EDITORIAL

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Is there a role for prophylactic collagen crosslinking in laser *in-situ* keratomileusis?

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Laser *in-situ* keratomileusis (LASIK) is one of the most common corneal refractive procedures. It involves lifting a corneal flap, ablation of the stromal bed with excimer laser to reshape the cornea, and re-placing the flap. Although LASIK has an excellent outcome and long-term safety record, iatrogenic ectasia and regression remain a concern, as lifting a flap and ablation of tissue inevitably weaken the corneal integrity. Such complications are more common following correction of high myopia, as more corneal tissue is ablated. Particularly in Hong Kong, there is a high prevalence of high myopia. Using swept-source optical coherence tomography, fluctuation of the posterior cornea during the first year following LASIK has been reported, demonstrating a possibility of postoperative corneal instability.[1]

Corneal collagen crosslinking (CXL) uses ultraviolet A (UVA) irradiation and riboflavin to induce crosslinks within the corneal stroma to increase the tensile strength and stability of the cornea.[2] It has been approved by the U.S. Food and Drug Administration for the treatment of keratoconus, which is an ectatic disorder due to biomechanical weakening of the cornea. The success of CXL in stabilizing keratoconus has led to its prophylactic application during LASIK (LASIK-CXL) to restore corneal biomechanical strength and prevent regression and ectasia.

In our review of 11 studies of LASIK-CXL in myopic and hyperopic eyes followed up for 1 month to 4.5 years,[3] outcome measures including postoperative manifest refraction spherical equivalent and uncorrected and corrected distance visual acuity (UDVA and CDVA) were evaluated following LASIK-CXL or LASIK. Compared with LASIK, LASIK-CXL achieved better efficacy (defined as the ratio of postoperative UDVA / preoperative CDVA) with a similar safety profile (defined as the ratio of postoperative CDVA / preoperative CDVA). Manifest refraction spherical equivalent after LASIK-CXL or LASIK showed no significant difference at a median follow-up duration of 12 months. A stronger inflammatory reaction and slight transient corneal haze was noted during the early postoperative period following LASIK-CXL. Nonetheless, no permanent side effects including corneal endothelial damage, stromal scarring or unintended flattening effect on keratometry were observed. Demarcation line, which indicates the crosslinking effect, was reported below the flap interface. It was harder to re-lift the flap during LASIK enhancement, indicating a stronger adhesion between the flap and the residual stromal bed. No iatrogenic ectasia developed following LASIK-CXL or LASIK.

In addition, we reported increased variance of postoperative

spherical equivalent and sphere in highly myopic eyes from 1 week up to 6 months after LASIK-CXL, compared with LASIK.[4] Transient delay in visual rehabilitation was also observed following LASIK-CXL. The increased variability in refractive outcome during the early postoperative period following LASIK-CXL may be due to an induced change in the healing process in the eyes.

There is no consensus on the optimal CXL protocol for LASIK-CXL. Following excimer stromal ablation, riboflavin solution is applied onto the stroma for 1-2 minutes with the flap lifted up. After residual riboflavin is thoroughly washed away, the flap is returned to its original position, and UVA irradiation performed. To save time, accelerated CXL protocols are adopted to shorten the irradiation duration by increasing the irradiation intensity to 10 to 30 mW/cm^2. The corresponding irradiation duration varies from 1 to 30 minutes with a total energy dose of 1.25 to 5.4 J/cm^2. These protocols are modified from the standard Dresden protocol for treating keratoconus that uses 5 mW/cm^2 for 30 minutes, with a total dose of 5.4 J/cm^2. We compared the early corneal morphological changes between two different protocols of LASIK-CXL in contralateral eyes.[5] There was no difference in the depth of stromal demarcation line or amount of postoperative corneal haze, despite a 50% difference in the irradiation duration as well as total energy dose. Insufficient diffusion of oxygen to fuel the photochemical reaction despite additional irradiation time may explain our observation.

There is a lack of studies of LASIK-CXL with sufficient patient numbers and follow-up duration. The main indication of LASIK-CXL is eyes at risk of iatrogenic ectasia or regression in patients with thin corneas or high refractive errors. The preliminary results are reassuring regarding the safety of the procedure. Stricter patient selection criteria, more long-term results and a standardized treatment protocol are needed to support the routine use of CXL in refractive surgery. LASIK-CXL has potential to improve the outcome of LASIK by restoring the biomechanical strength of the cornea, but it is still at an infant stage of development.

References

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