Computed tomography imaging of orbits in thyroid orbitopathy

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Abstract: The aim of this study was to present the authors' experience with identification and classification of thyroid ophtalmopathy activity. A total of 46 orbits from 23 patients with thyroid ophthalmopathy symptoms were evaluated on computed tomography images in terms of diameters and density of extraocular muscles, muscular index, proptosis, width of the optic nerve, width of superior ophthalmic vein and lacrimal gland position. Radiological symptoms of proptosis were present in 78.3% patients, while 80% cases of diagnosed proptosis were bilateral. The most frequently affected eye muscle was the inferior (61%) and medial (54%) rectus prior to superior (39%), lateral rectus (37%) and superior oblique (26%). The highest correlation between muscle enlargement and proptosis was noted in the case of inferior rectus (77%) and medial rectus (70%). 78% of muscle enlargement was bilateral. Anterior displacement of the lacrimal gland was observed in 58% of cases. Width of the superior ophthalmic vein and the optic nerve (sheath complex) did not differ significantly from normal population ranges. All muscles measured in the study had a lower density when compared to reference data; the density of the thickened muscles was lower than the density of muscles with an unmodified diameter.

Key words: thyroid orbitopathy, computed tomography imaging, proptosis

INTRODUCTION

Thyroid opthalmopathy (TO) is an organ specific auto-immune inflammation, centered on the extraocular muscles and orbital connective tissue. It is associated with Graves' disease in 90% of cases, less frequently with Hashimoto thyroiditis, thyroid carcinoma, primary hyperthyroidism, and neck irradiation. Associated with hyper (80%), hypo or euthyroid, TO can coexist, precede or follow the onset of thyroid dysfunction, without any parallel between ophthalmopathy intensification and exacerbation of hyperthyreosis. The incidence of TO is approximately 16/100,000 in females and 3/100,000 in males (TO is more severe in males) and typically occurs in those aged 20-50 years (most prevalent in the fourth and fifth decade of life) [1-5]. An estimated 25-50% of Graves' disease sufferers demonstrate clinical signs of TO, while 90% have radiological evidence of extraocular muscle involvement; optic nerve involvement can occur with any degree of exophthalmus [2, 3].

Thyroid orbitopathy must also exclude distinctions other than those connected with thyroid: orbital myositis (inflammatory pseudotumour of the orbit), primary and metastatic tumours, lymphoma, sarcoidosis, infection, acromegaly, trauma, cavernous sinus thrombosis, histiocytosis X, lacrimal gland tumour, orbital varices, cavernous haemangioma of the orbit, amyloidosis.

There are 2 distinct stages of thyroid orbitopathy – the active inflammatory phase, which usually encompasses an average period of 18-36 months, characterised by lymphocytic infiltration, interstitial oedema and glycosaminoglycans deposition in enlarged extraocular muscles and retroorbital fat, and the inactive disease with fibrosis and fat infiltration of the orbital tissues (fibroblast and preadipocytes' induction towards lipogenesis) [2, 4, 6, 7]. Thyroid orbitopathy is diagnosed by the presence of ocular signs and symptoms, estimation of the thyroid hormones level, and presence of antibodies (anti-thyreoglobulin, anti-microsomal and anti-thyrotropin receptor antibodies). The clinical manifestations include periorbital soft tissue inflammation, lid retraction, lid lag, proptosis, restrictive myopathy, corneal exposure leading to corneal erosion, conjunctival injection, conjunctival oedema, and compressive optic neuropathy (5%-10% of patients) [8] occurring as double vision, afferent pupillary defect, reduced visual acuity, dyschromatopsia, central or paracentral scotoma, nerve head swelling or atrophy [7]. Optic neuropathy is usually bilateral, but up to one third of cases may be unilateral [9]. Although the inflammatory orbitopathy tends to improve spontaneously, optic neuropathy generally requires treatment, as progressive irreversible visual loss may result in up to 30% of cases [8]. Therefore, patients at risk of development of dysthyroid optic neuropathy should be closely monitored clinically to treat the disease in the earlier stages. Treatment of Grave's disease depends largely on the severity of signs and symptoms and includes: local steroids application, radiotherapy, surgical orbital decompression or strabismus surgery.

