ORIGINAL ARTICLE

Outcomes of Orbital Decompression Surgery for Thyroid Eye Disease: Clinical and Computed Tomography-Based Analysis

Cirurgia de Descompressão Orbitária na Orbitopatia Tiroideia: Análise Clínica e Imagiológica

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Recebido/Received: 2023-08-04 | **Aceite/Accepted:** 2023-10-23 | **Published online/Publicado online:** 2024-03-11 | **Published/Publicado:** 2024-06-27

DOI: https://doi.org/10.48560/rspo.32537

ABSTRACT

INTRODUCTION: Orbital decompression surgery has been widely used in thyroid eye disease (TED). It is performed in the active stage, in sight-threatening cases of dysthyroid compressive optic neuropathy (DON), or severe corneal exposure unresponsive to steroids, and also during the quiescent phase to address proptosis. The purpose of this study is to analyze both clinical and imagiological outcomes of patients with TED who underwent orbital decompression.

METHODS: A retrospective analysis of patients undergoing orbital decompression in Centro Hospitalar Universitário de Lisboa Central and Hospital Cuf Descobertas, between 2018 and 2021, was performed. Demographic and clinical data were collected. The procedures included lateral, inferior-medial, balanced (lateral and medial) and three-wall decompressions. Main clinical outcomes included best corrected visual acuity (BCVA), proptosis reduction and complications. A group of patients underwent orbital computed tomography (CT) scanning before and after surgery, and differences in globe displacement in the horizontal, vertical and anteroposterior planes were measured for each type of surgery.

RESULTS: Forty-six orbits from 28 patients (18 females and 10 males) underwent decompression surgery. Mean age at time of surgery was 49.43 ± 11.63 years old. Orbital decompression was performed during the inactive phase in 19 patients (67.4%) and was required to treat sight-threatening active TED in 9 patients (32.6%). Lateral, inferior-medial, balanced and three-wall decompression were carried out in 12 (26.1%), 8 (17.4%), 14 (30.4%) and 12 (26.1%) orbits, respectively. From baseline, statistically significant improvements were observed after surgery in logMAR BCVA ($p<0.05$) and proptosis ($p<0.001$). Larger proptosis reduction occurred in three-wall decompression, followed by balanced decompression ($p<0.001$). New-onset strabismus occurred in 3 of the 28 patients (10.7%): 1 endoscopic inferior-medial decompression, 1 three-wall decompression with an endoscopic approach to the inferior and medial walls and 1 transorbital three-wall decompression. All the 3 cases presented DON non-reversible with high dose intravenous steroids.

CONCLUSION: Orbital decompression is an effective procedure to address proptosis in TED, being also an important resource in cases of DON unresponsive to systemic steroids. The reduction in proptosis is associated with the number of orbital walls addressed. An individualized approach is crucial during surgical planning in TED cases.

KEYWORDS: Decompression, Surgical; Graves Ophthalmopathy; Orbit/surgery; Tomography, X-Ray Computed.

RESUMO

INTRODUÇÃO: A descompressão cirúrgica da órbita é um procedimento amplamente utilizado no tratamento da orbitopatia tiroideia (OT). Está indicado tanto na fase ativa da doença, em casos de neuropatia ótica compressiva (NOC) ou de exposição corneana não reversíveis com corticoterapia sistémica, como na fase inativa para correção da proptose. O objetivo deste trabalho é analisar os resultados clínicos e imagiológicos de doentes com OT submetidos a cirurgia de descompressão orbitária.

MÉTODOS: Avaliação retrospetiva de doentes submetidos a descompressão orbitária no Centro Hospitalar Universitário de Lisboa Central e no Hospital Cuf Descobertas, entre 2018 e 2021. Foram realizadas descompressões da parede lateral, ínfero-medial, balanceada (lateral-medial) e de três paredes. Resultados referentes à melhor acuidade visual corrigida (MAVC), redução da proptose e complicações pós-operatórias foram analisados. Um subgrupo de doentes foi submetido a tomografia computorizada (TC) das órbitas antes e depois da cirurgia, de forma a quantificar o deslocamento do globo ocular nos planos horizontal, vertical e ântero-posterior consoante o tipo de descompressão orbitária.

RESULTADOS: Quarenta e seis órbitas, de 28 doentes, foram incluídas no estudo. A média de idades à data da cirurgia foi de 49,43 ± 11,63 anos. Nove doentes (32,6%) encontravam-se em fase ativa aquando da cirurgia e 19 (67,4%) foram intervencionados durante a fase inativa. Descompressões da parede lateral, ínfero-medial, balanceada e de três paredes foram realizadas em 12 (26,1%), 8 (17,4%), 14 (30,4%) e 12 (26,1%) órbitas, respetivamente. Após a cirurgia objetivou-se uma melhoria significativa na MAVC (p<0,05) e no grau de proptose (p<0,001). A redução mais acentuada da proptose foi observada na descompressão de três paredes, seguida da descompressão balanceada (p<0,001). Três doentes (10,7%) com NOC refratária a terapêutica médica no período pré-operatório desenvolveram estrabismo após a cirurgia.

CONCLUSÃO: A descompressão cirúrgica da órbita é um procedimento eficaz na redução da proptose de doentes com OT e no tratamento de casos de NOC não responsiva a corticoterapia sistémica. O grau de redução da proptose está relacionado com o número de paredes abordadas. A abordagem individualizada de cada caso de OT é fundamental para a obtenção de bons resultados clínicos e imagiológicos.

