Orbital Morphology in Exophthalmos and Exorbitism

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Background: Exophthalmos is a protrusion of the eyeball due to an increase in orbital contents in a normal bony orbit. Exorbitism is a protrusion of the eyeball due to a decrease in capacity of the orbital container, with a normal orbital content volume such as seen in a congenital form termed nonsyndromic exorbitism. High myopia can enhance proptosis. The purpose of this study was to provide values for orbital measurements from computed tomography and to suggest computed tomography criteria for nonsyndromic exorbitism.
Methods: Seventy-three computed tomography scans were collected (57 of Graves' ophthalmopathy and 16 of nonsyndromic exorbitism). Thirty-two scans from nonproptotic patients constituted a control series. Nine measurements and two indexes, performed on a reference axial computed tomography slice transecting the neuro-ocular plane, were obtained from each scan.
Results: The angle between the sagittal axis and the lateral orbital wall, as well as the width of the ethmoid bone (midinterorbital distance), was found to be more open in the nonsyndromic exorbitism population. A lateral orbital wall angle greater than or equal to 42 degrees and a midinterorbital distance greater than 30 mm were chosen as cutpoints. The association of these two criteria allowed the authors to obtain a sensitivity of 62 percent, a specificity of 78 percent, a positive predictive value of 80 percent, and a negative predictive value of 86 percent for nonsyndromic exorbitism.
Conclusions: The different mechanisms of globe protrusion have to be taken into account before an orbital expansion/decompression procedure is planned. Only a preoperative morphological analysis of the orbital shape permits a precise analysis of the relative position of the ocular globe and orbital structures, in addition to clinical examination. (*Plast. Reconstr. Surg.* 117: 542, 2006.)

The surgical treatment of ocular globe protrusion is a challenging task, and only good comprehension of the mechanisms leading to this protrusion will allow the results to be optimized. Exophthalmos and exorbitism are both manifestations of an abnormal protrusion of the ocular globe beyond the confines of the bony orbit.[1]

Protrusion of the eye in exophthalmos is due to an increase in orbital contents, with the bony orbital container being normal. Graves' disease is one of the most common causes of exophthalmos. Exophthalmos due to tumor or vascular abnormalities will not be discussed here.

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Graves' disease is caused by circulating autoantibodies that react with thyroid tissue and antigens located in the extraocular muscles, orbital fat, conjunctiva, and lacrimal gland. The resulting Graves' ophthalmopathy and toxic diffuse goiter may appear simultaneously or with delay or may exist separately. Exophthalmos is caused by lymphocyte infiltration, edema, and proliferation of endo-orbital connective tissue. These changes involve the extraocular muscles, intraconal and extraconal fat, lacrimal gland, and optic nerve.[2]

Exorbitism implies that the protrusion of the eye is due to a decrease in the capacity of the orbital container, with the volume of the orbital contents being normal, such as seen in a congenital form that we call nonsyndromic exorbitism. It can be defined as an idiopathic protrusive eye caused by a decreased orbital capacity, due to a shallow orbit, despite a normal volume of the globe.

High myopia, characterized by a distension of the posterior segment of the eyeball, is defined by an ocular axial length equal or superior to 26 mm.[3] The volume of an emmetropic eye is nearly 5 cm^3, for a mean ocular axial length of 23.5 mm. The volume of a myopic eye may be three or four times bigger than the volume of an emmetropic eye.

Graves' ophthalmopathy, nonsyndromic exorbitism, and high myopia can be associated problems.

Computed tomography is a well-established key modality in the diagnosis, surgical planning, and follow-up of craniofacial anomalies.[4] There is no significant enlargement or distortion of the image, overlap of structures, or tracing error, and the number of anatomic landmarks is vast. Computed tomography is an accurate and reproducible means of recording quantitative information.[5] In the literature, computed tomography proptosis is graded only in three degrees using the computed tomography oculo-orbital index.[6] To our knowledge, there is no classification of exophthalmos that takes into account the shape of the orbit.

