

Strabismus Surgery in Thyroid-related Ophthalmopathy

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Abstract

Background: Restrictive strabismus is a common feature of Thyroid-Related Ophthalmopathy (TRO) causing intractable diplopia. We reviewed the surgical outcome for TRO patients.

Methods: We retrospectively reviewed patients of TRO who underwent strabismus surgery from January, 1998 to September, 2012. Preoperative characteristics were recorded such as age, sex, disease severity, presence of compressive optic neuropathy or elevation of intraocular pressure, symmetry of orbitopathy, duration between onset of TRO and surgery, smoking status, and treatment. The length of muscle recession and the numbers of strabismus surgeries was recorded for further analysis.

Results: Twenty-four patients were enrolled with twelve female and twelve male in a mean age of 55.5 years (SD + 10.71). The mean number of surgery was 1.29 (SD + 0.46). Patients with asymmetric involvement at onset, presence of elevated intraocular pressure, and longer intervals between the onset of TRO and first surgery needed significantly more surgeries to correct strabismus. Factors such as age, gender, smoking status, medical treatment before surgery, presence of compressive optic neuropathy or previous orbital decompression procedure had no statistically significant effect on the number of surgery required.

Conclusion: Strabismus surgery showed favorable outcomes in correcting diplopia induced by thyroid-related ophthalmopathy. The average number of surgery needed is 1.29 (± 0.46) in this study, and the mean surgical effect we got was 4.09+0.26 PD/mm of rectus muscle recession.

Keywords: Restrictive strabismus; Thyroid-related ophthalmopathy; Surgery

the possible factors for multiple surgeries, we reviewed the surgical outcome and analyzed the surgery-related features.

Introduction

Thyroid-related ophthalmopathy [1]/ orbitopathy (TRO), also known as thyroid associated ophthalmopathy [2]/orbitopathy (TAO) [3], thyroid eye disease (TED) [4,5], or Graves's ophthalmopathy [6]/ orbitopathy [7], is considered an autoimmune disease which is characterized by chronic inflammation of orbital soft tissue, extraocular muscles, conjunctiva and even eyelids [1,8]. It may cause social and visual problems to patients by disturbing appearance and visual function. In the acute phase of the disease, patients may report orbital pain, diplopia and ocular movement limitation which result from lymphocytic infiltration and congestion of orbital tissues. In the chronic phase, restrictive strabismus occurs due to adipose tissue infiltration and fibrotic change of the extraocular muscles [6,9]. Among these signs of TRO, impaired ocular motility and alignment have been found to profoundly influence the quality of life of affected individuals [6,10]. Clinically, TRO most frequently involves the inferior and medial rectus muscles [4,5]. The diplopia caused by TRO may progress from intermittent to constant disability which needs surgical intervention to relieve. Due to the tightness and poor elasticity of involved muscle, patients may need more than one surgery. To present the outcomes of strabismus surgeries for TRO and investigate

Material and Method

We performed a retrospective chart review of consecutive patients with TRO who underwent strabismus surgery, based on medical records of patients in a tertiary referral center, Kaohsiung Veterans General Hospital, from January, 1998 to September, 2012. Patients were identified from hospital electronic diagnostic database according to ICD-9 codes (376.21: Thyrotoxic exophthalmos) combined with a hospital surgical coding system (strabismus surgery). The inclusion criteria are as following:

1. Age older than 18 and younger than 80 years old.
2. Patients in euthyroid status during follow-up
3. Stable deviation in at least 3 month's follow-up, which means a variation of less than 2 prism diopter between two consecutive visits
4. Received at least one strabismus surgery, including muscle weakening or strengthening procedures.
5. Complete 6 month's follow-up postoperatively

Cases with previous strabismus surgeries, or postoperative follow-up less than 6 months were excluded. The hospital Institutional

Review Board and Ethics Committee approved this study, which adhered to the tenets of the Declaration of Helsinki.

