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Computed tomography in Graves' ophthalmopathy – evaluation regarding the muscle size and density units

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Abstract

60 patients with Graves' ophthalmopathy were examined with CT before starting therapy. The muscle sizes were evaluated according to a staging, whereby more muscles were found to be enlarged in the group of patients with a short course of less than 2 years in comparison to the other group with a duration of disease of more than 2 years. These differences were particularly evident in the medialis and superior rectus muscle. However a long course of disease did not coincide with a reliable reduction in eye protusion. Additionally the density values differed according to the duration of disease, the lower ones being found in the group of patients with a long duration of disease. It can be assumed that fatty degenerations and/or fibrous alterations during the course of disease are responsible for this decrease in the density values.

Keywords: Graves' ophthalmopathy, computed tomography, density values, duration of disaese, muscle size

1 Introduction

Examinations of the orbit with computed tomography have proven to exhibit alterations in the case of Graves' ophthalmopathy. The indication for the examination is mainly given if the diagnosis cannot be established clinically and other diseases like myositis, pseudotumor or tumor of the orbit have to be taken into consideration [8, 12]. Morever, determining the orbital alterations may help in planning appropriate therapy because exact details on the morphological patterns of the disease can be obtained. The severeness of the changes in the retrobulbar space is clearly recognizable, so that the effect of a therapeutic procedure may be monitored.

Systematical evaluations by some working groups led to more exact information about the pattern of alterations in the orbit muscles and the other retrobulbar structures [3, 4, 9, 10]. In a previously published study we were able to demonstrate an effect of the duration of disease on the size of the muscles and conversely no effect on the values of Hertel [9]. However, these preliminary results were obtained on a small group of patients. It is the purpose of this study to analyse the effect of the duration of disease on the size of the muscles in a group of 60 patients who came to CT before starting therapy. Moreover we evaluated the density values of the muscles in order to answer the question of whether also the density values of the muscles allow conclusions on the duration of the disease to be drawn. Furthermore we wanted to know if these density values became altered by the inflammatory process of the muscles.

2 Material and Methods

The computed tomography examinations of 60 patients with Graves' ophthalmopathy were retrospectively evaluated. The CT examinations had been performed in a standardized manner with both coronal and axial slices and 2 mm slice thickness without overlapping, the evaluations being made on an off line unit with constant window and level. This is important for obtaining comparable values, because every change in the window and level of the evaluation unit results in different values in respect to the muscle size. The coronary cut behind the bulbus was taken for measurement of the muscle size, the length and width of every muscle being measured. The superior rectus muscle and levator palpebrae muscle were measured together, because a differentiation between these two muscles is often not possible behind the bulbus. The evaluation of muscle size was made by using a staging published earlier [6, 9]. The stages are based on the fact, that the muscles appear nearly rectangular on coronal scans, so multiplication of length and width is justifiable. The staging is summarized in Table I. The scans were also made in order to measure the density values of the muscles, values of the coronary and axial scans being added and the mean values calculated.

Table I. Staging of enlargement of the orbit muscles (in mm)

	med. rect. m. up to	inf. rect. m. up to	lat. rect. m. up to	sup. rect. m./lev. palp. up to
Stage 0	40	45	36	50
Stage I	41–55	46–60	37–50	51–60
Stage II	56–66	61–77	51–66	61–84
Stage III	67 and more	78 and more	67 and more	85 and more