Computed tomography (CT) scanning is an accurate imaging procedure for the diagnosis of thyroid ophthalmopathy. Beside the visualization of the enlarged extraocular muscles and the proptosis extent, CT scans provide the surgeon with depictions of the bony architecture of the orbit when orbital decompression is required. The most characteristic CT finding in thyroid orbitopathy is fusiform configurated enlargement of the extraocular muscles with normal tendinous insertions onto the globe (this differs from cylindrical configuration in idiopathic inflammation of the muscles or myositis). Muscle involvement is generally bilateral (90%) and asymmetric (70%) [9]. The most commonly involved extraocular muscles

are (from most to least frequent) the inferior rectus, medial rectus, superior rectus, oblique muscles, and lateral rectus [2]. Increase of width of medial rectus muscle also seems to be most reliably connected with optic neuropathy development [10, 11]. Other findings include proptosis and anterior prolapse of the orbital septum due to enlargement of (fat infiltrated and decreased attenuated) muscles and orbital fat compartment and intracranial fat prolapse. Patients at risk of developing optic neuropathy may also have severe apical crowding, dilated superior ophthalmic vein, enlargement and anterior displacement of the lacrimal gland and bowing of the medial lamina papyracea to accommodate the swollen bulge of the medial rectus muscle. Of all the above mentioned, apical crowding seems to be the most sensitive indicator for the presence of optic neuropathy. While there appears to be no selective inflammation of the optic nerve meninges or the perineural connective tissues, enlargement of the extraocular muscle bulges converged at the crowded orbital apex brings compression of the optic nerve, impairs its function, and thus causes visual decrease [12].

MATERIALS AND METHODS

Forty-six orbits of 23 patients (5 males, 18 females) with thyroid opthalmopathy (ophthalmologically assessed before CT examination) were retrospectively evaluated in this study. Patients ranged in age from 36-70 years (mean 55.5 years). Computed tomography examination was performed in axial 2 mm thick, pitch=1 scans, parallel to the infraorbitomeatal line with a spiral CT scanner (Somatom, Siemens; 512×512 image matrix). Coronal and multiplanar reconstructions of the orbits were postprocessed. All scanning was performed without intravenous contrast material, at constant window level and width settings of 50 and 250 HU, respectively, to eliminate measurement distinctions; patients were asked to maintain forward gaze and gentle eye closure during the scanning process to prevent asymmetric extraocular muscle contraction [13].

Diameters and density of extraocular muscles, length of the interzygomatic line, proptosis (distance from the interzygomatic line to the posterior margin of the globe), width of the optic nerve-sheath complex, muscular index, width of superior ophthalmic vein, and lacrimal gland position were calculated on direct axial and reconstructed coronal CT scans, and interpreted as correct or incorrect according to standard CT data for orbital structures described in other references [14-17].

Ranges for the maximal diameters of extraocular muscles were measured perpendicularly to the orbital wall in the planes parallel to its course – in axial scans: medial rectus, lateral rectus and in coronal scans: inferior rectus, superior group (indistinguishably superior rectus and the levator palpebrae superior muscle) and superior oblique. Further, a muscular diameter index (MDI) was achieved by adding these diameters. Ranges for the densities of extraocular muscles were assessed in axial scans. The mean optic nerve-sheath complex was measured perpendicularly to its course in the axial CT sections in retrobulbar and middle portion (waist) of the nerve. The mean length of the interzygomatic line (IZL), responding with the transversal head size, was measured on the anterior extent of the lateral bony orbital rims at the midglobe section (section imaging lens, optic nerve head and

