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Orbital MRI in thyroid-associated orbitopathy

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ABSTRACT

Aim: Thyroid-associated orbitopathy (TAO) is the most common cause of proptosis in adults and the clinical picture is mostly associated with thyroid dysfunction. MRI is frequently used because of its advantages, such as high soft tissue resolution, multiple plane evaluation, and no risk of ionizing radiation exposure to the lens. The research aim was to present cases of thyroid orbitopathy with MRI findings and to compare the findings with existing literature.

Material and Method: Patients who visited our radiology clinic with a preliminary diagnosis of TAO between April 2015 and February 2021 and underwent orbital MRIs were included in the study. We evaluated parameters such as age, sex, presence of proptosis, orbital muscle involvement, increase in orbital fatty tissue, and lacrimal gland involvement.

Results:A total of 35 patients were included in our study. The mean age was 40.6 (18-60) years, 19 (54%) patients were female, and 16 (46%) were male. All patients were diagnosed with Graves' disease, whereas no patient was diagnosed with Hashimoto's thyroiditis. The most common findings were proptosis in 33 (94%) patients, inferior rectus involvement in 27 (77%) patients, and medial rectus muscle involvement in 25 (71%) patients. No significant correlation was found between the presence of uni/bilateral involvement and TSH values (p = 0.008).

Conclusion: In conclusion, since the presence of orbital involvement is crucial for treating thyroid diseases, all orbital structures involved should be reported by imaging. Orbital MRI is an effective imaging modality in the detection and differential diagnosis of TAO.

Keywords: Thyroid, orbita, proptozis, magnetic resonance imaging

Our research's data was presented as a poster presentation at the 42nd National Radiology Congress (TURKRAD-2021, Antalya, 26-31 October 2021).

INTRODUCTION

Thyroid-associated orbitopathy (TAO) is the most common cause of proptosis in adults and the clinical picture is mostly associated with thyroid dysfunction (1-3). Besides proptosis, TAO is characterized by the involvement of extraocular muscles and an increase in orbital fat volume. While TAO is more common in women, the prevalence of severe orbitopathy is higher in men. The onset of TAO usually begins between the ages of 30-50 years and is more severe in older ages. It is the most common extrathyroidal involvement of Graves' disease. Orbitopathy develops in 25%-50% of patients with Graves' disease and a few (2%) with Hashimoto's thyroiditis. TAO may precede, occur simultaneously, or follow the onset of abnormal thyroid function (4-7).

Ultrasonography (US), magnetic resonance imaging (MRI) and computed tomography (CT), can be used as imaging modalities. Although US does not involve radiation exposure and provides a quick evaluation, not all orbital structures are examined using US and it is operator dependent. Whole orbital structures can be visualized using CT and MRI. CT has high sensitivity in revealing extraocular muscle enlargement; however, ionizing radiation exposure is a major disadvantage while performing CT. MRI is frequently used because of its advantages, such as high soft tissue resolution, multiple plane evaluation, and no risk of ionizing radiation exposure to the lens (8-11). Proptosis, muscle thickening, and increase in orbital fatty tissue can be easily visualized via MRI. Additionally, MRI is an essential imaging modality for the differential diagnosis of diseases that can be confused with thyroid orbitopathy (5-9). The research aim was to present cases of thyroid orbitopathy with MRI findings and to compare the findings with existing literature.

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MATERIAL AND METHOD

This research was designed as a retrospective study. Patients who visited our radiology clinic with a preliminary diagnosis of TAO between April 2015 and February 2021 and underwent orbital MRIs were included in the study. The study was initiated with the approval of Dicle University, Faculty of Medicine, Non-Interventional Clinical Researches Ethics Committee, (Date: 13.10.2021; Decision No: 423). All procedures were performed adhered to the ethical rules and principles of the Helsinki Declaration.

We evaluated parameters such as age, sex, TSh, ft3 and Ft4 values at diagnosis presence of proptosis, orbital muscle involvement, increase in orbital fatty tissue, and lacrimal gland involvement. In cases with involvement, localization of involvement, presence of uni/bilateral involvement, and their relationship with thyroid-stimulating hormone (TSH) levels were also evaluated.

Patients with a preliminary diagnosis of TAO but without a pathological appearance on MRI, patients whose imaging was not performed at our center, and patients with an unconfirmed diagnosis of TAO were excluded from the study.

