

## Factors Associated with Decompression and Strabismus Surgery in Thyroid Eye Disease

ALG Looi,<sup>1</sup>*M Med (Ophthalm), FRCS (Edin), FAMS*, CD Luu,<sup>2</sup>*PhD*, TY Wong,<sup>2,3,4</sup>*FRCS (Edin), MPH, FAMS*, LL Seah,<sup>1</sup>*FRCS (Edin), FRCOphth, FAMS*, J Rootman,<sup>1,5</sup>*FRCS*

### Abstract

**Introduction:** Prognostication of the thyroid patient with eye disease aids in the choice of treatment strategy. To facilitate this, we investigated factors associated with decompression and/or strabismus surgery in the Singaporean population. **Materials and Methods:** A 5-year retrospective study was performed. Patients who required strabismus and/or decompression surgery (n = 23) were compared to those who did not undergo either surgery (n = 44). Individual and multivariate age-adjusted odds ratios were calculated to determine significant associations. **Results:** Individually, male gender [odds ratio (OR), 4.5; 95% confidence interval (CI), 1.5 to 13.4], uncontrolled hyperthyroidism (OR, 4.0; 95% CI, 1.1 to 14.3), steroid therapy (OR, 7.4; 95% CI, 2.3 to 24), diplopia (OR, 7.3; 95% CI, 2.3 to 23.1), objective vertical myopathy (OR, 11.7; 95% CI, 1.4 to 96.0), elevated intraocular pressure in the primary position (OR, 3.4; 95% CI, 1.2 to 10.0) and clinical evidence of optic neuropathy (OR, 13.1; 95% CI, 1.4 to 124.6) were significantly associated with the need for surgery. Logistic regression analysis showed the greater impact of male gender (OR, 4.2; 95% CI, 1.2 to 15.4), optic neuropathy (OR, 13.0; 95% CI, 1.2 to 143.7) and previous steroid therapy (OR, 4.2; 95% CI, 1.1 to 16.2) on prognostication. **Conclusions:** Chances of requiring strabismus and/or decompression surgery are significantly higher for male patients and those with uncontrolled hyperthyroidism. In particular, male patients with optic neuropathy and a history of previous steroid therapy warrant a graver prognosis.

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**Key words:** Risk factors, Thyroid eye disease

### Introduction

Thyroid eye disease (TED) is a visually and socially disabling condition. Newly diagnosed patients are often fearful of sight-threatening complications that include optic nerve compression or restrictive strabismus. Although the current literature has pointed to age (>60 years), gender (male), abnormal thyroid function (both hyper- and hypothyroidism), smoking and radio-iodine treatment as risk factors for developing TED,<sup>1-11</sup> few reports on Asian populations are available. This study was performed to evaluate prognostic factors in the Singaporean population with the aim of improving patient counselling and management.

### Materials and Methods

From computer records, patients with TED treated at the Singapore National Eye Centre from January 1994 to December 1998 were identified through the medical diagnostic index. The time frame was chosen to allow for follow-up and correct allocation of patients who presented in December 1998. Only cases with good note-keeping and with at least 1 year of follow-up were studied.

All studied patients were subdivided into those requiring decompression and/or strabismus surgery, that is, severe thyroid eye disease (STED) and those who did not require either procedure, that is, non-severe TED. The STED and TED groups were compared using the following parameters:

<sup>1</sup> Oculoplastic Service, Singapore National Eye Centre, Singapore

<sup>2</sup> Singapore Eye Research Institute, Singapore

<sup>3</sup> Singapore National Eye Centre, Singapore

<sup>4</sup> Department of Ophthalmology, National University Hospital, Singapore

<sup>5</sup> Department of Ophthalmology and Visual Sciences, Faculty of Medicine, University of British Columbia, Canada

Address for Reprints: Dr Audrey Looi, Oculoplastic Service, Singapore National Eye Centre, 11 Third Hospital Avenue, Singapore 168751.

Email: audrey\_looi@yahoo.com.sg

age, gender, race, family history of thyroid disease, family history of TED, history of diabetes, smoking history (current, previous or nil), mode of treatment of thyroid disease, overall thyroid hormone status, rapidity of onset of TED and the duration between onset of thyroid disease and thyroid ophthalmopathy. Also studied were the subjective symptoms of diplopia, lid or conjunctival swelling and retrobulbar pain, and the objective evidence of proptosis, upper and lower lid retraction, motility dysfunction, intraocular pressure (IOP) in the primary position, optic neuropathy and mode of medical treatment.