The purpose of this study was to provide values for measurements of the proptotic eye and the orbit from computed tomography. Comparisons between normal values for Graves' ophthalmopathy and nonsyndromic exorbitism were made. These comparisons allowed us to suggest simple computed tomography criteria for nonsyndromic exorbitism. The final purpose was a rationalization of proptosis treatment planning, based on the comprehension of its mechanism.

In 1972, Paul Tessier stated that "measurement of skeletal dimensions is essential for accurate diagnosis and planned reconstructive surgery."

PATIENTS AND METHODS

Files from 110 consecutive patients who presented for proptosis treatment or who were operated on between 1986 and 2003 in our department were retrospectively reviewed. Seventy-three computed tomography scans were collected, 57 for Graves' ophthalmopathy and 16 for nonsyndromic exorbitism. Thirty-two scans from nonproptotic patients, taken for different other reasons (e.g., sinus disease) constituted a reference group. The mean age and sex ratio of this group corresponded to the mean age and sex ratio of the proptotic population. Among the 73 proptotic patients, eight were highly myopic (Fig. 1). All the patients reviewed were Caucasian adults.

A series of nine measurements and two indexes was obtained from the scans of each patient.

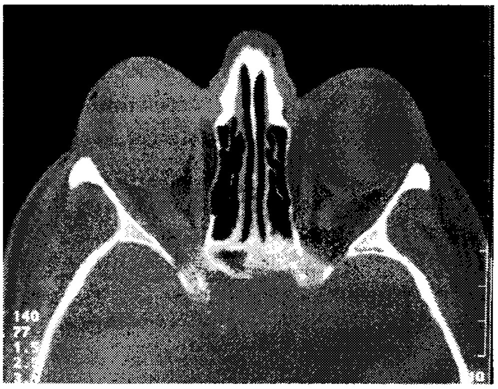

Fig. 1. High myopia.

All the measurements were performed by the same investigator, as described in Table 1 and in Figure 2. All measurements were obtained directly on the computed tomography slices with a piece of paper and a 1-degree protractor and then standardized according to the reference scale of the slide.

A reference axial computed tomography slice, chosen for its reproducibility and ease of identification, was studied for each subject. The axial slice transected the neuro-ocular plane described by Cabanis.[7] The neuro-ocular plane can be defined as a "horizontal slice of the head, with a millimetric height (1 to 5), in primary upgaze, showing a symmetric transection of both crystalline lenses, both heads of the optic nerves, and both optic struts." Each anatomically unilateral measurement was performed on the most proptotic eye of each patient.

Statistical Analyses

Statistical analyses were performed using Splus 4.5 software (Insightful, Seattle, Wash.). Statistical differences between group means were tested by the Wilcoxon rank-sum test. Group means, standard deviations, and 95 percent confidence intervals for mean values were calculated for the measurements, since the purpose of this study was to produce normative values. Statistical tests associated with probabilities of 0.05 or less were considered significant, and all p values quoted were two-sided.

To evaluate interobserver error, a full series of measurements was performed on the scans of a 10 percent sample of the population who were randomly selected. Measurements were done by two independent observers. The Altman and Bland correlation coefficient was used to compare the measurements.[8] The interobserver correlation was

Table 1. Computed Tomographic Measurements and Index of the Orbital Skeleton/Content

Measurement	Description
Orbital content	
Globe protrusion	Perpendicular distance between the anterior tips of the lateral orbital walls and the most anterior aspect of the globe (cornea) (Fig. 2, *above, left, "a"*)
Ocular axial length	Perpendicular distance between the most anterior aspect of the globe and the choroidoscleral posterior high density (Fig. 2, *above, left, "b"*)
Oculo–orbital index	Globe protrusion × 100/ocular axial length (Fig. 2, *above, left*)
Diameter medial rectus	Diameter of the medial rectus muscle measured at its maximum (Fig. 2, *above, right, "a"*)
Diameter lateral rectus	Diameter of the lateral rectus muscle measured at its maximum (Fig. 2, *above, right, "b"*)
Equatorial diameter of the globe	Diameter of the ocular globe measured at its maximum (Fig. 2, *above, right, "c"*)
Orbital shape	
Lateral orbital distance	Distance between the most anterior tip of each lateral wall (Fig. 2, *below, left, "a"*)
Midinterorbital distance	Width of the ethmoid bone between the midpoints between the lacrimal bone and the base of the optic strut on each medial wall of the bony orbit (Fig. 2, *below, left, "b"*)
Teleorbitism index	Mid interorbital distance/lateral orbital distance (Fig. 2, *below, left*)
Lateral orbital–wall length	Distance between the most anterior tip of the lateral orbital wall and the superior orbital fissure (Fig. 2, *below, right, "a"*)
Lateral orbital–wall angle	Angle between a line joining the most anterior and posterior ends of the lateral orbital wall and the sagittal axis (Fig. 2, *below, right, "b"*)

