Variation in the Best Fit Sphere Radius of Curvature as a Test to Detect Keratoconus Progression on a Scheimpflug-Based Corneal Tomographer

Nishant Gupta, MS, FRANZCO; Bruno L. Trindade, MD, PhD; Joobin Hooshmand, MBBS; Elsie Chan, FRANZCO

ABSTRACT

PURPOSE: To evaluate the variation in the best fit sphere radius (BFSR) of curvature on a Scheimpflug corneal tomographer as a test to detect keratoconus progression.

METHODS: In this retrospective, comparative, case-control study, two groups of eyes with stable or progressive keratoconus were identified based on keratometric, refractive, and visual acuity criteria. Two sequential scans were used to assess the variation in topometric variables. Receiver operating characteristic analysis was conducted for anterior and posterior BFSR values.

RESULTS: A total of 94 eyes of 62 patients were included in the study; 43 eyes were included in the progressive group and 51 eyes in the stable group. In the progressive group, these differences were found to be statistically significant in sequential scans for the analyzed variables: steepest axis keratometry value (K2) = 1.94 ± 1.70 D (P < .001), maximum keratometry value (Kmax) = 2.62 ± 3.08 D (P ≤ .001), apex pachymetry = 12.23 ± 13.728 µm (P ≤ .001), anterior BFSR = 0.116 ± 0.107 mm (P ≤ .001) and posterior BFSR = 0.082 ± 0.075 mm (P ≤ .001). In the stable group, changes in K2, Kmax, apex pachymetry, anterior BFSR, and posterior BFSR were not found to be statistically significant. Analysis of the area under the receiver operating characteristic curve (AUROC) showed that the best tests for discriminating between progressive and stable groups were the variation in the anterior BFSR and variation in K2 (AUROC = 0.940, 95% confidence interval [CI] = 0.884 to 0.996 and AUROC = 0.935, 95% CI = 0.881 to 0.990, respectively). Variation in the posterior BFSR had an AUROC of 0.863 with a 95% CI of 0.775 to 0.950.

CONCLUSIONS: Steepening of the BFSR of anterior and posterior surface elevation maps could be used as indices for keratoconus progression.

PATIENTS AND METHODS

This was a retrospective, comparative, case-control study of patients attending the keratoconus clinic at the Royal Victorian Eye and Ear Hospital in Melbourne, Australia, between 2013 and 2015. Inclusion criteria were a minimum follow-up period of 6 months and a reliable corneal tomographic scan over at least two consecutive visits. Tomography was performed using the Pentacam HR 6.07r29 (Oculus Optikgeräte GmbH). Scans with an “OK” quality for both anterior and posterior corneal surfaces were considered reliable. Eyes were divided into two groups: a progression group in which patients showed signs of keratectasia progression over the follow-up period and a stable group with eyes having no signs of progression. Criteria for progression were defined as either an increase of 1.00 diopter (D) or more in the maximum keratometry value (Kmax) or in the maximum keratometry value on the steepest axis (K2), an increase of 0.75 D or more of the subjective refraction cylinder, or loss of corrected distance visual acuity of one or more lines. All patients in the progressive group were treated with CXL.

Variables recorded for analysis were age, gender, subjective refraction, follow-up time, K2, Kmax, apex pachymetry (corneal thickness at the thinnest point), and anterior and posterior corneal surface BFS radius of curvature on a fixed 8-mm corneal diameter (anterior BFSR and posterior BFSR) (Figure A, available in the online version of this article). Keratoconus severity was graded by the Amsler–Krumeich criteria.7 Variables were recorded from scans performed on different visits and were compared for each eye independently, in both groups. For patients with more than two sequential scans, variation of topometric variables was calculated between the initial and most recent scan. All data in the progressive group were collected before CXL was performed.

A receiver operating characteristic (ROC) curve was used to determine the overall predictive accuracy in comparing the progressive and stable groups as described by the area under the curve for the variation of each individual parameter. This area ranges from 1 (100%), representing perfect discrimination, to 0.5 (50%), representing discrimination being no better than chance. Between that range, 0.90 to 0.99 = excellent discrimination, 0.80 to 0.89 = good, 0.70 to 0.79 = fair, 0.60 to 0.69 = poor, and 0.51 to 0.59 = very poor.8 The area under the ROC curve (AUROC) was calculated, as well as the sensitivity and specificity for each observed test value.

Normality was tested by the Shapiro–Wilk test. A paired Student’s t test was used for parametric variables and a paired Wilcoxon test for non-parametric variables. Categorical variables were compared using either the Fischer’s exact test or the Pearson chi-square test. A P value of less than .05 was considered statistically significant. Statistical analysis was performed using SPSS for Windows software (version 19.0.0; SPSS, Inc., Chicago, IL).

The study protocol was approved by The Royal Victorian Eye and Ear Hospital’s ethics committee and adhered to the tenets of the Declaration of Helsinki.

