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

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The Influence of Previous Orbital Irradiation on the Outcome of Rehabilitative Decompression Surgery in Graves’ Orbitopathy

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Abstract

**Purpose:** To investigate whether orbital irradiation influences the outcome of decompression surgery in Graves’ orbitopathy.

**Design:** Retrospective, comparative case series.

**Methods:** The medical records of all the patients with Graves’ orbitopathy treated with a three-wall orbital decompression through a coronal approach at our institution between January 1, 1990 and December 31, 2000 were reviewed. Only patients who underwent bilateral surgery for aesthetic rehabilitation, without preoperative diplopia, and who, in the active phase of the disease, had received orbital radiotherapy alone (20 Grays (Gy) in 10 daily fractions of two Gy over a period of two weeks; group R), systemic glucocorticoids alone (daily administration for more than three months independently from the dosage; group G), or both radiotherapy and glucocorticoids (group RG) were selected. Groups were compared for demographics, smoking habits, predecompression characteristics, and surgical outcome (mean reduction of exophthalmos, reduction of lid retraction, persistence of periorbital swelling requiring cosmetic eyelid surgery, onset of diplopia within 20 degrees of the central position of gaze, and variations in the peripheral field of diplopia).

**Results:** Sixty-one of 376 patients were selected for this study. There were no differences between group R (n = 29), group G (n = 15), and group RG (n = 17) with respect to demographics or predecompression characteristics, whereas the number of smokers was significantly greater in group RG ($P = 0.019$). We could not find differences in surgical outcome by comparing the three groups.

**Conclusions:** The total radiation dose, fraction size, and irradiated volume commonly used to treat active Graves’ orbitopathy do not adversely interfere with the outcome of rehabilitative decompression surgery.
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Introduction
Since 1913, external beam irradiation therapy has been used for the treatment of Graves’ orbitopathy.\(^1\) Initially, when exophthalmos was thought to be the result of dysfunction of the hypothalamus and the pituitary gland, radiotherapy was aimed at these structures. It later became clear that only those patients with iatrogenic orbital irradiation resulting from poorly collimated radiation delivery systems improved. Radiotherapy subsequently was directed to the orbital tissues behind the globe.\(^2\)

Although its efficacy was questioned recently\(^3\), orbital radiotherapy continues to represent a mainstay in the management of active Graves’ orbitopathy. This is largely the result of its superiority of optimal tolerance and almost no short-term side effects, as opposed to the alternative of systemic immunosuppression with glucocorticoids.\(^4\) Issues of concern with radiotherapy in benign diseases are the long-term adverse effects of ionizing radiation to tissue, which in the case of Graves’ orbitopathy may lead to an increased risk of malignancy in the head and neck region, retinopathy, cataract formation, and diffuse fibrosis of the retroocular soft tissues. So far, no secondary tumors have been observed in long-term follow-up studies, and ocular complications, such as retinopathy or cataract, do not seem to represent real aftermaths of orbital irradiation for Graves’s orbitopathy.\(^5\) Fibrosis of the orbital soft tissues secondary to radiation therapy may influence the results of later surgical procedures such as squint or decompression surgery. Preoperative radiotherapy was demonstrated not to affect squint surgery adversely\(^6\), but its effect on orbital decompressions remains undetermined. Although this issue has been mentioned incidentally in the literature\(^7,8\) and is a source of debate at meetings, we are unaware of previous reports that link orbital radiotherapy to the effects of decompression surgery in patients with Graves’ orbitopathy, and a computerized search using MEDLINE failed to reveal any references. This study sought to determine whether orbital irradiation in Graves’ orbitopathy influences the outcome of rehabilitative decompression surgery.
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Patients and Methods

Our study was a retrospective, comparative case series. The medical records of all the patients with Graves’ orbitopathy who underwent three-wall orbital decompression performed via a coronal approach at the Orbital Center, Department of Ophthalmology, University of Amsterdam, between January 1, 1990 and December 31, 2000 were evaluated retrospectively.