3 Results

Pathological muscle changes were seen more often on the right than on the left (Figure 1). On the right the medialis rectus muscle was enlarged in 50% of examinations, on the left only in 34.5%. The inferior rectus muscle was affected on the right in 38.5% of all cases in contrast to 10.7% on the left side. The lateralis rectus muscle was enlarged on the right in 12.3% of all patients, in contrast to 5.4% on the left. The difference between the right and left side was particularly evident in the superior rectus muscle/levator palpebrae, because 71.9% of all patients revealed an affection of the right side and 44.6% of the left. These differences were significant in the x-square-test for the inferior rectus muscle at $p < 0.001$ and the superior rectus muscle/levator palpebrae at $p < 0.05$. When the patients were divided into two groups depending on whether the disease had lasted for less than 2 years (A; 60% of all patients) or more than 2 years (B; 40% of all patients) the following results (Figure 2 and 3) were found: the medialis rectus muscle was affected on the right side in 57% of all cases in group A, in 42% in group B and on the left in 38% in group A in contrast to 20% in group B. The inferior rectus muscle displayed enlargement on the right in 45% of the cases in group A, in 37% in group B and on the left in 11% in group A and in 5% in group B. The lateralis rectus muscle was enlarged on the right in 16% of the patients in group A, in 14% in group B, and on the left in 5% in group A in contrast to 4% in group B. And the superior rectus muscle/levator palpebrae was altered on the right side in 87% of all examinations in group A and in 58% in group B, on the left in 57% in group A and in 25% of the examined cases in group B (Figures 2 and 3). When the x-square-test was used, these results were significant at $p < 0.001$ for the superior rectus muscle/levator palpebrae. They were not significant for the medialis rectus muscle or, as expected, for the other orbital muscles.

Again using the staging, differences could be seen not only in respect to muscle enlargement on the right and left side, but also between patients with a

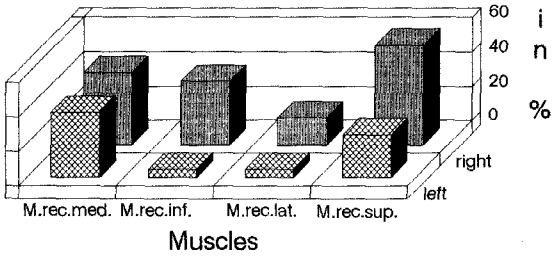

Figure 1 Muscle enlargement (in %) divided into right/left.

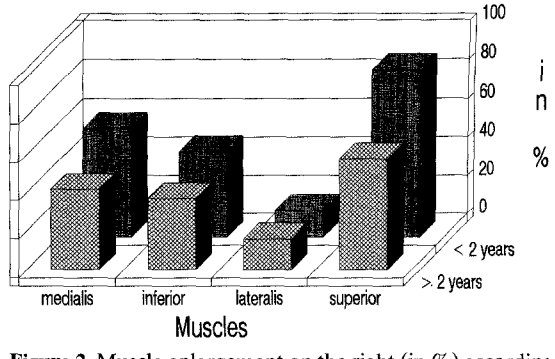

Figure 2 Muscle enlargement on the right (in %) according to the duration of disaese.

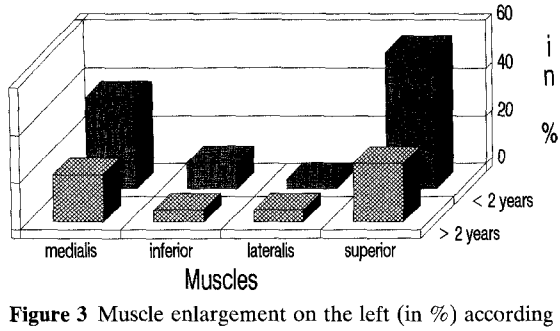

Figure 3 Muscle enlargement on the left (in %) according to the duration of disaese.