Fig. 2. Axial computed tomography scans in the neuro-ocular plane demonstrating (*above, left*) (*a*) the globe protusion and (*b*) the ocular axial length (*oculo-orbital index* = *globe protusion* × 100/*ocular axial length*); (*above, right*) (*a*) the diameter medial rectus, (*b*) diameter lateral rectus, and (*c*) equatorial diameter of the globe; (*below, left*) (*a*) the midinterorbital distance and (*b*) the lateral orbital distance (*teleorbitism index* = *midinterorbital distance/lateral orbital distance*); and (*below, right*) (*a*) the lateral orbital wall length and (*b*) lateral orbital wall angle.

found to be optimal for all the measurements (values of the concordance coefficient between 0.93 and 0.99, with a mean error of measurement between 0.3 and 1 mm) except for the lateral orbital-wall length, due to a difference in the location of the posterior limit (superior orbital fissure). After harmonization, the correlation became optimal.

To choose the most discriminating criteria between a normal orbit and nonsyndromic exorbitism, the distributions of measurements showing a significant difference and reflecting the shape of the orbit were plotted on a two-dimensional graph to determine graphically a cutpoint between these distributions.

RESULTS

The measurements in our reference population are comparable to the normal values obtained in the general population by Waitzman et al.[5] and Ozgen and Ariyurek.[9]

The mean values of the different measurements obtained in the Graves' ophthalmopathy population and in the reference population, as well as their comparison, are given in Table 2. Compared with the reference population, Graves' ophthalmopathy patients are, as expected, more exophthalmic (Fig. 3). The mean values for globe protusion ($p < 0.0001$), the oculo-orbital index ($p < 0.0001$), and the diameters of the extraocular muscles ($p < 0.0001$) were significantly higher.

Table 2. Comparison between the Mean Values of the Measurements for the Graves' Ophthalmopathy and Reference Populations

Measurements	GO Population (mm)	Reference Population (mm)	p
Orbital content			
Globe protrusion	23	16	**< 0.0001**
Ocular axial length	24	25	**0.038**
Oculo-orbital index	94	66	**< 0.0001**
Medial rectus	6.1	4.2	**< 0.0001**
Lateral rectus	4.6	3.4	**0.0001**
Equatorial diameter globe	24	24	0.077
Orbital shape			
Lateral orbital distance	98	97	0.38
Midinterorbital distance	28	28	0.84
Teleorbitism index	29	29	0.94
Lateral orbital wall length	41	41	0.66
Lateral orbital wall angle	42	40	**0.0034**

GO, Graves' ophthalmopathy.
Statistically significant results are printed in boldface type.

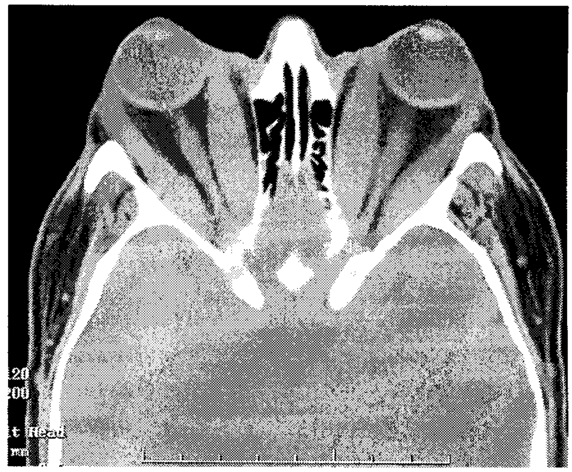

Fig. 3. Graves' ophthalmopathy.

