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

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Chapter 4

A Novel Method for Measuring Outcome of Orbital Decompression in Graves' Orbitopathy by Evaluating an Infero-medial Decompression Technique

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Manuscript in preparation
**Abstract**

**Purpose:** To evaluate outcome of a graded bone removal infero-medial orbital decompression in Graves’ orbitopathy (GO) by means of a novel stratified appraisal (NSA) versus a traditional group analysis (TGA).

**Design:** Prospective observational case series.

**Participants:** All the orbits decompressed at our institution, for rehabilitative reasons by one surgeon (L.B.), using the technique under evaluation, between June 1999 and December 2005.

**Methods and main outcome measures:** NSA assessed or quantified: (1) the invasiveness of surgery from minimally (25%) to maximally (100%) invasive, allowing to calculate a mean index of invasiveness per orbit (MIIO) and per patient (MIIP) (25%≤values≤100%); (2) at ≥ 6 months postoperatively the surgical targets recorded prior to surgery (amount of desired exophthalmos reduction, improvement of retroocular tension, reduction of periorbital swelling / edema, resolution of lagophthalmos) were scored allowing to calculate a mean index of targets achieved per orbit (MITAO) and per patient (MITAP) (0≤values≤1); (3) an index of diplopia (ID) (ratio of central 20° of gaze decompression-induced / cured diplopia) was calculated based on orthoptics at ≥ 3 months postoperatively and before any strabismus surgery; (4) demographics and preoperative characteristics were compared after stratification of the included orbits for surgical target; surgical outcomes were assessed after stratification for amount of desired exophthalmos reduction and invasiveness of surgery.

TGA examined the entire series as a single homogeneous cohort independently of the different targets and invasiveness of surgery.

NSA and TGA were compared and complications noted.

**Results:** 151 orbits of 84 patients (78% female, mean age 45.5±9.7 years) were included. The NSA detected differences among groups within the studied cohort, the overall achievement of surgical targets was very high, indices precisely quantified the extent of applied surgery and surgical results, at variance with those obtained with TGA. A negligible complication rate was recorded.

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Introduction

For roughly a century decompression surgery has been used to treat Graves’ orbitopathy (GO).\textsuperscript{1} Initially it was utilized to address sight threatening conditions such as optic neuropathy, or exposure keratopathy. More recently the indications for orbital decompression were extended to the treatment of the typical disfigurement, and symptoms caused by the disease, which include globe and eyelid displacement, periorbital swelling, and raised retroocular tension. At present, it is also used as a preliminary step before squint surgery when space is required for recession of enlarged extraocular muscles, and functional indications of orbital decompression have been further expanded for the treatment of globe subluxation, postural visual obscuration in patients with congestive inactive GO\textsuperscript{2} and choroidal folds of recent onset due to globe indentation by enlarged extraocular muscles.\textsuperscript{3,4}

Despite the multiple indications for rehabilitative decompression surgery, mean exophthalmos reduction and incidence of new onset diplopia have been the main outcome measures reported in most of the published series. Through the years most authors have linked effectiveness and reliability of the reported techniques to the highest extent of exophthalmos reduction and the lowest incidence of induced diplopia.

We perceive this perspective as suboptimal since the data which have been generated / reported are incomplete, often imprecise and most likely misleading.

Data are incomplete because most of the effects of decompression surgery other than those on exophthalmos and binocular single vision have remained unmeasured.

Data are also often imprecise because many series inappropriately mix patients decompressed for disfigurement, with those presenting with compressive dysthyroid optic neuropathy, in whom the reduction of exophthalmos was not the reason to undertake decompression surgery and in whom the true incidence of decompression induced diplopia could have been confounded by the low pre-decompression visual acuity.

Data are most likely misleading because it is assumed that decompression surgery is always performed to obtain the maximal possible exophthalmos reduction when in reality any decompression technique can be used with different extent of osteotomies, fat removal or periorbita manipulation to achieve any degree of desired reduction of exophthalmos in the single orbit. In addition, high exophthalmos reduction is not an index of effectiveness as any excessive exophthalmos reduction is to be regarded as a complication of...
decompression surgery. Similarly the incidence of decompression induced diplopia is not itself most appropriate to describe surgical outcome because it does not take into account the cases of preoperative diplopia that are cured by decompression.

Based on these considerations it appears evident that the results of decompression surgery deserve a more adequate, comprehensive and reliable evaluation. We tried to make a move towards this goal by evaluating the outcome of a graded, bone inferomedial rehabilitative decompression technique performed through a minimally invasive suture-less trans inferior fornix approach, under a novel perspective which possibly overcomes the existing “time honoured” limitations.

**Patients and methods**

Our survey is a prospective observational case series. The study was carried out following the tenets of the Declaration of Helsinki and of the “CODE of CONDUCT” of the Dutch Federation of Biomedical Scientific Societies (http://www.federa.org/) as recommended by the Review Board of the Academic Medical Center University of Amsterdam. The same Review Board ruled that for this type of study its permission need not to be requested, nor was patients’ informed consent necessary if data are collected anonymously from the medical records used by the authors in their every day practice.