Inclusion Criteria

We included all patients who: 1) had undergone bilateral surgery for aesthetic rehabilitation, 2) did not have preoperative diplopia within 20 degrees of the central position of gaze, and 3) had been treated, in the active phase of Graves’ orbitopathy, with bilateral orbital radiotherapy alone (total dose of 20 Grays (Gy) in 10 daily fractions of two Gy over a period of two weeks), systemic glucocorticoids alone (for a period of at least three consecutive months independently from dosage regimens), or with both retrobulbar radiotherapy and systemic glucocorticoids.

Exclusion Criteria

We excluded patients who: 1) had undergone unilateral surgery; 2) were decompressed for optic neuropathy or exposure keratopathy; 3) did not receive bilateral orbital radiotherapy, systemic glucocorticoids or both the treatments in the active phase of Graves’ orbitopathy or did not receive these treatments as specified in the inclusion criteria; 4) had preoperative diplopia; 5) had been treated with thyroidectomy or iodine 131 in the six months preceding decompression or in the six months preceding postoperative evaluation; 6) had concurrent orbital or periorbital diseases, injuries, or surgeries (except for postdecompression blepharoplasty) within six months after decompression; and 7) whose records did not clearly state the duration of Graves’ orbitopathy at decompression; smoking habits at surgery; the date and method of administration of predecompression orbital radiotherapy or systemic corticosteroids; the results of an immediate preoperative clinical examination, including standard ophthalmologic evaluation, NOSPECS (no signs or symptoms, only signs, soft tissues involvement with symptoms and signs, proptosis, extraocular muscle involvement, corneal involvement, sight involvement) classification,9 Hertel exophthalmometry, measurements of eyelid fissure and respective upper and lower eyelid positions; the results of at least one postoperative clinical examination performed six months or more after surgery; the results of preoperative and postoperative orthoptic
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We considered smokers to be those patients who were smokers on admission to the hospital at the time of surgery. In our center, the clinical work-up preceding rehabilitative orbital decompression consists of several ophthalmologic and endocrinologic examinations. Patients who smoke are strongly encouraged to give up smoking at all times. We assume that those patients who maintain their habit up to the time of decompression, despite multiple health warnings, will not refrain from smoking after surgery.

The postoperative data we used to assess the surgical outcome were: 1) reduction of exophthalmos; 2) reduction of upper or lower lid retraction, or both, when these signs were present before surgery; 3) persistence of periorbital swelling requiring cosmetic eyelid surgery; 4) occurrence of postdecompression diplopia within 20 degrees of the central position of gaze; and 5) variations in the peripheral field of diplopia. Postoperative Hertel readings and postoperative eyelid positions were those measured at the first clinical examination carried out six months or more after surgery.
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The included patients were divided into three groups based on the immunosuppression treatments administered in the active phase of Graves’ orbitopathy: those who had received orbital radiotherapy alone were included in group R, those who had received systemic glucocorticoids alone were included in group G, and those who had received both orbital radiotherapy and systemic glucocorticoids were included in group RG. Patients in group R were compared with those of groups G and RG for demographics, smoking habits, and preoperative and postoperative data by means of a database created using version 11.5.2 of the SPSS statistical analysis software package (SPSS, Inc, Chicago, Illinois, USA.). Right and left sides were not evaluated separately except for reduction of upper and lower lid retraction. For those patients presenting with a predecompression score ≥ a 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. Postoperative orthoptic data were based on the first orthoptic examination performed between three and six months after decompression.

Statistical Analysis

Univariate comparisons were carried out using a one-way analysis of variance 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.

Orbital Radiotherapy

Orbital irradiation was delivered with a 5- or 6-mV accelerator in 10 daily fractions of two Gy over a period of two weeks. Localization and verification films with lead markers on the lateral canthus of each eye were performed for each patient on a simulator. The dose was calculated at the midline and given by two three degree anterior angled lateral portals of 5 × 5 cm, with the patient’s head fixed by an individual full-head shell.

