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Letter to the Editor

Factors affecting keratoconus progression and corneal collagen cross-linking

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Keratoconus is a corneal ectasia where progression can lead to decreased visual acuity and significant morbidity. Corneal cross-linking (CXL) may halt the disease in cases of worsening keratoconus, however, there is no universal definition for disease progression¹. It is also not known what factors influence the success of CXL, although some studies report that K2 (mean keratometry on the steepest axis) greater than 54 dioptres², age between 18 and 39 years old³ and a central cone⁴ are associated with greater flattening following treatment. One factor that has not been investigated is whether the degree of pre-CXL progression affects post-CXL outcomes. It is also unclear if CXL should be offered on first presentation to individuals who have more risk factors for progression.

We performed a retrospective study on patients with progressive keratoconus who underwent CXL at the Royal Victorian Eye and Ear Hospital, Melbourne, Australia between July 2007 and February 2016. The aims of this study were to 1) investigate the preoperative factors that may influence the outcomes after CXL; 2) to determine whether the rate of pre-operative progression affects treatment outcomes; 3) examine the percentage of fellow eyes which were treated within the follow-up period. Only patients who had CXL at our institution with at least 2 pre-operative visits, and follow-up of at least 11 months after CXL were included in the study.

CXL in each patient was performed using the epithelium-off, Dresden protocol. Epithelium was removed manually with a blade or following 20% alcohol for 20 seconds. Riboflavin 0.1% (with 20% dextran) was applied topically for 30 minutes and ultraviolet A irradiation (370nm) was delivered for 30 minutes at 3mW/cm². The corneal thickness was measured every 10 minutes; if the thickness was below 400µm, hypotonic riboflavin was used until the thickness was above 400µm. Data was analysed between the baseline (visit 1) and immediate pre-operative visit (visit 2), and with the 11 month post-operative visit (visit 3).

A total of 110 patients were included in this study. The baseline characteristics shown in Table 1. Visit 1 was a mean of 8 months prior to CXL, visit 2 was two months prior to CXL, and visit 3 was a mean of 14 months after CXL.

Table 1: Patient characteristics. K1, K2 and Kmax were measured using the Pentacam (Oculus, Germany).

	Median (IQR) / N (%)
Total	110 (100%)
Age	21 (18, 26), range 11 - 53
Sex (male)	69 (63%)
Baseline parameters	
K1	47.6 (45, 51.2)
K2	53.1 (49.7, 57.1)
Kmax	60.6 (56.5, 66.8)
Thinnest corneal thickness	436 (413, 460)
Refractive sphere	1.5 (-0.5, 3)
Refractive cylinder	-4.5 (-7, -2.8)
Outcome of fellow eye during follow-up period	
Corneal Graft	9 (9%)
CXL	53 (48%)
Advanced keratoconus (unsuitable for CXL)	4 (4%)
Stable keratoconus	44 (40%)

Table 2: Changes in outcome parameters between visits.

	Visit 1-2		Visit 2-3	
	Coefficient, 95% CI	p	Coefficient, 95% CI	p
K1	1.34 (0.65, 2.04)	<0.001	0.51 (0.11, 0.90)	0.011

K2	1.96 (1.23, 2.68)	<0.001	0.40 (-0.01, 0.81)	0.054
Kmax	2.04 (0.85, 3.22)	0.001	0.36 (-0.30, 1.03)	0.284
Corneal thickness	-10.34 (-18.57, -2.10)	0.049	-13 (-18, -8)	<0.001
Sphere	0.45 (-0.65, -1.56)	0.422	0.13 (-0.53, 0.78)	0.706
Cylinder	-0.49 (-0.52, 1.50)	0.343	-0.70 (-1.29, -0.10)	0.022

Pre-operatively, there was a correlation between a younger age and greater steepening of K1 (average keratometry on the flatter axis) and K2 over the two visits prior to CXL (visits 1 and 2). There was also a moderate to strong correlation between a steeper baseline K2 and progression in K2 ($r=0.608$) and a steeper Kmax (maximum keratometry value) and progression in Kmax ($r=0.616$). Sex had no effect on K1, K2 or Kmax (Table 2).

Post-operatively, K1, K2, Kmax, corneal thickness at the thinnest point and cylinder on subjective refraction remained stable with no correlation with age, sex or rate of pre-CXL progression. Patients with a larger change in spherical error prior to surgery had a larger decrease in spherical error following CXL (interaction coefficient -0.01, 95% CI -0.02, -0.00, $p=0.010$) (Table 2).

The outcomes of the fellow eyes over the follow-up period are shown in Table 1. Forty-four (40%) of eyes had stable keratoconus in the fellow eye. Four (4%) had advanced keratoconus and were not eligible for CXL.

This retrospective study demonstrates that risk factors for pre-CXL progression are a younger age and steeper keratometry values, which is consistent with the findings of Ferdi *et al*⁶. These results are important when counselling patients regarding the risk factors for pre-CXL progression and should influence the time interval between repeat examinations to detect progressive disease. However, the rate of progression

prior to CXL did not affect the success of the treatment in halting the disease following CXL.

40% of fellow eyes in this study had stable keratoconus over the follow-up period, which suggests that routinely treating fellow eyes before documenting progression would also lead to overtreatment. Thirteen percent of patients presented with advanced keratoconus in their fellow eye where CXL was no longer suitable or where a corneal transplant indicated, suggesting that 1 in 8 patients are still presenting to our clinic late in the course of the disease.

The limitations of this study are in its retrospective design. During the follow-up period, there was a change in the ultraviolet A device during this time, and there were different operators performing the CXL and assessing the patients pre- and post-CXL. A larger sample size would be required to validate these findings.

In conclusion, we found that a younger age and steeper keratometry values are risk factors for progression of keratoconus. The rate of pre-CXL progression did not affect treatment outcomes.

REFERENCES

1. Gomes JA, Tan D, Rapuano CJ *et al*, Group of Panelists for the Global Delphi Panel of K, Ectatic D. Global consensus on keratoconus and ectatic diseases. *Cornea* 2015; **34**: 359-69.
2. Wittig-Silva C, Chan E, Islam FM, Wu T, Whiting M, Snibson GR. A randomized, controlled trial of corneal collagen cross-linking in progressive keratoconus: three-year results. *Ophthalmology* 2014; **121**: 812-21.

3. Vinciguerra R, Romano MR, Camesasca FI, *et al.* Corneal cross-linking as a treatment for keratoconus: four-year morphologic and clinical outcomes with respect to patient age. *Ophthalmology* 2013; **120**: 908-16.
4. Godefrooij DA, Boom K, Soeters N, Imhof SM, Wisse RP. Predictors for treatment outcomes after corneal crosslinking for keratoconus: a validation study. *Int Ophthalmol* 2017; **37**: 341-8.
5. Ferdi AC, Nguyen V, Gore DM, Allan BD, Rozema JJ, Watson SL. Keratoconus Natural Progression: A Systematic Review and Meta-analysis of 11 529 Eyes. *Ophthalmology* 2019; **126**: 935-45.