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What is the Main Potential Factor Influencing Ocular Protrusion?

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Background: The aim of the present study was to establish the normal-range orbital parameters and to explore the relationships between ocular protrusion and various orbital morphological factors.

Material/Methods: A retrospective, non-comparative case series was conducted from January 2014 to December 2015. We recruited 56 subjects (112 orbits), including 27 males (21 to 87 years of age) and 29 females (22 to 88 years of age) in this study. Nine length measurements, 2 angle measurements, and 2 volume measurements of various aspects of the orbit were obtained using Mimics v18.0 software. The data were collected manually using a 3D measurement technique. Statistical analyses using *t* tests and Pearson's correlation analyses were performed to evaluate the differences and relationships between the parameters, respectively.

Results: Ocular protrusion in both sexes was closely related to the following values: orbital soft tissue volume (OSTV) (males: r=0.61, p<0.001; females: r=0.39, p=0.003), orbital soft tissue volume/bony orbital volume (OSTV/BOV) (males: r=0.90, p<0.001; females: r=0.87, p<0.001), orbital width (males: r=0.40, p=0.003; females: r=0.53, p<0.001), orbital height (males: r=0.29, p=0.038; females: r=0.45, p<0.001), and globe diameter (males: r=0.52, p<0.001; females: r=0.48, p<0.001). No differences were found between the right and left orbits.

Conclusions: The study provides insight into the potential factors that influence ocular protrusion, which include the OSTV/BOV ratio, the shape of the orbital aperture, and the ocular axial length. The results of orbital surgery can be made more predictable by accounting for these 3 factors. The database and regression formula might provide support for surgical planning in the future.

MeSH Keywords: **Anthropometry • Exophthalmos • Orbit • Orbital Diseases**

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Background

Ocular protrusion is measured from the most posterior point of the lateral orbital rim to the apex of the cornea and plays an important role in the function and appearance of the upper face [1,2]. Exophthalmos, exorbitism, and enophthalmos are pathological changes in the globe-orbit relationship that are closely related to several orbital or craniofacial disorders, including orbital tumors, high axial myopia, Graves' ophthalmopathy, and orbital fractures [3–5]. The evaluation of ocular protrusion is a critical part of orbital morphometry and plays important roles in preoperative planning and evaluation of postoperative outcomes of craniofacial and orbital surgery [6].

The bony orbital volume enlarges after orbital fracture, which can result in enophthalmos. In our previous study [7], we found that a 1 cm^3 increase in orbital volume causes 0.89 mm of enophthalmos in blow-out fractures. Thus, restoring orbital volume is a key point in restoring globe position in orbital surgery. However, in some delayed or severe cases, the reduction of globe protrusion is not correlated with the result of orbital wall reconstruction, which suggests that fat atrophy might be important in influencing ocular protrusion.

This study aimed to determine the normal range of orbit parameters and to explore the relationships between ocular protrusion and various orbital morphologic factors, which have not been addressed in detail previously. These data can be used to support computer-assisted surgery plans in orbital surgery to achieve effective and predictable treatment.

Material and Methods

Subjects

This study was approved by the Ethics Committee of the hospital and adhered to the tenets of the Declaration of Helsinki. The medical data of adult patients (over 20 years old) who presented to Shanghai Ninth People's Hospital from January 2014 to December 2015 and underwent craniofacial computed tomography (CT) scans were collected. The inclusion criteria were as follows: (1) no history of craniofacial or eye trauma, (2) no history of craniofacial or eye surgery, (3) no history or presence of local or systemic disease affecting the orbit or globe, and (4) no craniofacial deformity or other pathological change. Patients with anophthalmia and microphthalmia were excluded from the study.

Image set acquisition

Craniofacial CT scans were collected using a multislice CT scanner (LightSpeed 16, GE Medical Systems, Milwaukee, WI, USA). Continuous high-resolution scanning with a slice detection (r) of 16×1.25 mm, reconstructed thickness of 1.25 mm, and slice increment of 1.25 mm was performed. The reconstructed field of view was 23 cm, and the reconstruction matrix was 512×512. All CT images were loaded in DICOM format.

