

## Ultrasonic measurement of ocular rectus muscle thickness in patients with Graves' ophthalmopathy

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**Key words:** Graves' ophthalmopathy; extraocular muscle; proptosis; ultrasonography.

**Summary.** The aim of this study was to evaluate changes in extraocular muscle thickness and to assess its correlation with the degree of proptosis in patients with Graves' ophthalmopathy (GO).

**Material and methods.** A total of 242 patients (207 females and 35 males) with Graves' ophthalmopathy were enrolled into the study (GO group). Their mean age was  $53.83 \pm 14.49$  years. In addition, we examined an age-matched ( $53.51 \pm 12.79$  years) control group of 40 healthy persons. All the participants underwent ophthalmological examination, including eye protrusion measurement and ultrasonographic evaluation of extraocular muscles thickness.

**Results.** The mean exophthalmos in the GO and control groups was  $17.84 \pm 2.79$  mm and  $16.0 \pm 1.58$  mm, respectively. The enlargement of inferior rectus muscle was recorded in 92.1% of patients, lateral rectus muscle in 81.2%, and medial rectus muscle in 50.8% ( $P < 0.001$ ). A significant correlation between exophthalmos and muscle thickness sum was found in the GO group (Spearman correlation coefficient, 0.515;  $P < 0.0001$ ).

**Conclusions.** Graves' ophthalmopathy is more frequent in medium-aged women than men. A significant enlargement of inferior, lateral, and medial straight muscles was noticed in the GO group. With increasing proptosis, the sum of the muscle thickness was increasing, and exophthalmos moderately correlated with muscle thickness sum.

### Introduction

Graves' ophthalmopathy (GO) is a thyroid-associated ophthalmopathy, a process in which the orbital tissues become inflamed and are remodeled (1). Eye changes result from either an autoimmune abnormality or a regulatory cell disorder that allows some antibodies to attack the ocular muscles, which leads to inflammation and other signs of discomfort (1–4).

GO is also known as thyroid eye disease, thyroid-associated ophthalmopathy, or endocrine ophthalmopathy. The process is associated with one of three thyroid disorders: Graves' hyperthyroidism (80%), Hashimoto's thyroiditis (10% to 15%), or unclassified thyroid immunologic abnormality (5%) (5).

More than 25–50% of individuals with Graves' disease have clinical involvement of the eyes (6). Clinically, the classic ocular signs of the disease include proptosis, lid lag or retraction, periorbital edema, extraocular muscle involvement causing diplopia, and the most feared complication – visual loss (5). The most obvious pathological change within the orbit is the enlargement of extraocular muscles (3, 4, 7, 8). The swelling of the extraocular muscles pushes the eye forward causing it to protrude.

Imaging of the extraocular muscles and orbital soft tissues in Graves' orbitopathy provides valuable information for both diagnosis and treatment decisions (8, 9). Helpful radiological techniques include orbital ultrasound (US), magnetic resonance imaging, and orbital computerized tomography.

Detection of extraocular muscle defects with US is more sensitive than clinical examination (8, 10). Using orbital US, both the A-scan and B-scan techniques may be employed to screen the straight and oblique extraocular muscles for lesions. The A-scan is particularly sensitive in indicating the thickening or thinning of muscles and in differentiating the underlying pathologies, while the B-scan is very helpful in their topographic evaluation, for determination if individual rectus muscles are enlarged (11).

In clinical practice, it is used to measure and evaluate each rectus muscle separately and to determine it to be pathological if the muscle thickness is more than 5.0 mm. Ossoinig states that the thickness of the extraocular muscles varies greatly from person to person, but is very similar in the two orbits of the same person (11). Scientists suggest evaluating the sum of muscle thickness in patients

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with GO (9, 12). Comparison of the difference in thickness between the pair rectus muscle and the sum of muscle thickness in the two orbits of the same person may obtain reliable information to determine the degree of extraocular muscle involvement in order to choose an appropriate treatment.

The aim of this study is to evaluate the changes in extraocular muscle thickness and to assess its correlation with the degree of proptosis in patients with Graves' ophthalmopathy.

