Corneal Deformation Response with Dynamic Ultra-high-speed Scheimpflug Imaging for Detecting Ectatic Corneas

1-3Marcella Q Salomão, 2-6Fernando F Correia, 2-7Isaac Ramos, 1,2,8Allan Luz, 1-3Renato Ambrósio Jr

ABSTRACT

Purpose: To test the ability of metrics derived from corneal biomechanical response using ultra-high-speed 8 mm horizontal Scheimpflug photography to noncontact tonometry (NCT) to distinguish between normal and ectatic cases.

Materials and methods: The prototype of CorVis ST (Oculus, Wetzlar, Germany) was used for assessing corneal biomechanical response using ultra-high-speed 8 mm horizontal Scheimpflug photography, taking 4,330 frames per second during NCT. Patients were stratified based on clinical data, including rotating Scheimpflug corneal tomography (Oculus Pentacam HR). Biomechanical data from one eye randomly selected of 177 patients with normal corneas (N) and from 79 patients with bilateral keratoconus (KC) were investigated. Group keratoconus suspect (KCS) had 16 eyes from 16 patients with topographic patterns suspicious of KC but documented stability over 3 years and normal tomographic findings. A combination of deformation parameters using linear regression analysis (Prototype Factor 1, pF1) was created by the BrAIn (Brazilian Artificial Intelligence on Corneal Tomography and Biomechanics) study group in order to provide the best possible separation of KC and normals.

Results: Statistical significant differences were found for normal tomographic findings. A combination of deformation parameters using linear regression analysis (Prototype Factor 1, pF1) was created by the BrAIn (Brazilian Artificial Intelligence on Corneal Tomography and Biomechanics) study group in order to provide the best possible separation of KC and normals.

Conclusion: Corneal deformation response analysis by ultra-high-speed 8 mm horizontal Scheimpflug photography provides relevant data for distinguishing ectatic and nonectatic corneas but cannot be used independently to detect KC. This data may be integrated with corneal tomography data for enhancing sensitivity and specificity for screening ectasia.

Keywords: Corneal biomechanics, CorVis ST, Forme fruste keratoconus, Keratoconus.


Source of support: Nil

Conflict of interest: None

INTRODUCTION

Keratoconus (KC) is an ectatic corneal dystrophy that has been described and studied for several decades.1,2 There was considerable progress related to refractive surgery over the past three decades, which boosted significant improvements in the diagnosis and management of ectatic conditions.3-5 Patients with ectatic disorders frequently present with subclinical disease as refractive surgery candidates. Such cases should be identified because these cases typically have unsatisfactory results and are at very high risk for progressive ectasia after laser vision correction (LVC).6,7 Furthermore, the identification of early stages of the disease turned out to be indispensable considering new treatment modalities, such as corneal collagen cross-linking (CL).8,9 Since the first report of post-LASIK ectasia by Seiler in 1998, the concept of biomechanical decompensation caused by corneal ectasia was ventured.5,6 Hence, preventing ectasia is related to the identification of cases at a higher risk for biomechanical failure. Definitely, the advent and evolution of corneal topography10,11 and tomography12 enhanced our ability to detect these milder forms of ectatic diseases, with no clinical signs or visual acuity loss.13 However, curvature and pachymetric changes

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should probably be secondary events, while abnormalities in biomechanical properties and architecture stability should be expected primarily.\textsuperscript{14}

The goal of this study was to test the ability of corneal biomechanical metrics derived from Dynamic Ultra High-Speed Scheimpflug Photography (the CorVis ST prototype) to distinguish normal from ectatic cases.

**MATERIALS AND METHODS**

This study adhered to the tenets of the Declaration of Helsinki. Patients from Instituto de Olhos Renato Ambrósio (Rio de Janeiro, Brazil) were retrospectively enrolled in the study. All eyes were examined by a fellowship-trained cornea and refractive surgeon (RA). Corneal biomechanics was assessed by the prototype of the Oculus CorVis ST (Oculus, Wetzlar, Germany), a new device with an ultra-high-speed 8 mm horizontal Scheimpflug camera that takes 4,330 frames per second during noncontact tonometry (NCT).

