Effect of orbital decompression on dysthyroid optic neuropathy
A retrospective case series

Qiao-Wen Liang, MD\textsuperscript{a}, Huasheng Yang, MD\textsuperscript{b}, Wenjing Luo, MD\textsuperscript{c}, Jian-Feng He, MD\textsuperscript{a,}\textsuperscript{*}, Yi Du, MD\textsuperscript{b,}\textsuperscript{*}

Abstract
In this study, we try to explore the effect of orbital decompression treatment on severe dysthyroid optic neuropathy. We retrospectively collected demographic and clinical characteristics of thyroid eye disease patients who performed orbital decompression. Then we analyzed the change of best-corrected visual acuity and exophthalmometry after surgery and the correlations among clinical parameters.

A total of 22 cases (30 eyes) were included in the study. After orbital decompression, visual acuities improved in 16 eyes, declined in 8 eyes, and had no change in 5 eyes. Best-corrected visual acuity was significantly improved (0.1 vs 0.4, \(P = .039\)) and exophthalmometry was significantly declined (22.0 mm vs 16.5 mm, \(P = .001\)) after orbital decompression. Better postoperative best-corrected visual acuity was significantly correlated with better preoperative best-corrected visual acuity (\(r = 0.718, P < .05\)), and with normal optic disc (\(r = 0.568, P < .05\)), but not with age, exophthalmometry, keratopathy, and clinical activity score.

These results showed that orbital decompression is a useful approach to manage dysthyroid optic neuropathy. The optimal time for surgery should be chosen based on clinical parameters, such as visual acuity and degree of crowding of orbital apex.

Abbreviations: BCVA = best-corrected visual acuity, CAS = clinical activity score, DON = dysthyroid optic neuropathy, RNFL = retinal nerve fiber layer, TED = thyroid eye disease.

Keywords: compressive optic neuropathy, Graves’ ophthalmopathy, Graves’ orbitopathy, thyroid associated ophthalmopathy, thyroid eye disease

1. Introduction
Thyroid eye disease (TED), also known as Graves’ ophthalmopathy/orbitopathy and thyroid associated ophthalmopathy, is the most common orbital disease, affecting nearly 50\% of Graves’ disease patients\textsuperscript{[1,2]} TED is thought to relate to plenty of glycosaminoglycan composed by fibroblast deposited in the orbit. Signs and symptoms of TED occur due to inflammation of the orbital connective tissue, expansion of the extraocular muscles, and adipogenesis\textsuperscript{[3]}. The increase of intraorbital pressure and expansion of the extraocular muscles can compress the optic nerve, resulting in dysthyroid optic neuropathy (DON), which is a potentially blinding complication\textsuperscript{[4,5]} Occasionally, there are no enlargement of extraocular muscles, but protopsis due to increasing orbital fat volume may stretch optic nerve, thus can also lead to DON. In general, 4\% to 8\% of cases with TED are affected by DON\textsuperscript{[5]} which can lead to visual loss.

Orbital decompression is considered to be an effective therapy for DON\textsuperscript{[4,6]} It can reduce orbital inflammation, decrease intraorbital pressure, and improve visual acuity\textsuperscript{[7]}. However, it remains unclear which clinical parameters are correlated with the visual acuity after orbital decompression. The purpose of the present study is to determine what factors are predictive of the postoperative visual outcome and explore the effect of orbital decompression.

2. Methods
2.1. Patients
The medical records of all TED patients with optic neuropathy who underwent orbital decompression in the Zhongshan Ophthalmic Center, Sun Yat-sen University between November 2010 and December 2012 were reviewed. TED diagnoses were determined based on Bartley’s criteria\textsuperscript{[8]} DON was categorized according to the criteria proposed by Dayan and Dayan\textsuperscript{[9]} The study was approved by the ethics committee of Zhongshan Ophthalmic Center. All patients provided the written informed consent according to the Declaration of Helsinki. Clinical
parameters, including age, gender, exophthalmometry (Hertel), optic disc morphology, severity of disease\cite{10}, clinical activity score (CAS)\cite{11}, preoperative and postoperative best-corrected visual acuity (BCVAs), were obtained for analysis. We also collected clinical materials including noncontact intraocular pressure, keratopathy, whether the patients suffer from eye pain or diplopia, whether the patients receive steroids pulse therapy, methylprednisolone pulse therapy ≥ 24 mg\textsuperscript{2} and 6 mg\textsuperscript{2} for patients with DON (CAS ≥ 3) with intravenous methylprednisolone pulse therapy first. If optic nerve function poorly responds to this therapy, orbital decompression would be carried out\cite{11}.

2.2. Inclusion and exclusion criteria
Patients with DON were included if they were Chinese and ≥ 18 years old, had no overt hypo- or hyperthyroidism, and had no other ocular diseases that may affect the assessment of visual function (e.g., exposure keratitis, severe pterygia, and age-related cataract). Patients were excluded if they had postoperative follow-up < 28 days, or had no orbital CT/MRI scan with axial and coronal views.