*Inclusion criteria:*

We included all the patients decompressed mono or bilaterally for rehabilitative reasons, who were clinically and biochemically euthyroid for at least 3 months, and who had undergone a graded bone inferomedial rehabilitative decompression performed through a minimally invasive suture less trans inferior fornix approach by one surgeon (L.B.), between June 1999 and December 2005.

*Exclusion criteria:*

We excluded all the patients 1) who had been treated with thyroidectomy or $^{131}$I in the 6 months preceding decompression or in the 6 months preceding postoperative evaluation; 2) who had concurrent orbital or periorbital diseases, injuries or surgeries (except for postdecompression blepharoplasties) within 6 months after decompression; 3) whose surgical targets were not listed in the respective medical files and whose pre and post operative notes were not filled out by means of the GO case record form in use in our clinic at the time of the study. It included all the necessary information for an adequate
clinical assessment of patients with GO, and was very similar to the EUGOGO case record form being one of its precursors.

Surgical technique

In bilateral cases, surgery was always initially performed on the more protruding eye if any. After the exposure of the inferior fornix by mean of a Desmarres’ retractor and a malleable orbital retractor, both electrically insulated, the conjunctiva and lower lid retractor complex were severed en-bloc with a Colorado needle and the inferior orbital rim was exposed. The periorbita was incised at this level and the medial and inferior orbital walls exposed by developing a subperiosteal plane. In order to obtain the best possible exposure of the medial wall, the bone insertion of the inferior oblique muscle was partially detached, and the conjunctival incision extended up to the caruncle.

Once the medial orbital wall and the orbital floor were exposed a Frazier suction tip was used to fracture the delicate bone of the medial orbital wall and of the floor and Blakesley forceps were used to remove bony fragments and mucosa of the sinuses. If necessary bone-nibbling rongeurs were also used. The bulla ethmoidalis underneath the fronto-ethmoidal suture was opened towards the orbit from the posterior lacrimal crest up to the orbital apex, and then the orbital floor medial to the infra-orbital canal was removed from about 1 cm behind the inferior orbital rim up to the posterior wall of the maxillary sinus.

Starting from this point, on the basis of intra operative estimations of eye position and resistance to retropulsion of the globe, and considering the targets to be pursued in the single orbit, surgery was graded to the specific patient’s needs. Clear surgical notes were prepared so that 4 progressively invasive surgical classes could be defined in the single orbit (A = minimally invasive to D maximally invasive, with an attributed index of invasiveness orbit (IIO) ranging from 25% for class A to 100% for class D).

Surgical class A: Osteotomies were terminated at this stage, and the periorbita left intact.

Surgical class B: The periobita was opened inferiorly and medially sparing the anterior portion of its inferior and medial surfaces for roughly 1.5 cm behind the arcus marginalis.

Surgical class C: The bony infraorbital canal and the orbital floor lateral to it were completely removed, the periorbita was addressed as for class B.

Surgical class D: The posterior two thirds of the maxillary ethmoidal strut were removed creating a wide antrostomy between the maxillary sinus and the nasal cavity. The bony infraorbital canal, the orbital floor lateral to it, and periorbita were addressed as for class C.
At all times possible sources of bleeding were controlled with cautious bipolar diathermy. In all cases, at the end of surgery the fornix incision was not sutured and a pressure bandage was applied on the operated eye, after absence of bleeding was assessed.

Immediate postoperative care:

Pupil reflexes, visual function, ductions and versions were checked when the patient was awake postoperatively, then daily up until the morning of postoperative day 2 when patients were discharged from the hospital. Pressure bandages were removed and reapplied daily after clinical examination up until discharge. At surgery, postoperative day 1 and 2 intravenous ceftriaxone (1 g/day) was administered; patients left hospital without medications except for artificial tears.

Evaluated data

The following data were evaluated: 1) gender; 2) age at surgery; 3) duration of GO at decompression; 4) smoking habits at surgery; 5) possible administration of systemic immunosuppressive treatments, and/or orbital radiotherapy before decompression; possible treatments with I^{131} or thyroidectomy before and after decompression; 8) pre and postoperative best corrected visual acuity, exophthalmometric values, measure of possible lagophthalmos, NOSPECS, and CAS scores; 9) expected targets of inferomedial decompression surgery; 10) information useful for defining IIO; 11) pre and postoperative orthoptic evaluations including information on central diplopia defined as double vision within 20° of the central position of gaze, field of peripheral diplopia, namely extension of diplopia beyond 20 degrees of the central position of gaze, measures of ductions in degrees performed with a modified perimeter; 12) any information concerning intraoperative, perioperative or medium term complications other than strabismus.

Clinical preoperative data were those of the last ophthalmic examination before decompression, while postoperative data and scoring of the single targets as achieved or not achieved referred to the first ophthalmic examination performed 6 or more months after surgery. In the case of postdecompression blepharoplasties performed earlier than postdecompression month 6 the achievement of the target “reduction of periorbital oedema” referred to the last ophthalmic examination preceding blepharoplasty.

