Orbital decompression in Graves’ orbitopathy: state of the art and novel perspectives
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Chapter 2

Early versus Late Orbital Decompression in Graves’ Orbitopathy
A Retrospective Study in 125 Patients

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Abstract

Purpose: To determine if early rehabilitative orbital decompression in Graves’ orbitopathy (GO) leads to a more effective postoperative outcome than the same intervention performed at a later, more likely, fibrotic stage.

Design: Retrospective comparative case series.

Participants: The medical records of all GO patients treated with a 3-wall orbital decompression at our institution between 1990 and 2000 were reviewed retrospectively. Only patients operated bilaterally for aesthetic rehabilitation, without preoperative diplopia, were included. They were divided into group 1 (duration of GO < 4 years) and group 2 (duration ≥ 4 years).

Methods and Main Outcome Measures: The 2 groups were compared for demographics, smoking habits, preoperative characteristics (immunosuppressive treatments, Hertel values, score in NOSPECS [no signs or symptoms, only signs, soft tissue involvement with symptoms and signs, proptosis, extraocular muscle involvement, corneal involvement, sight involvement] class 2, degree of extraocular muscle enlargement), and surgical outcome (mean reduction of exophthalmos, symmetry of exophthalmos reduction, reduction in upper and lower lid retraction, any persistent periorbital swelling requiring cosmetic eyelid surgery, postdecompression diplopia).

Results: The medical records of 125 of 376 patients were selected for this study. There were no differences between group 1 (n = 70) mean GO duration (2.2±0.8 years) and group 2 (n = 55) mean GO duration (9.0±5.4 years) with respect to demographics, smoking habits, and preoperative characteristics except for the degree of extraocular muscle enlargement, which was significantly greater in group 1 (P = 0.039). There was no difference in surgical outcomes between the 2 groups, with the exception of postdecompression diplopia, which was significantly more frequent in group 1 than in group 2 (29% vs. 13%, P = 0.033).

Conclusions: In GO, early rehabilitative orbital decompression does not improve surgical outcome and is associated with a higher risk of postdecompression diplopia.
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Introduction
Graves' orbitopathy (GO) is an inflammatory disorder characterized by autoimmune activity against orbital fibroblasts and adipocytes. The increased volume of the extraocular muscles, orbital connective tissues, and adipose tissues that develops leads to a mass effect, and may cause venous obstruction and congestion. Orbital fibrosis, which characterizes the final stage of GO, is a consequence of the long-lasting inflammatory and congestive involvement of the soft orbital tissues.

Prompt restoration of euthyroidism and, when necessary, immunosuppression represent the front line in the management of GO. Unfortunately, medical therapy alone is insufficient for many patients, and surgical intervention may be required for psychosocial rehabilitation and/or functional reasons. Rehabilitative surgery mostly consists of minor eyelid procedures, but in more severely affected patients, orbital decompression has to be considered.

Orbital compliance, which refers to the distensibility and plasticity of the orbital tissues, is reduced by orbital fibrosis in patients with GO. Reduced orbital compliance more likely occurs in the later stages of GO and may diminish the effectiveness of orbital expansion surgery due to the fact that orbital soft tissues can fail to prolapse maximally into the newly created spaces. The relationship between duration of GO at time of surgery and results of decompressive procedures, although incidentally mentioned, has never been specifically studied.

This study aimed to determine whether early orbital decompression is associated with a better postoperative outcome in terms of reduction of exophthalmos, symmetry in reduction of exophthalmos, reduction of periorbital swelling, reduction of eyelid retraction, and occurrence of the most frequent complication—namely, postdecompression diplopia.

Patients and Methods
Our study is a retrospective comparative case series. The medical records of all the patients affected by GO and treated with a 3-wall orbital decompression performed via a coronal approach at the Orbital Centre, Department of Ophthalmology, University of Amsterdam between January 1990 and December 2000 were evaluated retrospectively. Institutional review board approval was not required for this study.
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Inclusion Criteria

We included all patients (1) who were operated bilaterally for aesthetic rehabilitation and (2) who did not present with preoperative diplopia within 20° of the central position of gaze.