PALAVRAS-CHAVE: Descompressão Cirúrgica; Orbita/cirurgia; Orbitopatia de Graves; Tomografia Computorizada.

INTRODUCTION

Thyroid eye disease (TED), also known as thyroid-associated orbitopathy or Graves' orbitopathy, is the most common autoimmune inflammatory disorder of the orbit and the major extrathyroidal manifestation of Graves' disease,[1] occurring in 20%–50% of patients.[2] It is a relatively rare condition, with an estimated incidence of 3.3–8.01 cases/100 000/year in women and 0.54–1.62 cases/100 000/year in men.[3] Although severe disease is rare, it carries a major risk of irreversible vision loss due to corneal exposure, orbital congestion and optic neuropathy, and such patients should be treated urgently.

Even though we are still far from a complete understanding of its pathophysiology, the increase in volume of intraorbital tissues, such as orbital fat and extraocular muscles (EOM), within a limited bony space, explains most of the clinical signs and symptoms of TED, such as proptosis, diplopia and, in severe cases, vision loss.[4] TED may also cause significant disfigurement, severely impacting patients' quality of life.

Surgical decompression of the orbit is an established component of the surgical management of TED. Its goal is to provide space to accommodate the larger soft tissue volume, thus reducing proptosis and orbital pressure.[5] The indications for orbital decompression have evolved over the past decades. It is an urgent procedure in the active phase of TED, specifically in vision-threatening conditions, as severe exposure keratopathy and dysthyroid compressive optic neuropathy (DON), with poor or absent response to high-dose intravenous (iv) steroids. It is also performed during the stable stage of TED, for cosmetic improvement.

Several techniques, such as one-, two-, three-, and four-wall decompression have been described in the literature, though current data suggest that there is little need to decompress the orbital roof.[6–8] Any combination of the medial, inferior or lateral walls can be targeted and the number of walls removed determines the amount of proptosis reduction. The decision should be individually tailored to each case, in order to achieve the minimal but effective surgical results with an acceptable complication profile. To date, there are no evidence-based guidelines that recommend how much decompression to perform in TED.

The main purpose of this study is to analyze both clinical and imagiological outcomes of patients with TED who underwent orbital decompression.

METHODS

Retrospective observational case-series of patients with TED undergoing orbital decompression surgery in Centro Hospitalar Universitário de Lisboa Central and Hospital CUF Descobertas.

STUDY POPULATION

All patients undergoing unilateral or bilateral orbital decompression surgery in the abovementioned tertiary referral hospitals, between January 2018 and September 2021, were included in this study. Patients were retrospectively evaluated based on age at time of surgery, gender, laterality, smoking history and orbital disease activity. History of steroid, immunosuppressive and/or orbital radiotherapy was registered.

TED activity categorization was based on the Clinical Activity Score (CAS), amended by the European Group of Graves' Orbitopathy after Mourits *et al*[9] (being a CAS≥3 considered as active disease), and also on the duration of signs and symptoms suggestive of recent inflammatory disease activity.

PRE- AND POSTOPERATIVE EVALUATION

Patients underwent a complete ophthalmologic examination before and after surgery. The outcomes of orbital decompression surgery were assessed at the most recent evaluation, considering a minimum of 4 months of follow-up. Main clinical outcomes included best-corrected visual acuity (BCVA), differences in globe position in the antero-posterior, horizontal and vertical axes and complications. BCVA, TED activity, diplopia and/or muscle restrictions were evaluated pre- and postoperatively, as well as subsequent strabismus and/or lid retraction surgery.

SURGICAL TECHNIQUE

The surgical procedures performed included lateral-wall, inferomedial-wall, balanced-wall and three-wall decompressions, all of them executed by the same surgeon (A.D.).

In lateral-wall decompression, both rim-off and *ab-interno* approaches were used. A lateral upper eyelid crease incision provided exposure of the lateral orbital rim (Figs. 1A1, 1A2). A subperiosteal plane was opened until the superior orbital fissure was reached, exposing the greater wing of sphenoid bone, the zygomatic process of frontal bone, and the zygomatic bone. From 2018 to 2020, a rim-off approach was used. After retraction of the temporalis muscle, two osteotomies were created on the lateral rim, one above the zygomatic arch and another one above the frontozygomatic suture. The lateral wall was subsequently removed and enlarged with an electric burr (Fig. 1A3), and the periosteum was opened for prolapse of the orbital contents. Finally, the lateral rim was reshaped and secured in place with osteosynthesis titanium microplates (Fig. 1A4). In cases of significant proptosis, the lateral rim was not repositioned. Since 2021, the lateral-wall decompression was performed without removal of the orbital rim (*ab-interno*). For inferior and medial walls decompression, a transconjunctival approach was preferred, through a retrocaruncular (Fig. 1B1) and pre-septal access (Fig. 1B2), respectively. This approach adressed the lamina papyracea of ethmoid bone, the orbital process of palatine bone and the maxillary bone. Medially, decompression was performed from the posterior lacrimal crest, anteriorly, to the anterior border of the optic foramen, posteriorly (Fig. 1B3). The frontoethmoidal suture marked the superior limit and the inferomedial strut the inferior one. The inferior wall was decompressed between the inferomedial strut and the infraorbital nerve, from the posterior wall of the maxillary sinus until the orbital rim, leaving at least 10 mm of bone under the globe (Fig. 1B4). Some patients with active disease and DON were managed together with an otorhinolaryngology surgeon, and an endoscopic approach was used to address the inferomedial walls. The balanced two-wall decompression technique involved decompression of the medial and lateral walls, while leaving the orbital floor intact. Three-wall surgery entailed simultaneous decompression of lateral, medial, and inferior walls. Cases were respectively categorized according to type of surgery. The number of walls decompressed was tailored to the presence of DON, patient's phenotype (mainly myopathic or lipogenic), and severity of proptosis. Patients with significant proptosis and muscle enlargement underwent maximal bone excision, with removal of an increasing number of walls. Conversely, a more conservative approach was adopted for patients with less severe proptosis. All cases of active TED with DON were managed with an inferomedial-wall decompression, which included the removal of the posterior third of the strut. In selected cases with greater degree of proptosis, a lateral-wall decompression was added. Patients with bilateral disease underwent simultaneous bilateral surgery. Nonetheless, in certain cases, different surgical techniques were applied to each orbit within the same patient.

