.

**Eye discomfort** This is a common symptom, with a prevalence of 43–50% in patients with Graves' disease (9, 17). In the study by Bartley *et al.* (23) mentioned earlier, pain or discomfort was present in 30% of

patients, excessive, lacrimation in 21% and photophobia in 16%. Orbital pain was a major cause of distress in a cohort of 102 patients with GO (6, 9). A cohort of 60 patients with GO showed that 55% of patients reported symptoms of orbital pain, 65% excessive eye watering, 70% grittiness and irritation in one or both eyes and 55% photophobia (24); 97% of patients suffered from one or more eye discomfort-related symptoms. Orbital pain (either spontaneous or gaze-evoked) had a profound effect on QOL in one study (9). Using the MOS-24 questionnaire, marginally lower scores for 'bodily pain' were recorded among 70 patients with GO when compared with a large reference population (2). Health-related QOL seems to be primarily affected by physical and emotional problems with work or other daily activities.

### **Disfigurement**

Reference has already been made to the study by Bartley *et al.* (17) who reported that after 10 years of follow-up, 61% of patients with GO reported that the appearance of their eyes remained abnormal and 38% were unhappy because of it. Among a cross-sectional group of patients with GO, 63 out of 70 patients (90%) reported a change in their appearance as a result of GO, and the majority (53%) rated it as severe (11). Another study (24) demonstrated that in a cohort of 60 patients, 85% regarded themselves as having an altered facial appearance, 70% were aware of swelling of the lids and 67% regarded themselves as having bulging or protruding eyes. Park *et al.* (8) found in their assessment of patients with GO that 63% felt their disfigurement had significantly interfered with psychosocial functioning. Yeatts (10) has also found that patients with GO tend to have a significantly poor self-image when compared with control groups.

Disfigurement is difficult to define and is perceived differently by various people including patients. Terwee and co-workers (25) performed an interesting study whereby panels of endocrinologists, ophthalmologists, patients with GO and lay people were asked to rate the severity of disfigurement in 100 patients with GO shown in standard slides. There was a wide variation between individuals within the same panel and wider still between different panels. Highest concordance was between ophthalmologists (interclass correlation coefficient of 0.79). Patients with GO overrated and endocrinologists underrated the severity of disfigurement. The most important determinants of disfigurement were lid retraction, lid swelling and proptosis.

The mechanisms by which disfigurement leads to psychological dysfunction have been studied in diseases other than GO. Interference of disfigurement with social interaction appears to be a major contributor (26–28). The specific changes in the eyes associated with GO have

a particularly profound effect on social interaction. Engaging in eye contact and blinking play an essential role in sustaining the flow of social interaction (29), yet patients with GO stare and blink infrequently. Society expects non-verbal and verbal behaviour to be concordant (30). When people observe an inconsistency between what is said and what the body conveys, the non-verbal communication is usually taken as conveying the 'true' message. Proptosis, lid retraction and conjunctival redness are cues which are associated with aggression, surprise or fear (31). Six primary emotions associated with six universal facial expressions have been identified. Each facial expression is defined by the eyes and to a lesser extent of the mouth. The facial expression representing fear is that of a person with retracted upper and lower lids (31). It is interesting that Terwee *et al.* (25) demonstrated that proptosis (which is associated with lower lid retraction in patients with GO) had a negative influence on patients' perceived QOL. The eyes play an important role in human communication, particularly expression of emotion and determine how an individual is perceived by others (32). Examples are glaring, narrowing the eyes and blinking. Patients with GO may be unable to use these behaviours, or inadvertently appear to express emotions of anger or fear, due to the effects of the disease on the appearance of their eyes. It is not surprising that many patients with GO choose to avoid social interaction, although some patients, despite having severe facial changes appear to be psychologically unaffected. This may relate to personality traits and coping mechanisms employed by the patient.

Coping mechanisms are a conscious way of trying to adapt to stress and anxiety in a positive and constructive way, using thoughts and behaviours orientated towards searching for information, problem solving, seeking help from others, recognising one's true feelings and establishing goals and objectives (30). The ability to cope differs from individual to individual, depending on their resources (33). There are several different strategies used to help patients cope with disfigurement (34–36), but none has been assessed in patients with GO. Experience from other disfiguring conditions suggests that strategies which help the individual to confront rather than to avoid social situations are likely to be beneficial (37). Furthermore, the distress an individual feels may in part be associated with the stress of attempting to conceal a particular feature (38).

