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A Novel Method of CT Exophthalmometry in Patients With Thyroid Eye Disease

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Purpose: Conventional computed tomography (CT) exophthalmometry requires an intact lateral orbital wall and is therefore not feasible in patients who have undergone any form of lateral orbital wall surgery where the normal bony landmark may be lost or displaced. The purpose of our study is to validate an alternative method of CT exophthalmometry utilizing the posterior clinoid (PC) process as a new reference point that will allow for reproducible comparison of the anterior-posterior globe position in the preoperative and postoperative settings.

Design: Cohort study.

Methods: This is a retrospective study of 48 patients with clinically diagnosed thyroid eye disease who had undergone cross-sectional CT imaging in the pre- or postoperative settings. CT exophthalmometry was performed using both the conventional interzygomatic method and our proposed PC process method on all pre- and postoperative CT imaging by two independent observers. Interobserver variability analysis was performed with intraclass correlation coefficient. Correlation and agreement between the two methods were analyzed with Pearson correlation coefficient and linear regression method. All analyses were conducted at 5% level of significance with Stata MP V14.

Results: Interobserver variability analysis showed an intraclass correlation coefficient of >0.9 for both interzygomatic and PC methods. There is good correlation between the two different measurements observed in both the pre- and postoperative groups ($r = 0.68$ and $r = 0.72$, respectively, $P < 0.001$). Linear regression showed good agreement between the two different measurements with most of the points lying within the 95% limits.

Conclusions: Our new method agrees well with the conventional method and has the added benefit of being able to reliably assess the anterior-posterior globe position in patients who do not have intact lateral orbital walls after decompressive surgery.

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Submitted May 6, 2019; accepted August 1, 2019.

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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ISSN: 2162-0989
DOI: 10.1097/01.APO.0000617908.29733.84

Key Words: computer tomography, Hertel exophthalmometry, proptosis, thyroid eye disease

(*Asia Pac J Ophthalmol (Phila)* 2020;9:39–43)

Exophthalmos is one of the most common clinical manifestations of thyroid eye disease (TED) and is also one of the common indications for orbital decompression.[1] Therefore, accurate exophthalmometry is extremely important, in both the diagnosis and follow-up of patients with TED.

Clinical tools such as the Hertel exophthalmometer have been used for decades in the clinical assessment of exophthalmos.[2,3] However, these mirror-based tools are operator dependent and also suffer from parallax errors.

Computed tomography (CT) on the hand is a reliable method of exophthalmometry, being commonly used in the preoperative planning of orbital decompression surgery and occasionally used for postoperative quality control. Measurement of exophthalmos on cross-sectional imaging utilizes the same principle as the Hertel exophthalmometer, first requiring a reference line to be drawn between the anterior portions of the zygomatic arches (lateral orbital rim), before a perpendicular measuring line is drawn from this line to the anterior cornea. Therefore, we found that as with the clinical Hertel exophthalmometry, this radiological method is not feasible in patients who have undergone lateral orbital rim surgery where the lateral orbital rim may be displaced or removed.

The purpose of our study is to validate an alternative method of measuring anteroposterior globe position on cross-sectional imaging using the posterior clinoid (PC) process as a new reference point.

METHOD

Patients

A select group of patients from our institution's TED clinical database were analyzed between 2005 and 2018. All patients who had undergone cross-sectional CT imaging of their orbits were selected for the study. Patients with no intact lateral orbital wall, which precluded accurate CT exophthalmometry via the conventional method, were excluded from our study.

Our study involved a total of 48 patients. Group 1 comprised of 31 patients who were conservatively or medically treated with baseline CT imaging. The clinical activity scores for the patients in this group were not fully documented. The majority of patients had mild–moderate clinical activity severity.

TABLE 1. Types of Surgery in Group 2

Types of Orbital Decompression in Group 2	No. Patients
Bilateral three-wall decompression	4
Bilateral two-wall decompression	7
Bilateral one-wall decompression	3
Unilateral decompression	3

Group 2 comprised of 17 patients who underwent surgical orbital decompression. 16 patients had both baseline and postoperative CT studies and 1 patient only had postoperative CT without baseline imaging. The majority of our patients underwent balanced decompression of bilateral orbital walls, with only 3 patients having unilateral wall decompressions based on surgeon preference (Table 1).

