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Radiographic volumetric risk factors for late enophthalmos prediction in orbital blow-out fractures: a retrospective study

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Abstract:

Introduction: The aim of this study was to assess the correlation between volumetric risk factors, orbital volume (OV), orbital volume ratio (OVR), herniated volume (HV), and the newly described herniated volume ratio (HVR), with the occurrence of late enophthalmos.

Method: Patients presenting a unilateral unoperated blow-out fracture were retrospectively included. OV and HV were measured using planimetry on the initial CT scan images. OVR and HVR were then calculated. Enophthalmos was measured on the 2 months of follow-up CT scan images. Population was divided into two groups according to their enophthalmos status. Correlations and multiple linear regression model were used.

Results: 17 patients out of 45 presented a late enophthalmos of 1 mm or more.

There were significantly higher OVR (107 (3.76) ; $p < 0.0001$), HV (0.8 (0.47) ; $p < 0.0001$) and HVR (3.3 (1.82) ; $p < 0.0001$) in the enophthalmos group. A very strong linear correlation between enophthalmos and OVR ($r_s = 0.806$), HV ($r_s = 0.948$) and HVR ($r_s = 0.951$) was found.

Conclusion: Enophthalmos prediction using these volumetric parameters can help the surgeon decision-making in orbital blow-out fractures in order to prevent late enophthalmos. Their measurement is simple and reproducible. However, larger prospective studies are needed to confirm these results.

Introduction:

Enophthalmos, a complication of orbital fractures, is generally considered clinically significant beyond 2 mm and their management can be a challenge (Nikunen et al., 2021). Several hypotheses explain its occurrence, such as the increase of the orbital volume following the displacement of orbital walls (Whitehouse et al., 1994 ; *Cornelius et al., 2021*), but orbital soft tissues fibrosis and retraction may also play a significant role (Kim et al., 2017 ; Cohen et al., 2020 ; Falkhausen et al., 2021). Unfortunately, it is often not detected until later in the follow-up due to the initial swelling. Furthermore, enophthalmos measurement can be realized clinically with Hertel's exophthalmometer or radiographically with Computed Tomography (CT) imaging. However, Hertel's exophthalmometer underestimates enophthalmos (Ebrahimi et al., 2019) and has greater inter-observer variability than CT imaging, which is more accurate and reproducible (Delmas et al., 2018 ; Nightingale and Shakib, 2019). Unfortunately, CT is not used to measure enophthalmos in some publications. Finally, the timing of the evaluation of enophthalmos is vastly different between studies, potentially inducing a selection bias (Schlund et al., 2020). These are the reasons why an accurate prediction would allow proper management: surgical or not.

The development of volumetry is associated with the design of various parameters used to predict posttraumatic enophthalmos, such as orbital volume (OV), orbital volume ratio (OVR), herniated tissue volume (HV). However, measurement protocols and results vary. Planimetry is currently considered as the gold standard (Kim et al., 2019). Nevertheless, it is very time-consuming and difficult to apply in clinical practice because it requires a slice-by-slice measurement (Sentucq et al., 2020). OV has been the first parameter described; it is known that its increase lead to enophthalmos

appearance (Whitehouse et al., 1994 ; Fan et al., 2003 ; Sugiura et al., 2017 ; Schlund et al., 2020). However, the precise relationship between OV and enophthalmos is highly variable (Schlund et al., 2020), some studies even found no link between them (Alinasab et al., 2011 ; Zhang et al., 2012 ; Schöneegg et al., 2018). Furthermore, OV being variable between both orbits of the same individual and between two individuals, OVR has been developed as standardized parameter. It has been described as better correlated to the development of enophthalmos (Oh et al., 2013; Choi et al., 2016). However, there is still variability in the relationship between OVR and enophthalmos (Yang et al., 2019 ; Schlund et al., 2020). HV is the volume of soft tissue out of the normal orbital boundaries in the maxillary sinus or ethmoid. This parameter has been described as less correlated with the occurrence of enophthalmos than the OVR (Yang et al., 2019). The newly described herniated tissue ratio (HVR) may allow the standardization of this parameter.

The objective of this retrospective study was to assess the correlation between multiple orbital volumetric risk factors including the newly described HVR with late posttraumatic enophthalmos.