2.3. Orbital decompression procedure
Medial wall decompression can directly relieve the apical pressure by the hypertrophic medial rectus and it is necessary for patients with compressive optic neuropathy. In severe cases, medial wall decompression was used in combination with lateral decompression to relieve apical pressure and exophthalmos more effectively. If a patient had anosmia strabismus, medial wall decompression was used in combination with inferior decompression. For particularly severe cases, 3 wall (medial, lateral, and inferior) decompression was performed.

General endotracheal anesthesia is administered before surgery. Medial, lateral, and inferior wall decompression were all performed via skin approach and part of the orbital fat was removed during surgery. The procedure of medial and inferior wall decompression was as follows: firstly made a skin incision, exposed orbital rim and medial/inferior wall, then removed medial and inferior wall to make the orbital fat extrude into ethmoid sinus and maxillary sinus, finally layered sutured the incision. The procedure of lateral wall decompression was as follows: firstly made a skin incision, exposed lateral orbital rim, cut the periosteum to expose the bone substance, then removed lateral wall to make the orbital fat extrude into fossae temporalis, finally trimmed the removed lateral wall to make it thinner and replaced it, sutured the periosteum and incision.

2.4. Statistical analysis
The corrected decimal BCVAs were converted to the LogMAR scores for statistical analysis. Eyes without form visual acuity were assigned decimal visual acuity according to previous scores for statistical analysis. Eyes without form visual acuity were assigned decimal visual acuity according to previous

\begin{table}[h]
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\begin{tabular}{|l|c|}
\hline
\textbf{Parameter} & \textbf{Value} \\
\hline
Female, n (%) & 13 (59) \\
Age at surgery, years, median (range) & 50 (32-63) \\
Visual loss duration, months, median (range) & 2 (0.3-24) \\
Ophthalmoptosis duration, months, median (range) & 12 (2-36) \\
Subjective diplopia, n (%) & 7 (32) \\
Steroids pulse therapy & \\
Preoperative, n (%) & 4 (18) \\
Postoperative, n (%) & 18 (82) \\
Previous history & \\
\hline
\hline
\end{tabular}
\caption{Demographic characteristics in thyroid eye disease patients (n = 22).}
\end{table}

The relationships among age, exophthalmometry, optic disc morphology, keratopathy, clinical activity score, preoperative and postoperative best-corrected visual acuity, were evaluated using the Spearman test. For each patient, if there were bilateral DON in one patient, we used data of right eye for Spearman test. \( P < .05 \) was considered statistically significant.

3. Results

3.1. Demographic and preoperative clinical characteristics
Total 29 patients were included in the present study. Among them, 2 patients without coronary MRI scan and 3 patients who had follow-up < 28 days were excluded. Finally 22 patients (30 eyes) were included (9 males and 13 females). The median age was 50 years (32-63 years). The follow-up duration ranged from 1.2 to 12.8 months, with a median duration of 4.7 months.

The duration of visual loss ranged from 10 days to 2 years, with a median duration of 2 months. Seventeen cases of the 22 patients had ophthalmoptosis with a duration from 2 months to 3 years. Seven patients had a complaint of diplopia. Eighteen cases were treated with steroids after orbital decompression, and 4 before orbital decompression. Five patients received \( \text{I}^{131} \) therapy and 2 patients had subtotal thyreoidectomy in previous history.

Preoperative BCVAs ranged from no light perception to 0.7. Intraocular pressure ranged from 13 to 55 mm Hg, with a median of 24 mm Hg. Of these 30 eyes, 8 had optic disc edema, 3 had optic disc pallor, 18 had optic disc normality. The median preoperative exophthalmometry was 22 mm (15-25 mm). CAS ranged from 0 to 7, with a median of 2. Of the 30 eyes, 10 had corneal epithelial punctate defect, 3 had keratitis, 1 had corneal ulcer, and 16 eyes were normal (Tables 1 and 2).

3.2. Visual acuities and exophthalmometry
Preoperative BCVAs ranged from count fingers to 1.0. BCVAs improved in 18 eyes, declined in 6 eyes, and had no change in 6 eyes. The median preoperative exophthalmometry was 16.5 mm (12-19 mm). Exophthalmometry was declined by 5.1 mm (±3.0 mm) after surgery. BCVAs were significantly improved (\( P = .039 \)) and exophthalmometry was significantly declined (\( P = .001 \)) after orbital decompression.

