The Effect of Systemic Steroids and Orbital Radiation for Active Graves Orbitopathy on Postdecompression Extraocular Muscle Volume

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• PURPOSE: To evaluate the effect of orbital radiation prior to surgery on the clinical course and extraocular muscle (EOM) radiologic volume changes after decompression in Graves orbitopathy (GO).
• DESIGN: Retrospective, interventional case series.
• METHODS: The medical records of patients treated with orbital decompression for GO and who underwent postoperative orbital computed tomography were reviewed. Only patients who underwent rehabilitative decompression in the inactive phase and who received systemic corticosteroids alone (ST group) or combined orbital radiation and systemic corticosteroids (SRT group) in the active inflammatory phase of the disease were selected. The main outcome measure was the comparison of preoperative and postoperative EOM volumes. Secondary outcome measures were changes in proptosis and diplopia after decompression.
• RESULTS: Thirty-seven of 114 patients were selected for this study. There were no differences between the ST group (n = 22, 42 eyes) and SRT group (n = 15, 30 eyes) in terms of demographics or predecompression characteristics. After decompression surgery, the total EOM volume significantly increased by 15% in the ST group, but radiated EOMs in the SRT group did not expand, resulting in decreased induction of postoperative diplopia. The percentages of patients showing increased diplopia after decompression differed significantly between the groups (ST group, 40.9% vs SRT group, 13.3%, $P = .04$). However, there was no difference in exophthalmos reduction after decompression between the 2 groups.
• CONCLUSIONS: Orbital radiation prior to orbital decompression can reduce both the postoperative increase in EOM volume and deterioration in diplopia. (Am J Ophthalmol 2016;171:11–17. © 2016 Elsevier Inc. All rights reserved.)

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GRAVES ORBITOPATHY (GO) REFERS TO A PATHOLOGIC autoimmune condition characterized by lymphocytic infiltration and edema of the retrobulbar tissues, with potential thickening and fibrosis of the extraocular muscles (EOMs) and orbital fat.[1] It can lead to a discrepancy between the bony orbital cavity and the volume of the intraorbital soft tissue contents, resulting in disfiguring proptosis, motility disturbance, and optic neuropathy in GO patients.[2]

The mainstay therapy for GO in the active inflammatory phase is high-dose glucocorticoids and orbital radiotherapy (OR).[3] OR has been widely used to treat patients with active-phase GO for more than 70 years, and numerous previous retrospective and prospective studies have supported the efficacy of radiotherapy treatment for active GO.[4–7] In these previous studies, OR was well tolerated and effective in preventing exacerbations of active inflammation, in reducing soft tissue changes and proptosis, and especially in improving ocular motility impairment.[8–10] The main mechanism of OR is the anti-inflammatory effects caused by inducing apoptosis or disrupting the functions of radiosensitive lymphocytes and fibroblasts.[3,11]

Once the inflammation associated with GO becomes quiescent and a period of stability has been achieved, rehabilitative surgical therapy, such as orbital decompression, strabismus surgery, eyelid repositioning, and blepharoplasty, may be performed. Among these surgical treatments, orbital decompression is the primary treatment during the inactive or stable phase of the disease for correcting exophthalmos or exposure keratopathy, whereby the removal of portions of the bony orbit creates space for the enlarged orbital contents. However, some previous studies have reported EOM enlargement after orbital decompression; EOM enlargement may contribute to reducing the effect of orbital decompression, leading to the recurrence of orbital complications, such as proptosis, exposure keratitis, and compressive optic neuropathy.[12–14] Interestingly, we noted that EOM volume expansion after orbital decompression was less common in GO patients who underwent OR during the active phase than in those who did not undergo OR. Therefore, this study evaluated the effect of OR prior to surgery on the

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clinical course and postoperative EOM volume changes after decompression in GO patients.

METHODS

ALL PATIENTS WITH GO WHO UNDERWENT ORBITAL 2-WALL decompression by 1 surgeon (J.S.Y.) between January 2008 and December 2014 were retrospectively reviewed. The study protocol, which involved a retrospective chart review of all patients meeting the study criteria, was approved by the Institutional Review Board of the Severance Hospital of Yonsei University and adhered to the tenets of the Declaration of Helsinki. All patients provided their written informed consent.