Coordinate system redefinition and the reslice project

After DICOM data were imported into Mimics (Materialise, Leuven, Belgium), the coordinate system was redefined to ensure that all measurements were completed in the same environment. The new coordinate system was defined according to the protocols of the "Online Reslice" and "Reslice Project" functions. The axial plane was defined as a plane parallel to the Frankfurt plane, passing through the inferior margin of the left orbit and the upper margin of each of the external auditory meatuses. The sagittal plane was defined as the median plane passing through the midpoint of the nasion, sella turcica, and foramen magnum. The oblique sagittal plane was defined as the plane passing through the optic nerve in the orbit and was perpendicular to the axial plane. The coronal datum plane was defined as the coronal plane passing through the most posterior point of the lateral orbital rim (Figure 1).

Measurement methods

A series of 8 length parameters and 2 angle parameters, which included ocular protrusion, the lengths of the orbital walls, shape of the orbital aperture, and ocular axial length, were measured from the CT scans of each patient. Standard anatomical points that were previously determined and used in other studies [8–11] were applied for the measurements of the orbital parameters. To reduce inter-observer variation, all of the measurements were performed by 2 independent observers (YW Li and Y Su).

Using the "Measure and Analyze" tool, the landmarks indicated in Figure 1, such as the reference plane and distance, were defined. The orbital width, orbital height, roof length, floor length, medial wall length, and lateral wall length parameters were calculated automatically after the landmarks were defined. The ocular axial length was measured at the axial optical lens level. The orbital middle length was measured at the axial optic canal aperture level. The angle between lateral and medial wall (ALM) was measured in the axial plane passing through the optic nerve canal aperture, and the angle between roof and floor was measured in the oblique sagittal plane (Figure 2).

The multislice edit tool was used to select the bony orbital volume (BOV) and the orbital soft tissue volume (OSTV) using a mask setting of –150 to +150 HU. The BOV was defined as the space inside the frontal bone, frontozygomatic suture,

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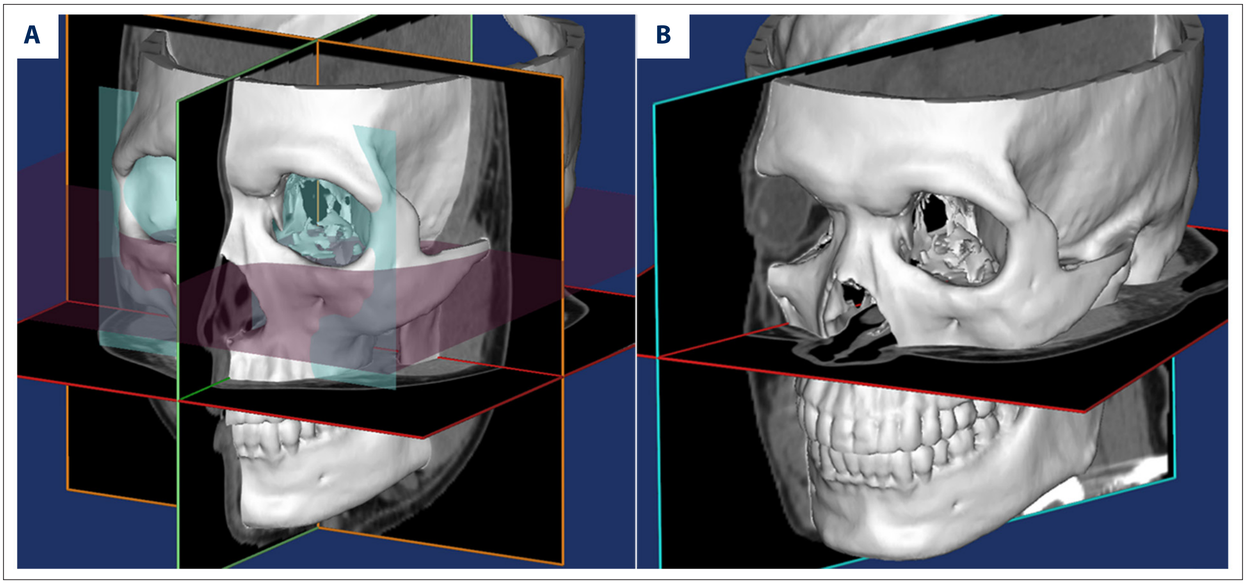

Figure 1. The new coordinate system was defined according to the protocols of the "Project Reslice", "Online Reslice", and "Reslice Project" functions. (**A**) The axial plane was defined as a plane parallel to the Frankfurt plane (purple) passing through the inferior margin of the left orbit and the upper margin of each external auditory meatus. The sagittal plane was defined as the median plane passing through the midpoint of the nasion, sella turcica, and foramen magnum. The coronal datum plane (cyan) was defined as the coronal plane passing through the most posterior point of the lateral orbital rim. (**B**) The oblique sagittal plane was defined as the plane passing through the optic nerve in the orbit and was perpendicular to the axial plane.

lateral orbital rim, inferior orbital rim, anterior lacrimal crest, orbital walls, superior and inferior orbital fissures, and optical nerve canal aperture. The OSTV was recorded as the sum of the BOV and the tissue volume anterior to the orbital aperture. The volume was determined after generation of the three-dimensional (3D) reconstruction (Figure 2).