The equatorial diameters of the globe were similar to the values for the reference population ($p = 0.07$), but the ocular axial lengths were different ($p = 0.04$), probably because three patients in this group suffered from high myopia. In our Graves population, the orbital shape was similar to that of the reference population, except for the lateral orbital wall angle (42 degrees versus 40 degrees in the reference population).

The mean values of the different measurements obtained in the nonsyndromic exorbitism population and in the reference population, as well as their comparison, are given in the Table 3. The nonsyndromic exorbitism population was more proptotic than the reference population (Fig. 4). The orbital shape was different in this population, when compared with the reference population: the midinterorbital distance ($p = 0.0005$), the lateral orbital wall angle ($p = 0.0001$), and the lateral orbital distance ($p = 0.0001$), and thus the teleorbitism index ($p = 0.007$), were significantly different. The equatorial diameter was significantly superior in the nonsyndromic exorbitism population ($p = 0.001$). However, in the nonsyndromic exorbitism population, five patients presented with high myopia, given 31 percent of the population (versus three patients in the Graves' ophthalmopathy population, given 5 percent). In both populations, the grade of exophthalmos was larger for patients with high myopia (Fig. 1).

A sensitivity analysis was performed to check that high myopia was not a confusing factor: the same analyses were performed after exclusion of the myopic patients. The nonsyndromic exorbitism population without myopic patients was significantly more proptotic than the reference pop-

Table 3. Comparison between the Mean Values of the Measurements for the Nonsyndromic Exorbitism and Reference Populations

Measurements	NSE Population(mm)	Reference Population (mm)	p (Wilcoxon rank-sum test)
Orbital content			
Globe protrusion	22	16	**<0.0001**
Ocular axial length	26	25	0.09
Oculo-orbital index	83	66	**<0.0001**
Medial rectus	4.7	4.2	0.25
Lateral rectus	3.4	3.4	0.97
Equatorial diameter globe	26	24	**0.0014**
Orbital shape			
Lateral orbital distance	100	97	**0.04**
Midinterorbital distance	32	28	**0.0005**
Teleorbitism index	32	29	**0.007**
Lateral orbital wall length	39	41	0.21
Lateral orbital wall angle	45	40	**0.0001**

NSE, nonsyndromic exorbitism.
Statistically significant results are printed in boldface type.

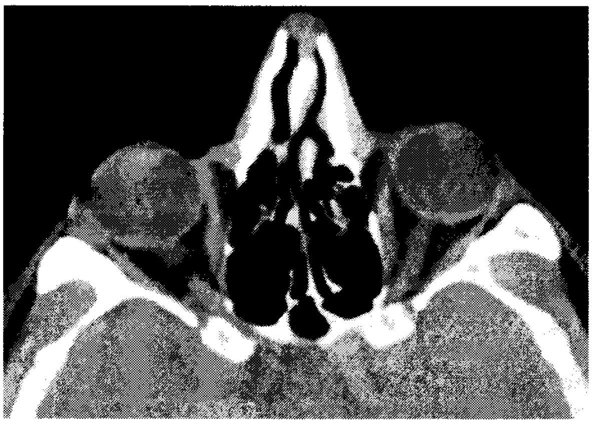

Fig. 4. Nonsyndromic exorbitism.

ulation (p = 0.0001 for globe protrusion and oculo-orbital index). The measurements related to the orbital shape in our nonsyndromic exorbitism population (lateral orbital distance, $p < 0.05$; midinterorbital distance, $p = 0.0005$; teleorbitism index, $p = 0.008$; lateral orbital wall angle, $p = 0.005$) remained significantly different from those of the reference population, but the equatorial diameter of the globe was not significantly different from that of the reference population ($p = 0.06$).

The mean values and 95 percent confidence intervals for the most informative measurements (i.e., oculo-orbital index, the diameters of the extraocular muscles, the lateral orbital distance, the midinterorbital distance, the teleorbitism index, and the lateral orbital wall angle) for the three populations are given in Table 4. The mean value of the lateral orbital wall length was 41 mm for the normal and Graves' ophthalmopathy populations and 40 mm for the nonsyndromic exorbitism population. No statistically significant difference was found for this measurement between the two types of proptosis and the reference population.