Table II. Staging of orbital muscle enlargement (in percent)

Stages	med. rect. m. right	left	inf. rect. m. right	left	lat. rect. m. right	left	sup. rect. m. right	left
no enlargement	50	65	62	89	88	94	28	55
I	19	12	19	2	–	4	16	4
II	7	9	12	4	5	2	17	12
III	24	14	7	5	7	–	39	29

Table III. Orbital muscle enlargement in patients with less than 2 years duration of disease (in percent)

Stages	med. rect. m. right	left	inf. rect. m. right	left	lat. rect. m. right	left	sup. rect. m. right	left
no enlargement	43	62	55	89	86	96	13	43
I	23	10	17	4	–	4	17	4
II	3	10	17	4	10	–	10	10
III	30	17	10	4	3	–	60	43

Table IV. Orbital muscle enlargement in patients with more than 2 years duration of disease (in percent)

Stages	med. rect. m. right	left	inf. rect. m. right	left	lat. rect. m. right	left	sup. rect. m. right	left
no enlargement	58	80	63	95	84	95	42	75
I	16	10	21	–	–	5	16	–
II	5	–	11	5	5	–	16	20
III	21	10	5	–	11	–	26	5

duration of the disease of less and patients with more than 2 years. The results are summarized in Tables II–IV. Figures 4 and 5 demonstrate muscle enlargement separately for the right and left sides, divided according to the stages and independent of the duration of the disease.

The orbit muscles revealed different density units as mean values. The highest values were obtained for the medialis rectus muscle with 50 HU, for the inferior rectus muscle 37 HU were measured, and for both the lateralis rectus muscle and the superior rectus muscle/levator palpebrae 30 Houndsfield units were calculated. Patients with a duration of disease of less than 2 years displayed higher average density

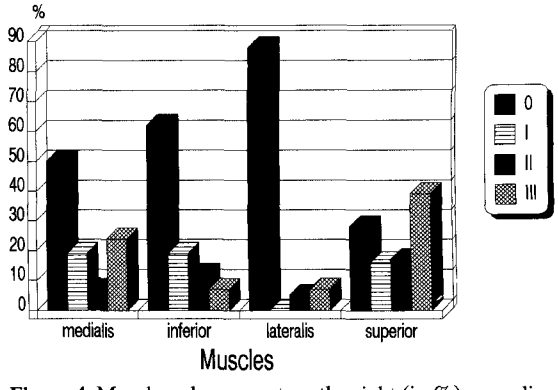

Figure 4 Muscle enlargement on the right (in %) according to stages.

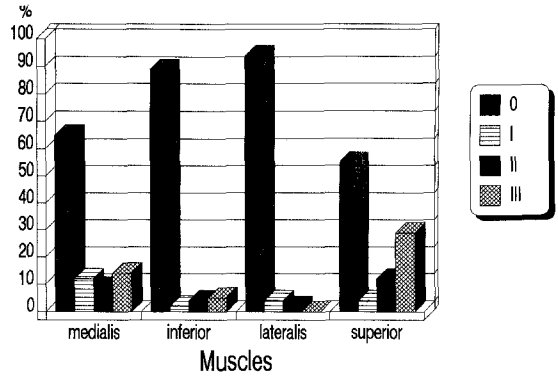

Figure 5 Muscle enlargement on the left (in %) according to stages.

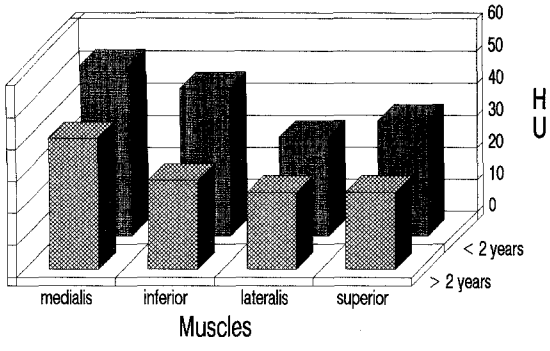

Figure 6 Density values on the right (HU) according to the duration of disaese.

values than the group of patients with a duration of more than 2 years (Figures 6 and 7), (Table V). These differences were significant for the medialis rectus muscle on both sides at $p < 0.05$, for the inferior rectus muscle on the left at $p < 0.05$ and for the superior rectus muscle/levator palpebrae at $p < 0.01$. The calculations were made with the significance test of MANN and WHITNEY. If the density values of the orbit muscles were classified according to the stages of muscle enlargement, significant differences dependent on the stage could not be found (Table VI).