Pre and postoperative data concerning eye motility were those collected at the orthoptic evaluations performed respectively not earlier than 6 months before decompression and not earlier than 3 months, but before any strabismus surgery.
Methodology

Predecompression characteristics and outcome by a novel stratified appraisal (NSA) were weighed against that of a traditional group analysis (TGA).

Novel Stratified Appraisal

Before surgery the targets to be achieved by the graded inferomedial decompression technique in the single orbit, were discussed with the patients and listed in their medical records.

Orbital targets were scored as achieved as desired or not, and were: (1) amount of desired exophthalmos reduction specified as a) none to minimal, i.e. ≤ 2 mm; b) moderate to maximal, i.e. ≥ 3 mm without causing enophthalmos and/or hypoglobus namely excessive reduction of exophthalmos, and/or eyeball dystopia for which surgical correction was advised or performed; (2) resolution of retroocular tension, defined as patient’s subjective perception of disappearance of such a symptom after decompression; (3) reduction of periorbital swelling oedema, defined as decrease of at least 1 point in NOSPECS class 2 after decompression; (4) cure of lagophthalmos, defined as disappearance or reduction of ≥ 3 mm of preoperative lagophthalmos.

In addition symmetry in exophthalmos reduction was considered as a constant patient target to be pursued. We considered symmetry as achieved when post operative Hertel readings were right = left ± 1 mm.

In order to characterize different groups according to the invasiveness of surgery a mean IIO, named mean index of invasiveness orbit (MIIO) was calculated, as well as a mean index of invasiveness patient (MIIP) which was based on the formula 0.5 x Σ IIO / number of patients included into the group (the coefficient 0.5 in the formula was chosen because in a patient the contribution of each orbit to invasiveness is 50%). IIO, MIIO, and MIIP express invasiveness in percentages from 25-100%.

For measuring in different groups the average amount of achievement of the desired surgical targets, a mean index of targets achieved orbit (MITAO) and a mean index of targets achievement patient (MITAP) were calculated, respectively based on the formulas: Σ 1 or 0 point for each target respectively achieved as desired or not in the single orbit / overall number of desired targets in a group of orbits; Σ 1 or 0 point for each target respectively achieved as desired or not for targets concerning only one of the two orbits, and for target symmetry (constant) + Σ 0.5 or 0 points for each target respectively achieved
as desired or not for targets concerning both the orbits / overall number of desired targets in a group of patients (0.5 points for targets desirable in both orbits was chosen because in a patient the contribution of each orbit to the achievement of that target is 50%). MITAO and MITAP are numbers between 0 and 1; MITAO=1 and MITAP=1 when all the targets are achieved in a group of orbits or in a group of patients respectively.

Based on the ratio frequency decompression induced diplopia / frequency decompression cured diplopia, an index of diplopia (ID) was calculated. ID is =1 when the frequency of induced diplopia is the same as that of cured, is > 1 when the frequency of induced diplopia is higher than that of cured, is < 1 viceversa.

Orbits grouped for target “amount of desired exophthalmos reduction” and stratified for class of surgical invasiveness (IIO) were compared within groups and within classes in respect to mean exophthalmos reduction, mean decompression induced change in ductions. Central and peripheral fields of diplopia were assessed in patients in whom preoperative binocular vision was present and who did not have anomalous retinal correspondence. Patients stratified for decompression induced or cured central diplopia were compared.

**Traditional Group Analysis**

Surgical outcomes (mean post operative exophthalmos, mean exophthalmos reduction, decompression induced change in duction) of the entire cohort of orbits were evaluated as a whole in the TGA. Incidence of decompression induced diplopia was evaluated in the same cohort of patients as for NSA.

**Statistical analysis**

Pre and post operative data were inserted in a data base created in SPSS 16.0 Statistics UK and analysed.

Univariate comparisons: one-way ANOVA and Student's t test were used to compare continuous variables. In case of ordinal or not normally distributed variables the Mann-Whitney U test was used. Categorical preoperative and post-operative data were investigated using $\chi^2$ test. Significance was assumed if $P \leq 0.05$.

Multiple regression analysis was used to assess the independent influence of preoperative Hertel values and IIO on exophthalmos reduction, and decompression induced mean changes in ductions.
Results

Eighty-four patients (151 orbits) out of 295 patients decompressed within the study period were selected for this survey, 210 patients were excluded because they did not meet the inclusion criteria or the necessary data were not recorded. One patient, previously reported, was excluded because of delayed decompression related reactivation (DDRR)\(^9\), requiring high dose oral glucocorticoids starting from 1 month after surgery.

Preoperative characteristics

The 151 orbits had the following characteristics: 77.5% were feminine, mean age ± SD at decompression was 45.5±9.7 years, mean duration of GO ± SD at decompression 45.7±44.6 months; 51.3% were smokers, and 34.2% had received \(^{131}\)I and 11.6% thyroidectomy. Steroids, orbital radiotherapy, or combined steroids and orbital radiotherapy had been administered in 12.2%, 17.6%, and 10.1% respectively.