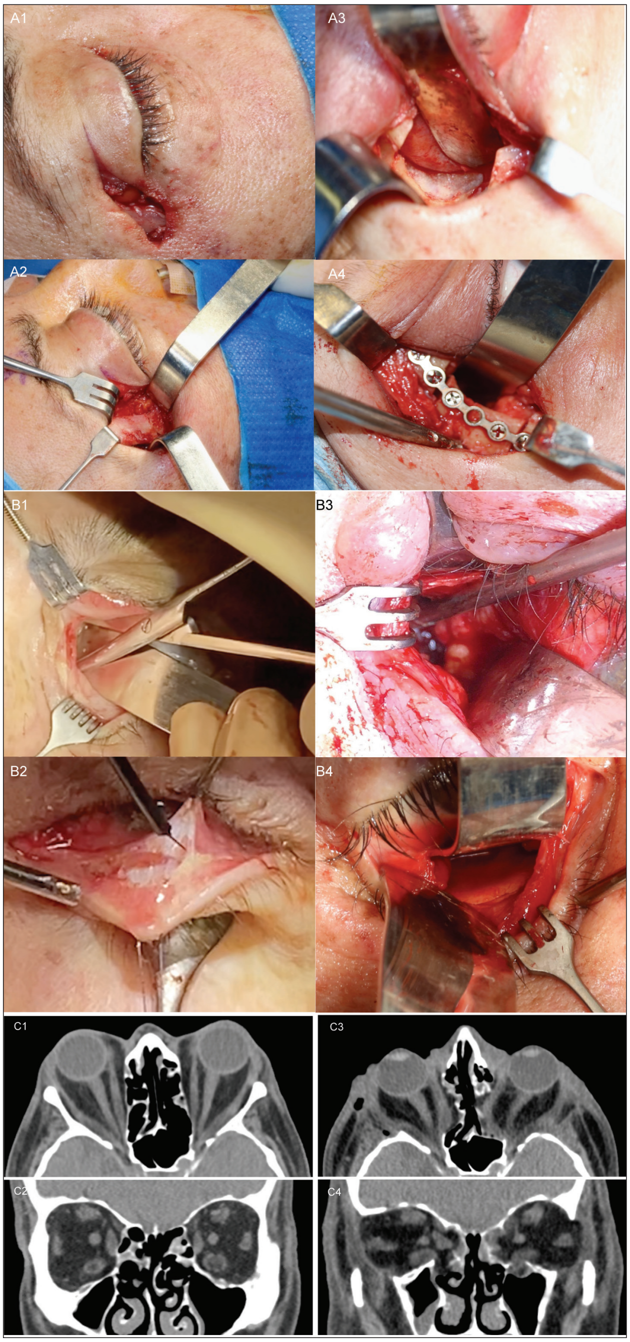

Figure 1. A: Lateral-wall approach with upper eyelid crease incision (A1) and lateral orbital rim exposure (A2) – while removing the lateral wall the orbital content is always protected with a malleable retractor (A3); the lateral orbital rim is refixed with an osteosynthesis titanium microplate in the end of the surgery (A4). B: Inferomedial-wall surgery through a transconjunctival retrocaruncular (B1) and preseptal (B2) approach, respectively. In the medial wall the lamina papyracea is removed from the posterior lacrimal crest to the optic canal (B3); 10 mm of the orbital inferior rim should be kept in place to support the globe (B4): C: Preoperative axial (C1) and coronal (C1) orbital CT images of a male patient with bilateral inactive TED, enlarged EOMs and proptosis, who was submitted to bilateral three-wall decompression surgery. The postoperative imaging (C3, C4) demonstrates the bony removal and decompression of the orbital soft tissues, with proptosis reduction of 4.0 mm in right eye and 6.6 mm in left eye.

COMPUTED TOMOGRAPHY OF THE ORBITS

A group of patients underwent orbital CT scanning before and after surgery. EOMs enlargement, proptosis reduction and differences in globe displacement in the horizontal, vertical and anteroposterior planes were measured for each type of surgery. Regarding those patients in whom an imagiological evaluation was not available, proptosis reduction was quantified based on pre- and postoperative Hertel exophthalmometric (HE) measurements (which excluded those whose orbital rim was not repositioned).

Pre- and postoperative orbital CT scans were performed with helical acquisitions, and the patients were positioned supine, asked to look at a fixed point and close their eyes while CT was taken. A stable head position was achieved by means of an adjustable head support.

The thin slice, high-resolution images obtained were then reformatted in axial and coronal images, parallel and perpendicular to the orbital axis, respectively, and sagittal images perpendicular to the coronal ones.

The method for proptosis evaluation required drawing a line between the most anterior margins of the superior and inferior orbital rims and then finding a perpendicular line forward to the most anterior point in the surface of the cornea.