Along with a comprehensive ocular examination, all eyes were examined by a Placido-disk-based corneal topography (Atlas Corneal Topography System; Humphrey, San Leandro, California or Keratograph 4; Oculus, Wetzlar, Germany) and rotating Scheimpflug corneal tomography (Pentacam HR; Oculus, Wetzlar, Germany). Diagnosis of clinical KC was made based on Placido-disk-based axial topography, elevation-derived anterior corneal curvature maps, and criteria used in the collaborative longitudinal evaluation of KC.\textsuperscript{15} Cases with a history of corneal surgery or with extensive corneal scarring were excluded from the study. Contact lens wearers were asked to discontinue the use at least 3 weeks prior to the examinations.

One eye randomly selected from 177 patients with topo- and tomographically comprised the normal corneas group (N). One eye randomly selected from 79 patients with bilateral KC comprised the KC group (group KC). Twenty eyes with normal topographic patterns from patients with clinical ectasia in the fellow eye were included in group forme fruste KC (FFKC). The keratoconus suspect (KCS) group comprised 16 eyes with topographic patterns suspicious of KC from 16 patients with documented stability over 3 years and normal tomography (Stable-KCS). We considered this as normal tomography if the eye had normal corneal thickness spatial profiles\textsuperscript{16} along with normal anterior and posterior elevation values\textsuperscript{17} and final D value.\textsuperscript{18-20} The intraocular pressure, along with applanation and deformation responses, was extracted. The hypothesis on this study was that the non-ectatic groups (N and Stable-KCS) would have different deformation responses than groups with ectatic corneas (FFKC and KC groups).

Statistical analysis was accomplished using BioEstat 5.0 (Instituto Mamiraua, Amazonas, Brazil) and MedCalc 12.0 (MedCalc Software, Mariakerke, Belgium) according to Lopes et al.\textsuperscript{21} The unpaired nonparametric Mann–Whitney test (Wilcoxon ranked-sum) was used to assess if the parameters have different distributions among N and KC. A p-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) curves were calculated for the parameters with significant differences to determine the test’s overall predictive accuracy and area under the curve (AUC). A combined parameter using linear regression analysis (Prototype Factor 1, pF1) was created by the BrAIn (Brazilian Artificial Intelligence on Corneal Tomography and Biomechanics) study group in order to provide the best possible separation of KC and normals. The Kruskall–Wallis test with post hoc Dunn’s test was used to test differences among the four groups (N, KCS, FFKC, and KC) for pF1.

**RESULTS**

There were no statistical differences for patient age or gender between the groups. Table 1 demonstrates computed corneal deformation metrics. Considering N and KC groups, statistically significant distributions were found for all studied parameters (Mann–Whitney, p<0.05). However, there was a significant overlap that limits the diagnostic relevance. The best parameter was the radius of curvature at highest concavity, with an area

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st A Time</td>
<td>Moment at the first applanation of the cornea during the air puff (ms)</td>
</tr>
<tr>
<td>HC Time</td>
<td>Moment that the cornea assumes its maximum concavity during the air puff (ms)</td>
</tr>
<tr>
<td>2nd A Time</td>
<td>Moment at the second applanation of the cornea during the air puff (ms)</td>
</tr>
<tr>
<td>1st A Length (max)</td>
<td>The length of the applanation at the moment of the first applanation (mm)</td>
</tr>
<tr>
<td>2nd A Length (max)</td>
<td>The length of the applanation at the moment of the second applanation (mm)</td>
</tr>
<tr>
<td>Def.Amp. (max)</td>
<td>Measurement (mm) of the maximum corneal deformation during the air puff</td>
</tr>
<tr>
<td>W-Dist.</td>
<td>Length of the distance between the two peaks of the cornea at the moment of maximum deformation (mm)</td>
</tr>
<tr>
<td>Curv. Rad. HC</td>
<td>Corneal curvature radius at the time of maximum concavity during the air puff (mm)</td>
</tr>
<tr>
<td>Curv. Rad. Normal</td>
<td>Radius of curvature of the cornea in its natural state (mm)</td>
</tr>
<tr>
<td>(V_{in})</td>
<td>Maximum velocity of the cornea during the ingoing phase (m/s)</td>
</tr>
<tr>
<td>(V_{out})</td>
<td>Maximum velocity of the cornea during the outgoing phase (m/s)</td>
</tr>
</tbody>
</table>
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under the ROC curve of 0.845 (Graph 1). The combined parameter pF1 had AUC of 0.945 (Box 1 and Graph 2). Table 2 shows pF1 average and standard deviation values in each group and these data might also be appreciated in box plots on Graph 3. The distribution of pF1 was different among the groups (Kruskall–Wallis test). The post hoc Dunn’s test found no differences between the FFKC and KC groups and N and KCS groups, but there were significant differences for N × FFKC, for N × KC, stable-KCS × FFKC and stable-KCS × KC (Table 3).