The NSA disclosed the following differences among orbits stratified for surgical target:

The orbits that required “moderate to maximal exophthalmos reduction” were younger and had higher mean preoperative Hertel values than those that required “no to minimal exophthalmos reduction” (mean ± SD age at decompression (44.4±9.6 vs 52.3±7.6 years, \(P = 0.000\)) (mean ± SD preoperative Hertel 21.6±2.2 vs 19.6±1.5 mm, \(P = 0.000\)). In addition the orbits whose target was “no to minimal exophthalmos reduction” had received orbital radiotherapy less frequently than those whose target was “moderate to maximal exophthalmos reduction” (9.5% vs 30.7% \(P = 0.001\)). The orbits that required treatment of lagophthalmos had received combined radiotherapy and glucocorticoids less frequently (0%) as compared with those who did not (12%) \(P = 0.000\). The duration of GO ± SD at decompression was longer in those orbits that did not require reduction of the periorbital oedema (70.3±67.5 months) as compared with those who required it (40.7±36.8 months) \(P = 0.003\).

Surgical outcome

After decompression surgery there was no clinically relevant change in visual acuity in any patient.

The achievement of the desired targets in the operated orbits are outlined in table 1. Calculated MITAO and MITAP were 0.95±0.16 and 0.94±0.15 respectively, attained by
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**Table 1. Achievement of the Surgical Target in the Operated Orbit**

<table>
<thead>
<tr>
<th>Surgical targets</th>
<th>Operated orbits out of the whole series (n=151) in which the achievement of the surgical target was desired</th>
<th>Achievement of the surgical target as desired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exophthalmos reduction:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>moderate to maximal (≥ 3mm, &lt;enophthalmos/hypoglobus*)</td>
<td>130 (86.1%)</td>
<td>Yes = 127/130 (97.7%) No = 3/130 (2.3%)³²</td>
</tr>
<tr>
<td>none to minimal (≤ 2mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>21 (13.9%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes = 21/21 (100%) No = 0/21 (0%)</td>
</tr>
<tr>
<td>Reduction of retroocular tension</td>
<td>100 (66.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes = 100/100 (100%) No = 0/100 (0%)</td>
</tr>
<tr>
<td>Reduction of periorbital edema</td>
<td>122 (80.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes = 110/122 (90.2%) No = 12/122 (9.8%)</td>
</tr>
<tr>
<td>Reduction of lagophthalmos</td>
<td>24 (15.9%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes = 24/24 (100%) No = 0/24 (0%)</td>
</tr>
<tr>
<td>*enophthalmos / hypoglobus = excessive reduction of exophthalmos or eye globe dystopia for which surgical correction was advised or performed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>³² one patient operated bilaterally had monolateral enophthalmos / hypoglobus, another had bilateral hypocorrection.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MIIO and MIIP of 86.4±21.9% and 78.2±26.1% respectively. Symmetry in exophthalmos reduction was achieved in 78 (94%) of 83 patients, with post decompression Hertel values right side = left in 56.4%; asymmetry in exophthalmos reduction resulted in 5 (6%) of 83 patients with post decompression Hertel values right = left ± 2 mm and ± 3 mm in 40% and in 60% respectively. In one of the 84 patients symmetry in exophthalmos reduction could not be assessed nor MITAP calculated. Prior to decompression, he had been enucleated on one side without orbital implant, and he was not wearing any eye prosthesis or willing to do that at the time of decompression.

The number of other targets to be achieved were not different between groups in which the desired exophthalmos reduction was ≤ 2 mm or ≥ 3 mm.

Surgical outcome measures of the orbits grouped for target “amount of desired exophthalmos reduction” are given in table 2.

TGA mean decompression induced changes in abduction, adduction, elevation and depression (degrees ± SD, increase in negative numbers) were 3.8±7.8; -0.05±6.6; 5.6±7.7; -0.03±10.6 with significant decrease of abduction (P = 0.000) and elevation (P = 0.000), could be calculated on 93 orbits for which pre- and postoperative orthoptic evaluations
Table 2. Invasiveness of Applied Decompression Surgery and Its Effect on Exophthalmos and Overall Achievement of Surgical Targets in a Cohort of 151 Orbits Grouped for Target “Amount of Desired Exophthalmos Reduction”

<table>
<thead>
<tr>
<th>Description</th>
<th>Orbits which required moderate to maximal exophthalmos reduction (≥2mm; ≤enophthalmos/hypoglobus*) (n=130/151)</th>
<th>Orbits which required none to minimal exophthalmos reduction: (≤2mm) (n=21/151)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean index of invasiveness orbits (MIO) ± SD, %**</td>
<td>91.3±15.8</td>
<td>55.9±29.4</td>
<td>( P = 0.000 )</td>
</tr>
<tr>
<td>Mean index target achievement orbit (MITAO) ± SD</td>
<td>0.96±0.15</td>
<td>0.90±0.17</td>
<td>( P = 0.075 )</td>
</tr>
<tr>
<td>Mean post decompression Hertel values ± SD, mm</td>
<td>16.5±2.3</td>
<td>18.1±1.4</td>
<td>( P = 0.002 )</td>
</tr>
<tr>
<td>Mean exophthalmos reduction ± SD, mm</td>
<td>5.0±1.9</td>
<td>1.5±0.6</td>
<td>( P = 0.000 )</td>
</tr>
</tbody>
</table>