To quantify the eye globe displacement in the vertical and horizontal planes, we determined the difference, after and before surgery, between the distance of the inferior margin of the superior orbital rim and the anterior limit of the medial orbital wall to the axis of the orbit in these planes, respectively. The anteroposterior globe displacement was measured using the difference between the distances from the center of the globe to the point where the perpendicular line to the axis of the orbit intersects the anterior limit of the medial orbital wall in the axial plane.

When the obtained results from the evaluation of vertical globe displacement were positive numbers it meant the globe moved inferiorly after surgery. Conversely, negative values demonstrated superior displacement. In the other orientations, positive values indicated lateral and anterior displacement of the eye globe.

In the coronal sections of preoperative CT scans, with the EOM oriented perpendicularly to their long axes, we evaluated the maximum thickness of the medial, lateral, and inferior rectus, and the superior muscle group (superior rectus and superior oblique) and used the reference normal size ranges to classify which were enlarged. The reference size used to determine EOM enlargement were: inferior rectus>6.5 mm, medial rectus>5.0 mm, superior rectus>6.1 mm and lateral rectus>4.8 mm.

In one patient, in the absence of a pre-operative orbital CT scan, we used an available MRI study to determine the measurements mentioned above.

The DICOM PACS viewer used was Sectra IDS7, and the anatomical landmarks were identified, and measurements taken by a neuroradiologist resident.

STATISTICAL ANALYSIS

Statistical analysis was conducted using RStudio software, version 1.1.423, on Windows 10 environment.

Categorical variables were summarized by absolute frequency and percentage and compared using Pearson's Chi-squared test or Fisher's exact test, as applicable. Pre- and postoperative values of categorical variables were compared with McNemar's test.

Numerical variables were summarized by mean, standard-deviation and range and compared between groups using ANOVA or Kruskal-Wallis test, as applicable. ANOVA test assumptions were tested using Shapiro-Wilk test for normality and Levene's test for homogeneity of variances.

Pre- and postoperative values of numerical variables were compared in each surgery group with a paired t-test or a Wilcoxon signed-rank test, as applicable. T-test assumption of normality was tested using Shapiro-Wilk test. In each pre- versus postoperative comparison, the p-values obtained for each surgery group, as well as the total sample, were then corrected for multiple comparisons using Benjamini-Hochberg's correction.

Comparison of numerical variables between two groups was also performed using t-test or Wilcoxon rank sum test, as applicable.

All statistical tests performed were bilateral, for a significance level of 0.05.

RESULTS

Forty-six orbits from 28 TED patients underwent orbital decompression surgery. Mean age at time of surgery was 49.43±11.63 years-old. Eighteen females and 10 males were included, with a female-to-male ratio of 1.8:1. Mean follow-up time after surgery was 15.40±13.13 months (4.50 – 56.83). TED was associated with Graves' disease in all cases except for one, who had Hashimoto thyroiditis. Of the 28 patients, 10 (35.71%) presented asymmetric/unilateral TED, while 18 (64.29%) had bilateral disease and underwent bilateral surgery. This gave a total of 46 operated orbits. Orbital decompression was performed for cosmetic reasons during the inactive phase in 31 orbits of 19 patients (67.39%) and was required to treat sight-threatening active TED (non-responsive to high-dose iv steroids) in 15 orbits of 9 patients (32.61%). In total, and regardless of the stage of the orbitopathy at time of surgery, 20 patients (71.43%) had undergone anti-inflammatory, immunosuppressive or orbital radiotherapy: 20 (71.43%) were previously treated with steroids, 7 (25%) with immunosuppressive agents (including 4 with tocilizumab) and 2 (7.14%) with orbital radiotherapy. The remaining 8 cases were in the inactive stage at first observation and had never been treated during the active phase. Table 1 shows demographic and clinical characteristics of patients included in the study.

Lateral, inferomedial, balanced and three-wall decompressions were carried out in 12 (26.09%), 8 (17.39%), 12 (26.09%) and 14 (30.43%) orbits, respectively (Table 2).

Table 1. **Demographic and clinical characteristics of the 28 patients included in the study.**

	Total (n = 28)
Age at time of surgery	
Mean (SD)	49.43 (11.625)
Range	(29 – 76)
Gender (n,%)	
Female	18 (64.29%)
Male	10 (35.71%)
Female:Male ratio	1.8:1
Smoker (n,%)	
No	22 (78.57%)
Yes	6 (21.43%)
Laterality (n,%)	
Unilateral	10 (35.71%)
Bilateral	18 (64.29%)
Follow-up time (months)	
Mean (SD)	15.40 (13.134)
Range	(4.50 – 56.83)
Pre-op steroids (n,%)	
No	8 (28.57%)
Yes	20 (71.43%)
Pre-op RT (n,%)	
No	26 (92.86%)
Yes	2 (7.14%)
Pre-op Tocilizumab (n,%)	
No	24 (85.71%)
Yes	4 (14.29%)

Pre-op = preoperative, post-op = postoperative, RT = orbital radiotherapy

Among the inactive disease group (n=31), lateral, inferomedial, balanced and three-wall surgery were performed, respectively, in 12 (38.71%), 1 (0.03%), 12 (38.71%) and 6 (19.35%) orbits. In patients with active disease (n=15), either an inferomedial (n=7, 46.67%) or three-wall (n=8, 53.33%) decompression were performed. In all cases a transorbital approach was used, except for 3 patients who underwent endoscopic endonasal surgery due to DON during active disease: 2 inferomedial and 1 bilateral three-wall decompression with an endoscopic approach to the inferior and medial walls.