The preoperative and postoperative ocular examination included best-corrected visual acuity, color discrimination test (Ishihara color plate), intraocular pressure (IOP), deviation at primary position by alternate prism cover test, ocular motility, existence of exophthalmos (Hertel exophthalmometer), examination of external eye, anterior segment and posterior segment. The decision of surgical dose was based on preoperative deviation, the pattern of motility limitation and forced duction test during surgery. All surgeries were performed by the same surgeon, M.C. Lin with non-adjustable method.

Preoperative data included gender, age at onset of TRO, smoking status, laterality of TRO at onset, amount of horizontal and vertical deviation in prism diopter, secondary glaucoma, compressive optic neuropathy, previous orbital decompression procedure, treatment before strabismus surgery, interval between onset of TRO and strabismus surgery. Current smoker was defined as having smoked at least 100 cigarettes in his/her entire life and smoking cigarettes every day or some days [11]. Laterality of TRO was divided into bilateral and unilateral, according to first presentation of the patient. If the patient presented as redness, swelling, pain, or limitation of extraocular muscle of only one eye, or more than (or equal to) 2 mm of the difference of exophthalmia, he was classified into the unilateral group. If the patient presented with above symptoms of both eyes or less than 2mm difference of exophthalmia, he was defined as having bilateral TRO [12]. Secondary glaucoma was defined as newly diagnosed open-angle glaucoma (after diagnosis of TRO) with intraocular pressure more than 21 mmHg. The steroids responder was excluded from secondary glaucoma group in this study if the patient's intraocular pressure returned to normal within one month after discontinuation of steroids.

The treatment before strabismus surgery included intravenous pulse methylprednisolone therapy (3 eyes, 12.5%), retrobulbar injection with triamcinolone (7 eyes, 29.2%), and oral prednisolone (12 eyes, 50%). The intravenous methylprednisolone pulse therapy was given as 250 mg q6h for 3 days (total 12 doses) followed by oral prednisolone according to clinical condition. The retrobulbar injection of triamcinolone was given as 20 mg/0.5ml/shot, repeated in 3-4 weeks' interval. The oral prednisolone was started as 1 mg/kg/day, and then gradually tapered by 5-10 mg/day every 1-2 weeks.

The surgery performed on TRO patients included muscle recession, muscle resection, muscle detachment, and muscle tucking. When the muscle planned to be recessed was too tight and we were unable to even put suture on that muscle, we left the tight muscle detached from the globe. Maximally two rectus muscles in the same eye were operated in one surgery to prevent anterior ischemic syndrome; however, if detachment of one rectus muscle was performed, no other rectus muscle in this eye was operated in the six months to come. Operative data included the amount and the number of muscles recession (both horizontal and vertical). We followed patients at 1 week, 6 weeks, 3 months and 6 months postoperatively, and the follow-up time was counted from the last surgery if more than one surgery was done. Success was defined as patients have no diplopia in primary position at distant and near without abnormal head position. If the patient had persistent diplopia after six months' follow-up, a second surgery was considered. The preoperative, postoperative ocular alignments and the numbers of strabismus surgeries required were collected for analysis. Mean surgical effect was calculated from data of patients receiving only muscle recession, and the data of patients

receiving muscle detachment, recession-resection and the data of the second surgery were excluded. The mean surgical effect was expressed by the corrected deviation in prism diopters (PD) divided by the length of muscle recessed in millimeter (mm). All statistical analyses, including Fisher's test, Mann-Whitney U test were conducted using SPSS version 20.0 (IBM Inc., New York, United States).

Results

Twenty four cases were recruited in this study, twelve were female (50%) and twelve were male (50%). The mean age was 55.50 + 10.71 years (range, 32 to 73 years). The mean age of males was 57.17+10.28 years (range, 41 to 73 years) and females was 53.83+11.31 years (range, 32 to 69 years) (p=0.59). Eight patients (33.3%) had unilateral involvement of TRO at onset. Three current smokers (12.5%) at first presentation were identified. Nine patients (37.5%) were diagnosed as secondary glaucoma during follow-up before strabismus surgery.