MRI Protocol

Orbital MRI was performed with 1.5-T and 3.0-T (Achieva; Philips Medical Systems, Best, Netherlands) MRI devices using an 8-channel cranial coil, which is the most suitable setup for evaluating orbitals. Images parallel to the optic nerve (oblique axial) were taken covering the entire orbital cavity. Coronal STIR, axial T2, axial T1-SPIR, sagittal T1, and diffusion-weighted images were obtained before contrast agent administration. During the procedure, 0.1 mmol/kg intravenous paramagnetic contrast agent was administered at a rate of 2 ml/sec through the antecubital vein. After administering the contrast agent, T1 fat-suppressed axial and coronal images were obtained in the 3D turbo field echo (TFE) sequence.

MRI Findings

Orbital MRIs were examined by two radiologists with at least 5 years of experience. The examinations were performed on Philips Extended Brilliance Workspace (Philips Medical systems, Best, Netherlands) workstations. The interzygomatic line was accepted as the reference line for measuring proptosis. The interzygomatic line is a line joining the anterior margins of the zygomatic bones. The distance between this line and the posterior sclera is normally 9.9±1.7 mm, and the decrease in this distance supports the diagnosis of proptosis. Additionally, the distance from the interzygomatic line to the anterior of the eyeball should be <23 mm, and a greater distance indicates proptosis (12,13) (**Figure 1**).

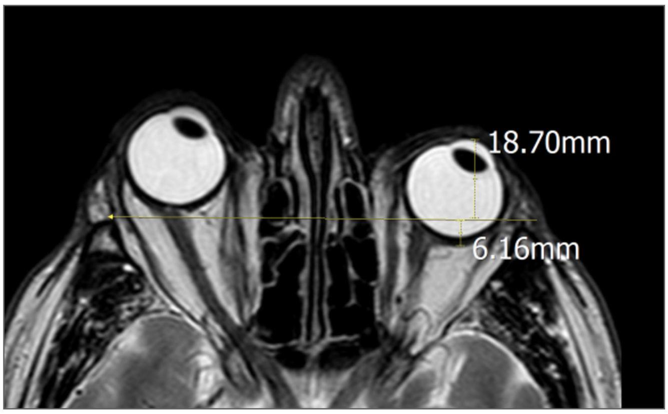

Figure 1. Evaluation of proptosis (proptosis on the right, normal appearance on the left)

While measuring orbital muscle thickness, muscle structures were observed on axial and coronal images and their average values were taken. The criteria for orbital muscle thickening were determined based on relevant literature (13-15). The criteria for normal muscle thicknesses were accepted as follows: 4.8 mm for the inferior rectus (3.2-6.5 mm), 4.2 mm for the medial rectus (3.3-5 mm), 4.6 mm for the superior rectus (3.2-6.1 mm), and 3.3 mm for the lateral rectus muscles (1.7-4.8 mm) (**Figure 2**) (**Table 1**).

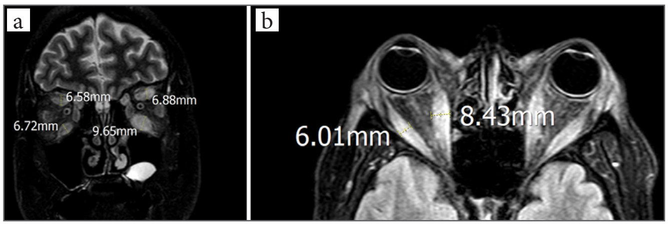

Figure 2. Orbital muscle thickness measurements (**a:** superior and inferior rectus muscle thickness measurements using coronal T2 image, **b:** lateral and medial rectus muscle thickness measurements using axial T1 image)

Table 1. Orbital muscle thickness normal reference values and orbital muscle thicknesses measured in cases with thyroid-associated orbitopathy

	Orbital muscle thicknesses in cases with involvement		Normal reference values of orbital muscle thickness	
	Muscle thicknesses (mm)	Average (mm)	Muscle thicknesses (mm)	Average (mm)
Inferior rectus	6.6-9	7.3	3.2-6.5	4.8
Medial rectus	5.3-8.5	6.2	3.3-5	4.2
Superior rectus	6.2-8.2	6.7	3.2-6	4.6
Lateral rectus	5-7.8	6.3	1.7-4.8	3.3

Increased orbital fatty tissue intensity, increased lacrimal gland size, and lacrimal gland herniation were also accepted as positive findings (**Figure 3**).