All 15 eyes that underwent surgery during active inflammatory phase of TED showed a significatively poorer preoperative BCVA (active TED 0.87±0.83 logMAR, inactive TED 0.21±0.63 logMAR, $p<0.01$). A significative visual recovery was observed in these eyes (postoperative BCVA 0.37±0.82 logMAR, $p<0.05$).

Preoperative orbital CT was performed in all patients for DON confirmation and/or surgical planning. In 8 cases (12 orbits), postoperative CT was not performed and HE values were analyzed. The lateral orbital rim had not been removed on these cases and did not interfere with measurements.

Considering the 20 patients (34 orbits) who underwent both pre- and postoperative orbital CT evaluation, mean preoperative proptosis measurements were different between groups (p<0.001): balanced and three-wall decompressions showed significatively greater mean preoperative proptosis values in contrast with lateral and inferomedial-wall decompressions (14.07±3.56 mm, 14.14±1.75 mm, 9.38±2.17 mm and 8.95±3.25 mm, respectively). Globally, mean proptosis demonstrated a statistically significant reduction of 3.79±2.19 mm after surgery, corresponding to a 30.21% general decrease (12.36±3.50 mm before surgery and 8.58±2.90 mm after surgery, p<0.001) (Table 2). Patients in three-wall group exhibited the greatest mean proptosis reduction after surgery (5.09±2.16 mm, 36.89% reduction, p<0.001) (Fig. 1C), followed by balanced-wall (4.17±1.79 mm, 29.04% reduction, p<0.001), inferomedial-wall (2.62±1.13 mm, 30.98% reduction, p=0.005) and lateral-wall surgeries (1.57±1.33 mm, 16.72% reduction, p<0.05). Table 2A shows CT proptosis measurements for each group. In the group of patients whose proptosis assessment was made using HE (n=12), 6 (50.0%) were submitted to lateral, 2 (16.67%) to inferomedial, 3 (25.0%) to balanced and 1 (8.33%) to three-wall decompression surgeries. A significative decrease was also observed in these patients (5.64±3.01 mm, p<0.001). Table 2B shows HE measurements for each group.

Differences regarding the globe position before and after decompression in the horizontal and vertical axes were assessed (Table 2). Considering the horizontal plane, a mild lateral displacement of the eye was observed in the lateral-wall decompression (0.85±0.80 mm). The other procedures exhibited, on average, a mild medial dislocation (p=0.016).

Table 2. **(A) Orbital CT measurements in study groups before and after surgery. Thirty-four orbits out of the 46 included in the study underwent imagiological evaluation. In globe displacement analysis, positive values indicate lateral and inferior shifts and negative values refer to medial and superior dislocations in the horizontal and vertical axes, respectively. (B) Hertel exophthalmometer measurements in study groups before and after surgery.**

A	**Type of surgery**					***p*-value** (test)
	Lateral-wall (n=6, 17.65%)	**Inferomedial-wall** (n=6, 17.65%)	**Balanced-wall** (n=9, 26.47%)	**Three-wall** (n=13, 38.24%)	**Total** (n=34)	
Pre-op proptosis (mm)						
Mean (SD)	9.38 (2.17)	8.95 (3.25)	14.07 (3.558)	14.14 (1.745)	12.36 (3.501)	<0.001*** (ANOVA)
Range	(7.2 – 11.8)	(6.8 – 15.4)	(8.1 – 18.4)	(11.9 – 18.4)	(6.8 – 18.4)	
Post-op proptosis (mm)						
Mean (SD)	7.82 (2.161)	6.33 (3.191)	9.9 (2.316)	9.05 (2.991)	8.58 (2.896)	0.094 (ANOVA)
Range	(4.1 – 9.4)	(3.4 – 12.2)	(5.9 – 12.2)	(3.1 – 1.2)	(3.1 – 13.2)	
Difference (post-pre)						
Mean (SD)	-1.57 (1.337)	-2.62 (1.134)	-4.17 (1.792)	-5.09 (2.162)	-3.79 (2.191)	0.002** (ANOVA)
Range	(-3.1 – 0.7)	(-3.9 – -1)	(-7.3 – -2.2)	(-9.8 – -1)	(-9.8 – 0.7)	
***p*-value** (test)	0.035* (t)	0.005** (t)	<0.001*** (t)	<0.001*** (t)	<0.001*** (t)	
Horizontal globe displacement (mm)						
Mean (SD)	0.85 (0.804)	-1.15 (0.446)	-0.34 (1.264)	-0.93 (1.374)	-0.50 (1.300)	0.016* (ANOVA)
Range	(-0.3 – 1.7)	(-1.6 - -0.4)	(-2.4 – 1.3)	(-4.1 – 1.2)	(-4.1 – 1.7)	
Vertical globe displacement (mm)						
Mean (SD)	-0.03 (1.093)	0.42 (1.447)	0.12 (0.556)	0.31 (1.159)	0.22 (1.042)	0.894 (K-W)
Range	(-1.2 – 1.4)	(-1.1 – 3.1)	(-0.7 – 1.2)	(-1.4 – 3.0)	(-1.4 – 3.1)	

