Surgical treatment of diplopia in Graves' Orbitopathy patients
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UNILATERAL AND BILATERAL MEDIAL RECTUS RECESSION IN GRAVES’ ORBITOPATHY PATIENTS

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ABSTRACT

Purpose: To evaluate the effect of uni- and bilateral medial rectus recession on squint angle and ductions in Graves’ Orbitopathy (GO) patients.

Design: retrospective case series.

Materials and Methods: Consecutive GO-patients seen between January 2000 and March 2012 who were operated on one or both medial rectus muscles were selected for the study. Data regarding squint angle, abduction and adduction were collected starting 3 months before surgery and 3 and 6–12 months after surgery.

Results: 102 patients were eligible for inclusion. Of these, 24 patients were operated on one medial rectus and 78 on two medial rectus muscles. The dose-effect response was 1.0 [-0.6 - 3.8]°/mm in the unilateral and 1.4 [0.2 – 3.0]°/mm in the bilateral group (p = 0.000). In the bilateral group, the maximal ab- and adduction changed significantly (p = 0.000). However, the total duction range remained unchanged (unilateral: p = 0.525; bilateral: p = 0.137). The extent of the preoperative abduction did not influence the dose-effect response (r = - 0.234; p = 0.040), nor did the muscle volume (unilateral p = 0.989; bilateral p = 0.397). Twenty-three patients (23%) needed additional horizontal squint surgery.

Conclusion: In this large series of medial rectus recessions in patients with Graves’ disease we found significantly lower dose-effect response ratios as compared to other studies. The amount of abduction deficit does not influence outcome.
INTRODUCTION

Approximately 50% of patients with Graves’ Orbitopathy suffer from double vision, with a tremendous impact on daily life activities (Yeatts, 2005; Wiersinga et al., 2004; Wiersinga, 2012; Gerding et al., 1997). Diplopia in GO-patients is caused by enlarged and fibrosis of extra-ocular muscles; in particular the inferior rectus and medial rectus. GO often affects both orbits in an asymmetric manner. This asymmetric involvement is particularly responsible for the most complicated motility patterns. Several studies have focused on surgical treatment, primarily for vertical squint (Esser et al., 2011; Esser, 1993; Coats et al., 1999; Hoog de et al., 2009; Sprunger & Helveston, 1993; Flanders & Hastings, 1997; Prendiville et al., 2000; Dal Canto et al., 2006; Baker & Ansons, 2001; Kalpadakis et al., 2002; Kose et al., 2002; Cormack et al., 2007; Esser et al., 2011). Until now, no consensus has been reached on how to treat this patient group. Variation exists in surgical approach (adjustable sutures (Scott & Thalacker, 1981; Lueder et al., 1992; Flanders & Hastings, 1997; Russo et al., 2004; Mocan et al., 2007), fixed sutures, relaxed muscle positioning (Dal Canto et al., 2006)), type of muscle surgery (recession or resection (Pitz et al., 2005)), amount of recession and outcome criteria. Only a few studies focus on horizontal strabismus surgery. Most have small sample sizes and different surgical procedures and outcome criteria (Table 1) (Mocan et al., 2007; Pitz et al., 2005; Kalpadakis et al., 2004; Eckstein et al., 2004; Schittkowski et al., 2004; Esser, 1993).

<table>
<thead>
<tr>
<th>Table 1. Literature overview</th>
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<tbody>
<tr>
<td>Number of patients</td>
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<tr>
<td>Prior decompression</td>
</tr>
<tr>
<td>Unilateral (degree / mm ± SD)</td>
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<tr>
<td>Bilateral (degree / mm ± SD)</td>
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<tr>
<td>Not specified uni / bil (range, degree / mm ± SD)</td>
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</table>

* included vertical surgery; n = number of patients
The purpose of this study is to analyze the surgical effect / success rate of recession of the medial rectus muscle(s) in GO-patients with horizontal diplopia. Our goal is to present our results, to give recommendations when to perform a uni- or bilateral medial rectus recession and to present the effect of surgery on horizontal excursion.

