LETTER TO THE EDITOR OF CORNEA

Ectasia Detection by the Assessment of Corneal Biomechanics

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We read with interest the article from Steinberg and coworkers entitled "Screening for Keratoconus With New Dynamic Biomechanical In Vivo Scheimpflug Analyses".[1] We commend the authors for their work and also thank and applaud their scientific spirit by allowing us to further analyze the raw data from the CorVis ST (Scheimpflug Technology [CST]; OCULUS Optikgeräte GmbH; Wetzlar, Germany) of their patients.

In this study, the ability to detect corneal ectasia by CST was tested. Despite the statistically significant differences found for some of the tested parameters, the discriminant ability to detect disease was relatively poor. Also, the analyzed CST parameters failed to detect abnormalities in the cases referred as having sub-clinical disease.[1] However, we do have a few comments that should provide a positive insight into this important subject for our field.

We agree with the authors that the detection of mild forms of ectatic corneal diseases (ECD) has gained substantial relevance because these cases are at very high risk for iatrogenic progressive ectasia (keratectasia) after corneal refractive procedures.[2,3] However, in addition to Refractive Surgery, early detection and monitoring ectasia progression have become of utmost importance because of the paradigm shift that happened in the management of ECD.[4] In addition, despite the evolution of corneal shape analysis, biomechanical understanding is paramount for augmenting the sensitivity in identifying cases with mild disease and characterizing the susceptibility for ectasia progression.[5] In fact, there is a consensus that the pathophysiology of corneal ectasia is related to altered corneal biomechanics.[6] The current understanding is that a focal abnormality in corneal biomechanical properties precipitates a cycle of decompensation and leads to localized thinning and steepening, which clinically define ectasia progression.[7]

Further, we would like to offer comments on the criteria that were used in the published paper to define the studied populations and on the clinical parameters that were analyzed. In fact, these are the foremost aspects for studies involving diagnostic technologies.[8] The authors wisely used objective front surface curvature indices (KISA, paracentral inferior–superior [I–S] asymmetry and the maximum keratometry [Kmax])[9] for defining the inclusion criteria for each group. This approach avoids problems related to subjectivity and variability of classifications of topographic maps.[10] Another positive aspect of the methods was the inclusion of one eye per patient, which avoids selection bias related to the use of both eyes from the same subject.[8] Nevertheless, they did not consider corneal tomographic data and solely considered topometric (front surface) evaluation at a single time point for each patient.

In this study, 87 eyes from 87 patients with normal topography maps were compared to 65 eyes from 65 cases with clinical keratoconus. Normal topography was defined as KISA lower than 60%, I-S lower than 1.4D and Kmax lower than 47D.[1] Even though this is relatively rare, it is possible that some of these cases have mild or susceptible forms of ectasia, as there are reported cases that, despite having normal topography and central corneal thickness, progressed to keratectasia after LASIK[11,12] or PRK.[13] Considering the preoperative state of stable LASIK cases with long term follow up would provide a more robust population for the normal control group.[14,15] The study also included 42 cases considered as keratoconus suspects (KCS), defined as cases with steep (Kmax>47D) and asymmetric corneas (I-S>1.4D), but with KISA lower than 100%.[1] Interestingly, stability of LASIK in corneas with such characteristics has been reported as these eyes may be classified as non-keratoconic by segmental or layered tomographic epithelial thickness mapping.[16] The study also included 27 cases considered as subclinical keratoconus, defined as the eye with normal topography (KISA<60%, I–S<1.4 D and Kmax<47D) from patients with clinical ectasia detected in the fellow eye.[1] While these eyes were referred to as forme fruste keratoconus by Klyce,[17] and have been widely used to develop and to test advanced screening algorithms for detecting mild ectatic disease,[15,18-20] some of these cases may be true unilateral ectasia. Interestingly, while there is a consensus that true unilateral keratoconus does not exist, secondary induced ectasia caused by a pure mechanical process may occur unilaterally.[6] These concepts are in agreement with the two-hit hypothesis, which proposes an underlying genetic predisposition coupled with external environmental factors, including eye rubbing and atopy.[4] In addition, the further exclusion of cases with central corneal thickness below 500µm and above 575µm may augment the population selection bias, limiting the relevance of the results on the cases referred to as subclinical.

Interestingly, the authors noted the relevance of KISA indices for the detection of mild ectatic diseases in a previous report,[21] but they also acknowledged the limitations of such criteria for group selections as part of the discussion.[1] Other topometric metrics such as the CMLI (Cone Location and Magnitude Index) may be of interest to objectively separate normal and ectatic cases.[22] However, longitudinal data is needed to improve definition of the groups. One closer to ideal population for representing cases with mild disease or with ectasia susceptibility would be the preoperative state of cases that developed ectasia after LASIK, which is relatively challenging.[14] Considering the published study, we advise for evaluating these patients longitudinally in order to better stratify normal and ectatic corneas. In addition, future studies should consider integrating tomographic data to further improve criteria to define the groups, as to combine parameters with biomechanical analysis.[5]

Nevertheless, the main criticism for the study is related to the clinical parameters from CST that were analyzed. In vivo characterization of corneal biomechanical response during non-contact tonometry using ultra high speed (UHS) Scheimpflug imaging enables the calculation of a variety of parameters,[23] which may be influenced by age, corneal thickness, IOP and other factors.[24,25] The authors found that maximum applanation length of the inward-moving cornea (A1 length), maximum applanation length of the outward-moving cornea (A2 length), radius of the maximal inward-bended cornea (“Radius”), the deflection length at the highest concavity (HC-DL) and new dynamic analyses generated "applanation length level" (ALL) and "deflection length level" (DLL) had statistically significant differences between normals and keratoconus, but with relatively poor performances on the receiver operating characteristic (ROC) curves, having less than 80% sensitivity and specificity.[1] Ectasia detection with the CST may, however, be improved by novel image analysis and processing methods such as higher harmonics of corneal deflection above 100Hz, which provided specificity of 98%, and sensitivity of 85% in a study involving 493 eyes of healthy subjects and 279 eyes of patients with keratoconus.[26]

New parameters from CST are described in Figure 1. The inverse concave radius of curvature during the concave phase of the deformation response and the deformation amplitude ratio between the apex and at 2mm from the apex (DA Ratio 2mm) provide AUC of 0.925 and 0.9 respectively. In addition to deformation characteristics, CST data includes the horizontal 8mm Scheimpflug image, which enables the calculation of the horizontal relational thickness (ARTh- Ambrósio Relational Thickness for the Horizontal meridian), considering the pachymetric increase from the thinnest position outwards.[27] ARTh had AUC of 0.961 with 93.1% sensitivity and 92.1% specificity. Interestingly, different combination of parameters from CST enabled a separation of normal and keratoconic corneas with less than 5% of false positives and false negatives. These parameters, along with combinations with tomographic data should be tested in future studies.

Figure 1. Novel Parameters from CST

A. Radius of Curvature during concave phase of deformation. B. The inverted radius is plotted graphically over time so that the integral sum of the inverse radius may be calculated; C. Deformation Amplitude (DA) Ratio between the apex and 2mm from it; D. Graphic representation of DA Ratio and 2mm over time.

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