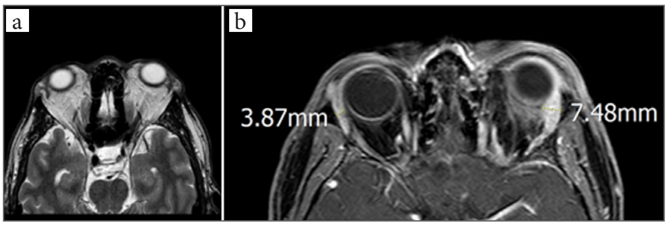

Figure 3. Increase in orbital fatty tissue **(a)** and left lacrimal gland involvement **(b)**

The SPSS package program was used for the statistical analysis of data. Standard deviation and mean values were calculated for age, sex, TSH, Ft3, Ft4 values; the presence of proptosis; orbital muscle, orbital fatty tissue, and lacrimal gland involvement. The chi-square test was used to investigate the relationship between TSH values and the presence of uni/bilateral involvement. Independent sample t-test was used for pairwise comparisons of normally distributed data, and Mann-Whitney U test was used for comparisons of non-normally distributed data.

RESULTS

Thirty five patients were included in our study. The mean age was 40.6 (18-60) years, 19 (54%) patients were female, and 16 (46%) were male. All patients were diagnosed with Graves' disease, whereas no patient was diagnosed with Hashimoto's thyroiditis. Contrast-enhanced orbital MRI was performed in all patients. The most common findings were proptosis in 33 (94%) patients (bilateral in 30 patients, unilateral in 3 patients), inferior rectus involvement in 27 (77%) patients (23 bilateral, 4 unilateral), and medial rectus muscle involvement in 25 (71%) patients (21 bilateral, 4 unilateral). Involvement of the superior rectus, lateral rectus, and superior oblique muscles was detected in 8 (23%), 4 (12%), and 2 (6%) patients, respectively. The findings showed unilateral involvement in 3 (9%) patients (right in 2 patients [**Figure 4**] and left in 1 [**Figure 5**)], whereas the involvement was bilateral in 32 (91%) patients (**Figure 6**) (**Table 2**).

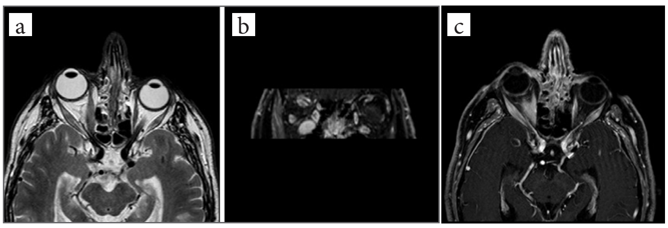

Figure 4. 60-year-old female patient (a: axial T2, b: coronal T1 fat suppression with contrast, c: axial T1 fat-suppressed sequence with contrast) with right proptosis and asymmetrical orbital muscle thickness with increased enhancement in the lateral and medial rectus muscles.

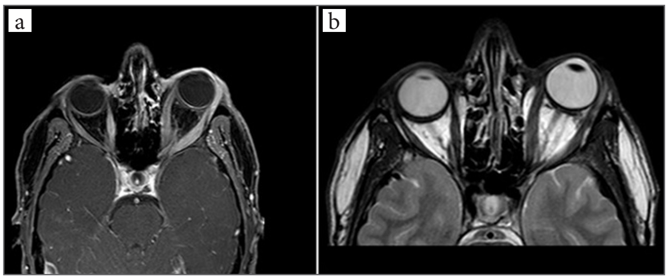

Figure 5. 28-year-old male patient (a: axial T1, b: axial T2 sequence fat suppression with contrast) with left proptosis, asymmetrical thickness and increased enhancement in the lateral and medial rectus muscles.

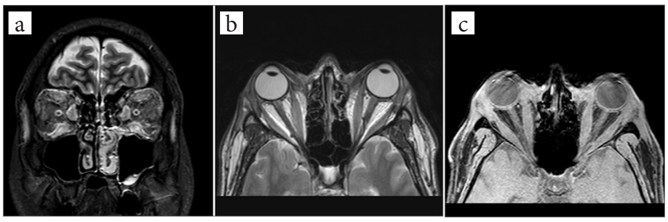

Figure 6. 35-year-old male patient, (a: coronal T2, b: axial T2, c: axial T1 sequence with fat-suppressed contrast) with bilateral proptosis, bilateral symmetric orbital muscle involvement and increase in periorbital fatty tissue and heterogeneity.