MATERIALS 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). The ethical board has reviewed the study and concluded that no approval was needed.

Consecutive GO-patients operated for horizontal diplopia between January 2000 and March 2012 were included in this study. Patients who underwent simultaneous surgery for vertical diplopia were excluded, as well as patients with pre-existent strabismus, a history of previous surgery on the medial rectus muscles, suppression, and/or vision < 0.2 in one or both eyes. Data were taken from the records starting 3 months before surgery until 6 – 12 months after surgery. The horizontal deviation was measured in primary position with the Maddox rod glass using the Maddox tangent screen at 2½ meters (Gutter et al., 2010). The abduction and adduction was measured with the modified perimeter as described by Mourits et al. (Mourits et al., 1994).

Surgery was only performed when the orbitopathy was inactive. The definition of inactivity was based on the clinical ophthalmic exam (Clinical Activity Score) and stable orthoptic findings for at least 3 months. Fixed sutures were used for surgery and carried out by different surgeons. Dose-effect response was assumed to be 1.5°/ mm. Using this dose-effect response, unilateral recessions were generally performed if the horizontal squint angle was ≤10°. In patients with larger squint angles, a bilateral recession of the medial rectus muscles was performed. In cases where there was an asymmetrical restriction of abduction, a greater recession was conducted on the more restricted side. Muscle thickness (graded as normal, mild, moderate, severe) was analysed, semi-quantitatively, for all available CT scans by a team of orbital experts. Dose-effect response was calculated by dividing the ‘preoperative – postoperative squint angle’ by the amount of recession. Statistical analyses were done with SPPS 19.0 (Statistical Package for the Social Sciences, Version 19.0, Chicago, Illinois, USA). Each variable was verified for normal distribution with
the Kolmogorov-Smirnov test. If the data met the requirements for normal distribution, parametric tests were applied. If not, non-parametric tests were used. Results were considered statistically significant for $p < 0.05$.

### RESULTS

In total, 157 patients underwent horizontal squint surgery. Fifty-five patients had to be excluded, 10 due to loss of follow up and 45 due to simultaneously performed vertical strabismus surgery. A total of 102 patients fulfilled the inclusion criteria. Thirty (29%) patients were male and 72 (71%) were female. Mean age was 52.5±9.4 years. Orbital wall decompression was performed in 90 (88%) patients before strabismus surgery of which 48 patients underwent a 3 wall, 30 patients an inferior-medial wall, 8 a medial-lateral wall and 1 a medial wall decompression. In 18 patients, the decompression was performed via the coronal approach. The others have been operated using a swinging eyelid approach.

Twenty-four (24%) patients underwent surgery of one medial rectus muscle and 78 (76%) of both medial rectus muscles. Mean duration of the GO prior to the strabismus surgery was 33 [8 – 120] months. Mean recession was 3.3 [2.0 – 5.0] mm in the unilateral group and 4.5 [2.5 – 7.0] mm per eye in the bilateral group ($p = 0.003$). Data regarding squint angle are listed in Figure 1 and Table 2.