RESULTS

A total of 94 eyes from 62 patients were included in this study. Eyes were divided into two groups: a progressive group (n = 43) in which patients showed signs of progressive keratoconus over the follow-up period and a stable group (n = 51) with eyes demonstrating no signs of progression. There were 33 men and 29 women with a mean age of 23.6 years (range: 14 to 35 years). Eyes in the progressive and stable groups were similar in relation to age (stable group: 24.1 ± 5.25 years; progressive group: 23.12 ± 4.86 years; P = .352), follow-up period (stable group: 27.78 ± 22.20 months; progressive group: 22.43 ± 17.10 months; P = .249), gender distribution (P = .534), and Amsler–Krumeich grading (stable group: 32 Grade 1, 17 Grade 2, 0 Grade 3, and 2 Grade 4; progressive group: 20 Grade 1, 16 Grade 2, 3 Grade 3, and 4 Grade 4; P = .125).

Comparisons between the initial and final readings of K2, Kmax, and anterior and posterior BFSR showed no statistically significant difference in the stable group (P = .111, .132, .215, and .969, respectively). Apex pachymetry was found to be significantly thinner in the final readings in the stable group but with no clinically significant difference (3.706 ± 9.352 µm, P = .007). The following variables were significantly different between groups: K2, Kmax, apex pachymetry, anterior BFSR, and posterior BFSR (Table 1).

A decrease of 0.035 mm of the anterior BFSR provided the maximum combination of sensitivity (85%) and specificity (94%) to discriminate between progressive and control cases. Using progression of K2 to differentiate between the groups, an increase of 0.95 D provided a sensitivity of 78% and specificity of 100% (Table 2).

DISCUSSION

Corneal tomography displays corneal elevation maps in relation to a derived best-fit reference surface. This surface can be a section of a sphere, ellipsoid, or toric ellipsoid. For it to be calculated, a radius of reconstruction needs to be set. Given the prolate shape of a normal cornea, with a steeper central area and a flatter periphery, the reconstructed reference surface tends to have a larger radius of curvature as the area of reconstruction is increased. For this study, a fixed
8-mm corneal diameter zone for the reconstruction of the BFS was used.

As the ectasia progresses, the steepening of the cornea will cause the BFS to have a progressively smaller radius of curvature. We have shown that the variation of the radius of curvature of the BFS for both the anterior and posterior corneal surfaces can be used to monitor the progression of keratoconus over time. These variables had an AUROC of 0.940 (95% confidence interval [CI]: 0.884 to 0.996; \( P < .001 \)) and 0.863 (95% CI: 0.775 to 0.950; \( P < .001 \)), indicating their excellent and good performance, respectively, in discriminating between the progressive and stable groups.\(^8\) In fact, the variation in the radius of curvature of the front corneal surface BFS had the highest AUROC in our study (0.940, 95% CI: 0.884 to 0.996, \( P < .001 \)). Greater correlation of the anterior BFSR to change in K2/Kmax could be related to the fact that they are the anterior surface variables and are more likely to be correlated than posterior BFSR, which is a posterior corneal surface variable. Analysis of the ROC curve showed a cut-off value of 0.035 mm in the variation of the radius of curvature of the anterior and posterior BFS that maximized the sensitivity and specificity for each of these tests. These values yield sensitivities of 85% and 94% and specificities of 83% and 88%, respectively, for the anterior and posterior corneal surfaces.

Due to the lack of widely acceptable criteria for progression, the current classification of progressive disease is mostly done using different variables in addition to clinical judgment. The purpose of this study...
was to present two new variables that could help in the discrimination between progressive and non-progressive disease. However, comparison between these two new variables and the more traditional ones (variation in K2 and Kmax) needs to be carefully analyzed. In the current study, variation in K2 and Kmax (and increase in refractive cylinder and loss of corrected distance visual acuity) were some of the variables used to define the progressive group. That way, AUROC statistics for these two variables might be questioned and should be carefully interpreted. However, the fact that anterior BFSR progression outperformed these two variables in the AUROC analysis increases its importance in that sense.

We believe that, in addition to the commonly used indices, the variation of the anterior and posterior BFSR should be calculated in every patient with keratoconus when evaluating for disease progression or stability. Moreover, refractive treatments such as topography-guided photorefractive keratectomy and conductive keratoplasty combined with CXL have also been described to visually rehabilitate patients with keratoconus. In these cases, the evaluation of the variation of the posterior BFSR can be potentially useful because the anterior surface of the cornea is altered and can no longer reliably serve as a reference for monitoring treatment efficacy and disease progression. The variation of the anterior and posterior BFSR can also be potentially used to monitor corneal stability after CXL, although that was not investigated in the current study.

The variation of the BFSR of the anterior surface of the cornea was shown to be an excellent test for discriminating between progressive and stable keratoconic eyes. Further tests are needed to assess this test as a useful tool for monitoring the effect of CXL.

**AUTHOR CONTRIBUTIONS**

Study concept and design (NG, BLT, EC); data collection (NG, BLT, JH); analysis and interpretation of data (NG, BLT, EC); writing the manuscript (BLT, JH, EC); critical revision of the manuscript (NG, BLT, EC); statistical expertise (BLT); supervision (NG)

**REFERENCES**

Figure A. Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany) 4-Maps-Refractive screen of the (A) initial presentation and (B) follow-up of a patient with progressive keratoconus. The anterior and posterior best fit sphere radius of curvature (BFSR) are circled. The variation in the radius of curvature of the best fit sphere (BFS) from these surfaces was calculated and recorded to assess keratoconus progression.