*enophthalmos / hypoglobus = excessive reduction of exophthalmos or eye globe dystopia for which surgical correction was advised or performed.
**Four progressively invasive surgical classes were defined in the single orbit (A = minimally invasive to D maximally invasive, with an attributed index of invasiveness orbit (IIO) ranging from 25% for class A to 100% for class D), MIO is the mean index of invasiveness for the orbits of a given group.
□□The mean index of targets achievement orbit (MITAO) is the average amount of achievement of the desired surgical targets for the orbits of a group. It was calculated based on the formula: \(\sum 1 \) or 0 point for each target respectively achieved as desired or not in the single orbit / overall number of desired targets for the orbits of a group.
□□Calculated excluding in this group the 3 orbits in which the target was no achieved (in one because of enophthalmos, in the other two because of hypo-correction) and which were considered failed surgeries in respect to desired exophthalmos reduction.

were available and were attained with a MIO of \(85±23.4\%\). The same measures stratified for target “amount of desired exophthalmos reduction” are given in table 3.

In table 4 orbits are grouped for target “amount of desired exophthalmos reduction” and, stratified for class of surgical invasiveness. Within and between group comparisons are specified for exophthalmos reduction, and decompression induced changes in ductions. Multiple linear regression analysis demonstrated that the amount of exophthalmos reduction was proportional to mean preoperative Hertel readings and IIO for the entire cohort of orbits \((P = 0.000 \text{ and } P = 0.000)\) and for those whose target was “moderate to maximal exophthalmos reduction” \((P = 0.000 \text{ and } P = 0.002)\), but not for those where “no to conservative exophthalmos reduction” was desired.

Multiple linear regression analysis demonstrated that decompression induced changes in abduction, elevation and depression were proportional to IIO \((P = 0.022; P = 0.047; P = 0.001)\) for those orbits where “moderate to maximal exophthalmos reduction” was desired but not for those whose target was “no to conservative exophthalmos reduction”.

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Table 3. Invasiveness of Applied Decompression Surgery and Its Effect on Ductions for Orbits Grouped for Target “Amount of Desired Exophthalmos Reduction”

<table>
<thead>
<tr>
<th>Mean Index of invasiveness orbit (MIIO) ± SD, %**</th>
<th>Orbits which required moderate to maximal exophthalmos reduction (≥3mm, &lt;enophthalmos / hypoglobus*), (n=82)</th>
<th>Orbits which required none to minimal exophthalmos reduction (≤2mm) (n=11)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>90.4±16.0</td>
<td>45.4±31.3</td>
<td></td>
<td>P = 0.000</td>
</tr>
</tbody>
</table>

Mean decompression-induced variations in ductions ± SD, degrees

<table>
<thead>
<tr>
<th>Abduction</th>
<th>4.0±8.2</th>
<th>2.6±5.0</th>
<th>P = 0.598</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adduction</td>
<td>-0.3±6.7</td>
<td>1.4±6.1</td>
<td>P = 0.426</td>
</tr>
<tr>
<td>Elevation</td>
<td>5.5±8.0</td>
<td>6.3±5.1</td>
<td>P = 0.722</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.2±10.7</td>
<td>1.7±10.4</td>
<td>P = 0.566</td>
</tr>
</tbody>
</table>

* enophthalmos / hypoglobus = excessive reduction of exophthalmos or eye globe dystopia for which surgical correction was advised or performed.

** Four progressively invasive surgical classes were defined in the single orbit (A = minimally invasive to D maximally invasive, with an attributed index of invasiveness orbit (IIO) ranging from 25% for class A to 100% for class D), MIIO is the mean index of invasiveness for the orbits of a given group.

Effects on central and peripheral fields of diplopia

The effect of decompression surgery on binocular vision was assessed based on retrievable information from medical records of 75 out of the 84 included patients. Nine patients were excluded because functional or anatomical monocularity, suppression, or anomalous retinal correspondence.

A MIIP of 78.33±25.5% was associated with a ID of 0.59: diplopia was induced by decompression in 8 (13.8%) of the 58 patients who had no preoperative central diplopia, and disappeared in 4 (23.5%) of the 17 patients who had preoperative central diplopia. In the other patients of this latter group, central diplopia improved in 2 (11.9%), worsened in 3 (17.6%) and remained unchanged in 8 (47.0%). Of the 50 patients without pre- or post-decompression central diplopia, 2 (4.0%) and 5 (10.0%) had decreased and increased extension of the field of peripheral diplopia after surgery.

The NSA did not disclose differences between patients with preoperative diplopia who were cured by decompression and those who were not and between those who developed post decompression diplopia and those who did not with respect to preoperative characteristics, MIIP and symmetry of surgery. The same results were found also by
comparing patients affected by preoperative diplopia and cured by decompression with those who presented decompression induced diplopia (Table 5).

