Orbital decompression in Graves’ orbitopathy: state of the art and novel perspectives
Baldeschi, L.

Citation for published version (APA):
Baldeschi, L. (2011). Orbital decompression in Graves’ orbitopathy: state of the art and novel perspectives

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Summary
The introductory Chapter 1 provides an overview of Graves' orbitopathy (GO) and its current treatment modalities. GO is one of the phenotypic appearances of Graves' disease, a multisystem disorder which usually leads to hyperthyroidism and goiter, less frequently to GO, and rarely to pretibial myxedema and acropachy. Its etiopathogenesis is poorly characterized and consequently a specific therapy is lacking. The European Group On Graves' Orbitopathy (EUGOGO) has published a consensus statement on indications and timing of the various medical and surgical treatment options in GO (Figure 2, page 14).

The current role of orbital decompression in the context of rehabilitative surgery for GO (the subject of this thesis) is reviewed.

The studies reported in chapters 2, 3 and 4 were designed to evaluate some unproven concepts in the existing literature on orbital decompression surgery. Chapter 2 evaluated the concept that outcome of orbital decompression is worse when performed rather late in the course of the disease, because there is more fibrosis and less compliance of orbital soft tissues in the late inactive stage of GO. In a retrospective study among GO patients without preoperative diplopia, outcome of surgical decompression was compared between 70 patients with GO duration <4 yr and 55 patients with GO duration of 4 yr or longer. Baseline characteristics of both groups were similar, except for greater extraocular muscle enlargement in the patients with early decompression. The surgical outcome (applying the same technique in all patients) was not different between both groups, except for more postdecompression diplopia in the group undergoing early decompression. It is concluded that a long duration of GO does not adversely interfere with the results of surgical decompression, and is associated with a decreased risk for developing postdecompression diplopia.

Chapter 3 evaluated the concept that outcome of orbital decompression is worse when patients have been treated with orbital irradiation prior to surgery, because radiotherapy might induce fibrosis and less compliant soft tissues. In a retrospective study among GO patients without preoperative diplopia, outcomes of 3-wall orbital decompression through a coronal approach was compared between 29 patients previously treated with radiotherapy (20 Gy), 15 patients previously treated with glucocorticoids, and 17 patients previously treated with radiotherapy and glucocorticoids. All preoperative characteristics except smoking behaviour were similar in the three groups. Surgical outcome did not differ...
The introductory Chapter 1 provides an overview of Graves’ orbitopathy (GO) and its current treatment modalities. GO is one of the phenotypic appearances of Graves’ disease, a multisystem disorder which usually leads to hyperthyroidism and goiter, less frequently to GO, and rarely to pretibial myxedema and acropachy. Its etiopathogenesis is poorly characterized and consequently a specific therapy is lacking. The European Group On Graves’ Orbitopathy (EUGOGO) has published a consensus statement on indications and timing of the various medical and surgical treatment options in GO (Figure 2, page 14). The current role of orbital decompression in the context of rehabilitative surgery for GO (the subject of this thesis) is reviewed.

The studies reported in chapters 2, 3 and 4 were designed to evaluate some unproven concepts in the existing literature on orbital decompression surgery.

Chapter 2 evaluated the concept that outcome of orbital decompression is worse when performed rather late in the course of the disease, because there is more fibrosis and less compliance of orbital soft tissues in the late inactive stage of GO. In a retrospective study among GO patients without preoperative diplopia, outcome of surgical decompression was compared between 70 patients with GO duration <4 yr and 55 patients with GO duration of 4 yr or longer. Baseline characteristics of both groups were similar, except for greater extraocular muscle enlargement in the patients with early decompression. The surgical outcome (applying the same technique in all patients) was not different between both groups, except for more postdecompression diplopia in the group undergoing early decompression. It is concluded that a long duration of GO does not adversely interfere with the results of surgical decompression, and is associated with a decreased risk for developing postdecompression diplopia.

Chapter 3 evaluated the concept that outcome of orbital decompression is worse when patients have been treated with orbital irradiation prior to surgery, because radiotherapy might induce fibrosis and less compliant soft tissues. In a retrospective study among GO patients without preoperative diplopia, outcomes of 3-wall orbital decompression through a coronal approach was compared between 29 patients previously treated with radiotherapy (20 Gy), 15 patients previously treated with glucocorticoids, and 17 patients previously treated with radiotherapy and glucocorticoids. All preoperative characteristics except smoking behaviour were similar in the three groups. Surgical outcome did not differ
between groups. It is concluded that previous orbital radiotherapy does not adversely interfere with the results of surgical decompression.