Exclusion Criteria

We excluded patients (1) who were operated unilaterally; (2) who were decompressed for optic neuropathy or exposure keratopathy; (3) who presented with preoperative diplopia; (4) who had been treated with iodine 131 in the 6 months preceding decompression or in the 6 months preceding postoperative evaluation; and (5) whose records did not clearly state (a) duration of GO at decompression, (b) smoking habits at surgery, (c) use of predecompression immunosuppressive treatments such as systemic corticosteroids and/or orbital radiotherapy, (d) results of an immediate preoperative clinical examination, including standard ophthalmological evaluation, NOSPECS (no signs or symptoms, only signs, soft tissue involvement with symptoms and signs, proptosis, extraocular muscle involvement, corneal involvement, sight involvement) classification, Hertel exophthalmometry, measurements of eyelid fissure, and the respective upper and lower eyelid positions, (e) results of at least one postoperative clinical examination performed ≥ 6 months after surgery, and (f) results of preoperative and postoperative orthoptic evaluations performed respectively not earlier than 6 months before decompression and between 3 and 6 months after surgery.

The following data were retrieved: (1) gender, (2) age at surgery, (3) duration of GO at decompression, (4) smoking habits at surgery, (5) use of predecompression immunosuppressive treatments, (6) preoperative Hertel values, (7) preoperative score in NOSPECS class 2, and (8) preoperative presence of upper and/or lower lid retraction with measurements of eyelid fissure and the respective upper and lower eyelid position. In addition to these, the degree of preoperative extraocular muscle enlargement was evaluated on coronal projections of orbital computed tomography scans, when available, and scored by a panel of 3 independent observers using a semiquantitative scale as absent, minimal, moderate, or severe. In case of discrepancy, the highest score was considered.

We considered as smokers those patients who were smokers on admission to the hospital at the time of surgery. The rationale for this choice is that in our center the clinical workup preceding rehabilitative orbital decompression consists of several ophthalmologic and
endocrinologic examinations. At all times, patients who smoke are strongly invited to give up smoking. We assume that those patients who maintain their habits up to the time of decompression despite multiple health warnings will not refrain from smoking after surgery.

The postoperative data that we used to assess the surgical outcome were (1) reduction of exophthalmos, (2) symmetry of exophthalmos reduction, (3) occurrence of reduction of upper and/or lower lid retraction when these signs were present before surgery, (4) persistence of periorbital swelling requiring cosmetic eyelid surgery, and (5) occurrence of postdecompression diplopia.

Based on the duration of the orbitopathy before decompression, the included patients were divided into 2 groups. Patients were included in group 1 when the duration of the orbitopathy before decompression was < 4 years and in group 2 when it was ≥ 4 years. The 4-year duration was chosen arbitrarily as a cutoff point because, in our view, such an interval may represent a reasonable border between the dynamic inflammatory phase and the static fibrotic stage of GO.

Demographics, smoking habits, and preoperative and postoperative data were compared between the groups by means of a database created in SPSS 11.5.2 Statistics UK (SPSS Inc., Chicago, IL). Right and left sides were not evaluated separately. Preoperative Hertel readings, NOSPECS class 2 score, and preoperative eyelid positions were the values measured at hospitalization for orbital decompression.

We considered as postoperative Hertel readings and postoperative eyelid positions the values measured at the first clinical examination carried out ≥ 6 months after surgery. For those patients presenting with a predecompression score ≥ a (mild) in NOSPECS class 2, persistence of periorbital swelling, implying the necessity for postdecompression cosmetic surgery, was defined as evidence in the medical record of upper or lower lid blepharoplasty proposed or performed at any time after orbital decompression. The presence of postoperative diplopia was assessed from the first orthoptic examination performed between 3 and 6 months after surgery.
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Statistical analysis

For univariate comparisons, Student’s t test was used to compare continuous variables. In case of ordinal or non-normally distributed variables, the Mann-Whitney U test was used. Categorical preoperative and postoperative data were investigated using the χ² test.