<table>
<thead>
<tr>
<th>Table 2. Pre- and postoperative orthoptic measurements</th>
<th>Unilateral group mean in degrees±SD ($n = 24$)</th>
<th>Bilateral group mean in degrees±SD ($n = 78$)</th>
</tr>
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<tbody>
<tr>
<td><strong>Horizontal deviation</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Primary position</strong></td>
<td></td>
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<tr>
<td>Preop</td>
<td>8.7 ± 4.9</td>
<td>18.1 ± 7.0</td>
</tr>
<tr>
<td>Postop &lt; 3 months</td>
<td>4.8 ± 4.2 ($p=0.000$)</td>
<td>5.1 ± 5.6 ($p=0.000$)</td>
</tr>
<tr>
<td>Postop 6 – 12 months</td>
<td>2.9 ± 5.0 ($p=0.423$)</td>
<td>4.6 ± 5.0 ($p=0.420$)</td>
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<tr>
<td><strong>Abduction</strong></td>
<td></td>
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</tr>
<tr>
<td>Preop</td>
<td>33.1 ± 8.1</td>
<td>29.4 ± 10.8</td>
</tr>
<tr>
<td>Postop &lt; 3 months</td>
<td>34.2 ± 7.8 ($p=0.368$)</td>
<td>33.5 ± 8.8 ($p=0.000$)</td>
</tr>
<tr>
<td>Postop 6 – 12 months</td>
<td>33.9 ± 6.5 ($p=0.745$)</td>
<td>35.8 ± 7.5 ($p=0.002$)</td>
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<tr>
<td><strong>Adduction</strong></td>
<td></td>
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<tr>
<td>Preop</td>
<td>40.2 ± 5.9</td>
<td>42.9 ± 6.9</td>
</tr>
<tr>
<td>Postop &lt; 3 months</td>
<td>38.1 ± 6.8 ($p=0.036$)</td>
<td>37.5 ± 7.8 ($p=0.000$)</td>
</tr>
<tr>
<td>Postop 6 – 12 months</td>
<td>38.4 ± 5.7 ($p=0.425$)</td>
<td>37.4 ± 7.3 ($p=0.877$)</td>
</tr>
<tr>
<td><strong>Total duction range</strong></td>
<td></td>
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</tr>
<tr>
<td>Preop</td>
<td>73.43 ± 12.17</td>
<td>71.9 ± 14.2</td>
</tr>
<tr>
<td>Postop &lt; 3 months</td>
<td>72.48 ± 12.7 ($p=0.525$)</td>
<td>70.7 ± 14.1 ($p=0.137$)</td>
</tr>
</tbody>
</table>

SD = standard deviation; $n$ = number
Figure 1. Squint angle measured with the Maddox rod glass at 2½ meter before and after surgery for unilateral (left boxplots) and bilateral (right boxplots) medial rectus recessions. *the outliers are two patients characterized by excessive squint angles ($\geq 30^\circ$) and severe limited abduction ($\leq 14^\circ$). This could be an explanation for their insufficient response to the surgery.

Figure 2. Mean abduction, adduction, and total duction range before and after surgery.
The preoperative squint angle was not influenced by the muscle volume \((p = 0.361)\), nor by the decompression approach (coronal versus inferior-medial; \(p = 0.436\)). Dose-effect response was \(1.0 [-0.6 \text{–} 3.8]^\circ/\text{mm}\) in the unilateral group and \(1.4 [0.2 \text{–} 3.0]^\circ/\text{mm}\) in the bilateral group \((p = 0.010)\). Overcorrection was observed in 3 patients. In 33\% of the unilateral group and in 20\% of the bilateral group a redo operation was considered necessary to correct the persisting horizontal deviation. Muscle volume did not influence the dose-effect response \((\text{unilateral} \ p = 0.989; \text{bilateral} \ p = 0.397)\) nor the incidence of a redo operation \((\text{unilateral} \ p = 0.921; \text{bilateral} \ p = 0.786)\).

As in the unilateral group only 2 patients underwent strabismus surgery without a preceding decompression, statistical evaluation of the influence of prior decompression surgery on dose-effect response was only possible in the bilateral group. We found no significant difference between prior decompression or no decompression \((\text{decompression} \ n = 67, \text{no decompression} \ n = 11; \ p = 0.748)\). The type of decompression also did not influence the dose-effect response \((p = 0.082)\).

In the bilateral group, the abduction increased after surgery \((p = 0.000)(\text{Fig. 2})\). No correlation was found between the dose-effect response and the preoperative abduction deficit \((r = -0.234; \ p = 0.040)\).

By 78 patients one operation was needed for their horizontal diplopia, 23 needed 2 and 1 needed 3 surgeries. With exception of the abduction of the bilateral group, all parameters were stable during the 6 – 12 months visit after surgery.