Isolated superior, lateral, and oblique muscle involvement was not observed in any patients, and all patients had proptosis, accompanied by inferior and medial muscle involvement. While isolated proptosis was detected in 6 (17%) patients, orbital muscle involvement without accompanying proptosis was observed in only 2 (6%) patients.

An increase in orbital fat tissue was observed in 12 (34%) patients (bilateral in 9 patients, unilateral in 3 patients). Lacrimal gland involvement was detected in 5 (14%) patients (bilateral in 3, unilateral in 2) (**Table 2**).

Table 2. Demographic data and magnetic resonance imaging findings

Age	40.6±6.4	
TSH	4.1± 0.8	
Ft3	2.2± 0.4	
Ft4	3.4± 0.6	
	n (number)	**% (percentage)**
Sex		
Female	19	54
Male	16	46
MRI FINDINGS		
Proptosis	33	94
Inferior rectus involvement	27	77
Medial rectus involvement	25	71
Superior rectus involvement	8	23
Lateral rectus involvement	4	12
Superior oblique involvement	2	6
Orbital fatty tissue involvement	12	34
Lacrimal gland involvement	5	14
Bilateral involvement	32	91
Unilateral involvement	3	9

In patients with TAO, the mean orbital muscle thickness measured at the levels of the inferior, medial, superior, and lateral rectus muscles was 7.3 mm (6.6-9 mm), 6.2 mm (5.3-8.5 mm), 6.7 mm (6.2-8.2 mm), and 6.3 mm (5-7.8 mm) respectively (**Table 1**).

All patients with TAO received medical treatment. Since post-treatment images of patients could not be accessed, the findings before and after treatment were not compared. TAO was detected in the first 5 years of disease onset in 14 (40%) patients, from 5-10 years in 12 (34%) patients, from 10-15 years in 7 (20%) patients, and at the time of initial diagnosis in two patients (6%).

DISCUSSION

In this research, orbital MRI examinations of patients with TAO were evaluated and the most common finding was proptosis (94%). Proptosis is a spontaneous decompression resulting from the enlargement of the extraocular muscles and connective tissue, as well as the orbital tissue infiltration by orbital fat deposits, glycosaminoglycans (GAG), and leukocytes. Proptosis is bilateral in 90% of cases(6,14-16). Our findings were consistent with the literature, where bilateral proptosis was detected in 90% of cases and unilateral proptosis in 10% of cases examined.

Muscle enlargement occurs because of the separation of muscle fibers by fluid and fat deposits, fibrosis, scar formation, and leukocyte infiltration. Despite the enlargement of the extraocular muscles, muscle fibers are normal in TAO. Trunk involvement of muscles and frequent preservation of insertions are key findings for differential diagnosis and based on these characteristics, TAO is differentiated from other diseases, such as orbital pseudotumor, orbital arteriovenous malformation, orbital sarcoidosis, lymphoma, and metastasis (6,7).

The inferior rectus muscle is the most frequently involved extraocular muscle in patients with orbitopathy followed by the medial and superior rectus muscles (16-18). In our study, extraocular muscle involvement was detected in 83% of cases, and consistent with the literature, the inferior rectus was most frequently involved. It was followed by the medial, superior, lateral rectus, and superior oblique muscles. None of the patients exhibited isolated superior, lateral, and oblique muscle involvement. Orbital muscle involvement without accompanying proptosis was observed in only 2 (6%) patients.

TAO is 2.5-6 times more common in women and severe orbitopathy is more common in men. The onset is generally between the ages of 30 and 50 and is more severe after the age of 50. Orbitopathy develops in 25%-50% of patients with Graves' disease and rarely (2%) in patients with Hashimoto's thyroiditis. Severe orbitopathy is seen in 3%-5% of these cases (5,6). In our study, 55% of the patients were female and the mean age was 40, which is consistent with the literature. All patients were diagnosed with Graves' disease, whereas none were diagnosed with Hashimoto's thyroiditis.