These results show three discriminating measurements: the midinterorbital distance, the lateral orbital distance, and the lateral orbital wall angle. In our series, the shapes of these distributions were roughly Gaussian for the three measurements considered. However, the overlap be-

Table 4. Mean Values and Their 95 Percent Confidence Intervals of the Discriminating Orbital Measurements

	GO		NSE		Normal	
Measurements	Mean (mm)	95% CI	Mean (mm)	95% CI	Mean (mm)	95% CI
Orbital content						
Oculo–orbital index	94	91–98	83	80–86	66	62–70
Medial rectus	**6.1**	5.5–6.6	4.7	4.1–5.3	4.2	4.0–4.5
Lateral rectus	**4.6**	4.2–4.9	3.4	2.9–3.4	3.4	3.1–3.8
Orbital shape						
Lateral orbital distance	98	97–99	**100**	98–102	97	96–98
Midinterorbital distance	28	27–29	**32**	31–33	28	27–29
Teleorbitism index	29	28–30	**32**	30–33	29	28–30
Lateral orbital wall angle	42	41–43	**45**	43–47	40	39–41

GO, Graves' ophthalmopathy; NSE, nonsyndromic exorbitism.
Outlying measurements are printed in boldface type.

tween the distributions of the lateral orbital distance in the reference group and in the nonsyndromic exorbitism group was high, thus rendering a cutpoint difficult to find. On the contrary, the distribution of the lateral orbital wall angles and the midinterorbital distances was more distinct, with the third quartile of the distribution of the reference group corresponding to the first quartile of the distribution of the nonsyndromic exorbitism group. A lateral orbital wall angle greater than or equal to 42 degrees and a midinterorbital distance greater than 30 mm were thus chosen as cutpoints. The association of these two criteria allowed for a sensitivity of 62 percent, a specificity of 78 percent, a positive predictive value of 80 percent, and a negative predictive value of 86 percent for nonsyndromic exorbitism.

DISCUSSION

A computed tomography scan is ordered for all patients presenting with exophthalmos. The axial orbit computed tomography slices are parallel to the hard palate, so the neuro-ocular plane is systematically available, enabling us to obtain our biometric analysis. The measurements are reproducible and easy to perform. In a few scans, however, the neuro-ocular plane was not rigorously respected. In these cases, the measurements used were the mean of the measurements performed on both adjacent slides. The resulting error of measurement is tiny and should not significantly modify the diagnosis.

In the Graves' ophthalmopathy population, a significant increase in the size of the extraocular muscles was noted, providing evidence of the well-known observation common in this disease. The contents of the bony orbit were much increased. According to our measurements, the bone topometry was normal, comparable to that of our reference population and the general population,[5] except for the lateral orbital wall angle, which was significantly more open in our Graves population. Indeed, in our Graves group, five patients could retrospectively be considered, according to our criteria, to have an associated nonsyndromic exorbitism, thus increasing the proptosis.

Proptosis in our nonsyndromic exorbitism patients was less pronounced. On computed tomography scans, nonsyndromic exorbitism was associated with a lateral orbital distance that was longer than that in the general population and a lateral orbital wall angle that was more open, thus reducing the depth of the bony orbit. This lack of depth associated with a larger-than-normal ethmoid bone reduces the volume of the container of the eye. This situation can be worsened by a voluminous globe (high myopia) or by an increase of the orbital content (Graves' ophthalmopathy). In our Graves and nonsyndromic exorbitism populations, patients who suffered from high myopia were more proptotic than nonmyopic patients were, although isolated high myopia is not associated with a significant exophthalmos in the general population.[3,10] In proptotic patients, high myopia is a factor that contributes to aggravating exophthalmos. If associated with nonsyndromic exorbitism, high myopia can lead to a symptomatic proptosis that can justify a surgical procedure [case 1 (Fig. 5) versus case 2 (Fig. 6)].