Table 4. Orbits Grouped for Target “Amount of Desired Exophthalmos Reduction” and Stratified for Classes of Surgical Invasiveness Are Compared for the Effect of Surgery on Exophthalmos Reduction and Decompression Induced Changes in Ductions

<table>
<thead>
<tr>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Significance**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A IIO*=25%</td>
<td>B IIO*=50%</td>
<td>C IIO*=75%</td>
<td>D IIO*=100%</td>
<td></td>
</tr>
<tr>
<td>Mean exophthalmos reduction ± SD, mm:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>orbits which required moderate to maximal exophthalmos reduction (n=127/151)**</td>
<td>3.4±0.5</td>
<td>4.2±1.2</td>
<td>5.4±2.0</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>orbits which required none to minimal exophthalmos reduction (n=21/151)</td>
<td>1.5±0.5</td>
<td>1.5±0.6</td>
<td>1.8±0.4</td>
<td>P = 0.627</td>
</tr>
<tr>
<td>Significance***</td>
<td>P = 0.000</td>
<td>P = 0.000</td>
<td>P = 0.000</td>
<td></td>
</tr>
</tbody>
</table>

Mean decompression-induced variations in ductions ± SD, degrees:*

<table>
<thead>
<tr>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Significance**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A IIO*=25%</td>
<td>B IIO*=50%</td>
<td>C IIO*=75%</td>
<td>D IIO*=100%</td>
<td></td>
</tr>
<tr>
<td>Abduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>orbits which required moderate to maximal exophthalmos reduction (n=82)</td>
<td>-3.1±10.3</td>
<td>2.1±6.8</td>
<td>5.4±7.8</td>
<td>P = 0.017</td>
</tr>
<tr>
<td>Elevations</td>
<td>-7.4±6.8</td>
<td>3.0±8.1</td>
<td>-0.3±5.6</td>
<td>P = 0.002</td>
</tr>
<tr>
<td>Depressions</td>
<td>2.1±9.6</td>
<td>3.4±6.9</td>
<td>6.5±8.0</td>
<td>P = 0.199</td>
</tr>
<tr>
<td>orbits which required none to minimal exophthalmos reduction (n=111)</td>
<td>-16.7±16.8</td>
<td>-1.6±9.5</td>
<td>2.2±8.2</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>Significance***</td>
<td>P = 0.000</td>
<td>P = 0.000</td>
<td>P = 0.000</td>
<td></td>
</tr>
</tbody>
</table>

* Four progressively invasive surgical classes were defined in the single orbit (A = minimally invasive to D maximally invasive, with an attributed index of invasiveness orbit (IIO) ranging from 25% for class A to 100% for class D)
**Significance refers to comparisons among different classes of invasiveness, within 2 groups of orbits which required exophthalmos reduction “moderate to maximal” (≥ 3 mm) or “none to minimal” (≤ 2 mm).
***Significance refers to comparisons between 2 groups of orbits which required exophthalmos reduction “moderate to maximal” (≥ 3 mm) or “none to minimal” (≤ 2 mm), within different classes of invasiveness.

<table>
<thead>
<tr>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Class of surgical invasiveness</th>
<th>Significance**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A IIO*=25%</td>
<td>B IIO*=50%</td>
<td>C IIO*=75%</td>
<td>D IIO*=100%</td>
<td></td>
</tr>
<tr>
<td>Abduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adduction</td>
<td>4.6±3.9</td>
<td>4.0</td>
<td>-8.0</td>
<td>0.5±3.5</td>
</tr>
<tr>
<td>Elevations</td>
<td>1.9±6.6</td>
<td>1.0</td>
<td>5.0</td>
<td>-1.5±9.2</td>
</tr>
<tr>
<td>Depressions</td>
<td>3.3±9.1</td>
<td>0.0</td>
<td>6.0</td>
<td>-5.0±21.2</td>
</tr>
<tr>
<td>Significance***</td>
<td>P = 0.541</td>
<td>P = 0.165</td>
<td>P = 0.387</td>
<td></td>
</tr>
</tbody>
</table>

Mean decompression-induced variations in ductions was defined as the average difference between pre- and postoperative ductions measured in degrees by mean of a perimeter. Calculations were performed when pre- and post-decompression orthoptic data were available: orbits requiring “moderate to maximal exophthalmos reduction” = 82/130; orbits requiring “none to minimal exophthalmos reduction” = 11/21. Increased ductions are negative numbers, bold text when t test for paired data indicated a significant (P<0.05) variation in ductions after decompression.
Chapter 4

Table 5. Preoperative Characteristics, Surgical Outcomes and Surgical Invasiveness in Patients Whose Preoperative Diplopia Was or Was not Cured by Decompression Surgery, and in Patients with or without Decompression Induced Diplopia