In total, 64 CT studies were analyzed.

Imaging Analysis

CT exophthalmometry was performed in a blinded manner by two investigators in both groups of patients using the following two different methods.

Conventional interzygomatic (IZ) method: A reference IZ line was drawn on the axial view in which the lens was best seen (Fig. 1A). Subsequently, a measuring line was drawn from the anterior corneal surface to the IZ line, bisecting the lens. The length of this perpendicular line is taken as the primary measurement.

Proposed PC method: Using multiplanar reconstruction, an axial plane was obtained where both the ocular lenses and PC processes were best seen. A measuring line was drawn from the most anterior aspect of the PC process to the anterior corneal surface (Fig. 1B).

We performed the measurements using bone window with a window width of 1800 and window level of 400 because we found that this window setting allowed the best definition of bony landmarks while retaining the ability to delineate the corneal surface.

Statistical Analysis

Two observers carried out both examinations in a blinded manner and intraclass correlation coefficients were analyzed.

TABLE 2. Demographic of Patients

	Group 1	Group 2	Total	*P* Value
Male	12 (37.5%)	9 (56.3%)	21 (43.8%)	0.217
Female	20 (62.5%)	7 (43.8%)	27 (56.3%)	
Average age (y)	53.81 ± 14.12	49.75 ± 15.22		0.364

TABLE 3. Average Exophthalmometry Measurements With IZ and PC Methods

	Average Preoperative Measurements (n = 94)	Average Postoperative Measurements (n = 34)
IZ measurement (mm)	21.9 ± 3.2	21.4 ± 3.4
PC measurement (mm)	76.2 ± 4.5	75.2 ± 4.3

Correlation between the two different methods was analyzed with Pearson correlation.

Linear regression analysis was used to analyze the agreements between the two different types of measurements.

All analyses were conducted at 5% level of significance with SPSS V25 (2017).

RESULTS

Table 2 shows the demographic characteristics of our patients. There is no significant difference between group 1 and group 2 in terms of sex and age.

Table 3 shows the average measurements using both methods in both groups. There is significant difference between the pre- and postoperative measurements in group 1 (Table 4).

Interobserver variability analysis demonstrated near-perfect correlation between the two different observers using both methods in both the pre- and postoperative settings. For conventional exophthalmometry using the IZ method in both pre- and postoperative settings, the intraclass correlation coefficients were 0.989 [Confidence interval (CI) 0.983–0.993, $P < 0.001$] and 0.991 (CI 0.982–0.995, $P < 0.001$). For conventional exophthalmometry using the PC method in the pre- and postoperative settings, the

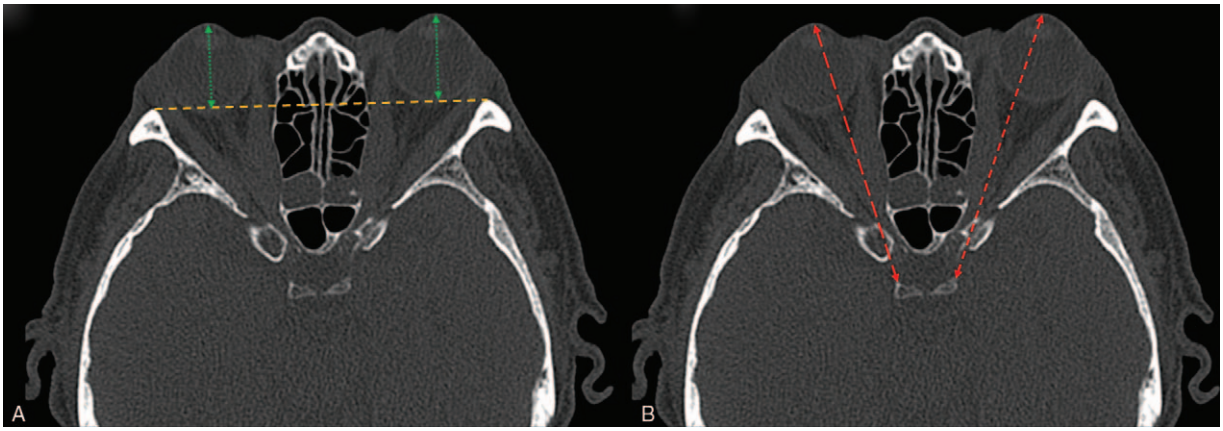

FIGURE 1. Axial CT orbit at the level of the mid-globes. A, Conventional method of assessing for proptosis using the interzygomatic line (yellow dotted line) as a reference for drawing the perpendicular measuring line to the anterior corneal surface (green arrows). B, Proposed posterior clinoid method using a single measuring line (red arrows).