Materials & Method:

Patients and data collection:

All consecutive patients presenting a unilateral unoperated blow-out orbital fracture, confirmed with CT imaging, from November 2018 to March 2020, in a regional specialized center for craniofacial trauma (Lille University Hospital, France) were retrospectively included. Conservative treatment was decided after two clinical evaluations performed immediately and at 15 days following the trauma, if the patient did not show functional (diplopia) or morphological (enophthalmos) consequences of the orbital fracture.

Patients administratively registered in pediatric surgery (under 15 years and 3 months old), having an associated zygomaticofrontal process fracture, not having at least a 2 months follow-up, or without a CT scan control after 2 months, were excluded from the study.

Age, gender, affected side, and fracture location were collected. Fractures were classified as orbital floor or medial wall.

All procedures performed in the study were in accordance with the ethical standards of the Helsinki Declaration. No IRB evaluation was required due to the retrospective nature of the study according to French law. All data were anonymized and the "Commission Nationale de l'Informatique et des Libertés" declaration was provided in accordance with French law.

Enophthalmos was defined as a qualitative and a quantitative variable.

The CT scan performed 2 months after the trauma was used to realize the late enophthalmos quantitative measurement. In axial slice in the neuro-ocular plan, the line between the zygomaticofrontal processes up to the posterior part of the lens was used to compare the position of the two eyeballs and define the size of enophthalmos in mm (**Figure 1**). Enophthalmos was then considered as a qualitative variable using a threshold of 1 mm. Patients having an enophthalmos ≥ 1 mm were classified in the enophthalmos group whereas those having an enophthalmos < 1 mm were classified in the group without enophthalmos. Enophthalmos was also considered as a quantitative variable.

Volume measurements were obtained, using manual segmentation, as described below after importing the initial CT scan DICOM data of each patient into 3D Slicer 4.10.2 freeware. Measurements were performed by two surgeons (one junior and one senior) twice in order to estimate intra and inter-observer variability.

- Orbital volume measurement:

The axial slices were placed according to the neuro-ocular plan. The sagittal and frontal plan were placed perpendicularly to the axial slices. Then, the orbit was measured slice-by-slice on the axial plan from top to bottom, using the cursor to delineate the surface to be calculated. The limits of the orbits were determined using Shuy et al. measurement method (Shyu et al., 2015): the zygomaticofrontal process laterally, the anterior lacrimal crest in the infero-internal part, the nasal process in the upper-internal part and the upper and lower margin of the orbit. The lacrimal canal was excluded from the measurement at the level of its upper orifice. The posterior limits correspond to the

optic foramen and the superior and inferior orbital fissures that are excluded from the measurement. At the fracture level, herniated soft tissues were also included in the measurement. The sagittal and frontal slices were used to check the quality of the measurement. The segment statistic tool finally provides orbital volume in cm³. The procedure was repeated to obtain the OV on both sides.

- Herniated tissue volume measurement:

HV was defined by the orbital tissue exceeding the fracture location in cm³. Slice-by-slice, in the axial plan for a medial wall fracture and in the frontal plan for a fracture of the orbital floor, a line was drawn from one edge to the other of the fracture side. The cursor was then used to delineate the hernia. The contrast modification allowed to visualize the limits of the measurement are, avoiding to include, for example, a hematoma in the measurement. (**Figures 2&3**)

- Orbit volume ratio and Herniated volume ratio calculation:

OVR and HVR were defined by the following equation:

$$\text{OVR} = (\text{volume of traumatized orbit} / \text{volume of healthy orbit}) \times 100$$

$$\text{HVR} = (\text{herniated volume of the traumatized orbit} / \text{volume of healthy orbit}) \times 100$$

Statistical analysis:

Descriptive statistics were calculated for the variables of interest. Continuous variables are presented as the means and standard deviations. Discrete variables are expressed as frequencies and percentages. Normality of distributions was assessed using histograms and the Shapiro-Wilk test.

Concordance of enophthalmos and volume measurements (volume of the healthy orbit, the volume of the traumatized orbit, and the volume of the herniated tissue) obtained from each observer and from each reading, were performed using intraclass

correlation coefficients (ICCs). The estimated ICCs were used to measure the interobserver and intraobserver reliability. ICC represents the proportion of variance in the data explained by between-subject differences; The ICC ranged from 0 to 1 and large values indicated high reproducibility. Categories of concordance were defined as follows: very poor for ICC 0.00-0.30, poor for ICC 0.31-0.50, moderate for ICC 0.51-0.70, good for ICC 0.71-0.90, and very good for ICC >0.91.