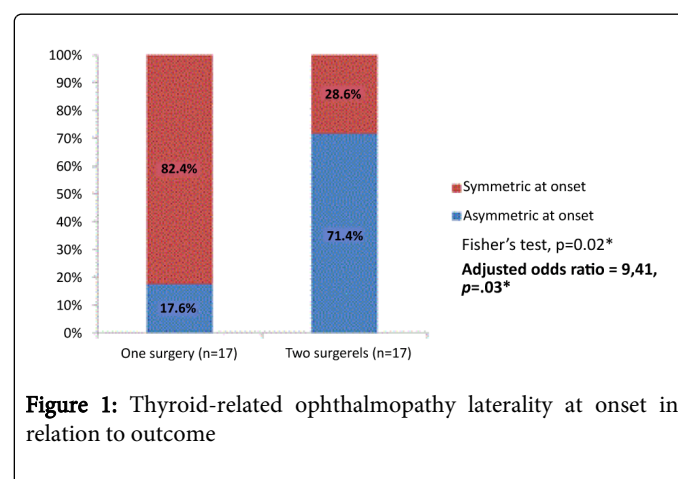


Figure 1: Thyroid-related ophthalmopathy laterality at onset in relation to outcome

Five patients (20.8%) had a history of compressive optic neuropathy related to TRO. Seven patients (7 eyes, 29.2%) had previous orbital decompression procedure. The mean duration from the onset of thyroid-related ophthalmopathy and the first strabismus surgery was 32.21+27.08 months (range, 6 to 114 months).

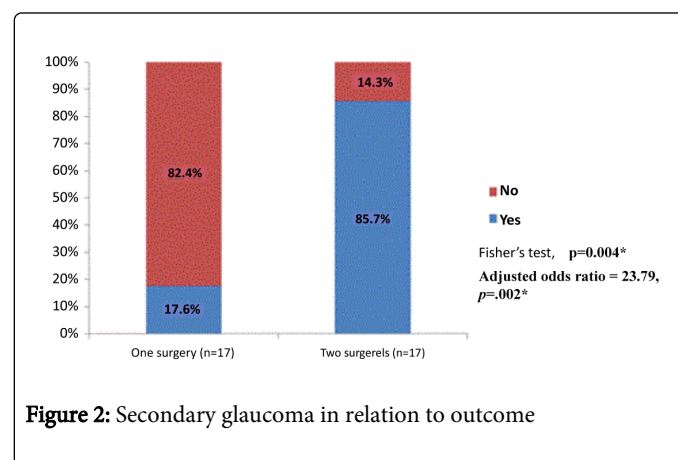


Figure 2: Secondary glaucoma in relation to outcome

The mean number of surgeries each patient received was 1.29+0.46 (range, 1 to 2). All patients, whether received one or more than one surgery, reached the status of diplopia-free at 6-month-follow-up after the last surgery. Outcomes were correlated with preoperative characteristics. The main outcome measurement was the number of

surgeries required for correcting diplopia, and the residual or recurrent strabismus after the first surgery. The maximal number of surgery each patient received is two. Seven patients received two surgeries, and seventeen patients just needed one surgery. The mean age of patients receiving one surgery and two surgeries were 55.35±10.83 (n=17, range, 32 to 72) and 55.86± 11.25 (n=7, range, 36 to 73) years ago, respectively (p=.71).

Patients with unilateral involvement at onset (p=.02*) (Figure 1), presence of secondary glaucoma (p=.004*) (Figure 2), and longer intervals between onset of TRO and first surgery (p=.01*) (Figure 3) needed more surgeries to correct strabismus significantly (Table 1).

Factors such as age, gender, smoking status, medical treatment before surgery, presence of compressive optic neuropathy or previous orbital decompression procedure had no statistically significant effect on the number of surgeries required (Table 1). However, there was a trend that retrobulbar injection with triamcinolone (p=.06) seemed to reduce the number of surgeries (Table 1). The surgical outcome calculated from the first muscle surgery was as following. The numbers of patients receiving only muscle recession without strengthening of antagonist was eight for horizontal deviation and eleven for vertical deviation respectively,

