Superior oblique enlargement in thyroid eye disease

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PURPOSE To determine the extent of superior oblique enlargement in thyroid eye disease (TED) by comparing the cross-sectional superior oblique areas of TED patients with those of unaffected control subjects.

METHODS The medical records of TED patients treated for strabismus from January 2005 to January 2016 were reviewed retrospectively for demographic and surgical data. The cross-sectional superior oblique area was compared to age-matched controls on high-resolution orbital computed tomography (CT) using a standardized protocol.

RESULTS A total of 46 TED patients and 18 controls were included. The mean superior oblique cross-sectional area in TED subjects was 250% larger than in controls (22.88 ± 6.64 mm^2 vs 9.32 ± 1.85 mm^2. The mean cross-sectional area was >3 standard deviations from the mean of the control group in 96% of TED patients.

CONCLUSIONS Superior oblique enlargement in TED may occur more frequently than generally recognized, challenging the notion that TED is primarily a disease of the rectus muscles. (J AAPOS 2019;23:252.e1-4)

Reoperation rates of 17%–45% in strabismus surgery for thyroid eye disease (TED) have been reported in the literature.[1] Unrecognized superior oblique involvement may contribute to this relatively high reoperation rate. Tight inferior rectus muscles may mask superior oblique involvement on sensorimotor examination, as proposed by Holmes and colleagues[2]; therefore, signs of a tight superior oblique muscle, including A-pattern strabismus and incyclotorsion, may only appear after inferior rectus recession, necessitating follow-up superior oblique surgery.

Orbital imaging in TED allows us to visualize the extent of extraocular muscle enlargement and can help guide surgical management. High-resolution orbital computed tomography (CT) can be used to objectively measure extraocular muscle cross-sectional area. The thickness and width of the superior oblique muscle has been studied in small cohorts of TED patients. Chen and colleagues[3] reported that the width of superior oblique muscle was significantly greater in 16 TED patients than in controls. Thacker and colleagues[4] showed that superior oblique enlargement on orbital imaging correlated with findings of A patterns, intorsion, and restricted elevation in adduction on intraoperative forced duction testing in a series of 4 patients. In their study of 45 TED patients, Wei and colleagues[5] found that preoperative superior oblique enlargement (thickness/width) correlated with postoperative intorsion. Thickness and width, as defined in previous studies, are one-dimensional measurements; cross-sectional area, a two-dimensional measurement, would provide a more accurate measurement of the true "size" of the superior oblique muscle. To our knowledge, the extent of superior oblique enlargement, measured in terms of cross-sectional area, has not been studied in a large cohort of TED patients.

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Subjects and Methods

The Moorfields Eye Hospital audit committee approved this study, which retrospectively reviewed the medical records, including imaging, of patients with a documented diagnosis of TED who had attended the strabismus clinic at Moorfields Eye Hospital, London, between January 2005 and January 2016. The diagnosis of TED was confirmed by endocrinological review and assessment by the adnexal team.

The following data were collected: age at imaging, sex, smoking status, statin use, and optic neuropathy. We examined treatment for hyperthyroidism, including radioactive iodine and thyroidectomy, and treatment for TED, including orbital radiation,

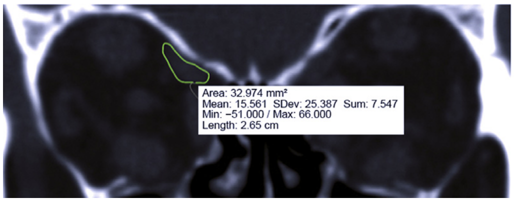

FIG 1. Technique for measuring the cross-sectional area of the superior oblique on a reformatted high-resolution coronal computed tomography scan.

steroids, orbital decompression, and strabismus surgery. A surgical audit was performed, including types of strabismus surgery performed during the first, and in some cases, second and third operations. TED patients were excluded from our study if they had not undergone high-resolution (1.0 mm isotropic resolution) orbital CT scans at our institution.

The DICOM viewer (v7.5.1; Osirix, Bernex, Switzerland) was used to measure the cross-sectional area of superior oblique muscle after the 1.0 mm data was reformatted in a coronal plane that was standardized by aligning the zygomatic arches in the axial plane and the sphenoid planum in the sagittal plane to ensure true and reproducible measurements. Superior oblique measurements were recorded by a neuroradiologist and an ophthalmologist. Each observer selected the three largest cross-sectional areas and quantified these on each side, then the mean and standard deviation of the measurements were calculated (Figure 1). Each of the patients had superior oblique measurements recorded bilaterally. Right and left eye measurements were kept separate because TED can be asymmetrical.

To estimate the superior oblique cross-sectional area in the normal population, age-matched controls without TED were selected from the imaging database at our institution (Table 1). These patients had undergone CT scanning using the same protocol as the TED patients. Imaging was performed to investigate for central neurological pathology or optic neuropathy. The scans of all of these patients were reported as normal by our radiologist; in particular, extraocular muscles were normal. Superior oblique measurements were recorded bilaterally using the same imaging method, and right and left eye measurements were kept separate to aid comparison with TED data.

