Discriminant Value of Custom Ocular Response Analyzer Waveform Derivatives in Forme Fruste Keratoconus

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• PURPOSE: To evaluate the performance of corneal hysteresis (CH), corneal resistance factor (CRF), 37 Ocular Response Analyzer (ORA) waveform parameters, and 15 investigator-derived ORA variables in differentiating forme fruste keratoconus (KC) from normal corneas.
• DESIGN: Case-control study.
• METHODS: Seventy-eight eyes of 78 unaffected patients and 21 topographically normal eyes of 21 forme fruste KC patients with topographically manifest KC in the contralateral eye were matched for age, the thinnest point of the cornea, central corneal thickness, and maximum keratometry. Fifteen candidate variables were derived from exported ORA signals to characterize putative indicators of biomechanical behavior, and 37 waveform parameters were tested. Differences between groups were assessed by the Mann-Whitney test. The area under the receiver operating characteristic curve (AUROC) was used to compare the diagnostic performance.
• RESULTS: Ten of 54 parameters reached significant differences between the groups (Mann-Whitney test, $P < .05$). Neither CRF nor CH differed significantly between the groups. Among the ORA waveform measurements, the best parameters were those related to the area under the first peak, p1area, and p1area1 (AUROC, 0.714 ± 0.064 and 0.721 ± 0.065, respectively). Among the investigator ORA variables, a measure incorporating the pressure-deformation relationship of the entire response cycle performed best (hysteresis loop area, AUROC, 0.694 ± 0.067).
• CONCLUSION: Waveform-derived ORA parameters, including a custom measure incorporating the pressure-deformation relationship of the entire response cycle, performed better than traditional CH and CRF parameters in differentiating forme fruste KC from normal corneas. (Am J Ophthalmol 2016;164:14–21. © 2016 by Elsevier Inc. All rights reserved.)

ECTASIA IS AN IMPORTANT COMPLICATION AFTER refractive surgery, and there is interest in the preoperative identification of patients at risk for developing this condition.[1,2] A topographic keratoconus pattern is the most important risk factor.[3] A major goal of preoperative evaluation is the detection of corneas with subclinical or early-stage keratoconus. Although clinical examination and computed corneal topography can be used to diagnose keratoconus in its clinical form, the detection of subclinical forms remains a challenge. Various terms, including keratoconus suspect and forme fruste keratoconus, have been used to describe the subclinical condition.[4]

The term "keratoconus suspect" was initially used to describe eyes at risk for developing keratoconus based on subjective impressions of topographic patterns. Videokeratography can be used to quantify the pattern of keratoconus and simplify the disease classification.[5] Using this approach, the progression of disease in keratoconus suspect eyes can be described using quantitative indices, and eyes with keratoconus can be confirmed.[6] Thus, the term keratoconus suspect can be reserved for corneas that display a topographic pattern characterized by specific quantitative indices. The term "forme fruste keratoconus" refers to topographic patterns that are insufficient to reach the threshold of keratoconus or keratoconus suspect based on computerized quantitative indices.[7]

Published studies have indicated that the corneal hysteresis (CH) value and corneal resistance factor (CRF) are lower in corneas with keratoconus and in corneas that have undergone laser in situ keratomileusis than in normal corneas.[8,9] In addition, new indices derived from the waveform signals obtained with an Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Depew, New York, USA) demonstrate the ability to distinguish keratoconus from normal corneas more accurately than the original pressure-derived parameters (CH, CRF).[10] A panel of candidate diagnostic variables using exported ORA data to characterize the temporal applanation signal intensity and the pressure features of the corneal response was also recently developed.[11]

Accepted for publication Dec 18, 2015.

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0002-9394/$36.00
http://dx.doi.org/10.1016/j.ajo.2015.12.020