TABLE 4. Average Measurements Using Both Methods in Group 1 Patients

	Average Preoperative Measurements (n = 32)	Average Postoperative Measurements (n = 32)	*P* Value
IZ measurement (mm)	23.3 ± 3.6	21.7 ± 3.3	<0.001
PC measurement (mm)	77.3 ± 4.6	75.5 ± 4.3	<0.001

intraclass correlation coefficients were 0.983 (CI 0.975–0.989, $P < 0.001$) and 0.99 (CI 0.976–0.994, $P < 0.001$), respectively.

There is good correlation between the two different measurements observed in both pre- and postoperative groups (Pearson correlation coefficient r = 0.68 and r = 0.72, respectively, $P < 0.001$).

Linear regression showed good agreement between the two different measurements with most of the points lying within the 95% limits (Fig. 2).

DISCUSSION

TED is a common autoimmune inflammatory orbitopathy that can be cosmetically disfiguring and not infrequently vision-threatening, if untreated. Although omnipresent, the pathophysiology of TED is complex and not fully understood to date. Current understanding revolves around orbital fibroblasts, which when activated sets off a cascade of reaction that ultimately leads to the hallmark inflammation, edema, and fatty proliferation of the orbital soft tissues.[4,5] Rundle and Wilson described the chronology of TED as having a self-limiting active phase that inevitably progresses to a chronic quiescent phase.[6] This forms the basis of assessment scales such as the Clinical Activity Score, European Group of Grave's Orbitopathy, and VISA-ITEDS scoring system, to name but a few, all of which help guide treatment thresholds and modalities.[7] As the disease is often self-limiting, most patients with TED only require reassurance with symptomatic supportive treatment and expectant observation. When indicated especially when the patients' quality of life is significantly affected, medical treatment with parenteral