optic canal). The globe position (GP) was measured as the perpendicular distance between the interzygomatic line and the posterior margin. The horizontal muscular index was expressed as the percentage of orbital width (C) occupied by the medial (A) and lateral (B) rectus muscles ($[(A+B)/C]/100$) at a point halfway between the posterior globe and the orbital apex (Figure 3). The vertical muscular index was expressed as the percentage of orbital height (F) occupied by the superior rectus/levator muscle complex (D) and inferior rectus muscle (E): ($[(D+E)/F]/100$) at a point halfway between the posterior globe and the orbital apex (Figure 4). The larger of the 2 indices represents the most significant impingement on the optic nerve space and was taken as the final muscular index [21]. The width of superior ophthalmic vein was measured in axial scans. Anterior displacement of the lacrimal gland was defined on axial images as displacement of at least half of the gland anterior to the frontozygomatic processus.

The paired-samples *t*-test was used to compare left and right orbit data. Correlations were calculated using the Pearson correlation coefficient.

Figure 1   Axial CT scan at midglobe demonstrates length of the interzygomatic line (IZL), the distance between the interzygomatic line and the posterior margin of the globe (GP), width of the optic nerve-sheath complex (retrobulbar and waist diameter), and muscle diameter measurement for the medial rectus and lateral rectus.
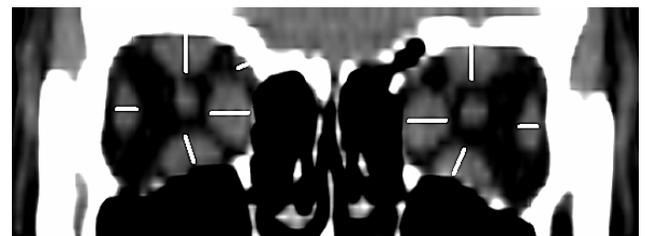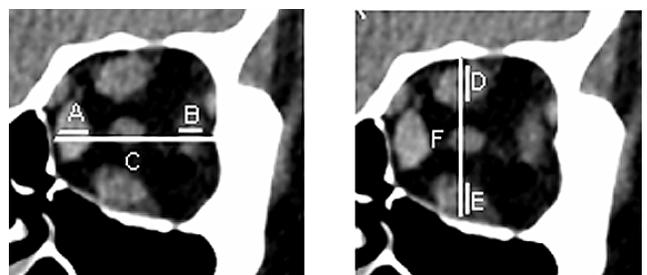

Figure 2   Coronal CT reconstruction of the orbit demonstrates the measurement of the extraocular muscle.

Figures 3 (left) and **4** (right)   Coronal CT reconstruction in measurement of horizontal muscular index and vertical muscular index.

Figure 5 Axial scan demonstrates width of superior ophthalmic vein (white arrows) and lacrimal gland position (grey arrow).

Table 2 Muscle density estimation.

Density ranges		All muscles	Involved	Normal
		mean (HU) ± 2 SD	muscles mean (HU) ± 2 SD	mean (HU) ± 2 SD*
Muscle	Medial rectus	36 ± 14	28 ± 9	45 (28-63)
	Lateral rectus	31 ± 14	24 ± 10	51 (24-78)
	Inferior rectus	30 ± 14	28 ± 14	41 (20-54)
	Superior group	30 ± 16	28 ± 13	44 (28-62)
	Superior oblique	40 ± 13	24 ± 9	

*According to Ozgen *et al*., 1999.

RESULTS

Assessment of the diameters and densities of extraocular muscles, the length of the interzygomatic line, distance between the interzygomatic line and the posterior margin of the globe, width of the optic nerve-sheath complex and superior ophthalmic vein and lacrimal gland position with regard to the normal data of other authors are given in Table 1. There were no statistically significant estimated differences between right and left orbit results. We also did not find statistical differences between males and females.