<table>
<thead>
<tr>
<th>Patients whose preoperative central diplopia was cured by decompression (n=4/17)</th>
<th>Patients whose preoperative central diplopia was not cured by decompression (n=13/17)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at decompression ± SD, yrs*</td>
<td>51.7±17.9</td>
<td>52.1±7.5</td>
</tr>
<tr>
<td>Mean duration of the orbitopathy at decompression ± SD, mts**</td>
<td>43.5±24.9</td>
<td>25.5±11.0</td>
</tr>
<tr>
<td>Mean pre decompression Hertel values ± SD, mm</td>
<td>20.1±1.8</td>
<td>20.1±2.1</td>
</tr>
<tr>
<td>Mean exophthalmos reduction ± SD, mm</td>
<td>5.1±4.3</td>
<td>3.5±2.0</td>
</tr>
<tr>
<td>IIO symmetry</td>
<td>Symmetric 50%</td>
<td>Symmetric 30.7%</td>
</tr>
<tr>
<td>MIIP</td>
<td>68.7±36.1</td>
<td>68.3±28.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients who developed diplopia subsequent to decompression surgery (n=8/58)</th>
<th>Patients who did not develop diplopia subsequent to decompression surgery (n=50/58)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at decompression ± SD, yrs*</td>
<td>43.6±6.7</td>
<td>44.0±9.7</td>
</tr>
<tr>
<td>Mean duration of the orbitopathy at decompression ± SD, mts**</td>
<td>44.3±29.6</td>
<td>50.4±51.5</td>
</tr>
<tr>
<td>Mean pre decompression Hertel values ± SD, mm</td>
<td>20.0±1.4</td>
<td>21.3±2.2</td>
</tr>
<tr>
<td>Mean exophthalmos reduction ± SD, mm</td>
<td>4.3±1.4</td>
<td>4.1±2.0</td>
</tr>
<tr>
<td>IIO symmetry</td>
<td>Symmetric 75%</td>
<td>Symmetric 66%</td>
</tr>
<tr>
<td>MIIP</td>
<td>90.6±18.6</td>
<td>80.7±24.0</td>
</tr>
</tbody>
</table>

*yr=years  
**mts=months

Four progressively invasive surgical classes were defined in the single orbit (A = minimally invasive to D maximally invasive, with an attributed index of invasiveness orbit (IIO) ranging from 25% for class A to 100% for class D). Symmetric IIO was when IIO right side = left; asymmetric IIO when IIO right side ≠ left or in any monolateral decompression.

In order to characterize different groups of patients for invasiveness of decompression surgery, a mean index of invasivity patient (MIIP) was calculated based on the formula 0.5 x Σ IIO / number of patients included into the group (the coefficient 0.5 in the formula was chosen because in a patient the contribution of each orbit to invasiveness is 50%).

Complications

No patients had relevant intraoperative or perioperative complications. One patient had an excessive correction of exophthalmos and developed 3 mm enophthalmos and 2 mm hypoglobus of the left side necessitating surgical correction (Figure 1). Another patient developed a posttraumatic neuroma of the infraorbital nerve, and has been previously reported.10
Discussion

Different techniques are used for decompression surgery in GO and each of them can be personalized at patient’s and surgeon’s convenience for invasiveness and technical variations. Most of the study up until now provide a careful description of the surgical procedures, but invasiveness and technical variations have been left undetermined. In this study, the uniform execution of surgery secured by selecting patients operated by one surgeon, and indices such IIO, MIIO and MIIP were aimed at a better classification of applied decompression surgery for the benefit of study comparisons.

There are multiple indications for decompression surgery in GO. Hence the evaluation of its results should be inseparable from the assessment of the achievement of the targets, for which it has been performed. Only a precise, quantitative assessment of target achievement can allow meaningful and straightforward comparisons of the effectiveness of decompression surgery within and among studies. Our input to this goal was represented by clear definitions of targets, scoring of target achievement and corresponding MITAO and MITAP indices. The NSA which includes descriptive figures (Table 1) and easily interpretable quantitative indices is specific for decompression surgery and can be regarded as a further step in defining the overall response to treatment as proposed by EUGOGO.11
In the NSA, all targets chosen for the assessment of rehabilitative surgery outcomes are direct consequences of decompression induced decrease of intra-orbital pressure and globe displacement; decompression allows to reach these goals based on intraoperative estimations of resistance to retropulsion of the globe, eye position and aspect of the periorbital region. Decompressions may influence eyelid positions and lid fissure width modifying vertical ductions, eyeball position, or as a consequence of eyelid scarring. Lid fissure width is therefore not controllable during decompression surgery and for this reason we did not consider it as a target in our study. Conversely dysthyroid lagophthalmos is a static consequence of eyelid retractions or of the relative eyelid shortening due to the presence of a protruding eye; its reduction can be assessed based on intraoperative estimations. The minimally invasive transinferior conjunctival fornix approach that we used in the present series, by minimally disrupting tissues, ease intra operative estimations. Similar exophthalmometric values can cause different degrees of disfigurement when anthropomorphic characteristics like gender, ethnicity, shell and face conformation are considered. This has implications on the extent of required exophthalmos reduction; hence it is within the context of the targets to be achieved, and not, as it was previously done, on the basis of preoperative Hertel values per se, that traditionally used measures such as the amount of exophthalmos reduction assumes a specific means. High values of mean exophthalmos reduction, which for decades has been linked to effectiveness of decompression surgery, may, on the contrary, represent a complication when excessive or not desired.

Data concerning the potential of a given approach for exophthalmos reduction can be relevant when counseling patients, but are of less interest to those patients about to be operated for other targets. The latter patients in fact might be more interested in opposite informations, or rather the possibilities to use a particular type of decompression avoiding the induction of unwanted reduction of Hertel values, while still taking advantage of its other possible beneficial effects.