**Material and methods**

A total of 242 patients (484 eyes) with GO and 40 healthy persons composing the age-matched control group were enrolled into the study. The inclusion criteria for patients into the study were as follows: clinical and laboratory signs of existing Graves' disease or a documented history of Graves' disease. Persons without eye diseases and clinical or laboratory signs of Graves' disease were enrolled into the study as controls.

All the participants underwent ophthalmological examination. Eye protrusion was measured using a Hertel's exophthalmometer. Orbital ultrasound was performed by the same doctor using the A/B mode Mentor™ Advent ultrasonic diagnostic imaging system. For each of the four (superior, inferior, lateral, and medial rectus) extraocular muscles, thickness was measured at the widest portion of the muscle.

We evaluated thickness (mm) of each extraocular muscle, calculated the sum of the muscle thickness in a given eye, paid attention to the difference in thickness between rectus muscles of paired eyes and the sum of muscle thickness in the two orbits of the same person.

Results were statistically analyzed using SPSS 13.0. Spearman's correlation and Student's *t* test were applied. *P* values less than 0.05 were considered as statistically significant.

**Results**

A total of 242 patients (484 eyes) with GO and a control group of 40 healthy persons (80 eyes) were enrolled into the study. There were 35 (14.5%) male and 207 (85.5%) female patients. The mean age of the patients was 53.83±14.49 years, and the

controls were age-matched (mean age, 53.51±12.79 years).

Proptosis of more than 16 mm was seen in 67.7% of the patients' eyes. The mean exophthalmos in the patients' group was 17.84±2.79 mm.

The mean thickness of extraocular muscles measured using ultrasound technique and the ranges of muscles thickness in the control and GO groups are showed in Table. Normal values for the rectus muscles have been determined by two different studies: one by McNutt et al. and the second more recent study by Byrne et al. (12).

A statistically significant enlargement of inferior, lateral, and medial straight muscles was noticed in the GO group (*P*<0.001) (Fig. 1).

The enlargement of inferior rectus muscle (thickness ≥3.6 mm) was found in 446 eyes (92.1%) of patients (*P*<0.001). Lateral rectus muscle was enlarged (thickness ≥3.8 mm) in 393 (81.2%) eyes (*P*<0.001), medial rectus muscle (thickness ≥4.7 mm) in 246 (50.8%) eyes (*P*<0.001), and superior rectus muscle (thickness ≥6.8 mm) in 11 (2.3%) eyes (*P*=0.716) (Fig. 2).

The sum of the four (superior, inferior, lateral, and medial rectus) extraocular muscle thickness in the control group ranged from 11.9 to 16.9 mm; the average was 16±2.24 mm. In 323 eyes of patients (67.7%), the sum of muscle thickness was more than 16.9 mm (*P*<0.001). The mean sum of muscle thickness in the entire cohort of patients was 18.9±3.88 mm.

The difference between the sums of muscle thickness of paired eyes in the control group was ≤1.2 mm. In 260 (46.3%) eyes of patients, the difference was >1.2 mm (*P*=0.102).

The difference of more than 0.4 mm between the inferior and lateral rectus muscles of pair eyes was recorded in 239 (49.4%) (*P*=0.7) and 231 (47.7%) (*P*=0.3) eyes of patients, respectively. The difference of more than 0.5 mm between the medial rectus muscles of paired eyes was found in 177 (36.6%) eyes of patients (*P*<0.001) and the difference of more than 0.8 mm between the superior rectus muscles of paired eyes in 64 (13.2%) eyes of patients (*P*<0.001) (Fig. 3).

A moderate statistically significant correlation between the exophthalmos and muscle thickness

Table. The mean thickness of extraocular muscle and ranges of muscle thickness

Muscle	Mean thickness of muscle, mm		Muscle thickness, range, mm	
	control group	GO group	control group	GO group
Superior rectus	4.0	4.22	3.9–6.8	2.23–8.4
Lateral rectus	3.0	4.76	2.2–3.8	2.72–10.76
Medial rectus	3.5	4.97	2.3–4.7	3.01–10.13
Inferior rectus	2.6	5.01	1.6–3.6	3.08–10.07

