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## CLINICAL ASSESSMENT OF PATIENTS WITH GRAVES' ORBITOPATHY

**Abstract:** Clinical examination is the basis of a good assessment of a patient with Graves' orbitopathy. This study gives recommendations of the European orbitopathy group related to the activity and severity of the disease. The activity of the disease is estimated on the basis of inflammation of the soft tissues and the sum of clinical activity is used here. Severity of the disease is estimated by measuring exophthalmos, palpebral aperture, infection of soft tissues, extraocular muscles, corneal infection and optical nerve.

The decision on the type of treatment is made on the basis of the assessment of severity and activity.

**Key words:** Graves' orbitopathy, clinical examination, activity, severity

Graves' autoimmune orbitopathy (GO) is the most important extrathyroid manifestation of autoimmune hyperthyroidism, although, quite rarely, it can appear in euthyroid and even in hypothyroid patients (within Hashimoto's thyroiditis) (1). About 50% of hyperthyroid patients have eye problems, mostly of a mild type, whereas in 20-30% clinically important symptoms are developed, and in only 3-5% there are symptoms of a severe disease (2). It usually appears as a bilateral disease although it may be unilateral as well. The beginning of the disease may be gradual, but it may also be abrupt. Typical initial symptoms are discomfort on the surface of the eye, photophobia and increased tearing, as well as diplopia and pain in the orbit. The most common clinical sign is the retraction of the upper eyelid (it appears in 90-98% of patients), and then swellings and redness of the eyelids, chemosis and conjunctival redness, proptosis (exophthalmos), lagophthalmos and motility disorders (3). Typical findings are swellings of extraocular muscles, particularly of the lower and medial rectus and they can be observed in both orbits even in cases in which the disease is clinically unilateral. Although motility disorders appear in as many as 60% of patients,

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some of them do not have diplopiae due to the symmetrical effects on both orbits, amblyopia or the fact that restriction happens in extreme situations which are not so important for everyday activities. Optical neuropathy appears rarely and may be observed in unclear eyesight which cannot improve even with one eye closed, reduced recognition of colours and problems in the visual field (4).

GO has its natural course which is very often changeable; eye symptoms may become worse, stay unchanged for a long period of time or spontaneously improve. Generally speaking, there is an inflammatory phase of the progressive course of the disease (active phase), after which there is a period without important changes (stable plateau phase) and finally the improvement phase (inactive phase) (5,6,7).

It is very important to separate the activity from the severity of the disease. Activity refers to the degree of inflammation of soft tissues, and severity determines the degree of functional and cosmetic changes. The fastest way to determine activity is a clinical examination using a clinical overview with the help of the score of clinical activity (Clinical activity score, CAS) (8), although some other visual and laboratory parameters are also considered to be indicators of the disease, e.g. TSH receptor Ab, reduced eye muscle reflectivity on A-mode ultrasonography, prolonged T2 relaxation time during magnetic resonance examination, positive octreoscan and increased values of GAG in urine.

European group for orbitopathies (EUGOGO) was founded in 1999 by nine European thyroid-ophthalmology centres. It expanded over the time and in 2011, Serbia also became a member of this association. It is an association of endocrinologists, ophthalmologists, epidemiologists and radiologists founded with the aim to improve the treatment of patients with Graves' orbitopathy. In order to do this, it is necessary to understand the disease (pathophysiological process, natural clinical course of the disease) as well as to do a detailed examination of the patient. Clinical examination is extremely important since the treatment depends on the activity degree and severity of the disease. E.g. medium and severe orbitopathy are treated with corticosteroids in case the disease is active, and if it is inactive it is treated by surgery (9,10,11). In order to standardise the examination of GO subjective components (inflammation of soft tissues), a specific methodology was suggested which related to the use of the ophthalmology atlas with colour photographs which would ensure precise definition of the eye symptoms and give examples for the assessment of severity of the disease (12,13).

### ***EUGOGO recommendations for the examination of patients with Graves' orbitopathy in specialised institutions -***

**(a) Activity** of the disease is estimated on the basis of classical clinical inflammation symptoms: CAS (8). The total number is obtained by adding points for the following parameters:

Retrobulbar pain when not moving  
 Retrobulbar pain when moving  
 Redness of the eyelids  
 Redness of the conjunctiva  
 Swollen eyelids  
 Swollen caruncula  
 Chemosis  
CAS  $\geq$  3/7 and more indicates an active orbitopathy

- (b) Severity** of the disease is estimated on the basis of the following parameters:
- Palpebral aperture (the distance between the edge of the eyelids in mm in a patient sitting in a relaxed manner, with the eyes in primary position and distant fixation)
  - Swollen eyelids (absent, mild, medium, severe) (14)
  - Redness of the eyelids (absent, present) (14)
  - Redness of the conjunctiva (absent, mild, medium, severe) (14)
  - Chemosis (absent, present) (14)
  - Swollen plicae or carunculae (absent, present) (14)
  - Exophthalmos (measured by means of Hertel exophthalmometre, expressed in mm)
  - Diplopie – subjective score (0=absent; 1= intermittent; 2=inconstant, e.g. in the extreme position; 3= constant, present in the primary position)
  - Infection of eye muscles (duction in degrees) (14)
  - Corneal infection (absent/punctiform keratopathy/ulcerations)
  - Infection of the optical nerve (visus corrected as much as possible, optical discus, colour eyesight, afferent pupillary defect (absent/present) with an examination of the visual field if the compression of the optical nerve is suspected).

Upon clinical examination, it is suggested to do the classification in the following way:

**EUGOGO recommendations for the classification of GO severity (11):**

1. GO endangering the eyesight: patients with dysthyroid optic neuropathy and/or damaged cornea. This demands urgent treatment.
2. medium to severe GO: Patients have one or more of the following symptoms: eyelid retraction  $\geq$ 2mm, medium to severe infection of soft tissues, exophthalmos  $\geq$ 3mm, constant or inconstant diplopie. Treatment is done by immunosuppressives or surgical decompression.
3. mild GO: Patients have one or more of the following symptoms: eyelid retraction  $<$ 2mm, mild infection of soft tissues, exophthalmos  $<$ 3mm, intermittent or no diplopie and corneal irritation (sensitive to lubricants). Changes in the

eyes have very little effect on daily activities so that immunosuppressives and surgical treatment are not justified.

EUGOGO recommends that doctors in primary health protection, general practitioners, specialists of internal medicine and inexperienced endocrinologists, when treating patients with Graves' orbitopathy, should send all of them except those with mild forms of the disease to tertiary institutions where teams of endocrinologists and ophthalmologists will do examinations in the above-mentioned way and thus make a decision on the type of treatment (9,11).

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