3.3. Correlations among clinical parameters
Better postoperative BCVAs were significantly correlated with better preoperative BCVAs (\( r = .718, P < .05 \)), and normal optic
In order to analyze the predictive factors of the postoperative visual outcome in visual acuity improved/unimproved patients, we divided the 30 eyes into 2 groups, 1 group with BCVAs improved (n=18) and the other group with BCVAs declined or unchanged (n=12). Then we compared the preoperative clinical characteristics between the 2 groups using Wilcoxon rank sum test and evaluated the relationships among clinical characteristics in each group using the Spearman test. We found that all of the preoperative clinical characteristics such as age, exophthalmometry, optic disc morphology, keratopathy, CAS, preoperative BCVAs between the 2 groups had no statistical differences. In the group of patients with BCVAs improved, better postoperative BCVAs were significantly correlated with better preoperative BCVAs ($r = 0.781$, $P < .01$), while in the group of patients with BCVAs declined or unchanged, better postoperative BCVAs were significantly correlated with better preoperative BCVAs ($r = 0.978$, $P < .01$) and shorter ophthalmoptosis duration ($r = -0.955$, $P < .01$).

### 3.4. Orbital decompression and complications

Among the 30 eyes, medial wall orbital decompression was done in 1 eye, medial and lateral wall orbital decompression was done in 8 eyes, medial and inferior wall orbital decompression was done in 6 eyes, and 3-wall (media, lateral and inferior) orbital decompression was done in 15 eyes (Fig. 2).

Broad-spectrum antibiotic was used after orbital decompression and no infection happened. Intraorbital hematoma happened in one of these patients, and we opened the incision, but not with age, exophthalmometry, keratopathy, and CAS (Table 3, Fig. 1).

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| Preoperative optic disc morphology | Postoperative BCVA (logMAR) | Postoperative BCVA (logMAR) |
|-----------------------------------|-----------------------------|-----------------------------|
| Optic disc normality              | 0.568 (P < 0.05)            | Postoperative BCVA (logMAR) |
| Optic disc edema                  | 0.568 (P < 0.05)            | Postoperative BCVA (logMAR) |
| Optic disc pallor                 | 0.568 (P < 0.05)            | Postoperative BCVA (logMAR) |

**Figure 1.** (A) Postoperative BCVA (logMAR) in patients with optic disc normality was better than that in patients with optic disc edema/pallor in the presented study. (B) Better postoperative BCVA (logMAR) was significantly correlated with better preoperative BCVA (logMAR) in the presented study. BCVA = best-corrected visual acuity.
removed the hematocèle, stopped bleeding with electrocoagulation, and then compressed with padding and a bandage.

4. Discussion

Orbital decompression is an effective and safe operation aimed at decreasing the raised intraorbital pressure and ophthalmoptosis, and treating exposure keratitis and dysthyroid optic neuropathy. In orbital decompression, removal of 1 to 3 bony orbit walls was done, usually in combination with removal of the orbital fat to make the intraorbital soft tissue extrude into paranasal sinuses. In this retrospective case series study among 22 patients with DON, we found that BCVAs were significantly improved and exophthalmometry was significantly declined after a mean 5.8 months of follow-up, and that patients with better preoperative BCVAs and/or normal optic disc had better BCVAs. To the best of our knowledge, this is the first report regarding prognostic factors of orbital decompression for DON.

Although few study specially addressing effect of surgery on visual recovery in patients with DON up until now, orbital decompression is an effective therapy for improvement of visual acuity in severe TED. West and Stranc reported that 22 patients (44 eyes) with severe TED, who failed to respond to steroids therapy, underwent four-wall orbital decompression. Fifteen of the 44 eyes (34%) had visual acuity of ≤0.1, and only 6 eyes had normal visual acuity (1.0) preoperatively. During long-term follow-up after surgery, visual acuity was normal in 34 eyes (77%). In the research of Korkmaz and Konuk, indicators of visual function (visual acuity and color vision) significantly improved after 2- and 3-wall decompression in DON patients. Proptosis reduction was higher after 3-wall than 2-wall decompression (7.2 ± 1.9 mm vs 5.1 ± 1.3 mm, P = .0001). We found that visual acuity was significantly improved and exophthalmometry was declined by 5.1 mm (±3.0 mm) after surgery. Our study further supports the existing data. Fatourechi et al reported a case series of 428 patients with severe TED who had undergone an initial transantral orbital decompression. They found that patients with more reduction of proptosis had more improvement in visual acuity using multifactor regression analysis. Our present study found that better postoperative BCVAs were significantly correlated with better preoperative BCVAs and normal optic disc, but not with preoperative exophthalmometry. The difference of these results may due to our smaller sample size.