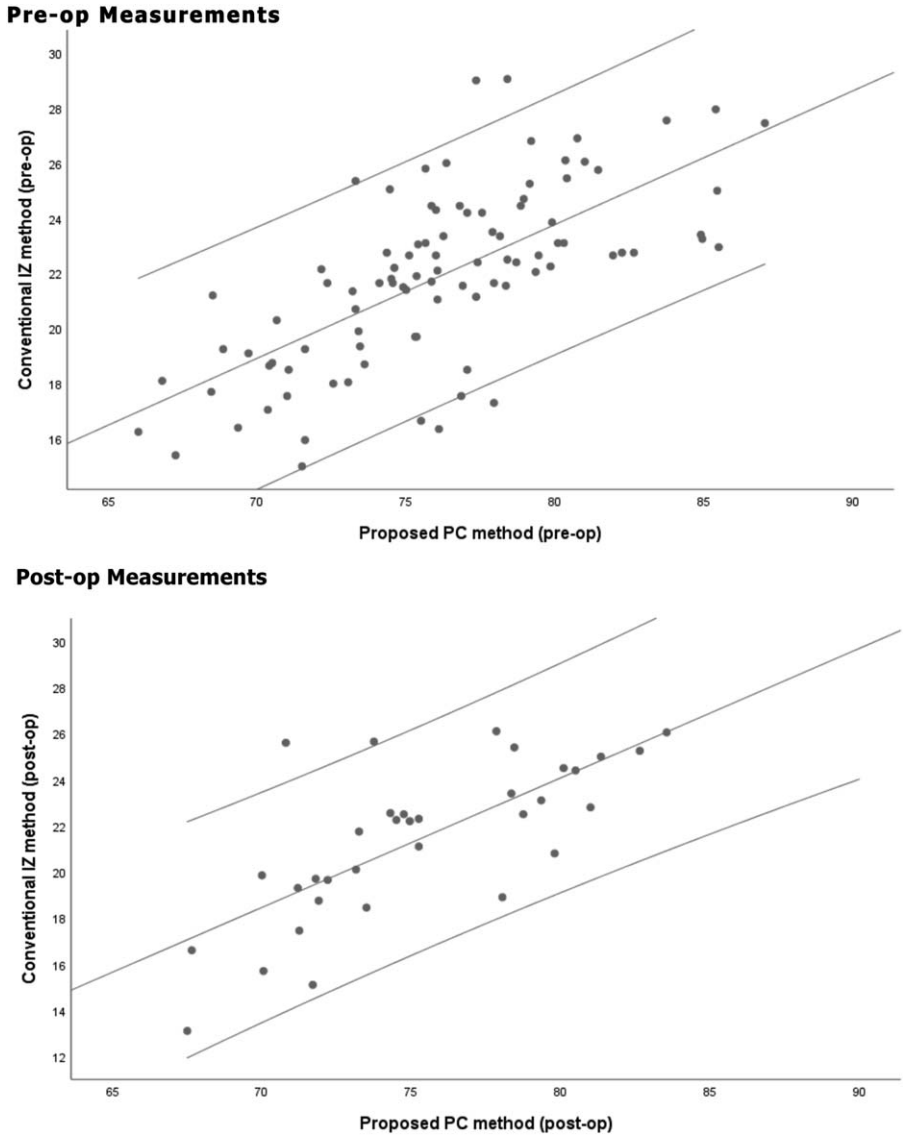

FIGURE 2. Linear regression analysis in pre-operative and post-operative patients. PC indicates posterior clinoid.

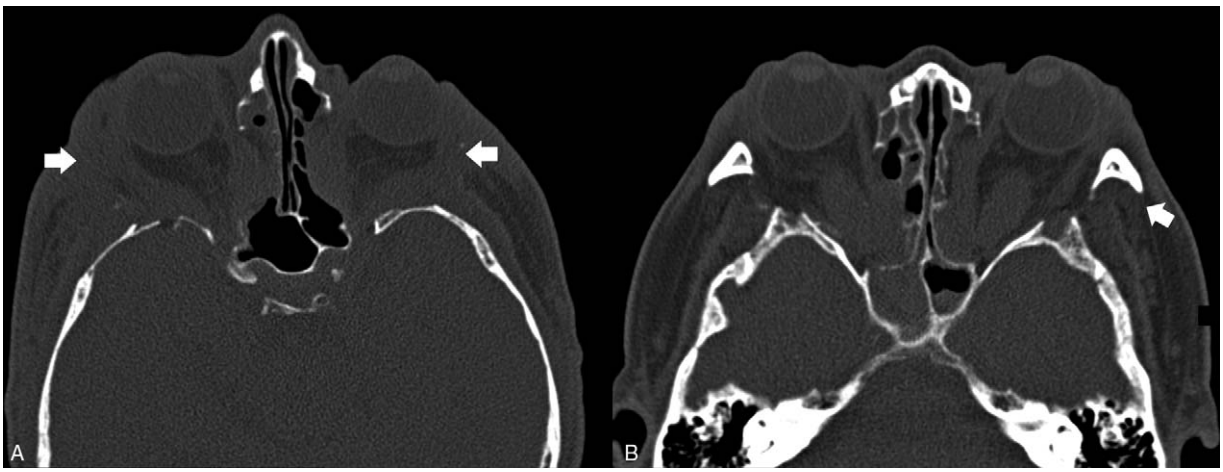

FIGURE 3. A, Pre-operative axial CT scan in a patient with bilateral proptosis and extraocular enlargement. Using the conventional IZ method of exophthalmometry, there is exophthalmos of 24 mm of both the right and left globes. B, Post-operative axial CT of the same patient who had undergone bilateral medial and lateral wall decompressions. Absence of the lateral rim (arrows) precludes exophthalmos assessment using the conventional method.