Surgical Technique

All the patients included in this study underwent standardized 3-wall decompression via a coronal approach, as is performed traditionally at our institution.11

A coronal incision was made with a no. 10 blade from ear to ear, 3 to 4 cm behind the hairline. In the central portion of the skull, a subperiosteal plane was created by blunt dissection, and laterally, a surgical plane was developed bluntly between the deep and superficial temporalis fasciae. The forehead flap thus created was then turned down to expose the superior and lateral orbital rims. The supraorbital nerve was set free by chiseling its bony foramen, when present, and the periorbita, including the trochlea, was dissected off the orbital bones. After this, the temporalis muscle was dissected from its anterior origin with a no. 10 blade and periosteal elevators, leaving sufficient tissue for suturing at the end of surgery. In this way, the lateral orbital wall was exposed. A small osteotomy was chiseled behind the lateral orbital rim, and bone-nibbling rongeurs were used to remove the middle portion of the lateral orbital wall. After this, a Frazier suction tip was used to fracture the delicate bone of the medial orbital wall and the floor, and Blakesley forceps nos. 1 and 2 were used to remove bony fragments and sinuses’ mucosa. The bulla ethmoidalis beneath the frontoethmoidal suture was opened towards the orbit from the posterior lacrimal crest up to the orbital apex, and then the orbital floor medial to the infraorbital canal was removed from 0.5 cm behind the inferior orbital rim up to the posterior wall of the maxillary sinus. The posterior two thirds of the maxillary ethmoidal strut was removed, creating a wide antrostomy, whereas the anterior one third of the strut was left intact to prevent globe displacement and the possibility of medial entropion or hypoglobus.

Finally, the periorbita was incised to promote maximal prolapsed of the orbital tissues into the newly created spaces, the temporalis muscle was sutured back into position with 4 to 5 interrupted 2/0 Mersilene sutures (Ethicon, Inc., Somerville, NJ), and after the insertion of a 3.3-mm-diameter end-perforated wound drain into each temporalis fossa, the scalp incision was closed with iron staples.
Results

Medical records of 125 of 376 patients were selected for this study; 251 were excluded because they did not meet the inclusion criteria or the necessary data were not recorded.

Demographics, Smoking Habits, and Preoperative Characteristics

There were no differences between group 1 (n = 70) and group 2 (n = 55) with respect to demographics, smoking habits, or preoperative characteristics, except for the degree of extraocular muscle enlargement, which was significantly greater in group 1 (P = 0.039) (Table 1).

Table 1. Demographics, Smoking Habits, and Preoperative Characteristics in Group 1 and 2

<table>
<thead>
<tr>
<th></th>
<th>&lt;4 yrs (n=70)</th>
<th>≥4 yrs (n=55)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>93%</td>
<td>93%</td>
<td>P = 0.978</td>
</tr>
<tr>
<td>Age at surgery (yrs ± SD)</td>
<td>40.0 (9.2)</td>
<td>40.4 (10.9)</td>
<td>P = 0.836</td>
</tr>
<tr>
<td>Duration of GO at surgery (yrs ± SD)</td>
<td>2.2 (0.8)</td>
<td>9.0 (5.4)</td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>56%</td>
<td>54%</td>
<td>P = 0.471</td>
</tr>
<tr>
<td>Preoperative immunosuppression:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>14%</td>
<td>11%</td>
<td>P = 0.301</td>
</tr>
<tr>
<td>Orbital radiotherapy</td>
<td>27%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>Neither corticosteroids nor orbital radiotherapy</td>
<td>16%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Hertel values (mm) (± SD)</td>
<td>21.8 (2.5)</td>
<td>22.5 (2.5)</td>
<td>P = 0.415</td>
</tr>
<tr>
<td>Score in NOSPECS class 2*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6%</td>
<td>15%</td>
<td>P = 0.312</td>
</tr>
<tr>
<td>a</td>
<td>63%</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>30%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>1%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Degree of extraocular muscle enlargement:†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>54%</td>
<td>79%</td>
<td>P = 0.039</td>
</tr>
<tr>
<td>minimal</td>
<td>27%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>moderate</td>
<td>16%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>severe</td>
<td>3%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

GO = Graves’ orbitopathy; NOSPECS = no signs or symptoms (class 0); only signs (class 1); soft tissue involvement with symptoms and signs (class 2); proptosis (class 3), extraocular muscle involvement (class 4), corneal involvement (class 5), sight involvement (class 6); SD = standard deviation.