**DISCUSSION**

Detecting milder forms of ectasia is fundamental for screening refractive surgery candidates as well as for indicating less-invasive surgery (i.e., CXL and intracorneal ring implantation). Iatrogenic ectasia is a rare complication after LVC, but due to the devastating nature of this complication, we must improve our understanding for prevention. Different studies have demonstrated the important role of corneal topography, tomography, and wavefront analysis in the screening of subclinical or mild ectatic disease. Nevertheless, the hypothesis that focal biomechanical distress precedes topographic and tomographic alterations of the cornea is well accepted and prevails among experts. Hence, analyzing biomechanical properties of normal and subclinical KC eyes has gained special relevance.

Biomechanical characterization is still challenging because of several biasing factors, such as the intraocular pressure and corneal thickness. While other noncontact tonometer, the Reichert ORA (Buffalo, NY, USA)

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**Box 1: Corvis Factor 1 Formula**

\[
0.033^* \text{IOP} - 0.004^* \text{Pachy Apex} - 0.448^* 1\text{st A Time} - 0.049^* \text{HC Time} + 0.093^* 2\text{nd A Time} + 0.026^* 1\text{st A Length(max)} - 0.105^* 2\text{nd A Length(max)} + 0.208^* \text{Def Amp (max)} - 0.619^* \text{W-Dist} - 0.021^* \text{Curv, Rad, HC} - 0.101^* \text{Curv, Rad, Normal} - 0.525^* V_{in} - 0.166^* V_{out} + 7.952
\]

**Graph 1:** Area under the ROC curve of the radius of curvature at highest concavity

**Graph 2:** The combined parameter pF1 had AUC of 0.945

**Graph 3:** Box plots demonstrating average and standard deviation values in each group

**Table 2:** Corvis Factor 1 average and standard deviation values in each group

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>FFKC</th>
<th>KC</th>
<th>ABT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ave</td>
<td>-0.00801</td>
<td>0.345529</td>
<td>0.506829</td>
<td>0.133745</td>
</tr>
<tr>
<td>SD</td>
<td>0.218348</td>
<td>0.196043</td>
<td>0.26691</td>
<td>0.181624</td>
</tr>
<tr>
<td></td>
<td>177</td>
<td>20</td>
<td>79</td>
<td>16</td>
</tr>
</tbody>
</table>

**Table 3:** The post hoc Dunn’s test found no differences between the FFKC and KC groups and N and KCS groups, but there were significant differences for N × FFKC, for N × KC, stable-KCS × FFKC and stable-KCS × KC

<table>
<thead>
<tr>
<th>Normal</th>
<th>KC</th>
<th>FFKC</th>
<th>ABT/IS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>KC</td>
<td>NS</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>FFKC</td>
<td></td>
<td></td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
monitors corneal applanation response through the reflex of an infrared beam with diagnostic capability to detect ectasia,29–31 ultra-high-speed Scheimpflug camera provides a dynamic visualization of the corneal deformation process with detailed information of the deformation response obtained during the NCT. A whole set of corneal deformation parameters is provided.32,33 The Oculus CorVis ST imaging system is based on the instrument we used for this study and has been the subject of many studies in the characterization of corneal biomechanical properties.34–36

In this study, we analyzed in vivo corneal biomechanical properties from corneal deformation during NCT using the prototype of the CorVis ST. The relevance of this study is related to the ability to distinguish normal and ectatic corneas, even in early stages of the disease. While the data were not enough for solely identifying clinical KC, we identified a strong potential for the data derived from corneal deformation response to integrate with tomographic data in order to enhance sensibility and also specificity.

CONCLUSION

Corneal deformation response analysis by ultrahigh-speed 8 mm horizontal Scheimpflug photography provides relevant data for distinguishing ectatic and nonectatic corneas but cannot be used independently to detect keratoconus. This data may be integrated with corneal tomography data for enhancing sensitivity and specificity for screening ectasia.

REFERENCES