A similar perspective applies to the effects of decompressions on extraocular eye motility. Till now the incidence of decompression induced diplopia was considered a good safety marker. Although extremely valuable when counseling patients unaffected by diplopia prior to surgery it is unhelpful to patients who already have diplopia, and who would be more interested about the potential benefits of decompression to their double vision. The
ID, which merges in one single number information concerning frequency of decompression induced and cured diplopia, represents an easy means to describe diplopia-related intervals. This can have distinct advantages for comparisons within and among studies.

Decompression induced changes in ductions which quantify the influences of surgery on extra-ocular monocular movements, are very valuable measures not only for study comparisons but also for counseling purposes. With respect to induced changes in ductions the NSA is specific for decompression surgery and consistent with EUGOGO suggestion for clinical trials.11

The above considerations were the rationale behind the NSA. Most of the novel observations are liable to speculative interpretations and might be cues for future studies.

We found that orbits for which “no to conservative exophthalmos reduction” was desired, had the lowest pre operative Hertel reading and belonged to the oldest patients, but did not have a longer duration of GO. This suggests a particular sub set of GO developing at older age. Additionally we showed that when combined steroids and radiotherapy were administered before decompression, orbits were less likely to need reduction of lagophthalmos. Reduction of periorbital oedema was needed less frequently in orbits with a longer duration of GO. This suggests that the use of medical options may reduce the need of surgical treatment of lagophthalmos, and that simply “tincture of time” may reduce the necessity of surgery for periorbital oedema.

Overall the inferomedial decompression approach with graded degree of invasiveness described in this paper resulted in a rather high degree of achievement of desired targets, with negligible occurrence of complications. In about 10% of the cases orbital decompression was not effective in reducing preoperative periorbital oedema, and indeed this target was achieved less frequently than the other.

When “no to conservative exophthalmos reduction” was desired, the observed MIIO was the lowest, and exophthalmos reduction was not related to the degree of surgical invasiveness. This latter finding is a substantial departure from the traditional concept that more extensive osteotomies result in higher mean exophthalmos reduction.13 Explanation of our finding can only be speculative; it can be linked (as observed at surgery) to the distinct lack of compliance of the soft tissues in many of the orbits included in the group whose target was “no to conservative exophthalmos reduction”. The statistically
significant less frequent administration of predecompression radiotherapy could have contributed to the stiffness of the soft orbital tissue observed in this group. Its differences in IIO were not relevant to decompression induced changes in ductions. Interestingly unlike for orbits whose target was exophthalmos reduction ≥ 3mm, a maximal surgical invasiveness of 100% was not associated with any change ductions. The explanation of this is again speculative and in line with the previous one. In this group of orbits, despite maximally sized osteotomies, reduced compliance of the soft orbital tissue might have resulted in minimal if any displacement (and scarring) of the soft orbital tissues, including extraocular muscles. In line with this perspective, a lower surgical invasiveness of 25% which was presumably associated with better compliance of soft orbital tissues, was related to reduction of preoperative abduction and elevation.

In all groups, independent of the amount of desired exophthalmos reduction, IIO 75% was neutral to ductions, while invasiveness 50% (which is a commonly used pattern of osteotomies for the treatment of disfiguring exophthalmos either through a trans cutaneous, or a swinging eyelid approach) was beneficial to altered adduction and depression.

Apart from the observed novel figures the main value of the NSA is that of providing a more comprehensive outlook. Although the NSA may appear more complete, precise and reliable than the TGA, the NSA it is far from being ideal. Variations in morphology of the orbital cavity and in orbital osteology might significantly influence the degree of exophthalmos reduction which can be obtained by standardized decompression procedures. In our study, the influence of different osteotomies weighed for invasiveness of applied surgery on outcomes of decompression surgery remains unexplored. Additionally in our analysis the lipogenic or myopathic nature of the orbital disease was not taken into account, nor was the orbital compliance which is not directly measurable before decompression. For these reasons the figures given by our method cannot be considered absolute when counseling patients about to undergo surgery. Depending on the soft tissue response to surgery, the invasiveness of the planned approach, if not the surgical technique itself, may need to be changed during surgery. Nevertheless when counseling patients, the observations generated by our novel approach can be offered to them as a possible case scenario. The same observation are also invaluable to the surgeon faced with intraoperative decision making for balancing risk benefits of his/her eventual choices.
Finally the time frame that we chose to study the outcome of decompression surgery was relatively short and therefore suboptimal for assessing long-term complications such as permanent dysaesthesias of the infraorbital nerve or sinus obstructions. We however regard our choice as justifiable because it was aimed at reducing the influence of confounding factors linked to further post decompression rehabilitative procedures.

Despite its shortcomings the value of this study lies in its innovative perspectives and in having pioneered a new path linking specific needs, and background characteristics of the patients to a detailed graded surgical approach. This therefore has the potential to be a step towards the final goal of a desirable, and as much as possible, evidence based customized approach to orbital decompression.
CHAPTER 4

References
5. www.eugogo.eu

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