Then, analysis population was separated into two groups according to patients had a late enophthalmos or not. All the available variables were used to evaluate the comparability of both groups. The primary objective was evaluated by comparing all volume measurements between both groups. The chi-square test was performed to compare categorical variables. The Mann–Whitney U test was applied to compare non-normally distributed means. Spearman's correlation was used to determine correlations between non-normal distribution variables, and a P value of 0.05 was considered statistically significant. The strengths of correlations were described for the absolute values of the ratios of the compared variables as follows: very weak (0–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (0.80–1.0). A multiple linear regression model was used to explain the relationship between the degree of enophthalmos and OVR, between the degree of enophthalmos and HV, between the degree of enophthalmos and HVR, and between the degree of enophthalmos and all volume measurements.

Tests were 2-sided, and p values less than 0.05 were considered significant. The analysis was performed using R statistical software.

Results:

Forty-five patients with an unoperated unilateral blow-out fracture and having a CT scan at 2 months of follow-up were finally included. Characteristics of the study population were listed in the **Table 1**.

Twenty-five males and twenty females, with an average age of 47.5 years were included. 28 patients had an enophthalmos of less than 1 mm, 12 patients between 1 and 2 mm, and 5 patients had enophthalmos greater than 2 mm. The main cause was fall (18 cases) followed by assault (17 cases).

Intra and interobserver reliability:

Inter and interobserver concordances were very good.

For interobserver reliability assessment, the ICCs of the enophthalmos and volume measurements (volume of the healthy orbit, the volume of the traumatized orbit, and the volume of the herniated tissue) ranged from 0.966 to 0.999. The ICC was 0.998 (95% CI, 0.996-0.999) for the enophthalmos measurement, 0.981 (95% CI, 0.966-0.990) for the volume of the healthy orbit, 0.979 (95% CI, 0.962-0.988) for the volume of the traumatized orbit and 0.999 (95% CI, 0.997-0.999) for the volume of the herniated tissue.

For intraobserver reliability assessment, the ICCs of the enophthalmos and volume measurements (volume of the healthy orbit, the volume of the traumatized orbit, and the volume of the herniated tissue) ranged from 0.977 to 1. The ICC was 0.999 (95% CI, 0.990-1) for the enophthalmos measurement, 0.989 (95% CI, 0.980-0.994) for the

volume of the healthy orbit, 0.987 (95% CI, 0.977-0.993) for the volume of the traumatized orbit and 1 (95% CI, 0.999-1) for the volume of the herniated tissue.

Comparison of the two groups according to the enophthalmos:

There was no significant difference between the two groups regarding age ($p=0.550$) and sex ($p=0.731$) of patients, suggesting that the two populations were similar.

There were significantly higher OVR ($p<0.0001$), HV ($p<0.0001$) and HVR ($p<0.0001$) in the enophthalmos group than in the non-enophthalmos group (**Table 2**).

Correlation between degree of enophthalmos and volume measurements

There was a significantly very strong correlation between the degree of enophthalmos, and OVR ($r_s = 0.806$), HV ($r_s = 0.948$) and HVR ($r_s = 0.951$) (**Figure 4**).

Linear regression models to explain the relationship between the degree of enophthalmos and volume measurements:

A simple linear regression was calculated to predict the degree of enophthalmos based on OVR. A significant regression equation was found ($F(1,43) = 116,860$; $p<0001$), with a R^2 of 0.731. Participant's predicted degree of enophthalmos is equal to $-20.38+0.20*OVR$, with OVR calculation described below. This model indicates that within the range of variation of the volumetric variables given by the observations, each time the OVR increases by 1%, the enophthalmos increases by 0.2mm (**Figure 5A**).

A simple linear regression was calculated to predict the degree of enophthalmos based on HV. A significant regression equation was found ($F(1,43) = 858,414$; $p < 0.0001$), with a R^2 of 0.952. Participant's predicted degree of enophthalmos is equal to $0.09 + 1.97 \cdot HV$, with HV calculation described below. This model indicates that within the range of variation of the volumetric variables given by the observations, each time the HV increases by 1cm^3 , the enophthalmos increases by 2mm (**Figure 5B**).