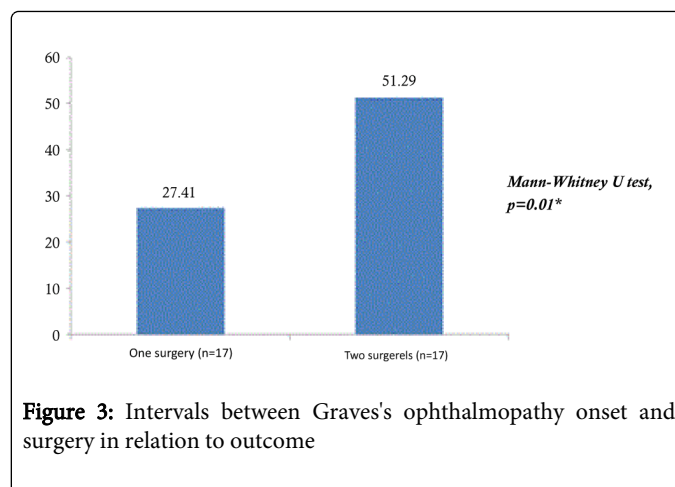


Figure 3: Intervals between Graves's ophthalmopathy onset and surgery in relation to outcome

and the mean surgical effect was 4.29±0.34 PD/mm recession of horizontal muscles and 3.99±0.24 PD/mm recession of vertical muscle, respectively. The average surgical effect was 4.09±0.26 PD/mm of muscle recession.

| | One surgery (N=17) | Two surgery (N=7) | P- value |
|--|--------------------|-------------------|----------------------|
| Age at surgery (mean, year old) | 55.35±10.83 | 55.86±11.25 | 0.71 ^a |
| Sex | 9F, 8M | 3F, 4M | 1.00 ^b |
| Unilateral at onset | 3(17.6%) | 5(71.4%) | 0.02 ^b , |
| Current smokers | 2(11.8%) | 1(14.3%) | 1.00 ^b |
| Seconadry Glaucoma | 3(17.6%) | 6(85.7%) | 0.004 ^b , |
| Compressive optic neuropathy | 3(17.6%) | 2(28.6%) | 0.61 ^b |
| Previous Treatment for TRO Intravenous pulse steroids therapy | 3(17.6%) | 0(0%) | 0.53 ^b |
| Retrobulbar steroids injection | 7(41.2%) | 0(0%) | 0.06 ^b |
| Oral steroids | 9(52.9%) | 3(42.9%) | 1.00 ^b |
| Decompression | 5(29.4%) | 2(28.6%) | 1.00 ^b |
| Mean time(months) between TRO onset and surgery | 27.41±24.97 | 51.29±29.92 | 0.01 ^a , |

F= female; M= male; TRO= Thyroid related Ophthalmopathy
^a= Mann Whitney U test, ^b= Fisher's test, ^c= Significant

Table 1: Preoperative parameters in relation to outcome

Discussion

Approximately 4% to 7% of patients with TRO require strabismus surgery. In general, staged surgeries may be needed to correct the strabismus induced by TRO. Most surgeons recommend an observation time up to 6 months after ocular deviation have stabilized [7,13-15]. Meyer, D.R suggested that a stable postoperative alignment is more likely reached after an extended period of stable preoperative alignment, and it minimizes the need for repeated strabismus surgery [7]. However, the re-operative rates for strabismus with TRO were reported to be between 17% and 45%, even in patients having had

stable deviations [6,7,16-19]. Of the twenty four patients in our study, seven (29.2%) received a second surgery. The reoperation rate is comparative to literature. Some of them had planned staged surgery due to very large deviation, and some of them were rescheduled due to unsatisfactory surgical result. Our previous study revealed that the severity of TRO was correlated with patients' age [20]. In this study, we noticed a trend that younger patients seemed to need more surgery to correct strabismus than aged group, although there is no statistically significant differences (p=.90) (Table 1). It suggested that younger patient might have more active inflammatory process, and therefore,

less predictable clinical courses. Mahmoud et al used CAS to assess the disease severity of their patients. They noted that although better postoperative outcomes were associated with earlier surgery, they did not have good correlation with the CAS score [6]. That means the CAS could not be used to predict the postoperative stability.