Statistical analysis

All statistical analyses were performed with SPSS 13.0 software (SPSS Inc., Chicago, IL, USA) for Windows. Independent sample *t* tests were used to evaluate the differences between sexes. Comparisons between the 2 orbits were analyzed with paired-samples *t* tests. Pearson's correlation analyses were performed to evaluate the relationships between ocular protrusion and the other parameters. A p-value <0.01 was considered statistically significant.

Results

In total, 56 subjects (112 orbits) were enrolled in this study, with a mean age of 50.34±15.75 years and a range of 21 to 88 years. Among the participants, 27 were males, with a mean age of 49.00±15.26 years and a range of 21 to 87 years, and 29 were females, with a mean age of 51.00±16.14 years and a range of 22 to 88 years. The CT image of each individual was analyzed to acquire the orbital parameters. There were no significant differences between the 2 observers (P>0.05). All data were normally distributed.

No significant differences were found between the right and left orbits. Table 1 provides the values of the orbital parameters for males and females. Both the soft tissues and orbital bony volumes were significantly larger in males than in females, with OSTVs of 34.88±3.42 ml versus 31.15±2.73 ml (p<0.001) and BOVs of 24.45±1.91 ml versus 22.13±1.95 ml (p<0.001), respectively. Moreover, the orbital width (p<0.001), orbital roof length (p=0.009), orbital floor length (p<0.001), and lateral orbital wall length (p<0.001) values were all significantly larger in males. However, none of the other parameters exhibited a sex difference.

The relationships between the ocular protrusion and the other orbital parameters are listed in Table 2. Among these parameters, 4 were closely related to ocular protrusion in both sexes: OSTV, OSTV/BOV, orbital width, and ocular axial length. Significant linear correlations were found between ocular protrusion and the OSTV/BOV (males: r=0.9, p<0.001; females: r=0.87, p<0.001). Figure 3 provides scatter diagrams of the linear correlations between ocular protrusion and the OSTV/BOV ratio in males (y=22.14x–14.67, y: ocular protrusion, x: the OSTV/BOV ration) and females (y=21.48x–14.44, y: ocular protrusion, x: the OSTV/BOV ration). Additionally, BOV (r=–0.39, p=0.003) and orbital height (r=0.45, p<0.001) were correlated with ocular protrusion in females.

