

Sir,
 Comment on, 'Factors affecting outcomes of corneal collagen crosslinking treatment'

We read with great interest the article by Toprak *et al*¹ regarding the evaluation of possible preoperative predictive factors influencing the outcome of cross-linking (CXL) in a group of 96 patients with progressive keratoconus (KC). The authors conclude that an older age (≥ 30 years), a worse corrected distance visual acuity (CDVA; $\leq 20/40$), and a thinner corneal pachymetry ($< 450 \mu\text{m}$) were positive predictive factors for CXL, whereas maximum K (K_{max}) did not affect the postoperative change.

Although we agree that age influences the outcome of the treatment,² our results, stratified into four subgroups (< 18 years, 18–28 years, 29–39 years, and over 40 years), demonstrated a better functional and morphological outcomes in the population between 18 and 39 years of age.

Furthermore, here we report a subset analysis of the data evaluated in *Ophthalmology*² based on preoperative curvature and thinnest corneal thickness (ThCT). In particular, the data have been stratified according to preoperative Simk1 ($< 45\text{D}$; 45–50D; $> 50\text{D}$) and ThCT ($< 400 \mu\text{m}$; 400–450 μm ; $> 450 \mu\text{m}$). Comparative analysis between curvature subgroups indicated the subgroup over 50D as the best responder with a significant

improvement in CDVA ($P < 0.05$) and in total aberration outcomes ($P < 0.05$; Figures 1a and b). Analysis based on ThCT showed a better reaction to CXL in the subgroup $< 400 \mu\text{m}$ with a significant difference in sphere change ($P < 0.05$; Figure 1c).

These results are in partial agreement with that of Greenstein *et al*,³ which showed that patients with a preoperative $K_{\text{max}} \geq 55\text{D}$ were more likely to have flattening $\geq 2\text{D}$.

Our main finding shows that eyes with progressive KC with higher curvature ($> 50\text{D}$) and low pachymetry ($< 400 \mu\text{m}$), representing more advanced cases, are more likely to have an improvement after CXL.

Moreover, we would like to comment on the reported use of the isotonic riboflavin solution.

It has been demonstrated that, in advanced KC (with thin corneas), using a standard isotonic solution, dextran, induces a decrease of thickness (CCT) that can cause endothelial damage and deep stromal opacities.⁴ To avoid these complications it is advisable to check intraoperative CCT and in case of the thickness reducing $< 400 \mu\text{m}$, use swelling solutions.²

Vetter *et al*⁵ in a recent report did not find a correlation between osmolality and CCT after riboflavin eye drop application but found an inverted correlation between dextran concentration and CCT. The authors explained that hypertonicity and hypotonicity of solutions do not have a significant effect on stromal thickness because

