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.

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

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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 (IZ line, bisecting the lens). 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.

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

| 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 |

| 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%) | 0.364 |
| 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 |

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).
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

|                        | 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      |

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

To date, Hertel exophthalmometry is the most widely used method of assessing exophthalmos clinically. However, this tool has been criticized for its reliability, which can be affected by operator’s experience and parallax. 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 peri-orbital soft tissue swelling that is commonly encountered in postsurgical patients. 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.

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. 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 peri-orbital soft tissue swelling. Several studies have shown good correlation between this method of CT exophthalmometry and the clinical Hertel exophthalmometry measurements.

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...
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.

REFERENCES

1. Jefferis JM, Jones RK, Currie ZI, et al. Orbital decompression for thyroid eye disease: methods, outcomes, and complications. Eye (Lond). 2018;32:626–636. doi:10.1038/ejey.2017.260.
2. Nkenke E, Maier T, Benz M, et al. Hertel exophthalmometry versus computed tomography and optical 3D imaging for the determination of the globe position in zygomatic fractures. Int J Oral Maxillofac Surg. 2004;33:125–133. doi:10.1054/ijom.2002.0481.
3. Kashkouli MB, Beigi B, Noorani MM, et al. Hertel exophthalmometry: reliability and interobserver variation. Orbit. 2003;22:239–245.
4. Shan SJ, Douglas RS. The pathophysiology of thyroid eye disease. J Neurol Ophthalmol. 2014;34:177–185. doi:10.1097/WNO.00000000000000132.
5. Khong JJ, McNab AA, Ebeling PR, et al. Pathogenesis of thyroid eye disease: review and update on molecular mechanisms. Br J Ophthalmol. 2016;100:142–150. doi:10.1136/bjophthalmol-2015-307399.
6. Rundle FF, Wilson CW. Development and course of exophthalmos and ophthalmoplegia in Graves’ disease with special reference to the effect of thyroidectomy. Clin Sci. 1945;5:177–194.
7. Barrio-Barrio J, Sabater AL, Bonet-Farriol E, et al. Graves’ ophthalmopathy: VISA versus EUGOGO classification, assessment, and management. J Ophthalmol. 2015;2015:249125. doi:10.1155/2015/249125.
8. Weiler DL. Thyroid eye disease: a review. Clin Exp Optom. 2017;100:20–25. doi:10.1111/cxo.12472.
9. Rootman DB. Orbital decompression for thyroid eye disease. Surv Ophthalmol. 2018;63:86–104. doi:10.1016/j.surophthal.2017.03.007.
10. Sleep TJ, Manners RM. Instrument variability in Hertel-type exophthalmometers. Ophthalmic Plast Reconstr Surg. 2002;18:254–257. doi:10.1097/0000000000001971.72318.95.
11. Lam AK, Lam CF, Leung WK, et al. Intra-observer and inter-observer variation of Hertel exophthalmometry. Ophthalmic Physiol Opt. 2009;29:472–476. doi:10.1111/j.1475-1313.2008.00617.x.
12. Tengroth B, Bogren H, Zaczkirsson U. Human exophthalmometry. Acta Ophthalmol (Copenh). 1964;42:864–874.
13. Vardizer Y, Berendschot TT, Mourits MP. Effect of exophthalmometer design on its accuracy. Ophthalmic Plast Reconstr Surg. 2005;21:427–430. doi:10.1097/01.IOP.0000180066.87572.39.
14. Chang AA, Bank A, Francis IC, et al. Clinical exophthalmometry: a comparative study of the Luedde and Hertel exophthalmometers. Aust N Z J Ophthalmol. 1995;23:315–318.
15. Genders SW, Mourits DL, Jasem M, et al. Parallax-free exophthalmometry: a comprehensive review of the literature on clinical exophthalmometry and the introduction of the first parallax-free exophthalmometer. Orbit. 2015;34:23–29.
16. Delmas J, Loustau JM, Martin S, et al. Comparative study of 3 exophthalmometers and computed tomographic biomtry. Eur J Ophthalmol. 2018;28:144–149. doi:10.5301/ejo.5001049.
17. Musch DC, Frueh BR, Landis JR. The reliability of Hertel exophthalmometry. Observer variation between physician and lay readers. Ophthalmology. 1985;92:1177–1180.
18. Siakallis LC, Uddin JM, Miszkiel KA. Imaging investigation of thyroid eye disease. Ophthalmic Plast Reconstr Surg. 2018;34:541–551. doi:10.1097/IOP.0000000000001139.
19. Kim IT, Choi JB. Normal range of exophthalmos values on orbit computerized tomography in Koreans. Ophthalmologica. 2001;215:156–162. doi:10.1159/000050850.
20. Segni M, Bartley GB, Garrity JA, et al. Comparability of proptosis measurements by different techniques. Am J Ophthalmol. 2002;133:813–818.