In most patients, orbitopathy develops within the first 18 months of diagnosis with Graves' disease. Consequently, TAO can develop anytime between 10 years before and up to 20 years after the diagnosis of Graves' disease (3). Orbitopathy findings are mostly bilateral, but unilateral or asymmetric findings have also been observed (11). In the current study, TAO was most frequently detected in the first 5 years of diagnosis with Graves' disease. We observed bilateral involvement in 92% of patients, whereas only 8% of patients exhibited a unilateral involvement. In patients with TAO, lacrimal gland involvement has been recognized as a potential cause of ophthalmopathy symptoms, and different studies have shown significant involvement of the lacrimal gland in patients with TAO compared to healthy controls. In these patients, decreased tear secretion and dry eyes can be observed due to lacrimal gland involvement. Active and inactive patients in terms of lacrimal gland involvement require different treatment strategies. Therefore, the lacrimal gland should be examined in imaging and its status should be reported. Lacrimal gland involvement can be observed as an increase in gland size or heterogeneity, or as herniation in the lacrimal gland. A high degree of proptosis, enlargement of retro-orbital structures, and accumulation of TSH-receptors in the lacrimal glands can be listed among the causes of lacrimal gland involvement (17,18). Lacrimal gland involvement was detected in 14% of patients in our study, and involvement was bilateral in 60% of these patients.

The relatively small number of patients and the lack of patients with Hashimoto's thyroiditis are the most important limitations of the current study. Moreover, patient findings before and after treatment could not be compared due to the lack of post-treatment imaging.

CONCLUSION

Since the presence of orbital involvement is crucial for treating thyroid diseases, all orbital structures involved should be reported by imaging. Orbital MRI is an effective imaging modality in the detection and differential diagnosis of TAO.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of Dicle University, Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee, (Date: 13.10.2021; Decision No: 423).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Ginsberg J. Diagnosis and management of Graves' disease. CMAJ 2003; 168: 575-585.
2. Chan LL, Tan HE, Teo F.T-H, L-H Lim, Seah L. Graves ophthalmopathy: the bony orbit in optic neuropathy, its apical angular capacity, and impact on prediction of risk. AJNR Am J Neuroradiol 2009; 30: 597-602.
3. North VS, Freitag SK. A review of imaging modalities in thyroid-associated orbitopathy. Int Ophthalmol Clin 2019; 59: 81-93.
4. Mishra S, Maurya VK, Kumar SA, Kaur A, Saxena SK. Clinical management and therapeutic strategies for the thyroid-associated ophthalmopathy: current and future perspectives. Curr Eye Res 2020; 45: 1325-41.
5. Bartalena L, Marcocci C, Pinchera A. Graves' ophthalmopathy: a preventable disease? Eur J Endocrinol 2002; 146: 457.
6. Şanlı E. Gündüz K. Tiroid Oftalmopati. Turk J Ophthalmol 2017; 47: 94-105
7. Davies MJ, Dolman PJ. Levator muscle enlargement in thyroid eye disease-related upper eyelid retraction. Ophthalmic Plast Reconstr Surg 2017: 33: 35-9.
8. Parmar H, Ibrahim M. Extrathyroidal manifestations of thyroid disease: thyroid ophthalmopathy. Neuroimaging Clin N Am 2008; 18: 527-36.
9. Ahn ES, Subramanian PS. Treatment modalities of thyroid related orbitopathy. Indian J Ophthalmol 2014; 62: 999-1002.
10. Hodgson NM, Rajaii F. Current understanding of the progression and management thyroid associated orbitopathy: a systematic review. Ophthalmol Ther 2020; 9: 21-33
11. Hennein L, Robbins SL. Thyroid-associated orbitopathy: management and treatment. J Binocul Vis Ocul Motil 2021: 1-15.
12. Haaga JR, Boll D. CT and MRI of the whole body. Mosby 2009; 2: 56-65
13. Ozgen A, Aydingoz U. Normative measurements of orbital structures using MRI. J Comput Assist Tomogr 2000; 24: 493-6.
14. Ozgen A, Ariyurek M. Normative measurements of orbital structures using CT. AJR. 1998; 170: 1093-6.
15. Monteiro ML, Gonçalves AC, Silva CT, Moura JP, Ribeiro CS, Gebrim EM. Diagnostic ability of Barrett's index to detect dysthyroid optic neuropathy using multidetector computed tomography. Clinics 2008; 63: 301-6.
16. Bahn RS. Graves' ophthalmopathy. N Engl J Med 2010; 362: 726-38.
17. Eckstein AK, Finkenrath A, Heiligenhaus A. et al. Dry eye syndrome in thyroid-associated ophthalmo- pathy: lacrimal expression of TSH receptor suggests involvement of TSHR-specific autoantibodies. Acta Ophthalmol Scand 2004; 82: 291-7.
18. Gagliardo C, Radellini S, Bubella RM, et al. Lacrimal gland herniation in Graves ophthalmopathy: a simple and useful MRI biomarker of disease activity. Eur Radiol 2020; 30: 2138-41