Patients who underwent orbital decompression during the inactive phase and met all of the following criteria were included: (1) euthyroidism before the operation, (2) steroid pulse therapy with or without OR in the active phase, (3) chronic phase lasting longer than 6 months before the operation, (4) preoperative orbit computed tomography (CT) scans obtained within 2 months before the operation, and (5) postoperative orbit CT scans obtained at least 6 months after the operation. The ST group, which was the control group, only underwent steroid pulse therapy. Indications for corticosteroid treatment were: (1) periocular soft tissue inflammation (clinical activity score [CAS] 3 or greater), (2) compressive optic neuropathy, and (3) strabismus. In addition to concurrent or previous treatment with corticosteroids, the SRT group underwent OR. The primary indications for adding OR after intravenous (i.v.) corticosteroids were as follows: (1) continuation or even progression of inflammation despite i.v. steroid, (2) intolerance of corticosteroids, and (3) development of significant restriction of ocular motility. The exclusion criteria were concurrent periorbital diseases, thyroidectomy, or radioactive iodine-131 within 6 months before the operation; a history of EOM surgery; and orbital trauma.

The following parameters were compared to evaluate the matching of the 2 groups: (1) demographics (age and sex), (2) smoking history, (3) previous anti-thyroid treatment, (4) duration of the active and inactive phases of GO before decompression surgery, (5) activity as evaluated using the CAS,[15] (6) severity of GO at the time of surgery as evaluated by the modified NOSPECS,[16] (7) the subtype of GO as assessed using the Nunery type,[17] and (8) biochemical characteristics at the time of surgery.

The primary outcome measure was radiographic EOM volume changes between preoperative and postoperative CT scans (after orbital decompression). Secondary outcome measures were (1) changes in proptosis after decompression and (2) changes in diplopia as determined using the Gorman score.[18] The Gorman score is graded from 0 to 3 (0 = none, 1 = diplopia with gaze, 2 = intermittent diplopia, and 3 = constant diplopia).

In the active phase, all patients with a CAS of 3 or greater were treated with i.v. corticosteroids (500 mg methylprednisolone weekly for 6 weeks and 250 mg weekly for 6 weeks). Orbital radiation was targeted at the retrobulbar space at a dose of 20 Gy in 10 fractions over a 2-week period. Two-wall orbital decompression with posterior strut removal was performed in a chronic phase lasting longer than 6 months. The inferior orbital floor was exposed by the swinging eyelid approach, after lateral canthotomy, and the medial orbital wall was accessed via a transconjunctival approach. The bone and fat were removed incrementally, and the degree of residual proptosis was checked periodically by viewing the patient superiorly. The volume of fat removed during decompression surgery was measured using a 10-mL syringe.[19]

Data were analyzed using SPSS statistical software version 20.0 (SPSS Inc, Chicago, Illinois, USA). Independent *t* tests were used to compare ages, CAS values, NOSPECS scores, exophthalmos, the volume of removed fat during decompression surgery, and the time of postoperative CT scanning between the study groups. Sex, smoking history, Graves disease treatment, and percent of diplopia were compared between the study groups using Fisher exact tests. The Mann-Whitney test was used to compare the duration of the active and inactive phases before surgery between the 2 groups. Total EOM measurements were calculated as the sum of the measured medial rectus (MR), inferior rectus (IR), lateral rectus (LR), and superior rectus (SR) muscle volumes. The change in volume was calculated as the difference between the postoperative and preoperative volume measurements. Differences in preoperative and postoperative measurements were tested for significance using the paired *t* test.

RESULTS

A TOTAL OF 114 CLINICAL CHARTS OF PATIENTS WHO UNderwent orbital wall decompression were reviewed, and 37 patients (73 eyes) fulfilled the inclusion criteria. The ST group consisted of 22 patients (43 eyes) who were administered corticosteroids only, while the SRT group consisted of 15 patients (30 eyes) who underwent OR in addition to corticosteroid treatment. The average age at the time of the operation was 46.65 ± 10.51 years (range: 20–65 years), and 59% (22/37) of the patients were women. There were no differences in terms of age, sex, or smoking history between the SRT group and ST group (Table 1). Furthermore, the median duration of the active phase and the inactive phase before decompression surgery did not differ significantly between the 2 groups. There were no statistically significant differences in the maximal CAS value in the active phase, preoperative and postoperative CAS values, or modified NOSPECS scores between the 2 groups. In terms of subtype of GO, type 2 accounted