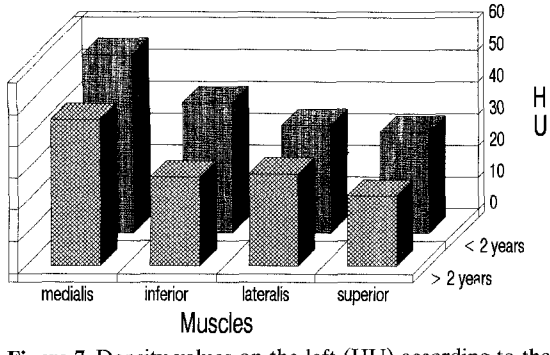

Figure 7 Density values on the left (HU) according to the duration of disaese.

Table V. Density values of the orbital muscles according to duration of disease (differentiation between less than and more than 2 years)

	med. rect. m.		inf. rect. m.		lat. rect. m.		sup. rect. m.	
	less than 2 years	more than 2 years	less than 2 years	more than 2 years	less than 2 years	more than 2 years	less than 2 years	more than 2 years
right side (HU)	56	46	41	28	34	29	32	21
left side (HU)	53	41	46	28	31	24	36	24

Table VI. Density values (in HOUNDSFIELD units) of the orbital muscles according to the duration of disease and the stage of muscle enlargement

Stage	med. rect. m.		inf. rect. m.		lat. rect. m.		sup. rect. m.	
	less than 2 years	more than 2 years	less than 2 years	more than 2 years	less than 2 years	more than 2 years	less than 2 years	more than 2 years
0	58	45	43	32	32	25	38	23
I	55	37	44	17	–	–	34	–
II + III	44	46	47	20	–	–	34	22

4 Discussion

The value of computed tomography in clarifying the alterations in the orbit in the case of Graves' ophthalmopathy has been underlined in several papers [3, 4, 6, 9, 10, 12]. There is agreement that only thin slices, wherever possible in both axial and coronal scan directions, guarantee a complete overview over the extent of the muscular alterations (Figure 8). If the sections are only made in axial direction, it is mainly the states of the superior rectus muscle/levator palpebrae and the inferior rectus muscle which are not sufficiently recognizable, because of the conus-like converging of these muscles in the orbit infundibulum. Both muscles can often not be scanned totally in their long axis [11]. The coronary scans, however, are sometimes difficult to manage because of the unpleasant position of the head of the patient. Deviations in the correct coronary position result in distorted image geometry with the consequence of oblique cuts of the muscles instead of cross cuts. This could lead to false positive measurements of the muscles [7]. Sagittal reconstructions of the scans would be ideal; however, the square of the muscles could not be calculated by this means, as is possible in the coronary position. For this reason, and because of the difficulty of reconstruction with the consequence of a great reduction in image quality we did not choose this way. Moreover our results do not support the view that the proportion of positive results is too high. The staging we used, based on a calculation of normal values by LANGENBRUCH [6], resulted in figures for the affection of the orbit muscles which were less high than those of ENZMANN and coworkers [2]. While that working group found the medialis and inferior rectus muscle to be affected in 75 and 77% of all patients respectively, in our group of patients it was 50% (medialis rectus muscle on the right) and 38% (inferior rectus muscle on the right). The evaluations of ENZMANN et al. do not contain information on what criteria were used to determine whether a muscle was enlarged.