Smoking has been well known to be associated with more severe TRO and smokers respond less well to treatment in the active phase of TRO [8,21-26]. Cytokine release following smoking-induced hypoxia may increase the inflammation of TRO [27,28]. Rajendram et al. points out that the strabismus surgery in TRO patients can be more difficult because of the post-inflammatory changes in the peribulbar tissues and the muscular contracture and fibrosis. They suggested that smoking at presentation aggravated the myopathy and the strabismus in TRO [29]. However, smoking might have no direct impact on the surgical result. Mahmoud et al found that an active smoker did not necessarily show worse surgical outcome in their study [6]. There were three current smokers in our study (12.5%) and they did not show higher reoperation rate than others (Fisher's exact test, $p=1.0$). However, we need more investigation to support this point because the sample size was too small. Furthermore, TRO in current smokers may not stabilize in months, and that's probably why we only recruited three smokers.

In this study we also found that the presence of secondary glaucoma, unilateral involvement at onset, and longer intervals between TRO onset and surgery were significantly correlated with increased numbers of surgeries. Clinically, although increased intraocular pressure was noted frequently in patients with TRO, the definite mechanism was not well known. In literatures, there are several theories on the causes of increased IOP in thyroid-associated ophthalmopathy, including increased mucopolysaccharide deposition in the trabecular meshwork, increased resistance to trabecular outflow, increased episcleral venous pressure resulting from orbital congestion and obstruction of venous outflow, a genetically linked predisposition to glaucoma, and restriction and compression of the globe by fibrotic and enlarged rectus muscle [2,30-36]. In our study, the reoperation rate in patients with secondary glaucoma was higher significantly. It suggested that patients with secondary glaucoma might have more severe orbital congestion, muscle fibrosis or muscle enlargement, thus increased the unpredictability and complexity of strabismus surgery. Soroudi et al analyzed the Hertel measurements of TRO patients before orbital decompression surgery and found that 36 of 391 patients (9%) had asymmetric proptosis with a difference equal to or more than two mm [12]. In our study, eight of the twenty four patients (33.3%) had unilateral involvement at onset which was significantly correlated with increased numbers of surgeries. Patients with unilateral involvement at onset may show more unpredictable disease course. Mahmoud et al also found that the outcome of patients with symmetric TRO is more favorable, and suggested that asymmetric orbital or muscle involvement would need asymmetric surgery also [6]. Patients with longer intervals between TRO onset and surgery might have a more eventful course, and it took longer to reach stable condition. The complexity also explained the need of more surgeries. We didn't use adjustable suture as surgical technique in our study, even though the surgical tables did not apply so well in cases of TRO [37]. Using adjustable suture on TRO patients was described broadly in the literature [38-41]. However, late or progressive overcorrection after inferior rectus muscle recessions has been reported [42,43]. Nicholas et al. reported that 11 of 54 patients (20%) with TRO and hypotropia who underwent adjustable suture on the inferior rectus muscle recession had an overcorrection at their last postoperative visit.

They suggested (1) including contralateral superior rectus muscle recessions to reduce the amount of the inferior rectus muscle recession needed, (2) using nonabsorbable suture when restrictive strabismus is severe, (3) including the contralateral inferior rectus muscle whenever restriction is present on that side, and (4) anticipating drift and leaving the patient initially undercorrected to reduce possible causes of late overcorrection of inferior rectus muscle recessions [37]. Further investigation is needed. In our cases, we also use non-absorbable suture for inferior rectus muscle recession.

Conclusion

Although patients with TRO may need more than one surgery to correct their strabismus, the overall outcome, including the elimination of diplopia and improvement of ocular movement and cosmetic appearance, is favorable. In this series, we got mean surgical effect of 4.09 ± 0.26 PD/mm of rectus muscle recession. This should be taken into consideration when planning surgical dosage. Although we expected multiple surgeries in such patients, the average number of surgery required to eliminate diplopia is $1.29 (\pm 0.46)$ which is encouraging. In conclusion, the outcome of strabismus surgery on TRO patients is good as long as the hormonal condition and the ocular deviation are stable. *The authors have no financial interest in the material presented.

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