Reliability of superior oblique measurements was calculated using the intraclass correlation coefficient (ICC). Statistical analysis was performed using SPSS Statistics version 21 (IBM Corp, Armonk, NY). A P value of <0.05 was deemed to be statistically significant.

Results

A total of 66 patients were initially identified, of whom 46 underwent CT analysis; 92 superior oblique muscles were analyzed by each observer. See Table 2. Results were compared with data from the 18 control subjects (36 superior oblique measurements).

Table 1. Age distribution of normal control and thyroid eye disease (TED) patients

Age, years	Control group,[a] no. (%)	TED group,[b] no. (%)
21-40	1 (5.6)	1 (2.1)
41-60	7 (38.8)	21 (45.7)
61-80	9 (50)	22 (47.8)
≥81	1 (5.6)	2 (4.4)

[a]Average age, 59.3 years; n = 18.
[b]Average age 62.4 years; n = 46.

Table 2. Basic demographic data for thyroid eye disease patients (n = 46)

	Yes, no. (%)	No, no. (%)
Female	32 (70)	14 (30)
Smoking status	23 (50)	23 (50)
Statin use	10 (22)	36 (78)
Optic neuropathy	11 (24)	35 (76)
Thyroidectomy	10 (22)	36 (78)
Radioactive iodine	9 (20)	37 (80)
Orbital decompression	27 (59)	19 (41)
Steroid treatment	26 (56)	20 (44)
Orbital radiation	11 (24)	35 (76)
Strabismus surgery	39 (85)	7 (15)

Imaging Results

The superior oblique cross-sectional area (mean with standard deviation) for the normal control group was 9.32 ± 1.85 mm^2 (95% CI, 8.40-10.24) for the right eye and 9.57 ± 1.56 mm^2 (95% CI, 8.79-10.34) for the left eye; for the TED group, 22.88 ± 6.64 mm^2 (95% CI, 20.91-24.85) for the right eye and 22.58 ± 6.88 mm^2 (95% CI, 20.54-24.62) for the left eye. See Figure 2. That is, the cross-sectional area was 250% larger in the TED group than in the control group ($P = 0.000$ for right and left eyes). The calculated observed power was 1.00. The cross-sectional area was slightly higher in the TED patients for the right eye compared to the left, but this was not statistically significant ($P = 0.83$). Of the 92 superior oblique muscles in this TED cohort, 88 (96%) had mean cross-sectional areas that were >3 standard deviations from the control group mean value.

There was excellent interobserver reliability with respect to superior oblique cross-sectional area for both control and TED data. For the control data, the ICC was 0.961 (95% CI, (0.734-0.989) for the right eye and 0.929 (95% CI, 0.753-0.976) for the left eye; for the TED data, 0.921 (95% CI, 0.843-0.947) for the right eye and 0.945 (95% CI, 0.899-0.970) for the left eye.[6]

Surgical Audit

Of the 46 TED patients, 39 (85%) chose to undergo strabismus surgery. The remaining 7 (15%) had conservative treatment, including Bangerter foil (4 patients), botulinum toxin injection (2 patients), or prism (1 patient). Overall, 31 of 39 (79%) initial strabismus surgeries involved recession

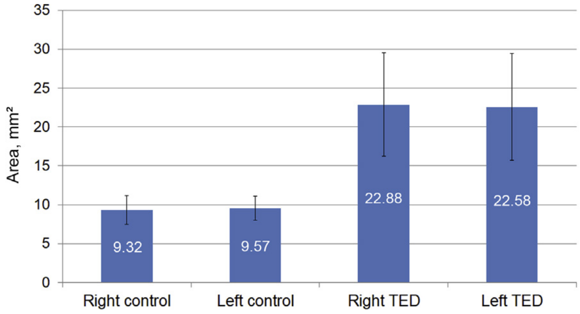

FIG 2. The superior oblique cross-sectional area in controls versus thyroid eye disease (TED) patients for the right eye and left eye. This represents a statistically significant difference between TED patients and controls (*P* = 0.000 for both eyes).

of the inferior rectus muscles. Adjustable sutures were used in 17 cases (44%). See Table 3 for a breakdown of initial surgeries performed. At our institution, the standard policy is to never recess the inferior rectus muscle more than 6.5 mm to avoid inducing A patterns or limitation of downgaze.

A second surgery was performed in 10 of the 39 cases (26%). Adjustable sutures were used in 3 cases (30%). Overall, 8 second strabismus surgeries (80%) involved recession of the vertical rectus muscle; 1 patient underwent superior oblique surgery as the second procedure. This patient was found to have very significant (greater >5 standard deviations from the mean) superior oblique enlargement on imaging. See Table 4 for breakdown of second strabismus procedures performed.