There is a difference between the two evaluations with respect to the distribution of muscle affection. While ENZMANN and coworkers found the medialis and inferior rectus muscle to be most frequently affected, our results showed an especially high affection of the superior rectus muscle/levator palpebrae and the medials rectus muscle. The fact of an evident and partly significant higher rate of enlargement of the muscles on the right side (Figure 9) is striking, and not, at present, explainable. ENZMANN and colleagues also demonstrated an asymmetrical pattern of affection but they did not describe a preference for the right side as opposed to the left. Our results confirmed that the extent of the muscle enlargements is dependent on the duration of disease. Not seldom could we see CT examinations of patients with a long duration of disease which revealed

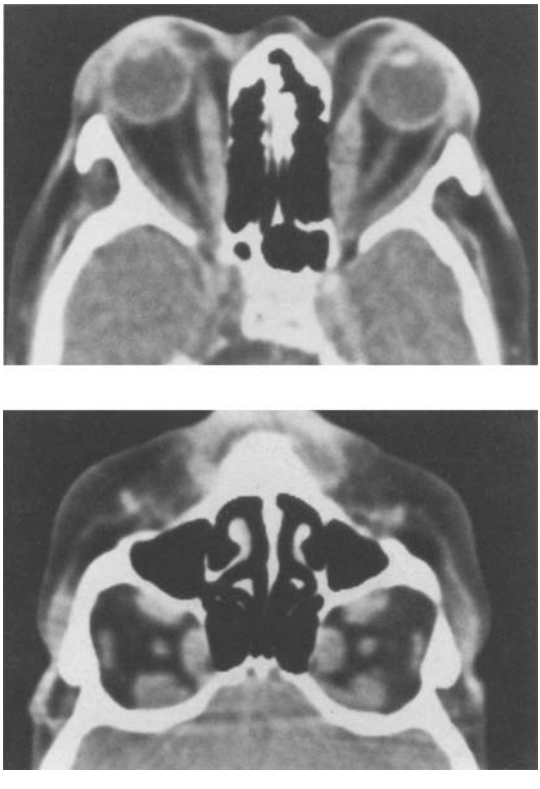

Figure 8 Axial cut of a patient with a short course of less 2 years (8a). Remarkable enlargement of the medialis rectus muscle on both sides. The coronary slice behind the bulbs demonstrates additionally an enlargement of both inferior and superior rectus muscles (8b).

Figure 9 Noticeable enlargement of the medialis rectus muscle on the right, in contrast only slight alteration of the same muscle on the left.

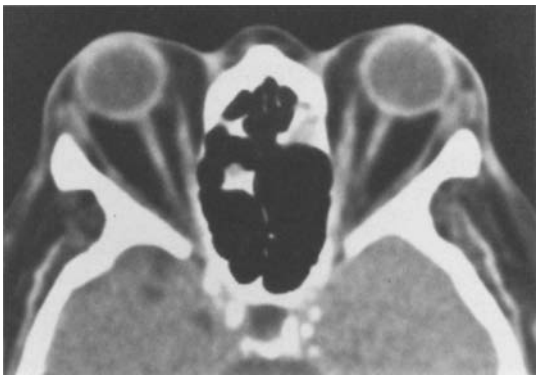

Figure 10 Patient with a long duration of disease. The CT reveals a striking protusion of both bulbs but no enlargement of the muscles. An increase of the retrobulbar fat must be presumed.

marked protrusion of the eyes but small muscles (Figure 10). These scarred and burned out muscles cannot develop an inflammatory reaction with cell infiltration and oedema. The persistent protusion is caused by an increase in retrobulbar fat, as some other authors also mention [1, 4]. It must be presumed that retrobulbar fat is more often involved in the inflammation than can be demonstrated with our imaging methods. The inflammatory process causes the development of fat cells and/or their enlargement, the storage of mucopolysaccharids and the growth of fibrous tissue [2]. This causes a persistent increase in retrobulbar volume without enlargement of the orbit muscles resulting in a protusion of the eyes.

Up to now there appear to have been no tests evaluating the density values of the muscles. The deviations in value seemed too large for a useful evaluation to be possible. The problems regarding the reliability of the density values of the orbit muscles are well known [5]. Problems arise from partial volume effects and beam hardening, from tooth material artifacts and eye movements. Therefore the main aim was not to calculate absolute figures but to correlate the values of the muscles in respect to different questions.