Smith described a form of congenital malformation called "hypoplastic malar eminence," which is associated with shallow orbits, enlarged globes, and hypoplastic malar eminence.[11] This association leads to an appearance of globe protrusion, reinforced by the shortness of the inferior lids. We agree with Wolfe and Kearney[1] that this "hypoplastic malar eminence" syndrome is a minor expression of Crouzon's disease. This syndrome is different from our definition of nonsyndromic exorbitism. Nonsyndromic exorbitism is an anatomical particularity that consists of a clinically obvious proptosis, a shallow orbit, and a normal volume of the globe with or without a hypoplastic malar eminence. The computed tomography scan criteria isolated in this study permit us to suggest a radiological definition for nonsyndromic exorbitism in proptotic patients: the association of a midinterorbital distance greater than 30 mm and a lateral orbital wall angle greater than or equal to 42 degrees in the neuro-ocular plane leads to a specificity and a positive predictive value close to 80 percent. The confidence in these values could be reinforced if these variables could be measured in a larger series. The choice of these cutpoints could have been different (i.e., smaller values could have been chosen) if a higher sensitivity was expected. However, as there was an overlap between the normal population and nonsyndromic exorbitism population, it seemed more pertinent to choose cutpoint values that would lead to an optimization of the specificity rather than the sensitivity.

Our choice to limit our measurements to a two-dimensional slice can, of course, be criticized. The measurement of the orbital volume would be an accepted standard. Numerous studies have raised this question.[12-14] However, it is not possible at this time to routinely measure the orbital volume, due to the natural convexity or concavity of the orbital walls. Our method provides a simple

Fig. 5. Case 1. (*Above, left*) Preoperative view of a 42-year-old woman with nonsyndromic exorbitism and myopia. On the preoperative computed tomography scan, her midinterorbital distance was 31 mm, her left lateral orbital wall angle was 40 degrees, and her right lateral orbital wall angle was 47 degrees. (*Above, right*) Postoperative view 5 years after three-wall expansion to the right orbit, two-wall expansion to the left orbit, and bone grafts, with levator palpebrae lengthening and lipofilling performed in a second step. (*Below*) Postoperative scan.

means of obtaining a reasonable estimate of orbital volume. The measurements are undertaken in the horizontal two-dimensional plane, where the effect of an orbital expansion procedure is susceptible to being maximal, given that the medial and lateral orbital walls will be expanded as a first step. It provides information that allows us to understand the mechanism of proptosis and to adapt the orbital expansion surgical procedure. Especially in cases of Graves' ophthalmopathy, a poor result of a two- or three-wall orbital expansion procedure is predictable in nonsyndromic exorbitism patients, due to the shallow shape of the bony orbit. After surgical enlargement, the major part of the orbital content expansion will be obtained in the coronal plane. It is likely, therefore, that the resection of a wide-angle lateral wall will provide less additional volume (Fig. 4).

High myopia can also limit the benefit of this procedure, as the excess volume of the ocular

Fig. 6. Case 2. (*Above, left*) Preoperative view of a 40-year-old woman with Graves' ophthalmopathy. Her preoperative midinterorbital distance was 27 mm, her left lateral orbital wall angle was 38 degrees, and her right lateral orbital wall angle was 43 degrees. (*Above, right*) Postoperative view 6 months after three-wall expansion to the right orbit and two-wall expansion to the left orbit. (*Below, left*) Preoperative scan. (*Below, right*) postoperative scan.

globe is anterior to the level of the orbital wall resections. We recommend the addition of bone grafts on the lateral orbital rims and eventually on the superior orbital rim and on the nasal bone after the orbital expansion in these patients.[15]

CONCLUSIONS

Graves' ophthalmopathy is due to an increase in the orbital contents, with the bony orbital container being normal. Nonsyndromic exorbitism is due to a decrease in the capacity of the orbital container, with the volume of the orbital contents being normal. This anatomical particularity can be defined by two computed tomography scan criteria: midinterorbital distance greater than 30 mm and lateral orbital wall angle greater than or equal to 42 degrees. High myopia is an aggravating factor for proptosis. These different mechanisms have to be taken into account before an orbital expansion/decompression procedure is planned. Only a preoperative topometric analysis of the orbital shape permits a precise analysis of the relative position of the ocular globe and the orbital structures, in addition to the clinical examination.

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