Quality of life improves after strabismus surgery in patients with Graves’ orbitopathy

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Abstract

Objective: To evaluate the influence of strabismus surgery on quality of life (QoL) in Graves’ orbitopathy (GO) patients.

Methods: Prospective study of case series.

The patients completed the GO-QoL questionnaire within 3 months before the surgery and 2–4 months after the surgery. A complete orthoptic examination, including the field of binocular single vision (BSV), was performed. Clinically relevant response (CRR) in the QoL was also evaluated.

Results: In this study, 28 patients were included. The GO-QoL score for visual functioning was 46.3 ± 24.2 before surgery and 65.7 ± 30.5 after surgery (P = 0.009). The GO-QoL score for appearance changed from 60.6 ± 25.9 to 69.5 ± 24.2 (P = 0.005).

After surgery, the field of BSV increased from 24.3 ± 34.8 to 68.5 ± 36.0 points (P = 0.000). A weak correlation was found between the field of BSV and the visual functioning score after surgery (r = 0.417; P = 0.034). CRR was found in 20 (71%) patients. Those with a CRR showed a larger field of BSV (P = 0.002) and better GO-QoL scores (P = 0.008).

Conclusions: GO-QoL score increases significantly for both visual functioning and appearance after the first strabismus surgery in GO-patients, showing the highest improvement for the visual functioning questions. Both the GO-QoL and field of BSV outcomes correlate well with the CRR.

Introduction

At least 40% of patients with Graves’ orbitopathy (GO) suffer from diplopia, which severely interferes with the activities of daily life such as working, driving a car or reading (1, 2, 3, 4). To assess the impact of the disease on functioning and appearance, the GO-quality of life (QoL) was developed in Dutch and English, validated and translated into six other languages (www.eugogo.eu) (2, 3, 4, 5). For both functioning and appearance, a total of 100 points can be scored. Terwee et al. (2001) (6) studied the effect of different surgical treatments on GO-QoL outcome and concluded that for strabismus surgery a minimum of six points of change has to be considered as minimal important change. However, to our knowledge, this minimal clinically important difference (MCID) was not confirmed by other studies.

The importance of QoL in evaluating the outcome of treatment has been extended by the European Group of Graves’ Orbitopathy and the Amsterdam declaration (6, 7, 8). Similarly, the goal of the present study is to assess the QoL before and after strabismus surgery in GO-patients. Approximately 170 new GO-patients are referred to our hospital each year and about 50 (29%) patients require strabismus surgery. This percentage is almost comparable with the numbers assessed in a previous study and a comparable setting (1). Improvement of QoL for the functional part can be achieved by creating the largest possible field of binocular single vision (BSV) (9). In the literature, this measurement is scarcely used as the outcome criteria (10, 11, 12, 13, 14). However, in the clinical setting, this instrument is the best available...
equipment for testing BSV in directions other than the primary position. The purpose of this study is to evaluate the effect of strabismus surgery on the QoL and to investigate the correlation between the GO-QoL and the field of BSV.

Subjects and methods

The study was conducted according to the principles of the Declaration of Helsinki (seventh edition, October 2008, Seoul) and in accordance with the Medical Research Involving Human Subjects Act (WMO). This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector. Our local ethical committee reviewed the research protocol and no approval was needed, because all interventions are normally carried out within the daily routine. Between December 2011 and September 2012, all consecutive GO-patients (clinically and biochemically euthyroid) in our tertiary referral center who needed a first strabismus surgery for diplopia were asked to participate in the study. The patients with pre-existent strabismus, suppression and/or vision <0.2 in one or both eyes were excluded. An informed consent form was signed by the patients who could be included in this study. Data regarding gender, date of first diagnosis of GO, prior treatment for their thyroid and eye disease and diplopia complaints before the strabismus operation were recorded. A full orthoptic examination was performed within 3 months before and 2–4 months after the surgery. This examination included the following: the prism cover test for near (30 cm) and distance (5 m) fixation, cyclo deviation at 2½ m using the Maddox Screen and the cycloforometer of Franceschetti (15), measurement of ductions by a motilitymeter (16), eye position measured in nine directions of gaze with the Maddox Glass and Maddox Screen (Amsterdam motility scheme) and the field of BSV at 2½ m using the Maddox Screen (17). A stable orthoptic examination during the last 3 months was part of the inclusion criteria. The choice of surgical procedure was based on the full orthoptic examination (17). There were no restrictions about the type of surgical procedure. The patients were operated by three orbital surgeons (R K, P S and M P M).