A simple linear regression was calculated to predict the degree of enophthalmos based on HVR. A significant regression equation was found ($F(1,43) = 1379,014$; $p < 0.0001$), with a R^2 of 0.970. Participant's predicted degree of enophthalmos is equal to $0.07 + 0.50 \cdot HVR$, with HVR calculation described below.

This model indicates that within the range of variation of the volumetric variables given by the observations, each time the HVR increases by 1%, the enophthalmos increases by 0.5mm (**Figure 5C**).

A multiple linear regression was calculated to predict the degree of enophthalmos based on OVR, HV and HVR. A significant regression equation was found ($F(3,41) = 558,301$; $p < 0.0001$), with a R^2 of 0.976. Participant's predicted degree of enophthalmos is equal to $-3.31 + 0.03 \cdot OVR - 0.20 \cdot HV + 0.50 \cdot HVR$, with OVR, HV and HVR calculation described below.

This model indicates that within the range of variation of the volumetric variables given by the observations, each time the HVR increases by 1%, the enophthalmos increases by 0.5 mm, and each time the OVR increases by 1%, enophthalmos increases by 0.033 mm (**Figure 5D**).

Discussion:

There are several hypotheses on the occurrence of enophthalmos: an increase of the OV for some authors and the soft tissue retraction for others (Kim et al., 2017). It is commonly accepted that an increase of the OV is accompanied by the appearance of enophthalmos (Whitehouse et al., 1994). However, OV is variable from one individual to another. Indeed, for Andrades et al., the average OV is $24.5 \pm 3.08 \text{ cm}^3$ and follows a normal distribution (Andrades et al., 2018). OVR is a parameter allowing to standardize this inter-individual variability. It is described as better in predicting the onset of enophthalmos (Yang et al., 2019). However, for McGurk et al., there is also an intra-individual variability with an OV difference between the two orbits of up to 0.6 cm^3 (McGurk et al., 1992). This study results showed that each time the OVR increases by 1%, enophthalmos increases by 0.2 mm. In other words, a significant enophthalmos of more than 2 mm is found for an $\text{OVR} \geq 110\%$. Yang et al. showed an OVR of 106.8% for a 2 mm enophthalmos, while Choi et al. found an OVR of 112.2% and 112.1% (Choi et al., 2016 ; Choi and Kang, 2017; Yang et al., 2019). In these three studies, the enophthalmos was measured with a Hertel exophthalmometer. OVR found in our study is an average of the results previously reported.

The use of an exophthalmometer requires experience, has a low reproducibility and underestimate enophthalmos (Musch et al., 1985 ; Nightingale and Shakib, 2019). It is a potential source of bias (Schlund et al., 2020) whereas CT imaging offer a more objective measurement with lower inter-observer variability (Ebrahimi et al., 2019). This may explain why the OVR is lower than that found by Choi et al. The most described method of measurement on CT was chosen in this study (Nightingale and Shakib, 2019). However, this requires the absence of fracture of the zygomaticofrontal

process in order to obtain a reliable result, which is why we decided to exclude patients with a fracture of the lateral rim.

The volume of herniated tissue is less described in the literature. It is defined as the orbital tissue protruding beyond the fracture line. For some authors it was not correlated with the appearance of enophthalmos (Alinasab et al., 2011), for others it was less correlated than OVR (Yang et al., 2019). In this study a very strong correlation between the HV and the degree of enophthalmos was found. Jin et al. found an enophthalmos of 2mm or more for an HV of 0.9 cm³, which is very close to this study results (Jin et al., 2000). A new parameter consisting in calculating the herniated volume ratio was introduced. In fact, just like the OVR, the theoretical principle that because of a normal distribution of the OV, the HV could also be impacted by the size of the orbit was applied. This parameter, which is not described in the literature, would allow to standardize the HV in relation to the healthy orbit. Thus, a very strong correlation of HVR and degree of enophthalmos was found, which is more important than that found between OVR and degree of enophthalmos. The main advantage of using HVR is that it requires less time to be evaluated. It is only necessary to measure the OV of the healthy orbit in the axial plane and the HV. This is less time-consuming than using the measurement of injured OV because the measurement of HV requires less slices and because in the axial plane, especially in orbital floor fractures, the measurement of injured OV can be made difficult by low CT resolution, the presence of a hematoma, of a comminuted fracture or of emphysema.