**DISCUSSION**

To the best of our knowledge, this study presents the largest case series of pure medial rectus recessions in GO-patients. The most intriguing question, e.g. how many patients benefitted from surgical intervention, cannot be answered, because till present no universally accepted definition of ‘success’ after squint surgery in GO-patients exists. However, in 77\% of our patients one surgical procedure was sufficient to correct their horizontal diplopia. We found significant lower dose-effect responses compared to other studies, especially in the unilateral cases. Bilateral medial rectus recession was found to have higher dose-effect response than unilateral medial rectus recession. Although the abduction changed significantly after bilateral surgery, the total duction range remained unchanged.
No more than 3 – 6 studies so far addressed the effect of the medial rectus recession in GO-patients until now (Mocan et al., 2007; Eckstein et al., 2004; Esser, 1993; Pitz et al., 2005; Kalpadakis et al., 2004; Schittkowski et al., 2004) (Table 1). In these studies, the dose-effect response in unilateral cases was markedly higher than found in this study. In Graves’ patients, Mocan et al. found approximately the same relationship as we did for bilateral medial rectus recessions (Mocan et al., 2007). However, in unilateral cases, we found no more than 1.0 degree per mm. This finding cannot be explained by the severity of the orbitopathy, because the choice for unilateral recession was based on a smaller squint angle, which most likely is associated with less severe GO. The discrepancy between our results and those of others, however, can be explained but not be compared by differences in inclusion criteria, operation technique, and differences in measuring the squint angle. In contrast to others, we calculated the amount of recession on the semi distance angle of 2½ meter as well as using a Maddox rod, both factors may influence the squint angle. This approach has no effect on the outcome of the dose effect response, because we measured the squint angle consistently, e.g. pre- and postoperatively in the same way. However, our way of assessing the squint angle does explain our relatively big residual esodeviation angle, as shown in Table 2, because the Maddox rod stimulates accommodation to which esodeviation is linked.

Following Eckstein et al. (2004), we excluded patients who underwent simultaneous vertical strabismus surgery because surgery in separate sessions gives less variability in outcome (Eckstein et al., 2004). Mocan et al. (2007) combined horizontal and vertical strabismus surgery which creates bias of the results (Mocan et al., 2007).

As observed in an earlier study about strabismus surgery in GO-patients we here again assessed that already 3 months after surgery the orthoptic status is stable (Jellema et al., 2012). This is of importance in planning further surgery. Mocan et al. (2007) mentioned an improvement towards orthotropia during their final evaluation, but it is unclear what their time frame was from surgery to their final evaluation.

Just as in previous studies, we found no clinically relevant correlation between the dose-effect response and the preoperative abduction deficit (Pitz et al., 2005; Nguyen et al., 2002). Although a significant change in ab- and adduction was found, we could only assess such a relationship in the bilateral group and, moreover, the amount did not exceed the ‘significant change of duction’ (i.e. 8°) as referred in literature (Prummel et al., 2004; Jellema...
et al., 2011). As found in vertical squint surgery, the total duction range remains stable after surgery (Jellema et al., 2012) which is very fortunate, because it creates a more centrally located field of binocular single vision.

The effect of preceding orbital decompression on squint surgery is unclear (Ruttum, 2000; Gilbert et al., 2005; Mocan et al., 2007). One study found more restriction of abduction if patients had a history of decompression (Mocan et al., 2007). We cannot support this finding: the results after orbital decompression in our series were comparable to those without previous orbital surgery. Our more precise measurement of ductions (0 – 60°) compared to measurement of Mocan et al. (0 – 4 grade) can account for this difference.

There are limitations to our study. The retrospective nature of this study creates bias, such as assignment bias. In the future, a prospective randomized controlled study can avoid this. Another limitation is that we do not have data about the squint angle at internationally accepted standard distances for comparison nor do we have data on how the patient is coping with his double vision. We cannot supply information on the subjective outcome of our operations, because patients did not yet fill in a quality of life questionnaire. Future studies should not only evaluate the objective, but especially the subjective outcome for squint surgery. A quality of life questionnaire has to be incorporated in research about diplopia treatment in GO-patients.

In conclusion, the outcome of strabismus surgery in GO-patients can be reasonably predicted taking into account the differences in the dose-effect response between the uni- and bilateral procedures. In almost 80% of these patients horizontal diplopia was resolved after one strabismus operation.
REFERENCES