B	**Type of surgery**					***p*-value** (test)
	Lateral-wall (n=6, 50%)	**Inferomedial-wall** (n=2, 16.67%)	**Balanced-wall** (n=3, 25%)	**Three-wall** (n=1, 8.33%)	**Total** (n=12)	
Pre-op proptosis (mm)						
Mean (SD)	22.5 (3.507)	26 (1.414)	23.33 (3.215)	29 (NA)	23.83 (3.46)	0.286 (ANOVA)
Range	(18 – 28)	(25 – 27)	(21 – 27)	(29 – 29)	(18 – 29)	
Post-op proptosis (mm)						
Mean (SD)	19.6 (2.608)	16 (1.414)	17.67 (1.155)	23 (NA)	18.73 (2.687)	0.101 (K-W)
Range	(18 – 24)	(15 – 17)	(17 – 19)	(23 – 23)	(15 – 24)	
Difference (post-pre)						
Mean (SD)	-3.8 (2.588)	-10 (0)	-5.67 (2.082)	-6 (NA)	-5.64 (3.009)	0.073 (ANOVA)
Range	(-8 – -1)	(-10 – -10)	(-8 – -4)	(-6 – -6)	(-10 – -1)	
***p*-value** (test)	0.122 (t)	0.692 (t)	0.692 (t)	1 (t)	<0.001*** (t)	

Pre-op=preoperative, post-op=postoperative

All eyes submitted to inferomedial-wall decompression presented a medial movement in the horizontal plane and showed the greatest medial shift (1.15±0.45 mm), followed by three-wall (0.93±1.37 mm) and balanced-wall (0.34±1.26 mm) groups. Regarding the vertical axis, an inferior movement was observed in the inferomedial, balanced and three-wall decompressions, especially in the first group (0.42±1.45 mm), followed by three-wall (0.31±1.16 mm) and balanced-wall (0.12±0.56 mm) groups (p=0.894). Importantly, these dislocations were not clinically significant and they were not noticed by the patients.

Furthermore, a comparison between CT measurements of patients with active (n=13, 38.24%) versus inactive TED (n=21, 61.76%) was performed. Preoperative proptosis did not differ significantly between these two groups (11.95±3.38 mm in active TED, 12.62±3.63 mm in inactive TED, p=0.632). Similarly, even though postoperative proptosis reduction was greater among patients with active (4.2±2.55 mm) than with inactive disease (3.53±1.96 mm), this difference did not prove to be statistically significant (p=0.429).

Patients with active TED underwent either inferomedial or three-wall decompression surgeries. Regarding these surgical techniques, postoperative results of active and inactive TED were compared. No statistical significative difference was found between the two groups of disease activity in proptosis reduction nor globe displacement in the horizontal and vertical axes (p>0.05) (Table 3).

Preoperatively, enlargement of the EOM was noted in 95% of cases. The superior rectus was enlarged in 77.5%, the medial in 85%, the inferior in 62.5% and the lateral in 70%. One muscle was enlarged in 2.5%, two in 15%, three in 35% and all four recti muscles were enlarged in 42.5% of cases.

Before surgery, 10 (35.71%) patients were orthotropic and diplopia was reported in 15 (53.57%). New-onset strabismus occurred in 3 of the 28 patients (10.71%): one endoscopic inferomedial decompression, 1 transorbital three-wall decompression and 1 three-wall decompression with an endoscopic approach to the inferior and medial walls; the latter 2 underwent strabismus surgery afterwards. All the 3 cases presented DON irreversible with high-dose iv steroids and significantly enlarged EOMs. Overall, 5 patients (17.86%) were submitted to strabismus surgery at the time of this report (Table 4).

Globally, 9 patients (32.14%) underwent eyelid surgery. Four patients were submitted to blepharoplasty, 4 to lid retraction correction and 1 to both procedures separately. Regarding the 5 cases in which a lid retraction surgery was performed, 3 were executed in a staged fashion after decompression surgery while 2 were done simultaneously: one bilateral endoscopic inferomedial decompression and 1 bilateral three-wall decompression with an endoscopic approach to the inferior and medial walls, both combined with lid retraction surgery. None of these cases of combined eyelid and orbital surgery had preoperative strabismus,

Table 3. **Orbital CT measurements in patients with active versus inactive TED. Thirty-four orbits out of the 46 included in the study underwent imagiological evaluation. Patients with active disease were submitted either to inferomedial or three-wall decompression surgery and therefore these were the two surgical groups compared in this section. In globe displacement analysis, positive values indicate lateral and inferior shifts and negative values refer to medial and superior dislocations in the horizontal and vertical axes, respectively.**

	Activity		p-value (test)
	Active (n = 13, 38.24%)	**Inactive** (n = 21, 61.76%)	
Proptosis reduction (mm)			
Inferomedial-wall (n=6)	(n = 5, 83.33%)	(n = 1, 16.67%)	
Mean (SD)	2.64 (1.266)	2.5 (NA)	>0.999 (Wilcoxon)
Range	(1– 3.9)	(2.5 – 2.5)	
Three-wall (n=13)	(n = 8, 61.54%)	(n = 5, 38.46%)	
Mean (SD)	5.17 (2.714)	4.96 (1.045)	0.844 (t-test)
Range	(1 – 9.8)	(4– 6.6)	
Horizontal globe displacement (mm)			
Inferomedial-wall (n=6)	(n = 5, 83.33%)	(n = 1, 16.67%)	
Mean (SD)	-1.06 (0.434)	-1.6 (NA)	0.373 (Wilcoxon)
Range	(-1.6 – -0.4)	(-1.6 – -1.6)	
Three-wall (n=13)	(n = 8, 61.54%)	(n = 5, 38.46%)	
Mean (SD)	-0.66 (1.078)	-0.86 (1.28)	0.782 (t-test)
Range	(-2.9 – 0.6)	(-2.3 – 1.2)	
Vertical globe displacement (mm)			
Inferomedial-wall (n=6)	(n = 5, 83.33%)	(n = 1, 16.67%)	
Mean (SD)	-0.02 (0.512)	-1.1 (NA)	0.333 (Wilcoxon)
Range	(-0.6 – 0.7)	(-1.1 – -1.1)	
Three-wall (n=13)	(n = 8, 61.54%)	(n = 5, 38.46%)	
Mean (SD)	0.07 (0.678)	1.25 (1.358)	0.182 (t-test)
Range	(-1.2 – 0.9)	(-0.2 – 3)	

Table 4. Surgical outcomes regarding strabismus and eyelid retraction.