### **Relative contributions**

Although we have highlighted distinct potential contributors to the psychological morbidity of GO, it is often the case that the features mentioned above exist concomitantly. For instance, a patient affected psychologically by the disfiguring symptoms of GO such as proptosis, strabismus and eyelid retraction are also

simultaneously affected psychologically by physical symptoms such as pain, lacrimation, grittiness and photophobia. In light of this, a consideration of the psychological impact that features such as visual impairment, eye discomfort and disfigurement play is limited by the undoubted difficulty that both the patient and the clinician have in distinguishing the relative contribution of each feature to psychological morbidity.

### **Psychological outcome associated with treatment of GO**

Clinicians tend to focus on measurable objective parameters of disease activity or severity. The overall QOL, however, is probably equally important (5), and influenced by psychological responses to the disease and its treatments.

Psychological well-being has not been specifically studied as a treatment outcome in GO, but data on overall QOL are available. Although not validated, the subjective eye score (SES) has been used to assess patients' perceptions of treatments (39). The SES consists of asking patients to rate their eye condition on a scale from 1 to 10. Steroid therapy, i.v. immunoglobulin and orbital radiotherapy were associated with improvements in the SES; other studies have also reported positive results with regards to patients' expression of satisfaction with surgical and other treatments (40). In a prospective study, Terwee *et al.* (4) showed that patients responding to major treatments (orbital decompression or radiotherapy) had a 10–20 point improvement in GO-QOL scores. Eye muscle surgery and lid surgery were associated with a 3–10 point improvement. Patients regarded changes of 6–10 points as important. Tehrani *et al.* (41) employed a 90-item study questionnaire to evaluate decompression surgery with respect to clinical benefit and the patient's satisfaction. Of note, 78% were content with their eye symptoms and 71% were satisfied with the cosmetic result. A clinically relevant increase in QOL was found following surgical decompression.

### **Correlation between objective measures of GO and psychological parameters**

Objective disease outcomes often correlate poorly with psychological responses (42) and this has also been observed in patients with GO (40, 43). In a cross-sectional study of patients with GO (14), double vision was associated with the most profound alteration in mood, as measured by the Profile of Mood State Questionnaire. Reduced visual acuity did not correlate with either of the mood assessing questionnaires used in the study (Profile of Mood State, Hospital Anxiety and Depression Scale). Of the appearance changing parameters measured by the ophthalmologist, proptosis, conjunctival redness and lid swelling had the greatest impact on the patients' anxiety and depression levels.

Using the Profile of Mood States survey, Farid *et al.* (16) found that compared with control groups, patients with disfiguring signs (proptosis) were much more likely to have experienced emotional distress than patients with diplopia as the predominant clinical feature.

## **Conclusions**

Psychological morbidity is common in patients with GO. Disturbances in visual function, the physical discomfort of the disease and disfigurement are major contributors to psychological dysfunction in this condition. The individual patient's pre-morbid level of physical, psychological and social function, the intensity of perception of symptoms by the individual patient and his/her ability to apply effective coping mechanisms, are additional relevant factors that determine the magnitude of the psychological burden of GO. A 'biopsychosocial' approach to care that addresses biological and psychosocial functioning as major determinants of health is an appropriate strategy when treating the patient with GO. As well as medical, surgical and radiological therapies, this approach to care may incorporate other services which may benefit the psychological functioning of the patient such as counselling, support groups, a regular port of call with a healthcare professional such as a nurse specialist and even referral to a disease-specific psychiatric service where necessary.