Extraocular muscle diameter measured in our study revealed significant and proportional enlargement according to normal data (32/46 orbits, 69.6% with increased muscular index), with respectively mean diameter ratio: medial rectus 1.32, lateral rectus 1.34, inferior rectus 1.39, superior group 1.33 and superior oblique 1.20. No muscle size was not gauge beneath the normal range. In our study, the most frequently swollen muscles were the inferior (61%) and medial (54%) rectus prior to superior (39%), lateral rectus (37%) and superior oblique (26%). The highest correlation between muscle enlargement and proptosis was remarked in the case of the inferior rectus (77%) and medial rectus (70%; p<0.05). Seventy-eight percent of muscle enlargement was bilateral and 22% unilateral. Mean muscle density, especially the mean density of only the enlarged muscles in this study, was significantly lower compared to normal population ranges, considering inflammatory oedema and fatty infiltration. Mean density of enlarged muscles was a very heterogeneous

group with densities hesitating from –17 HU-60 HU, and muscles with lower densities tended to have a more spotted pattern. Proptosis was the most frequent (36/46 orbits, 78.3 %) pathological indicator in our study and was bilateral in 80%. It existed even in the case of proper diameters of orbital the structures, leading to the conclusion that there may be 3 subpopulations of patients: those with increased extraocular muscle volume and orbital fat volume, those with increased extraocular muscle volume and normal orbital fat compartment volume (both groups in our study included 28/46 orbits, 60.9%), and those with normal extraocular muscle volume and increased fat volume (8/46 orbits, 17.4%). Proptosis caused mainly by expansion of the orbital fat was observed more often in patients under the age of 40 years old who were generally more likely to suffer from fat-derived proptosis and less likely to develop muscle alteration, strabismus and optic neuropathy [2,8]. Four among 46 orbits (8.65%), despite enlarged muscle diameter, did not manifest symptoms of proptosis. There was also a distinguished group of patients with dysthyroid orbitopathy symptoms but without proptosis and changes in muscle pattern (6/46 orbits, 13.1%). Muscular index exceeded 50% in all cases but 6 of the orbits mentioned above. This seems to confirm the thesis proposed by other researchers [18], that in excess of 50% in the muscular index is a positive indicator of apical crowding. Anterior displacement of the lacrimal gland was observed in 58% cases. Our study did not reveal any difference in mean axial SOV diameter, finding it an unreliable indicator of optic nerve compression. Also, optic nerve sheath complex width did not differ significantly from normal population ranges.

Table 1 Thyroid orbit measurement (mm) in comparison with normal data.

		Mean ± 2 SD	Normal ranges mean ± 2 SD*	Normal ranges mean ± 2 SD#	Normal ranges mean ± 2 SD§	Normal ranges mean ± 2 SD¶
Muscle	Medial rectus	5.4 ± 1.8	4.1 ± 0.5	3.3 – 5.0	3.7 ± 1.5	4 ± 1.8
	Lateral rectus	3.9 ± 1.6	2.9 ± 0.6	1.7 – 4.8	3.4 ± 1.3	3.4 ± 2.0
	Inferior rectus	6.5 ± 2.5	4.9 ± 0.8	3.2 – 6.5	4.2 ± 0.8	3.9 ± 2.4
	Superior group	5.3 ± 1.9	3.8 ± 0.7	3.2 – 6.1	4.0 ± 1.4	4.7 ± 2.6
	Superior oblique	2.9 ± 1.2	2.4 ± 0.4	-	-	-
	MDI	25 ± 5.7	18.2 ± 1.4	13.1 – 20.7	14.5 ± 4.5	-
Superior ophthalmic vein	Axial	1.8 ± 0.3	1.8 ± 0.5	-	-	-
Optic nerve sheath	Retrobulbar	5.2 ± 0.8	5.5 ± 0.8	3.2 – 5.6	4.2 ± 0.6	-
	Waist	4.3 ± 0.7	4.2 ± 0.6			
Interzygomatic line		96.3 ± 4.4	-	91 – 108	105.0 ± 5.1	96 ± 7.6
Globe position		3.7 ± 2.8	9.9 ± 1.7	5.9 – 12.8	11.1 ± 1.8	7.1 ± 5.2
Muscular index (%)		59.2 ± 8.67	-	-	-	-

*According to Nugent et al., 1990;   #According to Özgen et Ariyurek, 1998;   §According to Lee et al., 2001;   ¶According to Sheikh, 2007.