The patients completed both of the subscales within the GO-QoL: the visual functioning and the appearance questions (7). Questionnaires were self-administered, without supervision, following verbal and written instructions.

All the questions in the GO-QoL were scored as ‘severely limited’ (one point), ‘a little limited’ (two points) or ‘not limited at all’ (three points). The questions 1–8 and questions 9–16 were added up to two raw scores from 8 to 24 points, and then transformed to two total scores from 0 to 100 by the following formula: total score = (raw score / 16) × 100. Both the total scores hold that higher scores indicate better QoL. For questions 1 and 2, the answers ‘no drivers’ license’ or ‘never learned to ride a

Table 1

<table>
<thead>
<tr>
<th>Gaze position using the Maddox tangent screen</th>
<th>Score of BSV</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary position</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Up 5°</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Up 10°</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Up 15°</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Up 30°</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Down 10°</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Down 30°</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Right 10°</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Right 20°</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Right 30°</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Left 10°</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Left 20°</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Left 30°</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BSV, binocular single vision.

Table 2

<table>
<thead>
<tr>
<th>Gender</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>20</td>
</tr>
<tr>
<td>Age</td>
<td>54.5 ± 11.2</td>
</tr>
</tbody>
</table>

Diagnosis of GO

| Prior treatment | GO
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TDTC</td>
<td>36.5 ± 37.9 (7–216 months)</td>
</tr>
</tbody>
</table>

| Prior treatment | GO
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lubricants</td>
<td>11</td>
</tr>
<tr>
<td>Selenium</td>
<td>2</td>
</tr>
<tr>
<td>Steroids</td>
<td>2</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>3</td>
</tr>
<tr>
<td>Other immunosuppressive treatment</td>
<td>8</td>
</tr>
<tr>
<td>Decompression</td>
<td>16</td>
</tr>
</tbody>
</table>

Diplopia complaints

| Intermittent diplopia | 6 |
| Gaze-dependent diplopia | 12 |
| Constant diplopia | 9 |
| Abnormal head posture | 1 |

OG, Graves’ orbitopathy; GTD, Graves thyroid disease.

aMore therapies per patient are possible.
bike’ were scored as a missing value. When there were missing values for some items, total scores were calculated for the remaining completed items. The transformation was then adjusted as: total score $Z((\text{raw score} - K)/(2^K) \times 100)$ where $K$ is the number of completed items (6).

The outcome of the field of BSV was scored using a modified score system for diplopia by Holmes et al. (2005) (18) (Table 1). The original system is a subjective score system containing the questions about double vision during ‘reading’ (four points) and in ‘any position’ (one point). In addition, the question whether a person can get rid of the double vision ($K$1 point) is part of the score list. Those three questions were deleted and gaze positions, up $5^\circ$, right $20^\circ$ and left $20^\circ$, were added. Score points were reformatted and the score system was objectively used.

Two orthoptists (H M J and E M-T) independently defined the clinically relevant response (CRR) in each patient. The patients who showed clinically sufficient improvement on the Amsterdam motility scheme were called responders.

Statistical analyses were done using SPSS 19.0 (Statistical Package for the Social Sciences, Version 19.0). Each variable was verified for the normal distribution using the Kolmogorov–Smirnov test. If the data met the requirements for the normal distribution, parametric tests were applied; if not, non-parametric tests were used. To uncover the main and interaction effects of categorical independent variables on an interval dependent variable, ANOVA was used.

**Results**

In this study, 28 patients were included, and 21 patients were excluded because 13 of them needed a reoperation, two had suppression and thus no diplopia complaints, and for six of them the data were incomplete. Of the included patients, eight were male (29%) and 20 were female (71%). The mean age was $54.5 \pm 11.2$ years. All general data can be found in Table 2. The types of surgery are listed in Table 3.

The field of BSV changed from $24 \pm 35$ to $68 \pm 37$ points ($P=0.000$) (Fig. 1). The GO-QoL for visual functioning before surgery was $46 \pm 26$ points and increased to $66 \pm 31$ points after surgery ($P=0.009$).

The questions about appearance scored $61 \pm 26$ points before and $71 \pm 22$ points after surgery ($P=0.005$) (Fig. 2). A decompression that was performed earlier did not influence the outcome ($P=0.224$).

Between the diplopia groups (e.g. intermittent, gaze dependent, constant or abnormal head posture), no different outcome in the score of the preoperative field of BSV (ANOVA, $P=0.111$) or the score of the GO-QoL for visual functioning ($P=0.430$) was found.