Surgical Technique

All the patients included in this study underwent a standardized three-wall decompression via a coronal approach as is traditionally performed 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 cranium, a subperiosteal plane was created by blunt dissection, and laterally, a surgical plane was developed bluntly between the deep and the superficial temporalis
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Orbital irradiation was delivered with a 5- or 6-mV accelerator in 10 daily fractions of two Gy over a period of two weeks. Localization and verification films with lead markers on the lateral canthus of each eye were performed for each patient on a simulator. The dose was calculated at the midline and given by two three degree anterior angled lateral portals of 5 × 5 cm, with the patient's head fixed by an individual full-head shell.

Surgical Technique

All the patients included in this study underwent a standardized three-wall decompression via a coronal approach as is traditionally performed at our institution. 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 cranium, a subperiosteal plane was created by blunt dissection, and laterally, a surgical plane was developed bluntly between the deep and the superficial temporalis fascia. The forehead flap thus created was then turned down to expose the superior and lateral orbital rims. The supraorbital nerve was set free by chiselling its bony foramen when present and the periorbita, including the trochlea, was dissected off the orbital bones. The temporalis muscle then 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 chiselled behind the lateral orbital rim, and bone-nibbling rongeurs were used to remove the mid portion of the lateral orbital wall. 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 mucosa of the sinuses. The bulla ethmoidalis beneath the frontoethmoidal suture was opened toward 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 were 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 extensively to promote maximal prolapse of the orbital tissues into the newly created spaces. The temporalis muscle was sutured back into position with four to five interrupted 2-0 Mersilene sutures and, after the insertion of a 3.3-mm diameter end-perforated wound drain into each temporalis fossa, the scalp incision was closed with steel staples.

Results

The medical records of 61 of 376 patients were selected for this study, whereas 315 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 R (n = 29), group G (n = 15), and group RG (n = 17) with respect to demographics or preoperative characteristics, whereas the number of smokers was significantly greater in group RG (P = 0.019). It was not possible to compare group RG with the other two groups with regard to CAS at baseline because we could not retrieve enough data from the medical records of the patients included in this group (Table 1).
Table 1. Demographics, Smoking Habits and Predecompression Characteristics in Three Groups of Patients Affected by Graves’ Orbitopathy Who Had Been Treated with Different Immunosuppressive Strategies during the Active Phase of the Disease

<table>
<thead>
<tr>
<th></th>
<th>Group R* (n=29)</th>
<th>Group G* (n=15)</th>
<th>Group RG* (n=17)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>86%</td>
<td>93%</td>
<td>100%</td>
<td>P = 0.250</td>
</tr>
<tr>
<td>Age at surgery (yrs ± SD) (95% CI)</td>
<td>41.8 (8.5) (38.5-45.0)</td>
<td>43.0 (9.6) (37.6-48.5)</td>
<td>46.3 (10.0) (41.1-51.4)</td>
<td>P = 0.292</td>
</tr>
<tr>
<td>Duration of Graves’ orbitopathy at surgery (yrs ± SD) (95% CI)</td>
<td>3.6 (2.7) (2.6-4.7)</td>
<td>4.9 (4.4) (2.5-7.4)</td>
<td>5.1 (3.9) (3.0-7.0)</td>
<td>P = 0.321</td>
</tr>
<tr>
<td>Interval end immunosuppression by steroids or radiation, and time of decompression (mts ± SD) (95% CI)</td>
<td>15.1 (14.7) (9.5-20.7)</td>
<td>28.5 (28.4) (11.3-45.6)</td>
<td>15.9 (10.3) (10.7-21.2)</td>
<td>P = 0.070</td>
</tr>
<tr>
<td>Smokers</td>
<td>43%</td>
<td>31%</td>
<td>80%</td>
<td>P = 0.019</td>
</tr>
<tr>
<td>Radioactive Iodine</td>
<td>21%</td>
<td>40%</td>
<td>41%</td>
<td>P = 0.244</td>
</tr>
<tr>
<td>Thyroidectomy</td>
<td>7%</td>
<td>13%</td>
<td>29%</td>
<td>P = 0.114</td>
</tr>
<tr>
<td>Hertel values (mm ± SD) (95% CI)</td>
<td>23.3 (2.3) (22.4-24.2)</td>
<td>23.1 (2.5) (21.7-24.5)</td>
<td>21.9 (2.3) (20.7-23.0)</td>
<td>P = 0.130</td>
</tr>
<tr>
<td>Upper lid retraction:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monolateral</td>
<td>7%</td>
<td>20%</td>
<td>6%</td>
<td>P = 0.860</td>
</tr>
<tr>
<td>Bilateral</td>
<td>65%</td>
<td>40%</td>
<td>59%</td>
<td></td>
</tr>
<tr>
<td>Not present</td>
<td>28%</td>
<td>40%</td>
<td>35%</td>
<td></td>
</tr>
<tr>
<td>Lower lid retraction:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monolateral</td>
<td>7%</td>
<td>0%</td>
<td>12%</td>
<td>P = 0.750</td>
</tr>
<tr>
<td>Bilateral</td>
<td>69%</td>
<td>80%</td>
<td>59%</td>
<td></td>
</tr>
<tr>
<td>Not present</td>
<td>24%</td>
<td>20%</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Score in NOSPECS class 2:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7%</td>
<td>13.3%</td>
<td>6%</td>
<td>P = 0.372</td>
</tr>
<tr>
<td>a</td>
<td>52%</td>
<td>33.3%</td>
<td>76%</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>38%</td>
<td>53.4%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>3%</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>C.A.S. (+/7 ± SD) at the last examination preceding immunosuppression</td>
<td>3.6 (1.5)</td>
<td>3.44 (1.4)</td>
<td>§</td>
<td>P = 0.817</td>
</tr>
</tbody>
</table>