A third strabismus procedure was performed in 4 of 39 cases (10%). Of these, 2 (50%) underwent superior oblique–weakening procedures. One patient underwent right superior oblique tenotomy to treat 10° of incyclotorsion that developed after bilateral inferior rectus recessions (6 mm). The other underwent left superior oblique tenotomy to treat 19° of incyclotorsion that developed after bilateral inferior rectus recessions (4 mm). Both patients had notable superior oblique tightness on forced duction testing at the beginning of surgery. Neither patient had incyclotorsion prior to initial first strabismus surgery; Indeed, both had mild *excyclotorsion* prior to initial strabismus surgery. Both patients were found to have very significant (>5 standard deviations from the mean) superior oblique enlargement on imaging. Of the remaining 2 patients who underwent a third operation, one had a right medial rectus recession to treat esotropia following medial wall decompression. This was his second decompression on that eye due to reactivation of TED. The other had a right inferior rectus recession to treat 25 D of left hypertopia.

Discussion

In this study of TED patients with symptomatic strabismus, we confirmed a female predominance and found that 50% of patients were still smoking. Patients in our cohort tended to have severe TED: 24% suffered optic neuropathy, and the majority underwent decompression surgery (59%) and/or steroid therapy (56%). Vertical muscle surgery (either alone or combined with horizontal) was the most commonly performed procedure at both first (79%) and second (80%) strabismus operations.

We have described a technique for measurement of superior oblique with excellent inter-rater reliability. Of the 92 superior oblique muscles in this TED cohort, 96% had mean cross-sectional areas that were more than 3 standard deviations from the control group mean. Moreover, the superior oblique cross-sectional area was approximately 250% larger than age-matched controls.

Previous studies[3,5,7] have shown an increased width of superior oblique in TED compared to the normal population. To our knowledge, the present study is the first to demonstrate the true size (cross-sectional area) of the superior oblique in a large cohort of TED patients. The extent and frequency of superior oblique enlargement in this cohort challenges the notion that TED is primarily a disease of the rectus muscles. It is also likely that superior oblique involvement was not recognized previously because of the comparatively poorer image quality with older scanning techniques.[8]

Because this was a retrospective review, we were not able to rescan patients who had been scanned elsewhere and therefore had not undergone CT according to our protocol. The loss of 20 patients from our study cohort is one of the limitations of this study. We also acknowledge that it would have been useful to measure the cross-sectional area of the other muscles, especially the inferior oblique

Table 3. Breakdown of initial strabismus surgery performed for the 39/46 patients who chose to undergo strabismus surgery

Initial strabismus surgery	No. patients	Percentage of total (n = 39)
V alone	18	46
H alone	7	18
Combined V + H	13	33
IO	1	3
Total	39	100

H, horizontal muscle recession; *IO*, inferior oblique muscle weakening; *V*, vertical muscle recession.

Table 4. Breakdown of second strabismus surgeries performed for the 10/39 patients who required a second procedure

Second strabismus procedure	No. patients	Percentage of total (n = 10)
V alone	6	60
Combined V + H	2	20
IO	1	10
SO	1	10
Total	10	100

H, horizontal muscle recession; *IO*, inferior oblique weakening; SO, superior oblique weakening; *V*, vertical muscle recession.

muscles. We reformatted our CT data in the true standardized coronal plane using set anatomical landmarks. It was not possible to measure the cross-sectional area of the inferior obliques in the coronal plane because of its oblique angle of insertion on the globe. Another plane would need to be used, likely the sagittal, using a different standardized protocol from the one used in this study. The superior rectus muscle also contributes to incyclotorsion of the eye. We recognize that this muscle was not measured in our study. This is an important topic for further research.

Another study limitation was that we could not standardize the orthoptic measurements. We would have liked to assess how torsion measurements changed before and after vertical muscle recession and attempted to correlate intorsion with superior oblique enlargement. In our unit, all patients attending the motility clinics are seen by an orthoptist and an ophthalmologist. The standard policy is for all patients to be asked about the presence and nature of diplopia by their orthoptist. If torsion is identified on history, a synoptophore examination is undertaken (our institution uses the synoptophore rather than Maddox rods). If the patient does not identify torsion, this test is not undertaken. Therefore, it is possible that some patients in this cohort had torsion that was not measured. That is why we chose not to make the sensorimotor findings the main focus of this paper. In an ideal study, all TED patients would have torsion measured at each orthoptic assessment, although we appreciate that this may not be possible with very restricted eye movements. Ideally, all TED patients would also undergo intraoperative forced duction testing at the time of rectus muscle surgery on all of the rectus and the oblique muscles. Some of our patients did not undergo intraoperative forced duction testing.

Only 3 of the 31 patients who underwent inferior rectus recession in our study required superior oblique weakening (1 at second surgery and 2 at third). Meanwhile, 96% of this cohort demonstrated significant superior oblique enlargement. Therefore, counterbalancing of the extraocular muscles must be critical in determining which TED patients will develop torsion. The presence or absence of torsion after rectus muscle recession in TED is determined by a complex interplay between the rectus and oblique muscles. Under normal circumstances, there is a balance between the incyclotorting muscles (superior oblique and superior rectus) and excyclotorting muscles (inferior rectus and inferior oblique). Patients with significant inferior rectus involvement and minimal excyclotorsion often demonstrate ipsilateral superior rectus involvement counterbalancing the anticipated excyclotorsion. We anticipate that many of those with superior oblique involvement may also have inferior oblique involvement counterbalancing the anticipated incyclotorsion.

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