A weak correlation was found between the field of BSV and the GO-QoL for the visual functioning score after surgery ($r=0.417; P=0.034$) (Fig. 3), but not for appearance ($r=0.180; P=0.374$).

CRR was found in 20 (71%) patients. The responders showed significantly larger fields of BSV ($P=0.002$) after surgery and better outcome of GO-QoL for visual functioning ($P=0.008$) compared with the non-responders.

**Discussion**

The present study is, to the best of our knowledge and inspired by the Amsterdam declaration, the first prospective study focusing on the QoL after strabismus surgery in GO-patients. After this strabismus surgery, a significant improvement in the GO-QoL score for both visual functioning and appearance occurs. Both the field of BSV and GO-QoL score after surgery are significantly higher in the responders group.

In contrast to a previous study, we found a significantly higher GO-QoL score for the visual functioning after surgery (mean improvement of $19.4 \pm 34.5$ in the present study...
compared with the mean of 2.8 ± 25.4 in the study of Terwee et al. (2001) (6). The improvement of the GO-QoL score is also higher as the mentioned six points of MCID (6). The hospital setting, duration of GO, mean age, sex distribution and number of participating patients (n = 31 vs present study, n = 28) are comparable in both studies. The improvement in the subjective score observed in this study is more similar to what clinicians would expect. Terwee et al. (6) could not clearly explain why the improvement in the subjective score in her study was rather modest. Explanations for the differences in results between her and our studies are the following: i) Terwee et al. sent questionnaires 3 months after the operation via mail, while our questionnaires were embedded in the treatment protocol. ii) As the questionnaire was embedded in the protocol, the response rate was 100% in our study when compared with the response rate of 80% in Terwee’s study. The 20% difference may be because of the non-responders who were asymptomatic, which had a negative influence on the total score. iii) For the last 5 years, strabismus surgery in GO-patients has been the focus of research in our institute, which might have improved the outcome of strabismus surgery, and thus the outcome of the subjective evaluation. To ratify this, the CRR rate in the study of Terwee et al. was 50% as we found 71% of patients responding to the strabismus surgery. iv) In the present study, only primary strabismus surgeries were included, whereas in the study of Terwee et al. this item is not specified. This could also clarify the difference between the visual functioning scores before surgery, which is lower at the baseline in the present study.

Terwee et al. (2001) (6) suggested that the surgery is part of a larger surgery plan and that this minor invasive strabismus surgery does not change the outcome significantly. However, in our study group, 16 patients underwent decompression surgery which counts for a major invasive surgery. GO-QoL was not different between the groups with and without prior decompression surgery (P = 0.224).

In general, one should take into account that changes in the GO-QoL score can be influenced by the side effects, costs and possible available alternative treatments like prism therapy. In addition, total score changes at the lower end of the score scale may be less important than changes at the higher end of the score (6). However, in contrast to the results of Terwee et al. (2001) (6), we had a lower baseline GO-QoL score (due to stricter inclusion criteria) and despite that there was a higher treatment effect. The side effect aspect may explain the weak correlation found between the GO-QoL for visual functioning and the field of BSV after surgery. The field of BSV is a clinical measurement in a setting wherein the patient’s head is being moved slowly, which is different from the movements in daily life (question 4 of the visual functioning questionnaire).

Another aspect which can influence the outcome of the GO-QoL is the regression of the mean phenomenon (19). However, by merely asking the patients to fill in the GO-QoL one time before and one time after the surgery, we cannot distinguish between the influence of the surgery and that of the regression of the mean.

It would be interesting to see whether the GO-QoL outcome also applies to the results 6–12 months after the surgery for orthoptic stability, as was found in our previous results (20). Hatt et al. (2012) (21) found no changes in the health-related QoL questionnaire 1 year after the surgery (HR-QoL) in both the diplopic and non-diplopic patients following a successful strabismus surgery. GO-QoL was not different between the groups with and without prior decompression surgery (P = 0.224).

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surgery. A future study may reveal whether this is also applicable for the GO-patient group.

We are aware of the fact that we evaluated the GO-QoL and BSV scores after one strabismus surgery and that multiple strabismus surgeries are needed for many patients (20, 22, 23), and therefore undervalue the final outcome. For that reason, a future study will focus on the effect after two surgeries.

In conclusion, the GO-QoL and the field of BSV outcome both add in their own way to the information for the clinician regarding CRR in GO-patients who undergo strabismus surgery.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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