C.A.S. = clinical activity score; CI = confidence interval; SD = standard deviation; a = mild; b = moderate; c = severe; NOSPECS (classification of eye changes in Graves’ orbitopathy) = class 0, no signs or symptoms; class 1, only signs; class 2, soft tissue involvement with symptoms and signs; class 3, proptosis; class 4, extraocular muscle involvement; class 5, corneal involvement; class 6, sight involvement.

*Group R = patients in whom immunosuppression was obtained by means of orbital radiotherapy; Group G = patients in whom immunosuppression was obtained by means of systemic glucocorticoids; Group RG = patients in whom immunosuppression was obtained by means of orbital radiotherapy and glucocorticoids.

†Interval calculated based on the last of the two immunosuppressive treatments that was administrated.

§Only patients with upper lid retraction before surgery: Group R, 21 right 19 left; Group G, six right nine left; Group RG, 11 right 10 left.

| Mean exophthalmos reduction (yrs ± SD) (95% CI) | 4.6 (1.9) (3.5-5.7) (n=29) | 5.3 (1.9) (4.3-6.3) (n=15) | 5.7 (1.9) (4.3-7.0) (n=17) | P = 0.114    |

Surgical outcome

There were no statistically significant differences regarding mean reduction of exophthalmos, occurrence of diplopia consecutive to orbital decompression within 20 degrees around primary position of gaze, or variation in the peripheral field of diplopia among the groups. When the predecompression score in NOSPECS class 2 was ≥ a, there were no statistically significant differences among the groups with regard to persistence of postdecompression peri-orbital swelling requiring upper or lower lid blepharoplasty. The
reduction of upper and lower lid retraction also was not statistically different among groups when these signs were present before surgery (Table 2).