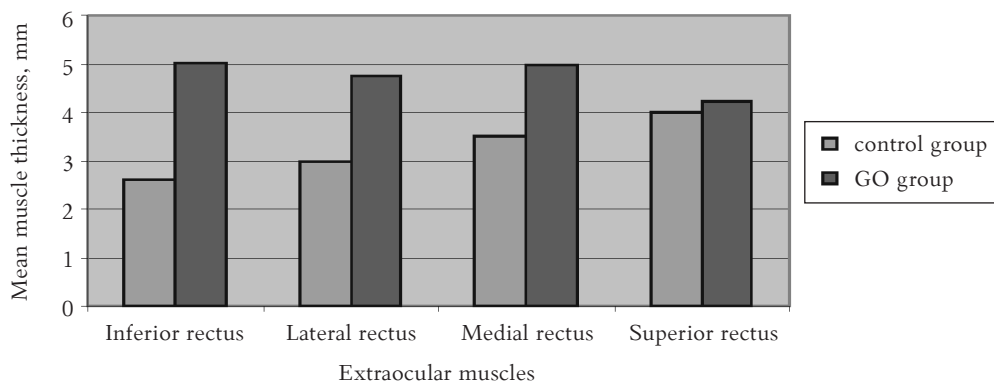


Fig. 1. Mean extraocular muscle thickness

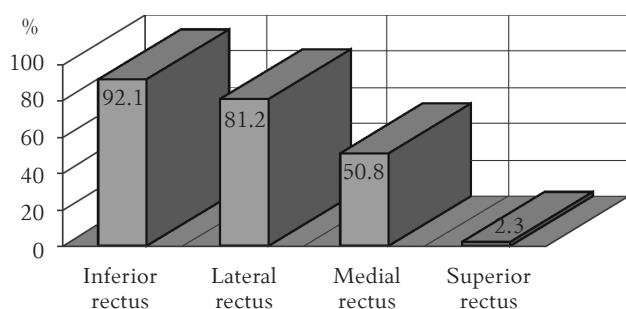


Fig. 2. The percentage of eyes with enlarged extraocular muscles in patients with Graves' ophthalmopathy

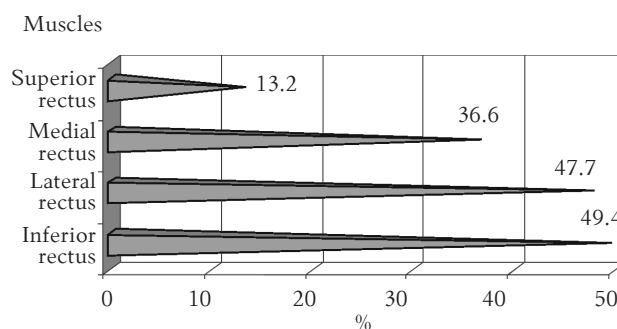


Fig. 3. The percentage of eyes with pathological difference comparing muscle thickness of paired eye

sum was found (Spearman correlation coefficient, 0.515;  $P < 0.001$ ). With increasing proptosis, the sum of the muscle thickness was increasing.

In 51.2% of patients, muscle sum thickness was enlarged and proptosis was normal ( $< 16.9$  mm).

### Discussion

Graves' ophthalmopathy is clinically relevant in approximately 50% of patients with Graves' disease (13). The disease is more frequent in women than men, although the female-to-male ratio is only 1:4 in severe forms of eye disease (13). In our study, the female-to-male ratio was 1:6, and the mean age of our patients was 54 years. Wiersinga et al. observed the highest GO incidence in patients in their fifth and seventh decades of life (13). Nagy et al. findings were similar; in their study group, the ages of the majority of GO patients were clustered around the fifth decade (9).

GO is the most common cause of both unilateral and bilateral proptosis in adults (14). In our series, the mean eye protrusion of patients was  $17.84 \pm 2.79$  mm. In the cohort study of 39 patients with Graves' disease by Robert et al., the mean proptosis was  $24.3 \pm 2.5$  mm (15). However, patients of their study had the disease of late stages before fat-removal orbital decompression.

External eye muscles are important contributors to the orbital process in Graves' ophthalmopathy (8, 9). We found that the inferior and lateral rectus muscles were the most frequently affected muscles (92% and 81% of cases, respectively). In a Japanese study on 349 thyroid patients, the inferior rectus was enlarged in 43%, the medial in 38%, and the lateral in 16% of cases (16). Villalodid et al. examined two groups of patients with Graves' disease: with clinical ophthalmopathy and without it. Both groups showed the inferior rectus muscle as the most frequently involved (56% and 77%, respectively) (17).