*On the basis of a semiquantitative scale (0, absent; a, mild; b, moderate; c, severe).
†Only when coronal projections of orbital CT scan were available: <4yrs (n=56); ≥4yrs (n=39).

Surgical Outcome

There were no statistically significant differences in mean reduction of exophthalmos and symmetry of exophthalmos reduction between the 2 groups. When the predecompression score in NOSPECS class 2 was ≥ a, there were no statistically significant differences
between the 2 groups in persistence of postdecompression periorbital swelling requiring upper or lower lid blepharoplasty. The occurrence of reduction of upper and lower lid retraction also did not differ statistically when these signs were present before surgery. In contrast, the occurrence of postdecompression diplopia was significantly ($P = 0.033$) more frequent in group 1 (Table 2), the relative risk and risk difference for decompressioninduced diplopia being 2.3 and 18.1%, respectively.

### Table 2. Postoperative Outcome

<table>
<thead>
<tr>
<th></th>
<th>&lt;4 yrs (n=70)</th>
<th>≥4 yrs (n=55)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exophthalmos reduction (mm ± SD)</td>
<td>4.5 (1.8)</td>
<td>4.2 (1.9)</td>
<td>$P = 0.456$</td>
</tr>
<tr>
<td>Symmetry in exophthalmos reduction</td>
<td>≤1mm (87%)</td>
<td>≤1mm (89%)</td>
<td>$P = 0.739$</td>
</tr>
<tr>
<td></td>
<td>&gt;1mm (13%)</td>
<td>&gt;1mm (11%)</td>
<td>$P = 0.502$</td>
</tr>
<tr>
<td>Occurrence of reduction of upper lid retraction *</td>
<td>58%</td>
<td>50%</td>
<td>$P = 0.771$</td>
</tr>
<tr>
<td>Occurrence of reduction of lower lid retraction ‡</td>
<td>65%</td>
<td>62%</td>
<td>$P = 0.911$</td>
</tr>
<tr>
<td>Persistence of post-decompression periorbital swelling requiring cosmetic surgery ‡</td>
<td>50%</td>
<td>49%</td>
<td>$P = 0.033$</td>
</tr>
<tr>
<td>Post-decompression diplopia</td>
<td>29%</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>

SD = standard deviation.
* Only patients who presented with this sign before surgery: <4yrs (n = 48); ≥4yrs (n = 47).
† Only patients who presented with predecompression score in NOSPECS (no signs or symptoms, only signs, soft tissue involvement with symptoms and signs, proptosis, extraocular muscle involvement, corneal involvement, sight involvement) Class 2 ≥ x: <4yrs (n = 66); ≥4yrs (n = 47).
‡ Only patients who presented with predecompression score in NOSPECS (no signs or symptoms, only signs, soft tissue involvement with symptoms and signs, proptosis, extraocular muscle involvement, corneal involvement, sight involvement) Class 2 ≥ x: <4yrs (n = 66); ≥4yrs (n = 47).

### Discussion

To the authors’ knowledge, the literature that evaluates the relationship between results of decompressive procedures and duration of the orbitopathy at surgery is scarce. At present, the assumption that links early intervention with more attractive results is hypothetical, often mentioned at meetings, and based on the natural course of the orbital disease.

McCord\(^{14}\) quantified the result of aesthetic orbital decompression by measuring the retrodisplacement of the globe in 23 patients. They concluded that the amount of retrodisplacement varied and depended strictly on orbital fibrosis, but neither duration of the orbitopathy at surgery nor explanations of the method to determine orbital fibrosis were given. Härting et al.\(^{11}\) advocated early intervention without providing data to support their preference. Kalmann et al.\(^{12}\) reported no significant relation between duration of GO and the amount of proptosis reduction after 3-wall orbital decompression in 250 orbits.
However, because that study was not carried out specifically to evaluate this particular aspect, patient characteristics according to duration of the orbitopathy were not given, and the mean duration of the orbital disease was only 4.35 years.