With regard to the mode of treatment of thyroid disease, the study looked at patients who received oral antithyroid medication alone, those who received both oral medication and radio-iodine therapy, and those who underwent thyroidectomy. As for the overall thyroid hormone status, the patient's free thyroxine (T4) and thyroid-stimulating hormone levels, which were repeated several months apart, determined whether the patient was euthyroid with treatment (with or without thyroid hormone replacement) or remained hyperthyroid. In other words, we looked at the overall control of hyperthyroidism and not the thyroid status at diagnosis. The rapidity of onset was classified as acute, subacute or chronic depending on whether symptoms developed over 1 month, 3 months or a longer period of time, respectively. The interval between the diagnosis of thyroid disease and that of TED was documented in months.

Proptosis was defined as an exophthalmometry reading of at least 20 mm. Upper and lower lid retractions were recorded as absent or present based on the clinician's observation. Patients were classified as having vertical dysmotility, horizontal dysmotility, both or none based on the Hess chart (performed with Lees screen which uses a mirror to dissociate right and left images, allowing underactions and overactions of extraocular muscles to be mapped on right and left Hess charts). A limitation of movement by 1 square (5 degrees) was required for a positive record of dysmotility. Optic neuropathy was present if clinical evidence that included a decrease in visual acuity, defective colour vision, relative afferent papillary defect and apical crowding on computed tomography (CT) scan were documented.

The mode of medical treatment refers to previous use of oral prednisolone or intravenous methylprednisolone.

The age-adjusted odds ratio was calculated for each studied factor. Significant factors were identified and a multivariate-adjusted odds ratio was then calculated using a logistic regression analysis. All odds ratios were computed with 95% confidence intervals.  $P < 0.05$  was considered statistically significant.

## Results

Sixty-seven cases were analysed. This represented about a third of all TED patients identified through computer records. Of these, 23 had STED and 44 were patients with TED. There is no significant difference in the mean age between groups ( $t_{(65)} = -0.924$ ,  $P = 0.359$ ). In the severe group, Chinese was the majority race. All control patients were Chinese and, therefore, the race variable was not included in the analysis. A summary of demographic data of the studied patients is presented in Table 1. The indication for strabismus surgery was diplopia with objective evidence of muscle restriction, while all cases of orbital decompression were performed to relieve optic nerve compression.

Table 1. Characteristics of Severe Thyroid Eye Disease (STED) and Non-severe Thyroid Eye Disease (TED) Groups

Variable	STED (n = 23)	TED (n = 44)
Age (y)	42.8 ± 13.6	39.7 ± 12.8
Male gender (%)	65.2	31.8
Race		
Chinese (%)	60.9	100
Malay (%)	26.1	0
Indian (%)	0	0
Others (%)	13.0	0

We found male gender, uncontrolled hyperthyroidism and the previous use of steroid therapy, whether oral or pulsed, to be significantly associated with the need for strabismus and/or decompression surgery. Symptomatic diplopia, the objective presence of vertical motility restrictions with or without a horizontal component, IOP of at least 21 mm Hg in primary position and clinical evidence for optic neuropathy were features of TED that also proved to be associated with a higher chance of developing severe disease (Table 2).

As symptomatic diplopia and/or vertical dysmotility are indications for strabismus surgery, and because raised IOP in this group of patients is likely related to a tight inferior rectus muscle, the multivariate analysis was performed with the exclusion of vertical dysmotility, diplopia and raised IOP. Optic neuropathy, as a parameter, was included in this analysis as some patients with clinical evidence of optic neuropathy had been treated adequately with steroid and/or radiotherapy and had not required orbital decompression. The multivariate analysis showed male gender, a previous history of steroid treatment and optic neuropathy to be significantly linked to severe disease (Table 3).