DISCUSSION

Thyroid ophthalmopathy is the most frequent extrathyroid symptom of Graves' disease, as well as one of the most difficult and deceptive in clinical presentation. The disease can significantly deteriorate the life quality of the patient and may lead to vision loss, resulting permanent disability. Therefore, diagnosis of the dysthyroid orbitopathy and assessment of the effects of its treatment should rely on relevant measurements, i.e. diameters of extraocular muscles, volume of retrobulbar fibro-adipose tissue, proptosis, lid fissure width, range of extraocular motion on perimeter, and quantitation of diplopia fields.

Sensitive spatial radiological diagnostic modalities (CT, MRI) can evaluate not only clinically noticeable infiltrative stage of the disease, but also muscle involvement in the latent phase. According to The European Group on Graves' Orbitopathy (EUGOGO) imaging of the orbits by CT or MRI scanning [19] is recommended when diagnosis based on the clinical or serologic findings is uncertain, in cases of apparently unilateral disease and suspected dysthyroid optic neuropathy. It is also used to indicate the degree of muscle involvement and its bi-laterality, to monitor patients for progression of the disease, to exclude coexisting pathology and to aid surgical planning and evaluating the result of orbital decompression surgery [20]. Computed tomography scanning provides a number of objective quantitative measures which identify patients at increased risk of orbital complications. It surpasses ultrasonography – with its imaging capability to evaluate extraocular muscles and optic nerve involvement at the orbital apex, and is complementary to MRI – with poorer soft tissue resolution but better bone architecture resolution.

Selection of the CT scanning plane is an intrinsic issue in the assessment of orbital content. Extraocular muscles are measured in the planes parallel to their course: in axial scans (medial rectus, lateral rectus) or in coronal scans (inferior rectus, superior group, superior oblique) and perpendicularly to the orbital wall, which provides accuracy, comparability and repeatability of the results. Postprocessed planar reconstructions enable the consultant to perform a survey of the orbits while the scanning is performed in single plane acquisition. Studies should be assessed both in soft tissue and bone algorithm.

Enlargement of the extraocular muscle diameter as well as density decrease was pertinent to all muscle groups, implying that fat and inflammation in dysthyroid orbitopathy usually do not incorporate individual orbital elements, but the entire orbit compartment, regardless of the fact that their reaction manifestation is not accurately similar. Computed tomography imaging enables highly sensitive and specific diagnostic of the development of optic neuropathy with apical crowding induced by the muscles and/or fat tissue that seems to be the most appropriate indicator of intraorbital pathology. In our study, the most frequently swollen muscle was inferior, followed by superior and lateral rectus and superior oblique. This result is a direct confirmation of the results of other studies [2, 17]. Similarly, the highest correlation between muscle enlargement and proptosis was presented by the medial rectus. The posterior and middle third of the muscle bulges were most affected, with relative sparring of tendinous insertions. On CT scans there was enlargement of one or more of the extraocular muscles, in different combinations. All muscles measured in our study had a lower density when compared to normal data, and the density of the thickened muscles was lower – sometimes in heterogeneous pattern – than density of those whose diameter was not enlarged. This suggests that muscle thickness and density decrease are correlated; which corroborates statements by other authors [17]. Multiple muscle involvement was much more common than isolated muscle involvement. The majority of patients undergoing the CT demonstrated bilateral involvement, despite unilateral clinical findings. Muscle diameters and density did not correspond with the Graves' disease span.

CONCLUSION

CT scanning is a valuable method of orbital assessment in Graves' disease as it enables the consultant to precisely evaluate and determine the ground of proptosis - extent of enlargement of respective extraocular muscle diameter or increased orbital fat volume, as well as differences in densities of extraocular muscles relevant to increased orbital fat compartment volume. Specification of parameters such as thickness and density in numerical values renders CT a beneficial monitoring method in thyroid orbitopathy.

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