The mechanism of optic nerve compression that can lead to vision loss remains unclear. Increased intraocular pressure and decreased perfusion pressure due to the increased intraorbital pressure might lead to ischemia of the optic nerve. In the present study, better postoperative BCVAs correlated with better preoperative BCVAs. This phenomenon in DON was similar with findings in other optic neuropathies (e.g., optic neuritis, traumatic optic neuropathy). It implied that patients had the more unbroken optic nerve fibers preoperatively, the better postoperative visual acuity they would have. However, it is surprising that visual acuities of two 61-year-old female patients were improved from no light perception to count fingers after orbital decompression. These 2 patients had some common clinical characteristics such as vision loss duration of half a month, ophthalmoptosis duration of one year, CAS of 4, optic disc swelling and exophthalmometry was declined by 6 mm (from 19 to 13 mm) after surgery. The improvement of visual acuity might be related to the relatively short duration of vision loss and the relatively large decreases of exophthalmometry. Since normal visual acuity does not preclude optic neuropathy and the optic

Figure 2. Axial (A) and coronal (B) CT scans of a 22-year-old man with bilateral DON showing apical compression of the optic nerve with apical crowding. Axial (C) and coronal (D) CT scans of the same patient, one month after bilateral 3-wall (media, lateral and inferior) orbital decompression.
disc in DON patients may be swollen, pale or normal, molecular markers and imaging examinations are necessary for the recognition of DON. Ponto et al. reported that serum thyroid-stimulating immunoglobulins was associated with DON of recent onset. Another study found that the rate of apoptosis in orbital fibroadipose tissue of TED patients was significantly higher in eyes with DON than in eyes without DON. In the aspect of imaging examination of optic nerve, Park et al. found that the mean temporal peripapillary RNFL thickness was thinnest in chronic DON compared to acute DON and control eyes, and patients with greater inferior peripapillary RNFL thickness and younger age were more likely to have better visual outcomes.

There are 2 subtypes of TED, including predominantly fat increase subtype and predominantly muscle increase subtype. Regensburg et al. calculated the fat volume and muscle volume of Caucasian TED patients and found that 70% of these patients had muscle enlargement while only 14% had fat increase. In Chinese TED patients, Du et al. found that DON rarely occurred in the predominant fat increase subtype, and visual impairment caused by DON was relatively mild compared to predominantly muscle increase subtype. In the present study, all of the TED patients were predominantly muscle increase subtype. In our experience, DON caused by muscle enlargement usually requires orbital decompression after failing to respond to steroids pulse therapy, while DON caused by fat increase rarely needs surgical treatment because steroids therapy is usually effective.

Since there is no guideline for orbital decompression at present, the surgical time window for our patients depends on visual acuity, degree of crowded orbital apex syndrome, etc. One patient with DON has indications for surgery if preoperative methylprednisolone pulse therapy does not improve visual acuity. In patients who do not have severe visual impairment, if their visual acuity continues to decline and have crowd apex syndrome on CT/MRI, we will still treat them positively. Thus, patients with DON might best benefited from orbital decompression. In patients with compromised optic neuropathy, decompression of medial orbit wall is a routine technique because optic nerve is close to medial rectus in orbital apex. However, because morbidity rate exotropia is far higher than that of exotropia in TED patients, and eye ball often moves toward medial after medial orbit wall decompression, this technique is usually used in combination with lateral orbit inferior wall decompression instead of used only. Additionally, as TED patients suffer from inflammation, tissue edema and hemangiectasis, postoperative orbital hematoma is common and it can decrease the visual outcome. Skin incision, orbital bone membrane separation, orbital fat and connective tissue removal may lead to orbital hematoma. In the present study, visual acuity in only one case was made worse by surgical complication because of postoperative orbital hematoma. In this case, the optic nerve was seriously stretched by antidisplacement of eye ball, resulting from retrobulbar hematoma. Preoperative coagulation function test, fully exposure and avoiding large blood vessels in operation may prevent orbital hematoma.

The follow-up duration is a major limitation of the present study. The follow-up duration of the patients ranged from 1.2 to 12.8 months, and 4 patients had relatively short follow-up duration shorter than 2 months. This may affect the outcomes to some extent.

In conclusion, as an effective and safe operation, orbital decompression can protect the residual visual function of DON patients. Patients with better preoperative visual acuity, with normal optic disc could have better postoperative visual acuity. The appropriate time for orbital decompression should be chosen based on clinical parameters, such as visual acuity and the degree of crowding of orbital apex. We should hold the indication of orbital decompression, prevent and treat complications to achieve better surgical outcomes.

Author contributions

Conceptualization: Huasheng Yang, Yi Du.

Data curation: Qiao-Wen Liang.

Formal analysis: Qiao-Wen Liang, Wenjing Luo, Yi Du.

Funding acquisition: Yi Du.

Investigation: Yi Du.

Methodology: Huasheng Yang, Wenjing Luo, Yi Du.

Resources: Huasheng Yang.

Supervision: Jian-Feng He, Yi Du.

Writing – original draft: Qiao-Wen Liang, Wenjing Luo, Yi Du.

Writing – review & editing: Jian-Feng He, Yi Du.

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