	Total (n = 28)
Pre-op strabismus (n,%)	
No	13 (46.43%)
Yes	15 (53.57%)
Strabismus (n,%)	
Never	10 (35.71%)
Only post-op	3 (10.71%)
Only pre-op	5 (17.86%)
Pre-op and post-op	10 (35.71%)
Strabismus surgery (n,%)	
No	23 (82.14%)
Yes	5 (17.86%)
Eyelid surgery (n,%)	
No	19 (67.86%)
Yes	9 (32.14%)
Eyelid procedure (n,%)	
No	26 (92.86%)
Yes	2 (7.14%)

Pre-op=preoperative, post-op=postoperative.

and in both cases no further interventions were needed. Botulinum toxin A injection was used in 2 (7.14%) patients to control lid retraction during the active phase (Table 4).

No severe intra- or postoperative complications were described.

DISCUSSION

Orbital decompression surgery is not only indicated as an urgent procedure for active sight-threatening TED but also for functional and aesthetic rehabilitation of patients with long-standing orbitopathy and disfiguring proptosis.[1] Surgery is performed by removing the lateral wall, medial wall and orbital floor in several combinations, with different approaches. Technical and conceptual advances have improved the surgical outcomes of this procedure in such an extent that, considering the low morbidity of modern orbital decompression techniques, indications have been expanded to include aesthetic deformities.

To date, there are no evidence-based guidelines that recommend how much decompression to perform in patients with TED. A graded surgical approach based on the presence of DON, muscle enlargement and desired proptosis reduction should be adopted.

There are various types of devices available for measuring the degree of proptosis.[10] The HE is the most widely used device to date.[11,12] It estimates the degree of proptosis from the lateral orbital rim to the corneal surface, perpendicular to the frontal plane.[13] However, the HE has been criticized for its low reliability and accuracy,[14] and the values obtained are less repeatable in serial measurements. Previous studies[15–17] demonstrated significative inter-observer differences. These differences in readings may result from misplacement of the foot plates, error in the base measurement, strabismus, asymmetry of the lateral orbital rims, compression of soft tissues, parallax errors or lack of a uniform measurement technique.[18,19] Furthermore, a drawback of its use is the influence of the surgical procedure on the readings. Conventional lateral rim-supported HE are not suitable for postoperative proptosis assessment after removal of the orbital rim during lateral wall decompression,[20] as proptosis reduction may be underestimated. Imaging becomes a more reliable and precise means of measuring proptosis, being, whenever possible, our preferred method. Neuroradiological imaging plays an important role in the differential diagnosis and interdisciplinary management of patients with TED.[1,21] Orbital CT findings, such as spindle-shaped thickness>4 mm of more than one EOM, without involvement of the corresponding tendon (with preferential involvement of the inferior and medial rectus), orbital tissue edema, increase in retrobulbar fat volume, compression of the optic nerve at the orbital apex ("crowded orbital apex syndrome") and absence of any space-occupying intraorbital process are the most important morphological diagnostic criteria of TED.[20] Orbital CT scan is recommended pre and postoperatively to define the site and extent of the bony decompression and evaluate anatomical results.[22,23]

In our study, lateral, inferomedial, balanced and three-wall decompressions were performed. There was a statistically significative difference in proptosis reduction between groups (p=0.002). Nonetheless, preoperative proptosis measurements also showed significative difference between groups (p<0.001), since balanced-wall and three-wall decompressions were performed on orbits with greater preoperative proptosis. Lateral, inferomedial, balanced and three-wall surgeries resulted in significative mean proptosis reduction on orbital CT measurements (1.57±1.33 mm, 2.62±1.13 mm, 4.17±1.79 mm and 5.09±2.16 mm, respectively) (Table 2). Activity of disease did not appear to affect significatively the postoperative measurements concerning the proptosis reduction and the globe displacement in the horizontal and vertical planes. However, eight out of nine patients with active TED were additionally treated with either TCZ or radiotherapy after surgery, which should be taken into account and may bias these results.

Lateral-wall decompression has been reported to achieve, on average, between 2.7 – 4.0 mm of proptosis reduction, measured using the HE.[24–27] In our study, and considering patients evaluated by CT imaging, a mean reduction of 1.57 mm was obtained. However, when considering patients evaluated with HE (n=6), a 3.8±2.59 mm reduction was found (p>0.05), which is compatible with the results obtained on reference studies.[25–27] This difference reinforces the importance of not comparing proptosis values using different measurement methods. Regarding inferomedial-wall decompression, pooled data from multiple centers,[28] meta-analysis[29,30] and retrospective case-series[25,26] suggest that a range of 2.5 – 4.7 mm of proptosis reduction can be expected. Studies suggest that inferomedial-wall decompression is an effective surgical option for DON: by removing the medial orbital wall and posterior floor, the optic nerve is immediately given space to decompress.[31] However, when addressing DON caused by TED, the amount of proptosis reduction drops to 3.1 mm.[32] In fact, all except one patient from inferomedial-wall group underwent surgery during active phase of TED to treat DON non responsive to systemic steroids, and therefore our results are in line with the literature. The amount of proptosis reduction via balanced-wall and three-wall decompression ranges from 4.1 – 5.3 mm[25,29,33–35] and 4.4 – 6.9 mm,[27,28,36] respectively, which is also consistent with the current study.