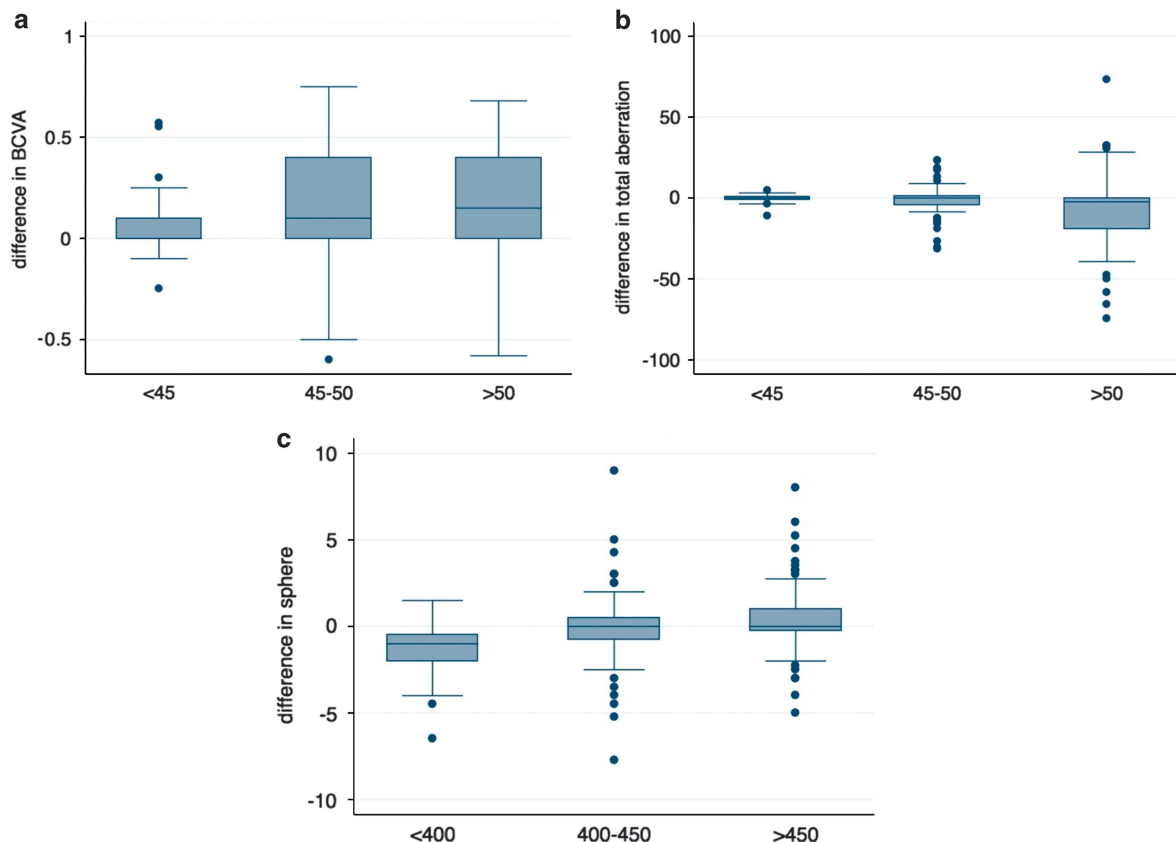


Figure 1 Box and whisker plot between follow-up and preoperative values with respect to preoperative curvature (a and b) and thickness (c). Differences divided by preoperative Simk1 for best-corrected visual acuity (BCVA) are shown in graph a, for total aberration outcomes are shown in graph b. Changes in sphere divided by preoperative pachymetry are shown in graph c.

only 2–3% of the corneal stroma volume consists of cells, conversely dextran possesses a high affinity for water because of its abundant hydrophilic hydroxyl groups leading to deswelling beyond the physiological level. For this reason we suggest to evaluate not only the osmolality of the solution but also the concentration of dextran.

In conclusion, our report confirmed the literature finding that a preoperative high keratometry is a positive predictive factor. Furthermore, our findings add that keratoconic corneas with very low pachymetry are more likely to improve. For this reason we suggest to treat advanced KC also and in case of ThCT <400 μm to use swelling solutions.

Conflict of interest

The authors declare no conflict of interest.

References

- 1 Toprak I, Yaylalı V, Yildirim C. Factors affecting outcomes of corneal collagen crosslinking treatment. *Eye (Lond)* 2014; **28**(1): 41–46.
- 2 Vinciguerra R, Romano MR, Camesasca FI, Azzolini C, Trazza S, Morengi E *et al*. Corneal cross-linking as a treatment for keratoconus: four-year morphologic and clinical outcomes with respect to patient age. *Ophthalmology* 2013; **120**(5): 908–916.
- 3 Greenstein SA, Hersh PS. Characteristics influencing outcomes of corneal collagen crosslinking for keratoconus and ectasia: implications for patient selection. *J Cataract Refract Surg* 2013; **39**(8): 1133–1140.
- 4 Vinciguerra P, Albe E, Romano MR, Sabato L, Trazza S. Stromal opacity after cross-linking. *J Refract Surg* 2012; **28**(3): 165.
- 5 Vetter JM, Brueckner S, Tubic-Grozdanis M, Vossmerbaumer U, Pfeiffer N, Kurz S. Modulation of central corneal thickness by various riboflavin eyedrop compositions in porcine corneas. *J Cataract Refract Surg* 2012; **38**(3): 525–532.

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Sir, Response to Vinciguerra *et al*

We thank Vinciguerra *et al*¹ for their interest and valuable comments on our article.² The rationale of our study was to determine the preoperative patient characteristics affecting visual and topographic outcomes of corneal collagen crosslinking (CXL) for progressive keratoconus. We found that patients with a worse preoperative corrected distance visual acuity (CDVA, $\leq 20/40$ Snellen equivalent) tend to experience more visual improvement after CXL treatment ($P < 0.001$).² However, an older age (≥ 30 years) and a thinner cornea (thinnest pachymetry <450 μm) appear to be positive preoperative predictors for more flattening in maximum keratometry ($P = 0.024$ and $P = 0.005$, respectively).² Similarly, Vinciguerra *et al*³ reported that age between 18 and 39 years has positive effect on the outcomes of CXL, and they found a significant association between the thinnest pachymetry and sphere change after CXL treatment.

Unlike the studies of Vinciguerra *et al*³ and Greenstein *et al*,⁴ our analysis showed no significant relation between initial maximum keratometry and postoperative improvement in visual acuity and maximum keratometry.² In our study, cut points were determined as 54 diopters (D) for the maximum keratometry and 450 μm for the thinnest pachymetry in accordance with the current literature and median values. A significant result could be found by shifting cut point to 58.5 D for maximum K, whereas inappropriate and unbalanced number of subjects between subgroups did not allow using this cut point in our study.

We agree with the comments of Vinciguerra *et al*¹ that intraoperative corneal thickness measurement is crucial and swelling riboflavin solutions should be used when the intraoperative minimum corneal thickness is <400 μm to prevent complications. However, in our study we excluded the eyes, which received swelling riboflavin solution during the CXL procedure.²

In conclusion, our results suggest that age, preoperative CDVA, and thinnest pachymetry seem to affect the outcomes of CXL treatment. Moreover, Vinciguerra *et al* and several studies concluded that preoperative maximum keratometry has an effect on the clinical improvement after CXL treatment.^{3–6} However, the predictive threshold values for each preoperative factor remain to be investigated.

Conflict of interest

The authors declare no conflict of interest.

References

- 1 Vinciguerra P, Romano V, Romano MR, Azzolini C, Vinciguerra R. Comment on, 'Factors affecting outcomes of corneal collagen crosslinking treatment'. *Eye (Lond)* 2014; **28**(8): 1032–1033.
- 2 Toprak I, Yaylalı V, Yildirim C. Factors affecting outcomes of corneal collagen crosslinking treatment. *Eye (Lond)* 2014; **28**(1): 41–46.