This study presents a number of biases. The first limitation was the absence of subgroup analysis based on fracture location. However, no significant difference in orbital volume between these subgroups was found, suggesting that these two groups

were similar. Moreover, no conclusion could be drawn concerning the effect of fracture location on the relationship between orbital volume and posttraumatic enophthalmos in a systematic review about enophthalmos prediction (Schlund et al., 2020). The second limitation was a selection bias because 172 of the 217 eligible patients were not included. 37 patients were operated earlier due to orbital symptomatology. 135 patients were lost to follow-up or did not perform a follow-up CT scan. Overall, there were two peaks in age and mechanism in the orbital fracture onset: the young adult presenting after an assault and the senior person after a fall. These patients showed a high rate of lost to follow-up. Patients were lost to follow-up probably because fractures were pauci- or asymptomatic and the recovery was complete without sequelae in the majority of cases (Jansen et al., 2020). Enophthalmos rate is therefore probably overestimated. However, no study has estimated the enophthalmos rate in patients with an unoperated fractured orbit. On the other hand, this study is representative of patients presenting in follow-up consultation at 2 months of trauma. Finally, there was a measure bias. While the posterior orbit landmarks are easy to find and measurements are reproducible (Shyu et al., 2015), even when there is reconstruction material in the orbit (Gomes de Oliveira et al., 2019). Indeed, Jansen et al. demonstrated intra-observer variability of 0.09 cm³ and inter-observer variability of 0.03 cm³ in the measurement of orbital volumes using the planimetry method. The difficulty of the measurement is due to the lack of consensus on the anterior limit of the orbit (Jansen et al., 2016 ; Chepurnyi et al.,2020). In this study posterior limits are the same (the optical foramen and the upper and lower orbital fissures), however a simple and reproducible anterior limit was chosen, which is the line between the zygomaticofrontal process and the anterior lacrimal crest. This limit is easier to use

and is highly reproducible as shown with our intra and inter-operator reliability assessment.

Conclusion:

Enophthalmos prediction using these volumetric parameters can help the surgeon decision-making in orbital blow-out fractures in order to prevent late enophthalmos. Their measurement is simple and reproducible. HVR predictive validity is promising but it was only shown retrospectively on a small number of patients, it should be confirmed in another larger and prospective follow-up study.

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Tables and Figures:

Table 1: Characteristics of the study population.

Table 2: Comparison of the two groups according to the enophthalmos.

Figure 1: Measurement of enophthalmos through the example of an orbital fracture of the medial wall. In axial slice in the neuro-ocular plan, the line between the zygomaticofrontal processes up to the posterior part of the lens was traced. The enophthalmos here is estimated perpendicularly to this line.

Figure 2: Measurement of OVs and HV through the example of an orbital floor fracture. HV is shown in brown.

Figure 3: Measurement of OVs and HV through the example of an orbital fracture of the medial wall. HV is shown in purple.

Figure 4: Correlation matrix between degree of enophthalmos and volumetric parameters according to the Spearman test. A black color indicates an absence of correlation, a green color indicates a very strong correlation (close to 1). Conversely, a red color indicates a negative correlation (close to -1). HV and HVR have a better correlation than traumatized OV and OVR.

Figure 5A: Relationship between the degree of enophthalmos in mm and OVR in %.

Figure 5B: Relationship between the degree of enophthalmos in mm and HV in cm³.

Figure 5C: Relationship between the degree of enophthalmos in mm and HVR in %.

Figure 5D: Relationship between the degree of enophthalmos in mm and volumes measurement jointly (with OVR in %, HV in cm³ and HVR in %).

Characteristics of analysis population	N=45
Age means (SD)	47 (28;63)
Females n (%)	20 (44.44)
Volume measurements:	
Healthy OV means (SD)	24.51 (2.44)
Traumatized OV means (SD)	25.78 (2.72)
OVR median (Q1;Q3)	103.77 (101.76;105.68)
HV median (Q1;Q3)	0.22 (0.03;0.56)
HVR median (Q1;Q3)	1.06 (0.16;2.16)
Enophthalmos n (%)	17 (37.77)
Degree of enophthalmos median (Q1;Q3)	0.70 (0.16;1.20)

	Enophthalmos N=17	Absence of enophthalmos N=28	p
OVR mean (SD)	107.02 (3.76)	101.90 (2.60)	<0.0001
HV mean (SD)	0.84 (0.47)	0.12 (0.14)	<0.0001
HVR mean (SD)	3.33 (1.82)	0.48 (0.56)	<0.0001