Differences regarding the globe position before and after decompression in the horizontal and vertical axes were assessed. As expected, all eyes submitted to inferomedial-wall decompression presented a mild medial displacement in the horizontal plane, being the procedure with the greatest shift in this axis, followed by three-wall and balanced-wall decompressions. In contrast, eyes from the lateral-wall group presented a mild lateral displacement. Regarding the vertical axis, almost all procedures exhibited a mild inferior globe dislocation, more prominent in the inferomedial-wall decompression and less evident in the balanced-wall group. All of these are expected results after these procedures and have no negative impact on the final cosmetic improvement. Whenever a two-wall procedure is needed, a balanced approach is preferable to the inferomedial surgery.

Diplopia is the most common complication following decompression surgery,[31] reported to be between 0% – 45%[37] depending on the type of surgery, with medial and inferior decompressions associated with higher rates. New-onset strabismus occurred in only 3 of the 28 patients (10.71%), all of them with DON: 1 endoscopic inferomedial decompression, 1 transorbital three-wall decompression and 1 three-wall decompression with an endoscopic approach to the inferior and medial walls. Out of these, one patient reported diplopia resolution with prism correction while the latter 2 underwent subsequent strabismus surgery. Importantly, all of these cases had a marked muscle enlargement, which is a known risk factor for strabismus,[38] and needed posterior struct removal, a maneuver performed in DON cases to increase the space of crowded apexes. Overall, 5 patients (17.86%) had undergone subsequent strabismus surgery at the time of this study. In 3, diplopia was already present before surgery.

Within our study, a significant proptosis reduction was observed in all patients except for one, in whom post-operative CT scan was performed after decompression and second-stage strabismus surgery. This specific case initially presented proptosis improvement after lateral-wall decompression. Muscle recession can theoretically allow the globe to move anteriorly by the release of tethering of the EOMs and may affect proptosis, especially in patients who have undergone previous orbital decompression.[39] Therefore, in patients with TED-associated restrictive strabismus, in whom we anticipate the need for future muscle recession, we may consider targeting a slightly higher decompressive effect.

Surgical treatment of TED has been traditionally conducted in a stepwise fashion. The classic approach suggests that decompression is the first procedure performed, as it can affect strabismus measurements and may be followed by postoperative diplopia.[40] The last procedure is eyelid surgery, which can be affected by both decompression41 and strabismus surgery.[42,43] Some have challenged this paradigm, suggesting that there is minimal change in upper eyelid position with decompression surgery[44] and therefore simultaneous upper eyelid and decompression surgery may be performed to shorten rehabilitation intervals.[45] In this study, simultaneous orbital decompression and eyelid retraction surgery was performed in 2 patients, mainly due to economic issues or the impossibility for frequent traveling. We prefer, whenever possible, a staged approach; however, in selected cases, this is a valid choice with good proptosis and eyelid results. Other authors also claimed that customized orbital decompression surgery combined with eyelid or strabismus surgery in TED is effective, has fewer side effects and leads to earlier recovery, decreasing the number of total procedures and the time needed for surgical rehabilitation.[5]

As possible limitations of this study, we highlight its retrospective nature. Also, it was not feasible to objectively analyze pre and postoperative orbital CT scans in all patients, due to the fact that some patients live in distant cities and usually undergo imaging procedures externally, precluding our access to the exams during the course of this analysis. It would also be interesting to increase the sample in each decompression group. As strong points of this work, all patients were operated by the same surgeon, thus eliminating the bias of the surgical technique. Also, CT examination provided a precise analysis of the vertical and horizonal displacement of the globe after surgery and allowed us to clarify the benefit of balanced-wall versus inferomedial-wall decompression when considering a two-wall decompression surgery.

CONCLUSION

TED is a potentially disfiguring and frequently disabling condition with an important impact on quality of life, posing a significant health burden. Severe proptosis remains a therapeutic challenge as of date. A great reduction of proptosis with a low complication rate is the key to address facial rehabilitation aimed at restoring function and enhancing appearance (Fig. 2). Orbital decompression surgery is an effective procedure to address proptosis in TED, being also an important resource in cases of sight-threatening disease unresponsive to systemic steroids. The amount of proptosis reduction is associated with the number of orbital walls removed and the combination of decompression with eyelid surgery presents good efficacy in selected cases. An individualized approach is crucial for surgical planning in TED.

Figure 2. Patients underwent: A: Bilateral three-wall decompression followed by strabismus surgery. B: right three-wall orbital decompression surgery; C: bilateral three-wall decompression surgery; D: right three-wall decompression surgery; E: right balanced and left lateral-wall decompression followed by bilateral upper eyelid retractors recession.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

CGM: Responsible for gathering the data, statistical analysis, presenting the results, creating the manuscript

PB: Responsible for CT evaluation, analysis and measurements.

DM: Contributed to data collection.

AM: Manuscript revision.

AD: Supervised this project, revised the manuscript and contributed with her expertise to its conclusion.

All authors approved the final version to be published.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

Provenance and Peer Review: Not commissioned; externally peer reviewed.

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