**Table 2. Outcome of Three-Wall Rehabilitative Orbital Decompression**
**Through a Coronal Approach in Three Groups of Patients Affected by Graves' Orbitopathy**
**Who Had Been Treated with Different Immunosuppressive Strategies during the Active Phase of the Disease**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group R* (n=29)</th>
<th>Group G* (n=15)</th>
<th>Group RG* (n=17)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean exophthalmos reduction ± SD, mm (95% CI)</td>
<td>4.9 (1.8) (4.2-)</td>
<td>4.6 (1.9) (3.5-)</td>
<td>5.3 (1.9) (4.3-)</td>
<td>P = 0.598</td>
</tr>
<tr>
<td>Reduction of upper lid retraction right/left†</td>
<td>52% / 47%</td>
<td>50% / 33%</td>
<td>36% / 40%</td>
<td>P = 0.683/P = 0.772</td>
</tr>
<tr>
<td>Reduction of lower lid retraction right/left‡</td>
<td>62% / 52%</td>
<td>67% / 67%</td>
<td>67% / 60%</td>
<td>P = 0.946/P = 0.719</td>
</tr>
<tr>
<td>Persistence of postdecompression periorbital swelling requiring surgery§</td>
<td>48%</td>
<td>46%</td>
<td>31%</td>
<td>P = 0.536</td>
</tr>
<tr>
<td>Onset of diplopia consecutive to decompression within 20° around primary position of gaze</td>
<td>28%</td>
<td>40%</td>
<td>41%</td>
<td>P = 0.563</td>
</tr>
<tr>
<td>Field of diplopia beyond 20° from primary position of gaze</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased</td>
<td>50%</td>
<td>72%</td>
<td>25%</td>
<td>P = 0.494</td>
</tr>
<tr>
<td>Decreased</td>
<td>17%</td>
<td>14%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Unchanged</td>
<td>33%</td>
<td>14%</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>

CI = confidence interval; SD = standard deviation.
*Group R = patients in whom immunosuppression was obtained by means of orbital radiotherapy; Group G = patients in whom immunosuppression was obtained by means of systemic glucocorticoids; Group RG = patients in whom immunosuppression was obtained by means of orbital radiotherapy and glucocorticoids.
†Only patients with upper lid retraction before surgery: Group R, 21 right 19 left; Group G, six right nine left; Group RG, 11 right 10 left.
‡Only patients with lower lid retraction before surgery: Group R, 21 right 21 left; Group G, 12 right 12 left; Group RG, 12 right 12 left.
§Only patients with NOSPECS score in class 2 ≤ 4: Group R, 27; Group G, 13; Group RG, 16.
¶Only patients who did have postdecompression diplopia within 20 degrees around the primary position of gaze: Group R, 18; Group G, 7; Group RG, 8.

**Discussion**

Orbital irradiation is a common method of treatment of Graves’ orbitopathy in its early, inflammatory, active phase. It seems to be effective on soft tissue inflammatory changes, recent extraocular muscle involvement, and optic neuropathy by inactivating orbital lymphocytes and fibroblasts, which are, respectively, the mediators and the effectors of the inflammatory reaction in the orbit. Ionizing radiation, however, may not be without negligible side effects even when low doses are used.

Histopathologic radiation-induced alterations mainly occur in a repetitive form in different structures, namely, epithelia and parenchymatous tissues, stroma, and blood vessels. Some alterations are characteristic of particular organs. All of them are delayed radiation injuries
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that appear months to years after exposure to ionizing radiation. Acute radiation injury is rare.