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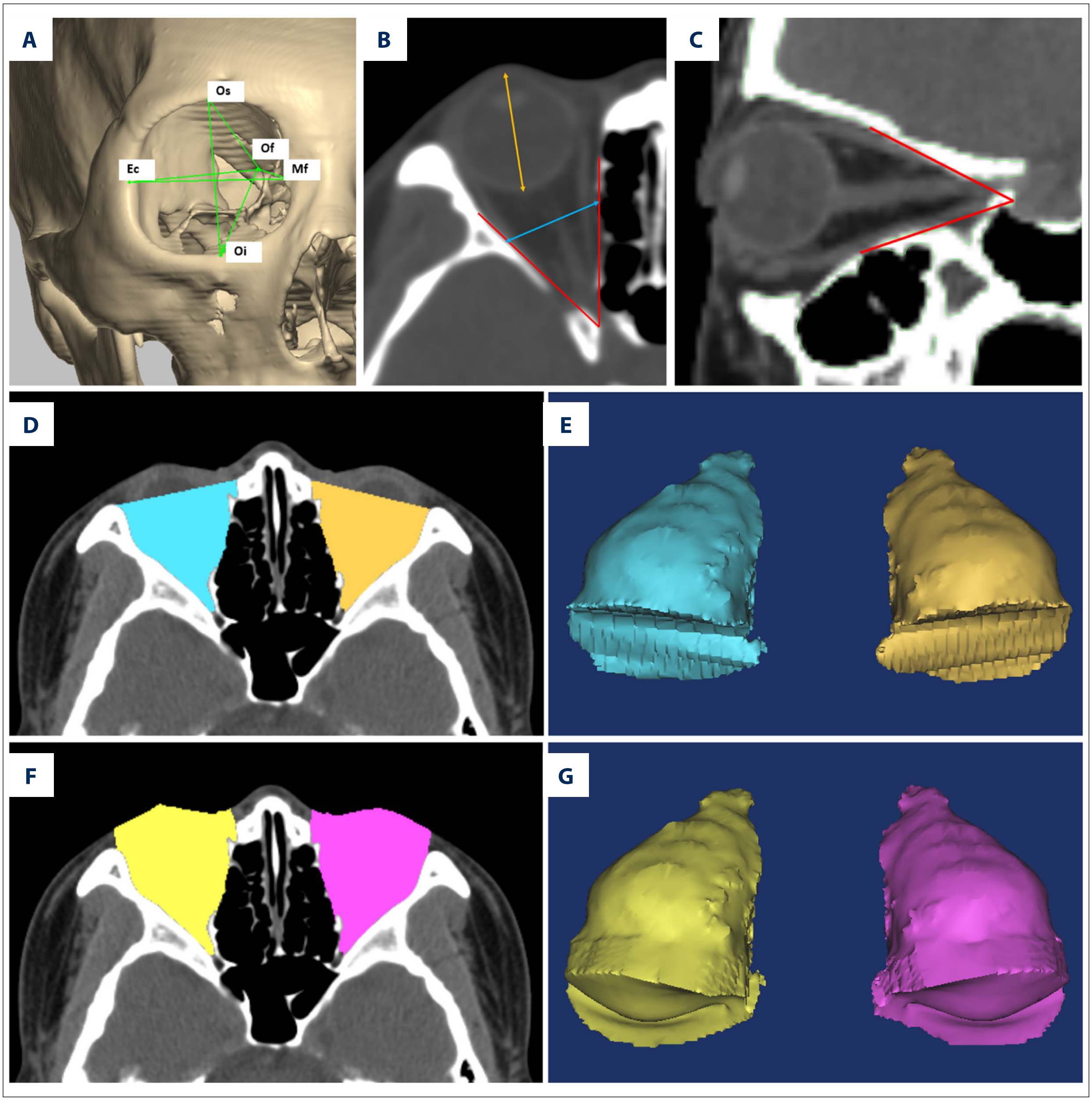

Figure 2. Distance, angle, and volume measurements. (**A**) The orbital width (Mf-Ec), orbital height (Os-Oi), roof length (Os-Of), floor length (Oi-Of), medial wall length (Mf-Of), and lateral wall length (Ec-Of) parameters were measured with the "Measure and Analyze" tool. (**B**) The ocular axial length (yellow line) was measured at the axial optical lens level. The orbital middle length (blue line) and the angle between the lateral and medial walls (ALM; red angle) were measured at the axial optic canal orifice level. (**C**) The angle between the roof and floor (ARF) was measured in the oblique sagittal plane. (**D**) Mask (–150 to +150 HU) of the bony orbital volume (BOV) marked with the multislice edit tool in the axial plane. (**E**) 3D reconstruction of the BOV. (**F**) Mask (–150 to +150 HU) of the orbital soft tissue volume (OSTV) marked with the multislice edit tool on the BOV mask. (**G**) 3D reconstruction of the OSTV.

Discussion

Ocular protrusion is an important clinical sign, and its evaluation is helpful in the diagnosis and surgical treatment of many orbital and craniofacial diseases. Pathological changes in ocular protrusion influence both the appearance and functional of the ocular adnexa. Proptosis caused by lymphocyte infiltration, the proliferation of orbital connective tissues, or edema is one of the clinical characteristics of Graves' ophthalmopathy [12]. Exophthalmos can also be found in cases with

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Table 1. Orbital parameter values of males and females.