## **References**

- 1 Testa MA & Simonson DC. Assessment of quality-of-life outcomes. *New England Journal of Medicine* 1996 **334** 835–840.
- 2 Gerding MN, Terwee CB, Dekker FW, Koorneef L, Prummel MF & Wiersinga WM. Quality of life in patients with Graves' ophthalmopathy is markedly decreased: measurement by the Medical Outcomes Study instrument. *Thyroid* 1997 **7** 885–889.
- 3 Egle UT, Kahaly GJ, Petrak F, Hardt J, Batke J, Best J & Rothenbacher M. The relevance of physical and psychosocial factors for the quality of life in patients with thyroid-associated orbitopathy (TAO). *Experimental and Clinical Endocrinology and Diabetes* 1999 **107** (Suppl 5) S168–S171.
- 4 Terwee CB, Dekker FW, Mourits MP, Gerding MN, Baldeschi L, Kalmann R, Prummel MF & Wiersinga WM. Interpretation and validity of changes in scores on the Graves' ophthalmopathy quality of life questionnaire (GO-QOL) after different treatments. *Clinical Endocrinology* 2001 **54** 391–398.
- 5 Terwee CB, Dekker FW, Prummel MF & Wiersinga WM. Graves' ophthalmopathy through the eyes of the patient: A state of the art on health-related quality of life assessment. *Orbit* 2001 **20** 281–290.
- 6 Kahaly GJ, Hardt J, Petrak F & Egle UT. Psychosocial factors in subjects with thyroid-associated ophthalmopathy. *Thyroid* 2002 **12** 237–239.
- 7 Terwee C, Wakelkamp I, Tan S, Dekker F, Prummel MF & Wiersinga W. Long-term effects of Graves' ophthalmopathy on health-related quality of life. *European Journal of Endocrinology* 2002 **146** 751–757.