Male gender, old age, and heavy smoking habits are patient characteristics that are known to be associated with a more severe orbital disease\textsuperscript{15-17}, whereas preoperative Hertel values have been regarded as a factor influencing the amount of exophthalmos reduction.\textsuperscript{12}

The 2 groups compared in this survey did not differ with respect to gender, mean age at surgery, or smoking habits. Because other predecompression characteristics, such as Hertel values, NOSPECS class 2 score, and use of immunosuppressive treatments also did not differ, it is conceivable that the 2 groups were not dissimilar in either severity of GO at surgery or its activity during the active phase of the disease. In addition, based on our inclusion criteria, only patients decompressed for aesthetic reasons and not presenting with diplopia within 20\degree of the central position of gaze were included. Therefore, groups 1 and 2 can be considered to be composed of a homogeneous population of Graves’ patients, only differing in duration of the orbitopathy at decompression. The observed difference in preoperative volume of the extraocular muscles is, in fact, just the tomographic representation of the different pathophysiological periods that characterize the 2 groups. Therefore, it should be regarded as a consequence of the duration of the orbitopathy in group 1 and 2, rather than a self-standing characteristic of the groups.

Our retrospective observations did not show any statistically significant correlation between duration of the orbitopathy at decompression and (1) reduction of exophthalmos, (2) symmetry of exophthalmos reduction, (3) persistence of postdecompression periorbital swelling requiring postdecompression cosmetic surgery, and (4) amelioration of upper or lower lid retraction, whereas in our series patients decompressed within 4 years from the onset of the orbitopathy seemed to run a higher relative risk of postdecompression diplopia than patients decompressed later than 4 years.

The higher frequency of postdecompression diplopia in group 1 can be explained by the greater preoperative enlargement of the extraocular muscles in this group as compared with group 2, despite similar preoperative Hertel values in the 2 groups. This implies a more consistent contribution of the extraocular muscle mass to exophthalmos in group 1. Therefore, it is feasible to deduce from the similar reduction of exophthalmos that was achieved in the 2 groups that, for group 1, there was a more consistent shift of extraocular
muscles into the spaces newly created by decompression surgery. This could have led to a greater decompensation of extraocular muscle balance in group 1. Differing motor and/or sensory capacities for compensation of induced muscle imbalance between the 2 groups also may have played a role. Further investigations are required to clarify this.

In conclusion, in contrast to the assumption that early intervention is related to a more desirable surgical outcome, our observation links early intervention with a higher risk of postdecompression diplopia. Our results, however, are far from conclusive, because the study might have been biased by systemic corticosteroid use, orbital radiotherapy, and relatively low preoperative Hertel values. The immunosuppressive effect of corticosteroids and/or radiotherapy has influenced the pathophysiological course of the disease and might have reduced the final orbital fibrosis in about half of our patients. On the other hand, the toxicity of radiation therapy to soft tissues, which includes fibrotic sequelae, might have reduced the distensibility and plasticity of the soft orbital tissues, decreasing the effect of decompression surgery. In addition, the low mean preoperative Hertel values in the 2 groups can be regarded as the epiphenomenon of a minimally to moderately increased intraorbital pressure, which reasonably induced only mild congestion, leading to scarce final fibrosis.

We acknowledge that, to overcome the shortcomings of our retrospective analysis, a prospective clinical trial would be needed, with some design difficulties. If only patients who did not require treatment with systemic corticosteroids or orbital radiotherapy were included, the study would enroll only those patients with milder disease who, presumably, are less prone to develop late fibrosis. On the other hand, it would be ethically questionable to design a study in which immunosuppression is not administrated to reduce biases, and patients are randomized to early or late decompression.

Patients with GO who do not have prompt access to diagnosis and medical treatment and who finally present to the orbital surgeon with advanced disease could offer an adequate population for a prospective study aimed to validate our major conclusions.
Chapter 2

References