**Chapter 4** evaluated the concept that -according to a time-honoured axiom- the outcomes of orbital decompression in GO for rehabilitative reasons can be described in a satisfactory manner in terms of exophthalmos reduction and postoperative diplopia. These conventional outcome measures were compared to a newly designed set of outcome criteria in a prospective study among 84 GO patients who underwent a graded inferomedial bone decompression of 151 orbits through a minimally invasive sutureless transinferior fornix approach. The novel criteria allowed to assess surgical outcome in relation to the extent of surgery. Surgical targets were recorded prior to surgery, and included: 1) desired degree of exophthalmos reduction, 2) resolution of retroocular tension, 3) reduction of periorbital swelling, 4) cure of lagophthalmos; it allowed to calculate a mean index of targets achieved per orbit (MITAO) and per patient (MITAP), with values ranging between 0 and 1. Also an index of diplopia (ratio of decompression-induced de novo diplopia to decompression-induced cure of diplopia) was calculated. Invasiveness of surgery was quantified from minimally invasive (25%) to maximally invasive (100%), allowing to calculate a mean index of invasiveness per orbit (MIIO) and per patient (MIIP) ranging from 25% to 100%. The novel methodology described surgical outcomes in relation to the extent of surgery more precisely and meaningfully as compared to traditional evaluation of surgical outcomes.

The studies reported in chapters 5 and 6 were performed in order to evaluate and review current trends in decompression surgery with regard to ostetomies and approaches. **Chapter 5** evaluated the -previously undetermined- contribution of maximal removal of the deep lateral wall of the orbit to exophthalmos reduction, and its influence on the onset of diplopia. In a case-control study among GO patients undergoing 3-wall decompression through a coronal approach, 15 patients in whom the deep portion of the lateral wall had been removed (cases, extended decompression) were compared to 15 patients in whom the deep lateral wall had been preserved (controls, conservative decompression). There were no differences in baseline characteristics between cases and controls, but mean exophthalmos reduction was 2.3 mm greater in cases than controls; onset of diplopia was similar. It is concluded that removal of the deep lateral orbital wall as part of a coronal approach 3-wall
decompression enhances the degree of exophthalmos reduction without increasing the risk of diplopia.

Chapter 6 reviews the advantages and disadvantages of small versus coronal incisions to orbital decompression surgery. An inferior fornix incision can be used for inferomedial bony decompression and/or for removing fat from the medial and lateral inferior orbital quadrants. Through the same route a lateral ostetomy can be performed, although an upper skin crease incision offers a wider access to the lateral orbital wall. The swinging eyelid technique provides adequate access to the bony orbit and to the orbital fat compartments; it is a versatile technique that can virtually be used as a standard approach for the majority of patients needing decompression surgery. Orbital decompression by coronal incision is an invasive technique, not to be used as a standard approach. Nevertheless, it should not be abandoned as it could be advantageous in particular patients who may benefit more from a tailored rather than a standardised approach. Practical implications of the choice between a standardized approach to orbital decompression surgery and a more desirable customized approach are discussed.

The studies reported in chapters 7, 8, 9 and 10 deal with rare conditions which may be encountered in GO patients who are about to undergo or who already had undergone orbital decompression surgery.

Chapter 7 describes two patients who developed clinical and radiological evidence of reactivated GO a few weeks after rehabilitative bony orbital decompression during the static phase of the disease. We reviewed the charts of 249 consecutive GO patients who had undergone the same treatment for the same reason (excluded were patients with perioperative glucocorticoids, concurrent periorbital diseases, or who were immunocompromised). The incidence of delayed decompression-related reactivation of GO (called DDRR) was 1.3%. The reactivation took place a few weeks after surgery, after a normal convalescence period. No further episodes of reactivation were observed during a mean follow-up of 7.5 yr.

Chapter 8 describes a patient with X-linked childhood cerebral adrenoleukodystrophy; he was treated for this condition with whole bone marrow transplantation from his sister, and developed Graves’ hyperthyroidism and GO six years later. His sister was euthyroid when she donated the bone marrow transplant, but developed Graves’ hyperthyroidism
afterwards. The case demonstrates passive transfer of thyroid autoimmunity from an asymptomatic donor during allogeneic stem cell transplantation.

**Chapter 9** describes a GO patient presenting with restrictive strabismus. Orbital CT scanning showed an enlarged supernumerary extraocular muscle, confirmed by biopsy. Supernumerary extraocular muscles are quite prevalent in cats but extremely rare in humans. The case underscores the importance of an accurate preoperative assessment of GO in order to avoid surgical mistakes.

**Chapter 10** describes a GO patient who after bilateral rehabilitative inferomedial decompression developed a traumatic neuroma of the left infraorbital nerve. This previously unreported but disabling complication is likely the result of unnoticed nerve trauma at the time of surgical dissection of the infraorbital canal. The lesion remained stable during 39 months follow-up. Symptoms of neuralgia could be controlled only partially with medical therapy.

The general discussion in **Chapter 11** puts the presented findings in GO patients who underwent rehabilitative orbital surgery into perspective. Sometimes astute clinical observations may contribute to better understanding basic mechanisms in the pathogenesis of GO. Systematic review of the results obtained with orbital surgical decompression proves to be invaluable in refining surgical techniques and improving surgical outcomes.