- 8 Park JJ, Sullivan TJ, Mortimer RH, Wagenaar M & Perry-Keene DA. Assessing quality of life in Australian patients with Graves' ophthalmopathy. *British Journal of Ophthalmology* 2004 **88** 75–78.
- 9 Kahaly GJ, Petrak F, Hardt J, Pitz S & Egle UT. Psychosocial morbidity of Graves' orbitopathy. *Clinical Endocrinology* 2005 **63** 395–402.
- 10 Yeatts RP. Quality of life in patients with Graves' ophthalmopathy. *Transactions of the American Ophthalmology Society* 2005 **103** 368–411.
- 11 Terwee CB, Gerding MN, Dekker FW, Prummel MF & Wiersinga WM. Development of a disease specific quality of life questionnaire for patients with Graves' ophthalmopathy: the GO-QOL. *British Journal of Ophthalmology* 1998 **82** 773–779.
- 12 Terwee CB, Gerding MN, Dekker FW, Prummel MF, van der pol JP & Wiersinga WM. Test-retest reliability of the GO-QOL: a disease-specific quality of life questionnaire for patients with Graves' ophthalmopathy. *Journal of Clinical Epidemiology* 1999 **52** 875–884.
- 13 Wiersinga WM, Prummel MF & Terwee CB. Effects of Graves' ophthalmopathy on quality of life. *Journal of Endocrinological Investigation* 2004 **27** 259–264.
- 14 Frewin SE, Dickinson AJ, Kendall-Taylor P & Perros P. Psychosocial morbidity in patients with thyroid-associated ophthalmopathy. *Journal of Endocrinology* 1999 **160** (Supplement) 241.
- 15 Bradley EA, Sloan JA, Novotny PJ, Garrity JA, Woog JJ & West SKW. Evaluation of the National Eye Institute Visual Function Questionnaire in Graves' ophthalmopathy. *Ophthalmology* 2006 **113** 1450–1454.
- 16 Farid M, Roch-Levecq AC, Levi L, Brody BL, Granet DB & Kikkawa DO. Psychological disturbance in Graves' ophthalmopathy. *Archives of Ophthalmology* 2005 **123** 491–496.
- 17 Bartley GB, Fatourechhi V, Kadmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA & Gorman CA. Long term follow up of Graves' ophthalmopathy in an incidental cohort. *Ophthalmology* 1996 **103** 958–962.
- 18 Holland SP, Chee C & Grimes M. The challenge of eye disease: the patient's perspective. *Journal of Ophthalmic Nursing and Technology* 1991 **10** 52–54.
- 19 Salive ME, Guralnik J, Glynn RJ, Christen W, Wallace RB & Ostfeld AM. Association of visual impairment with mobility and physical function. *Journal of the American Geriatrics Society* 1994 **42** 287–292.
- 20 Lee PP, Spritzer K & Hays RD. The impact of blurred vision on functioning and well-being. *Ophthalmology* 1997 **104** 390–396.
- 21 Brook A, Elder A & Zalidis S. Psychological aspects of eye disorders. *Journal of the Royal Society of Medicine* 1998 **91** 270–272.
- 22 Perros P, Crombie AL, Matthews JN & Kendall-Taylor P. Age and gender influence the severity of thyroid-associated ophthalmopathy: a study of 101 patients attending a combined thyroid-eye clinic. *Clinical Endocrinology* 1993 **38** 367–372.
- 23 Bartley GB, Fatourechhi V, Kadmas EF, Jacobsen SJ, Ilstrup DM, Garrity JA & Gorman CA. Clinical features of Graves' ophthalmopathy in an incidence cohort. *American Journal of Ophthalmology* 1996 **121** 284–290.
- 24 Frewin SE, Dickinson AJ, Neoh C, Perros P & Kendall-Taylor P. Is self assessment of value in the assessment of thyroid eye disease? *Endocrinology Abstracts* 2001 **1** 229.
- 25 Terwee CB, Dekker FW, Bonsel GJ, Heisterkamp SH, Prummel MF, Baldeschi L & Wiersinga WM. Facial disfigurement: is it in the eye of the beholder? A study in patients with Graves' ophthalmopathy. *Clinical Endocrinology* 2003 **58** 192–198.
- 26 Goffman E. *Behaviour in Public Places: Notes on the Social Organisation of Gathering*. New York: Free Press, 1963.
- 27 Macgregor F. *Transformation and Identity: The Face and Plastic Surgery*. New York: Quadrangle, 1974.
- 28 Clarke A. Psychosocial aspects of facial disfigurement: problems, management and the role of a lay-led organisation. *Psychology, Health and Medicine* 1999 **4** 127–142.
- 29 Davis L. Perceptual problems in thyroid eye disease. *Nursing Standard* 1995 **9** 36–39.
- 30 Gross R. *Psychology: The Science of Mind and Behaviour*, edn. 2. London: Hodder & Stoughton, 1992.
- 31 Russell JA & Fernández-Dols JM (eds). *The Psychology of Facial Expression*. Cambridge: Cambridge University Press, 1997.
- 32 Morris D. *Body Watching: A Field Guide to the Human Species*. London: Jonathan Cape, 1987.
- 33 Bradbury E. *Counselling People with Disfigurement*. Leicester: British Psychological Society, 1996.
- 34 Lazarus R. *Psychological Stress and the Coping Process*. New York: McGraw Hill, 1966.
- 35 Grasha AF. *Practical Applications of Psychology*. Boston: Little, Brown & Co, 1983.
- 36 Partridge J. The psychological effect of facial disfigurement. *Journal of Wound Care* 1993 **2** 168–171.
- 37 Clarke A. The psychological impact of disfigurement in visible eye conditions. *Ophthalmic Nursing* 2000 **4** 14–17.
- 38 Root S, Kent G & Al-Abadie M. The relationship between disease severity, disability and psychological distress in patients undergoing PUVA treatment for psoriasis. *Dermatology* 1994 **189** 234–237.
- 39 Prummel MF, Mourits MP, Berghout A, Krenning EP, van der Gaag R, Koornneef L & Wiersinga WM. Prednisone and cyclosporine in the treatment of severe Graves' ophthalmopathy. *New England Journal of Medicine* 1989 **321** 1353–1359.
- 40 Terwee CB & Gerding M. Quality of life measurement in patients with Graves' ophthalmopathy. In *Thyroid Eye Disease*, pp. 163–183. Ed RS Bahn. Norwell MA, USA: Kluwer Academic Publishers, 2001.
- 41 Tehrani M, Krummenauer F, Mann WJ, Pitz S, Dick HB & Kahaly GJ. Disease-specific assessment of quality of life after decompression surgery for Graves' ophthalmopathy. *European Journal of Ophthalmology* 2004 **14** 193–199.
- 42 Guyatt GH, Feeny DH & Patrick DL. Measuring health-related quality of life. *Annals of Internal Medicine* 1993 **118** 622–629.
- 43 Prummel MF, Terwee CB, Gerding MN, Baldeschi L, Mourits MP, Blank L, Dekker FW & Wiersinga WM. A randomized controlled trial of orbital radiotherapy versus sham irradiation in patients with mild Graves' ophthalmopathy. *Journal of Clinical Endocrinology and Metabolism* 2004 **89** 15–20.

---

Received 28 March 2007

Accepted 8 May 2007