Parameters	Min/Max		Mean		SD		t	p-value
	Males	Females	Males	Females	Males	Females		
OSTV	28.29/41.53	25.67/40.12	34.88	31.15	3.42	2.73	−6.39	<0.001*
BOV	18.35/27.27	18.45/27.10	24.45	22.13	1.91	1.95	−6.37	<0.001*
OSTV/BOV	1.21/1.70	1.12/1.62	1.43	1.41	0.12	0.10	−0.84	0.402
Ocular protrusion	11.93/22.75	6.69/19.78	16.97	15.89	2.87	2.55	−2.10	0.038
Orbital middle length	18.45/24.63	16.06/24.33	21.63	20.91	1.68	1.72	−2.26	0.026*
ALM	39.83/54.82	39.73/57.51	47.87	48.06	3.09	4.10	0.28	0.782
ARF	42.51/59.47	38.26/60.52	48.67	49.31	3.89	4.97	0.75	0.455
Orbital width	35.71/40.38	32.89/40.32	37.70	36.54	1.17	1.44	−4.68	<0.001*
Orbital height	30.36/39.72	30.97/40.10	35.63	35.31	2.13	1.84	−0.85	0.396
Roof length	43.12/52.14	43.02/51.95	47.49	46.39	2.18	2.18	−2.67	0.009*
Floor length	45.59/52.63	40.33/51.51	49.42	47.54	1.68	2.31	−4.90	<0.001*
Medial wall length	33.71/43.55	34.68/43.19	39.16	39.01	1.97	2.03	−0.39	0.695
Lateral wall length	42.84/51.78	40.04/50.61	47.03	45.55	1.84	2.00	−4.08	<0.001*
Ocular axial length	22.80/28.55	23.09/27.41	25.35	24.96	1.32	0.96	−1.84	0.069

OSTV – orbital soft tissue volume; BOV – bony orbital volume; ALM – angle between lateral and medial wall; ARF – angle between roof and floor. * Variables with statistical significance in t-tests.

Table 2. Results of correlation analyses of the ocular protrusion in the two genders.

Parameters	Males		Females	
	r	p-value	r	p-value
OSTV	0.68	<0.001*	0.39	0.003*
BOV	−0.09	0.518	−0.39	0.003*
OSTV/BOV	0.90	<0.001*	0.87	<0.001*
Orbital middle length	−0.23	0.091	−0.28	0.031
ALM	0.03	0.825	−0.28	0.031
ARF	0.06	0.690	−0.25	0.064
Orbital width	0.40	0.003*	0.53	<0.001*
Orbital height	0.29	0.038	0.45	<0.001*
Roof length	0.10	0.476	−0.16	0.219
Floor length	−0.12	0.393	0.05	0.711
Medial wall length	−0.06	0.672	0.17	0.193
Lateral wall length	−0.31	0.024	−0.20	0.133
Ocular axial length	0.52	<0.001*	0.48	<0.001*

OSTV – orbital soft tissue volume; BOV – bony orbital volume; ALM – angle between lateral and medial wall; ARF – angle between roof and floor. * Variables with statistical significance in Pearson's correlation analyses.

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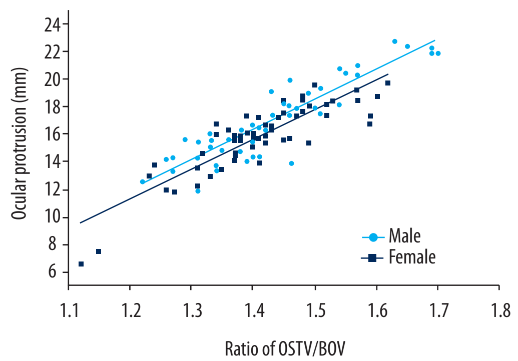

Figure 3. The scatter diagrams depict the correlations between the ocular protrusions and the OSTV/BOV ratios in males and females. The regression lines are illustrated in the figure (light blue line: males, y=22.14x–14.67; solid blue line: females, y=21.48x–14.44).

post-globe tumor [13]. Enophthalmos is a common symptom of orbital fracture that results from an enlargement of the orbit volume and can be accompanied by restricted ocular mobility, diplopia, or eye displacement [14].

Previous studies [7,15–17] found a linear correlation between ocular protrusion and bony orbital volume, which provides a good reference for orbital fracture reduction. However, these studies neglected the factors involving intra-orbital soft tissue. In some delayed or severe orbital fracture cases, even if the orbital bony structure is anatomically reconstructed, various degrees of enophthalmos can remain after surgery [18–20].