Table 2. Age-adjusted Odds Ratio for Severe Thyroid Eye Disease (STED)

Variable	STED (n = 23)	TED (n = 44)	Odds ratio	95% confidence interval
Gender (Male)*	15	14	4.5	1.5-13.4
Hyperthyroidism*	8	5	4.0	1.1-14.3
Interval between diagnosis of TD and TED ≤3 months	11	20	1.1	0.4-3.2
History of previous steroid therapy*	13	7	7.4	2.3-24.0
Presence of diplopia*	17	12	7.3	2.3-23.1
Presence of vertical myopathy*	22	29	11.7	1.4-96.0
IOP in primary position ≥21 mm Hg*	12	11	3.4	1.2-10.0
Presence of optic neuropathy*	5	1	13.1	1.4-124.6
Positive family history of TD	7	10	1.7	0.5-5.4
Positive family history of TED	1	3	0.7	0.7-7.1
Positive diabetic history	4	4	1.7	0.4-8.7
Smoker/Ex-smoker	7	3	4.6	0.8-25.1
Radio-iodine treatment	7	15	0.8	0.3-2.4
Acute and subacute onset of TED	5	5	0.4	0.1-1.7
Symptomatic conjunctival swelling or redness	13	16	2.6	0.9-7.7
Presence of orbital pain	3	1	7.5	0.7-78.3
Objective conjunctival injection/chemosis	16	22	2.4	0.8-6.9
Objective proptosis ≥20 mm	17	27	2.0	0.6-6.4
Presence of upper lid retraction	16	32	1.0	0.3-3.1
Presence of lower lid retraction	13	22	1.6	0.5-4.5

IOP: intraocular pressure; TD: thyroid disease; TED: thyroid eye disease

\* Significant association with STED

Table 3. Multivariate Analysis with Exclusion of Dysmotility, Diplopia and Raised Intraocular Pressure

Variable	Odds ratio	95% confidence interval	P value
Male gender	4.2	1.2-15.4	0.03
Hyperthyroidism	1.8	0.4-8.8	0.44
Previous steroid therapy	4.2	1.1-16.2	0.04
Optic neuropathy	13.0	1.2-143.7	0.04

## Discussion

Of all patients with thyroid ophthalmopathy, only 5% to 10% have severe disease.<sup>12,13</sup> What makes an individual develop more severe disease remains largely unclear. Previous research has established cigarette smoking as the single most important environmental factor for the development and progression of the disease.<sup>4-7</sup> This finding has shaped current counselling for patients with TED. Identification of factors linked to severe disease, especially modifiable factors, would not only improve patient counselling but also help to reduce progression to visual loss and the need for surgery. The present study shows results similar to published literature in that we found male gender and uncontrolled hyperthyroidism to be significantly associated with the development of more STED requiring surgical management.

A record of previous steroid therapy was also found to be associated with STED. However, the link between the use

of steroids and severe disease may be explained by the common clinical practice of prescribing steroids for patients assessed to have more severe disease. It is, therefore, unlikely that steroids play an aetiological role in more severe disease requiring decompression or strabismus surgery. The implication, however, is that frequently, patients who receive steroid therapy still require surgery later and this could indicate the ineffectiveness of steroids in altering the mechanical disease factors in thyroid orbitopathy once the inflammatory process is clinically evident.

Considering that patients with optic neuropathy frequently require surgical decompression, an association between the clinical features of optic neuropathy and STED is not surprising. As a parameter, it was still included in the multivariate analysis as some patients do respond to non-surgical forms of therapy. Logistic regression analysis showed that males with a previous history of steroid therapy and clinical features of optic neuropathy were likely to require orbital decompression and/or strabismus surgery.

Two important negative findings deserve comment. Although smoking was not found to be significantly associated with STED ( $P = 0.078$ ), the percentage of smokers/ex-smokers in the STED group (30.4%) was much higher than in the TED group (6.8%), supporting the well-described association of smoking with thyroid

orbitopathy. Radio-iodine treatment was not found to be linked to severe disease. This observation supports the local practice of prescribing prophylactic steroids in patients who require radioactive iodine treatment.

There were several limitations in this study. The number of patients in each group was small. Many of the cases which were excluded from the study because of inadequate record-keeping were deemed to have mild disease that did not require referral to the Thyroid Clinic. Those with more severe disease were frequently referred to the Thyroid Clinic, accounting for a third of the patients studied. This may have resulted in inter-observer differences between those with severe disease and those without. Also, race could not be studied as a prognostic variable.

Nevertheless, these findings are useful in patient counselling and education. In seeing a new patient with TED, clinicians are better equipped to prognosticate with regard to the likelihood of further progression to surgery and to advise good control of hyperthyroidism.

### Conclusion

In STED, male gender and uncontrolled hyperthyroidism are factors associated with the need for strabismus and/or decompression surgery. In particular, male patients with clinical evidence of optic neuropathy and a history of steroid therapy are likely to require surgical intervention.

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