Fibrosis, one of the most common delayed injuries of stroma, may affect soft orbital tissues, especially the fat and, in turn, may have an adverse effect on bone removal orbital rehabilitative decompression surgery. Fibrosis occurs in practically all tissues and organs exposed to ionizing irradiation, but the extent and severity vary from site to site and are dependent on the total radiation dose, fraction size, and treated volume. The typical radiation-induced fibrosis is inhomogeneous: some areas have very dense, acellular collagen, whereas next to them, other areas have only a few fibrous bands. The fibrous areas are within the irradiated field but do not fill it entirely. Such alterations are typical of irradiated adipose tissue. Classic theories of radiation effects not only indicate deoxyribonucleic acid double-strand breaks as the early lethal event, but also assert that tissues that are prone to late radiation fibrosis have slow reproductive rates that delay cell death and result in late reactions. Adipose tissue perfectly fits such characteristics. Eventual late radiation toxicity to orbital fat in Graves’ orbitopathy is not likely to be solely the result of delayed cell death and slow cell turnover. Orbital irradiation is administered in the active, inflammatory phase of Graves’ orbitopathy, and it has long been observed that inflammation worsens delayed radiation fibrosis. Inflammation is mediated largely by proinflammatory cytokines, including tumor necrosis factor α, which in injured tissue has been shown to be involved in the recruitment and activation of macrophages with the release of downstream fibrogenic cytokines. These cytokines include fibroblast growth factor 2 (FGF2) and transforming growth factor β 1 (TGFβ1). FGF2 is chemotactic and mitotic for fibroblasts, and TGFβ1 stimulates fibroblast proliferation and premature end differentiation, leading to excessive extracellular matrix glycoprotein production. Thus, irradiation dramatically alters the ability of macrophages to stimulate normal fibroblast populations, and fibrosis induced by radiation is a multicellular event in which the macrophage and fibroblast cell systems interact through intracellular communication mediated by specific growth factors such as FGF2 and TGFβ1. Orbital compliance, which refers to the distensibility and plasticity of the orbital tissues, may be reduced by fibrosis of the orbital soft tissues, and reduced orbital compliance may
diminish the effectiveness of orbital expansion surgery because orbital soft tissues can fail to prolapse maximally into the spaces newly created by surgery.\(^\text{25}\) In view of this possibility, orbital radiotherapy may be expected to have a negative effect on decompression surgery in patients with Graves’ orbitopathy. Because of the extreme heterogeneity of patients with Graves’ orbitopathy who need rehabilitative decompression surgery, the variation applied to surgical techniques, and the use of perioperative glucocorticoids, it may prove difficult to verify whether this affects the results of orbital surgery. The paucity of data available in literature seems to be in line with this viewpoint, which our results confirm further. In our retrospective survey, conducted in a tertiary referral center with an established tradition for the treatment of Graves’ orbitopathy\(^\text{11}\) and encompassing a period of 11 years, among 376 patients decompressed using the same technique, we could recruit only 61, meeting the criteria that we regarded as essential for a comparative case series.

Male gender, older age, and heavy smoking habits are patient characteristics that are known to be associated with more severe orbital disease\(^\text{26-28}\), whereas extension and location of the osteotomy performed during decompression surgery, differences in aperture of the periorbit, and preoperative Hertel values have been regarded as factors influencing the amount of exophthalmos reduction.\(^\text{25,29-36}\) In addition, the timing for assessment of surgical outcome can be an additional source of bias when evaluating the results of decompression surgery. As a consequence, any meaningful comparison of the results of rehabilitative decompression surgery in different cohorts of patients with Graves’ orbitopathy necessitates a careful evaluation of their baseline characteristics and a careful control of confounding factors by means of the methodology of investigation. We therefore compared the groups for baseline characteristics and we tried to control confounding factors and bias by means of our strict inclusion and exclusion criteria, timing for assessment of the results, and clear definitions for important symptoms such as diplopia or signs such as persistence of postdecompression periorbital swelling.

The three groups of patients included in our study were basically homogeneous at baseline, although smoking was a most common habit among the patients in the RG group. Considering the well-known negative influence of smoking on the course of Graves orbitopathy and its capacity to impair the response of Graves orbitopathy to radiotherapy and glucocorticoids\(^\text{37}\), it was not unexpected that group RG required the most intensive
immunosuppression regimen. By comparing the results of rehabilitative decompression surgery of the three groups, we did not find that patients treated with retrobulbar irradiation in the active phase of Graves’ orbitopathy had a different outcome than those treated with systemic glucocorticoids alone or with both retrobulbar irradiation and systemic glucocorticoids in the same phase of the disease.

We acknowledge that the results of our study should be weighed in light of its retrospective nature and its limitations. Our survey was a retrospective comparative case series, and the results of this type of study need to be confirmed by investigations with stronger study designs. The number of patients included was relatively small, the mean interval between retrobulbar irradiation and orbital decompression was relatively short, and patients were not allocated randomly to either of the three treatment groups. Despite these shortcomings, our results seem to suggest that the total radiation dose, fraction size, and irradiated volume commonly used to treat active Graves’ orbitopathy do not adversely interfere with the outcome of rehabilitative decompression surgery.
Chapter 3

References