A variance of more than 0.5 mm between the same muscles in the two orbits is consistent with the diagnosis of thyroid-associated ophthalmopathy (18). In our study, a statistically significant difference of more than 0.5 mm between the medial rectus muscles of paired eyes was found in 36.6% of cases and difference of more than 0.8 mm between the superior rectus muscles of paired eyes in 13.2% of cases ( $P < 0.001$ ).

Fledelius et al. in their study ultrasonically measured horizontal eye muscle thickness in 93 patients with thyroid-associated orbitopathy. The mean of the sum of all four muscles was 16.8 mm (range, 13.6–21.7 mm) in the control group versus 22.6 mm (range, 15.5–36.4 mm) in the thyroid

group (19). In our study, the mean thickness of the sum of all four muscles was 16.0 mm in the control group versus 18.9 mm in the GO group. We found the difference between the sums of muscle thickness of paired eyes, but the difference was not statistically significant. This may be explained by fact that GO is an immunologically mediated inflammatory disease and it affects both the orbits. In patients with GO, the straight muscles of both the eyes are involved in the process and the difference was not statistically significant. If we compared the difference between the sums of muscle thickness of the same person's healthy and impaired eyes, a statistically significant difference would be presumable.

We found a correlation between the degree of exophthalmos and the sum of muscle thickness for a given eye. The findings of the study by Nagy et al. were similar. Moreover, they reported that in their

series, a normal Hertel reading did not guarantee normal sized muscles (9).

### Conclusions

The disease is more frequent in medium-aged women than men. Pathological eye protrusion was documented in 67.7% of patients' eyes. A statistically significant enlargement of inferior, lateral, and medial straight muscles was noticed in the patients with Graves' ophthalmopathy. The difference between the sums of muscle thickness of paired eyes in patients' group was statistically not significant. Graves' ophthalmopathy is an immunologically mediated inflammatory disease, and extraocular muscle involvement is usually bilateral but it may be asymmetrical. That could be a reason why the difference was not large enough to be statistically significant.

## Akių išorinių tiesiųjų raumenų storio ultragarsiniai tyrimai sergantiesiems Greivso oftalmopatijomis

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**Raktažodžiai:** Greivso oftalmopatija, akių judinamieji raumenys, išverstakumas, ultragarsiniai tyrimai.

**Santrauka.** *Tyrimo tikslas.* Įvertinti akių judinamųjų raumenų pokyčius ir nustatyti sąsajas tarp raumenų storio bei išverstakumo Greivso oftalmopatija sergantiems pacientams.

*Metodai.* Ištyrėme 242 Greivso oftalmopatija sergančius pacientus (207 moteris ir 35 vyrus). Pacientų amžiaus vidurkis – 53,83±14,49 metų. Kontrolinę grupę sudarė 40 sveikų žmonių, kurių amžiaus vidurkis – 53,51±12,79 metų. Tiriamiesiems atliktas oftalmologinis tyrimas, kurio metu įvertintas išverstakumas, ultragarsiniu A/B skenavimu išmatuotas akių judinamųjų raumenų storis. Atlikta statistinė duomenų analizė.

*Rezultatai.* Išverstakumo vidurkis pacientų grupėje – 17,84±2,79 mm, kontrolinėje – 16,0±1,58 mm. Sergantiesiems Greivso oftalmopatija nustatytas apatinio (92,1 proc.), šoninio (81,2 proc.) bei vidinio (50,8 proc.) tiesiųjų raumenų sustorėjimas, p<0,001. Nustatyta koreliacija tarp išverstakumo ir raumenų storio sumos (Spearman koreliacijos koeficientas lygus 0,515), p<0,0001.

*Išvados.* Greivso oftalmopatija dažniau serga vidutinio amžiaus moterys nei vyrai. Pacientų grupėje nustatytas statistiškai reikšmingas apatinio, šoninio bei vidinio tiesiųjų akių judinamųjų raumenų sustorėjimas. Pastebėta, kad, didėjant išverstakumui, didėja raumenų storio suma, rasta statistiškai reikšminga vidutinio stiprumo koreliacija tarp išverstakumo ir raumenų storio sumos.

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