It is remarkable that mean density values differ from muscle to muscle. That cannot be explained by the possibility of partial volume effects. One might think the muscles which were less often enlarged had lower density values because partial volume effects during measurements are more likely. The medialis rectus muscle especially showed markedly differing values in comparison to the others, these data being confirmed by an isolated comparison of the density values of the nonenlarged muscles, as Table V shows. The highest values were found for the medialis rectus muscle, which showed 58 HU's in the unaffected form, and the lateralis rectus muscle had the lowest at 32 HU's in normal size, both in the group of patients with less than 2 years duration of disease. It is difficult to explain these differences. One explanation could be that the beam hardening effect is not present for the medialis rectus muscle because there is no absorption material in front of the muscle if the x ray beams from the tube come from the front. The bulb being located in front of the other muscles, not so the medialis rectus muscle, which usually shows a convex course directed to medial.

The result of our investigations was that partly significant differences in the density values were observed between patients with less and patients with more than 2 years duration of disease. Generally the lower values were found in the group of patients with the longer course of disease. This could be explained by the same factors discussed above for the differences in muscle size. The development of fibrous tissue within the muscle, the loss of muscle cells and the alteration in the muscle sheets could be responsible for the lower density values. In addition we saw, mainly in patients with a long course of the disease, noticeable fatty infiltrations of the muscles, probably the consequence of the degeneration of the muscle, which led additionally to a reduction of density values (Figures 11 + 12). Therefore, it is our opinion that two different courses of inflammation of the orbit muscles have to be considered: one with scarring of the muscles as an expression of the damage to them along with a remarkable reduction in

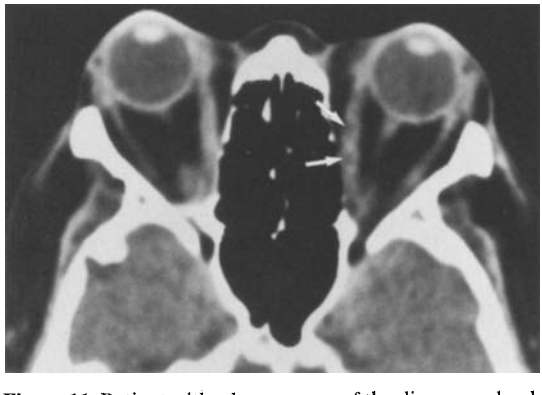

Figure 11 Patient with a long course of the disease and only slight increase in size of both the left and right medialis rectus muscle. Additionally patchy alterations with fat-like density values can be seen. These are the expression of muscle degeneration.

Figure 12 The slice demonstrates low density alterations in both medialis rectus muscles as an expression of fatty degeneration.

size, the second with a fatty degeneration of the orbit muscles. It is conceivable that both alterations coincide in the same patient.

The inflammation in itself does not seem to have a reliable influence on the density values of the muscles, because we were unable to see a significant difference in respect to the stages of muscle enlargement. The density values of the medialis rectus muscle showed a slight reduction when the values of stage 0 were compared with those of stages I and II/III; however, on the other hand the values of the inferior rectus muscle revealed a slight increase. Maybe further investigations are necessary to obtain more detailed information, so that not only the shape and size of the muscles but also the density values indicate inflammation.

Do these analyses of size and density of the orbit muscles have clinical relevance? The clinical aspect should be seen in the fact that a precise analysis of the status of the muscles and the other orbit structures may help in planning appropriate therapy, to decide whether conservative methods such as corticosteroid therapy, radiotherapy or autoimmunological drugs should be considered or whether a surgical management is necessary. It should be the aim to improve therapeutic procedures in respect to morphological classification of the orbit alterations.

In summary it is the result of the evaluation that more detailed information about orbit structures in respect to the course of the disease are possible, if an exact analysis of muscle size and density values is performed. The orbit alterations give us information about the activity of the inflammatory process and about the duration of the disease. These data may help to develop more useful therapeutical procedures.

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