Our findings update the concept that the OSTV/BOV ratio better represents the relative space of the orbit and the condition of ocular protrusion than does bony orbital volume. The correlation lines of the 2 sexes provide a valuable reference for orbital reduction or orbital decompression (Figure 3). In this study, the orbital soft tissue volume was included, and a strong correlation between this volume and the OSTV/BOV ratio was found (males: $y=22.14x-14.67$, $r=0.9$, $p<0.001$; females: $y=21.48x-14.44$, $r=0.87$, $p<0.001$) (Figure 3, Table 2). This relationship could explain postoperative enophthalmos in cases of delayed orbital fracture reduction. As the BOV increases together with different degrees of atrophy of the soft tissues, even where the BOV is restored to normal, the OSTV/BOV ratio still decreases, which leads to the reduction of ocular protrusion followed by symptoms of enophthalmos. Moreover, with the help of the 2-regression equation, it will be easier to design the surgery plan [21] and the surgical result would be predictable in cases of delayed orbital fracture reduction. The target BOV could be obtained by substituting the preoperative OSTV and target ocular protrusion into the regression equation. The difference of this target BOV and BOV of the contralateral orbit is the volume that needs to be compensated for. If the compensatory volume is not relatively large, additional implants such as polyethylene can be used to compensate the OSTV. If the compensatory volume is too large, clear and complete communication with the patient will be needed to discuss the unsatisfied result of enophthalmos correction.

In addition to the OSTV/BOV ratio, the ocular axial length contributed to ocular protrusion, showing a significant relationship (Table 2). Other studies have also reported a significant positive relationship of ocular axial length with ocular protrusion [22,23]. In patients with high levels of myopia or large ocular axial lengths, the OSTV is increased but the BOV remains unchanged; thus, the OSTV/BOV ratio increases, and the patient presents with exophthalmos. This finding highlights the importance of considering the length of the globe in planning orbital surgery for patients with high levels of myopia.

Furthermore, the shape of the orbital aperture, particularly the orbital width, exhibited a significant relationship with ocular protrusion in this study, which is in consistent with the study conducted by Weaver et al. [24] in a white population. Pessa et al. [25] also found an effect of the orbital aperture on eye measurements based on curve analysis of the orbital rims of human skulls. Ocular protrusion is usually measured from the most posterior point of the lateral orbital rim, and this point is influenced by the morphology of the orbital aperture. When measured using 3D-CT, the datum plane of measurement is also determined by the lateral margin of the orbit. This finding indicates that a change in the shape of the orbital aperture would also influence ocular protrusion. For example, the combination of orbital decompression and advancement of the lateral orbital margin would be helpful in treating patients with thyroid eye disease and shallow orbits [26].

However, some differences were observed between males and females. Orbital height and BOV were correlated with ocular protrusion only in females. This result might reflect the differences in orbital structures between the sexes. Regensburg et al. [27] reported that the orbital bony cavity volume, fat volume, and muscle volume are much larger in white males than in white females. Yoo et al. [28] similarly found larger orbital and muscle volumes in Korean males than in Korean females. In our study, we found that males tended to have larger orbits than females. The potential ramifications of differences between sexes for surgical plans and implant shapes require further study.

In the present study, we established an improved method based on using CT imaging in which a plane that passes through the most posterior point on the lateral margin of the orbit and parallel to the coronal plane is established as the datum plane for measurement. This plane is consistent with the datum plane used in Hertel exophthalmometry [29]. The data acquired by

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this method are of clinical significance and can be compared with data collected using Hertel exophthalmometry. CT imaging has been widely used for many years to observe inner structure from various angles, accurately measure orbital parameter values, and evaluate facial asymmetry [30]. Previous studies [2,31,32] have evaluated different methods of ocular protrusion measurement in a two-dimensional plane. However, typically, the apex of the cornea is not in the same CT imaging plane as the most posterior part of the lateral margin of the orbit, leading to some uncertainties or errors during measurements. With the help 3D CT, measurements of ocular protrusion and orbital morphology will be changed to a more efficient and accurate fashion than traditional 2D methods [33].

The potential limitations of this study must be considered. The orbital soft tissues include the tissues posterior to orbital septum, such as orbital fat, the globe, the optic nerve, and the rectus muscles. Because it was difficult to distinguish the eyelid from the orbital soft tissue on CT images, all of the soft tissue anterior to the orbital aperture was included. A more detailed study will be conducted in the future, which will divide the OSTV into several areas, such as fat and muscle, to explore the relationships of deeper anatomy using image fusion of CT and MRI. Furthermore, the sample size of subjects was small, which limits the power of this study in regard to group comparisons. For this reason, formal statistical analysis was not used to compare different age groups or race/ethnicity groups, thereby avoiding a type II statistical error.

Conclusions

The present study provides insight into the potential factors influencing ocular protrusion, which include the OSTV/BOV ratio, the shape of the orbital aperture and the ocular axial length. The results of orbital surgery can be made more predictable by accounting for these 3 factors, and the database and regression formula might provide support for surgical plans in the future.

Proprietary interest statement

The authors do not have any type of financial interest related to this study.

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