corticosteroids form the next line of treatment. Surgical treatment is usually considered in the late stage of the disease to address residual deformity from moderate-to-severe exophthalmos, before performing strabismus and/or eyelid surgery when indicated.[8] Occasionally, surgery is indicated in progressive vision-threatening cases that are unresponsive to medical treatment. In each of these cases, exophthalmometry serves as an important parameter to monitor progression, guide treatment, and monitor outcomes after orbital decompression.[9]

To date, Hertel exophthalmometry is the most widely used method of assessing exophthalmos clinically.[2] However, this tool has been criticized for its reliability, which can be affected by operator's experience and parallax.[10–12] The measurements can also be affected by varying the amount of pressure exerted by the operator when placing the footplate at the lateral canthal region and the presence of periorbital soft tissue swelling that is commonly encountered in postsurgical patients.[13] Several other clinical measurements such as the Luedde ruler and parallax free Mourits exophthalmometer have been described, with literature showing comparable reliability to Hertel exophthalmometer.[14–17]

Cross-sectional imaging is usually not required for the diagnosis of TED, but rather plays an adjunctive role in the early detection of orbital tissue remodeling such as orbital fat proliferation and extraocular muscle enlargement.[18] CT scan, in particular, provides accurate assessment of baseline globe position and degree of exophthalmos and it aids in the preoperative planning for patients being considered for orbital decompression. Due to its multiparametric capabilities, CT exophthalmometry is thought to be more accurate and reproducible with the added benefit of not being affected by periorbital soft tissue swelling.[19] Several studies have shown good correlation between this method of CT exophthalmometry and the clinical Hertel exophthalmometry measurements.[19,20]

However, as already mentioned, we noted that these methods are technically not feasible nor reliable in patients who have undergone lateral wall decompression surgery involving removal of the lateral orbital rim with or without replacement (Fig. 3). To the best of our knowledge, there is no current consensus method of exophthalmometry in this patient group on imaging, thus precluding follow-up assessment and monitoring of disease.

There are two main reasons we chose the PC process as a reference point. First, they form the superior bony tubercles of the dorsum sellae and are thus virtually unaffected in any forms of orbital surgery. Second, the PC processes are easily recognizable on CT scan as triangle-shaped structures with pointed anterior ends (Fig. 4). This morphology makes it an attractive landmark as there is no ambiguity when drawing the measuring line from the anterior pointed end to the anterior cornea. We decided on using a single measuring line from a fixed point as we believe simplifying the measuring process into a single-step may potentially reduce interobserver variability compared with the two-step IZ method.

Although not superior, our analysis showed that our new method has similar reliability to the conventional method with both having near-perfect agreement (intraclass correlation

FIGURE 4. CT scan demonstrating the normal posterior clinoid process on the A, axial, B, coronal and C, sagittal planes (arrows).

coefficient >0.9). This is not unexpected as CT exophthalmometry has been shown to be objective and readily reproducible.[20]

As for the correlation, we expected the two methods to conform to a linear relationship because the proposed method is simply based on a new reference point. This was proven with a strong positive association between the two methods with Pearson correlation coefficient of >0.5 in both pre- and postoperative measurements. Although there is strong association between these two measurements, this does not imply agreement. Hence, in addition to Pearson correlation, we regressed the IZ measurements onto the new IZ measurements to give us an analysis akin to "limits of agreement." This showed good agreement in both groups with most points lying within the 95% limits. However, this analysis is limited by the small sample of the postoperative measurements, something we hope to address in a future study. There were also several other limitations with our study. We only included patients with TED, thus we were unable to assess application of the proposed method in the normal population to estimate a normal reference range. Second, although clinical exophthalmometry measurements were available in our patient database, these measurements were not performed in a controlled setting at the same time as the CT studies. Different clinical tools were also used in the clinical setting by different clinicians, mostly Hertel or Mourits exophthalmometers. Therefore, although it would have been ideal, we were unable to assess the correlation between our proposed CT measurements and the clinical measurements.

CONCLUSIONS

The proposed method is reliable and agrees well with the conventional method of CT exophthalmometry in the assessment of the anterior-posterior globe position. We believe that our method will be beneficial in the follow-up of treated TED patients, especially those who do not have intact lateral orbital walls. Additionally, our study shows that other potential landmarks can be used for the same purpose, a prospect we hope to investigate in the future.

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