• Letter to the Editor •

Transepithelial photorefractive keratectomy without mitomycin-C for irregular astigmatism after femtosecond laser-assisted *in situ* keratomileusisflap complications

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Dear Editor,

We write to present a case report of transepithelial photorefractive keratectomy (TPRK) without mitomycin-C (MMC) for irregular astigmatism after femtosecond laser-assisted *in situ* keratomileusis (FS-LASIK) flap complications. Written informed consent was obtained from the patient to allow the publication of this case and associated accompanying images. The study was conducted in accordance with the Helsinki Declaration.

TPRK is a surgical procedure which uses an excimer laser to ablation of both the corneal epithelium and stroma, which is widely used in clinic[1-2]. The procedure may be conducted in cases where there is notable topographic irregularity or scarring following complications with the LASIK flap. Corneal haze is a potential complication following TPRK, and the use of MMC as a prophylactic agent against postoperative corneal haze has been demonstrated to significantly reduce its formation after TPRK/photorefractive keratectomy (PRK). However, the application of MMC in the treatment is currently controversial[3-5]. Here we report a patient who underwent FS-LASIK surgery for myopia and occurred epithelial ingrowth (EI) after femtosecond flap failure. We managed the flap complications at first, subsequently, TPRK without MMC was performed using the SCHWIND AMARIS technique and smart pulse technology (SPT), in order to correctirregular astigmatism and myopia. The patient achieved good uncorrected visual acuity after surgery and did not exhibit any corneal haze throughout the one-year follow-up period.

A 28-year-old woman initially presented to our department with refractive errors. Her preoperative manifest refraction was: right eye (OD), -4.50/0.25×30°=1.0; left eye (OS), -4.25/0.00×170°=1.0. The central corneal thickness was 524 μm and 523 μm in the right and left eyes, respectively. The patient underwent the FS-LASIK (LDV; Ziemer, Switzerland) procedure with the diameter of 8.5 mm and the pre-set depth of the flap of 100 μm on April 5th, 2019. The surgery in the right eye was uneventful. In the left eye, however, due to the movement of the eye position, the central region of the cornea did not open, the flap could not be lifted in the first operation. A similar difficulty was encountered in the second operation using the original suction ring. Thus, further surgery was postponed to allow a more efficient and individualized approach to her treatment. This was also important to prevent several potential risks, such as haze, pressure-induced stromal keratopathy (PISK), and EI.

At the initial follow-up in approximately 4wk following the FS-LASIK procedure, an EI was observed in the patient's left eye (Figure 1A), with the best-corrected visual acuity (BCVA) of 0.4. She was managed conservatively with continuing close and frequent follow-up, which might be more appropriate given this early post-operative period and also to allow for potential modifications in the treatment protocol when necessary. However, during the further follow up at 4wk, the EI appeared more apparent with the melting flap. There was an upheaval of the corneal flap and thinning of the corneal flap edge (Figure 1B-1C). The corneal densitometry measured 58.3 through the PentacamScheimpflug Image (Oculus Optikgeräte GmbH, Wetzlar, Germany). Thus, surgical treatment for the EI was performed. This involved lifting of a flap, removal of epithelial cells from the posterior surface of the flap and the stromal bed using a blunt instrument and 40% diluted alcohol. The epithelial flap was then restored to its original place, followed by thorough irrigation with a balanced salt solution. Following the surgery, the patient was required to wear a bandage contact lens.

At the 2-week follow up after surgery, the melting flap appeared stable and the cornea was more regular compared with the initial appearance following the FS-LASIK procedure (Figure 1D). Nevertheless, given the considerable difference in the sensitivity between a normal cornea and cornea with EI undergoing TPRK, two TPRK operations without MMC were planned to correct irregular astigmatism and myopia in her left eye (-4.25/1.25×35°=0.3). About 10mo later, during the first TPRK procedure, epithelial cells were removed and the refractive error was corrected partly, with the correction of the remaining refractive error planned in the second surgery.

Through the Pentacam Scheimpflug image, it revealed that the depth of corneal scarring was the deepest at 140 μm. Also, following a full examination, we decided to change the optical zone from 6.3 to 6.7 mm with the ablation zone set at 8.25 mm to cover the flap almost completely and the ablation depth was made at 145 μm. During the procedure of cornea ablation, the opacity of corneal stroma had decreased and the cornea was getting transparent. After surgery, the patient was also required to wear a bandage contact lens. In the early post-operative follow-ups, the uncorrected distance visual acuity (UDVA) had increased to 0.5 (20/40) and the corneal epithelia had healed at 4d after TPRK surgery. At the 16-day follow-up, the UDVA had improved further to 0.8 (20/25). Three months later, the UDVA was stable at 1.0 (20/20). One year postoperatively, compared to before TPRK surgery, the corneal density had reduced from 58.3 to 15.1 and the corneal topography was more regular (Figure 2A-2B). The assessment of the anterior segment by the Pentacam had also showed the irregular astigmatism of the cornea was corrected (-1.25/0.75×38°=1.0; Figure 2C-2D). The assessment of the slit-lamp microscopy revealed that the corneal epithelium appeared clear, while some scars remained at the periphery of the cornea and no corneal haze had appeared (Figure 3). The patient was satisfied with her vision and refractive correction. Therefore, we did not proceed with the second TPRK procedure to correct the remaining refractive error.

TPRK, a non-contact and gentle laser corneal procedure, has demonstrated significant efficacy in addressing corneal flap complications resulting from LASIK, including buttonhole formation, EI, and irregular astigmatism caused by scarring or EI. However, it is important to note that there is a notable risk of developing subepithelial fibrosis known as haze subsequent to the occurrence of flap complications[3,6].

MMC, an antibiotic isolated from *Streptomyces* species, exerts its anti-fibrotic effect by impeding myofibroblast cell division through the inhibition of DNA synthesis. The application of

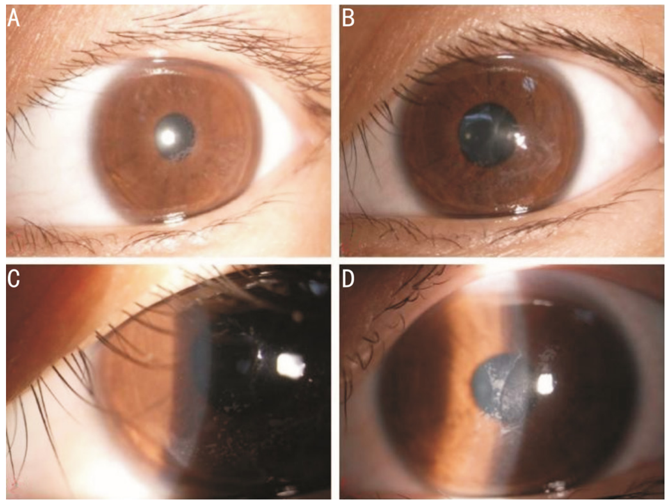

Figure 1 The anterior segment of the left eye A: The appearance of epithelial ingrowth in the patient's left eye; B: The epithelial ingrowth appeared more apparent with the melting flap; C: The corneal flap was upheaval and the edge was thinned; D: Two weeks after surgical removal of epithelial ingrowth.

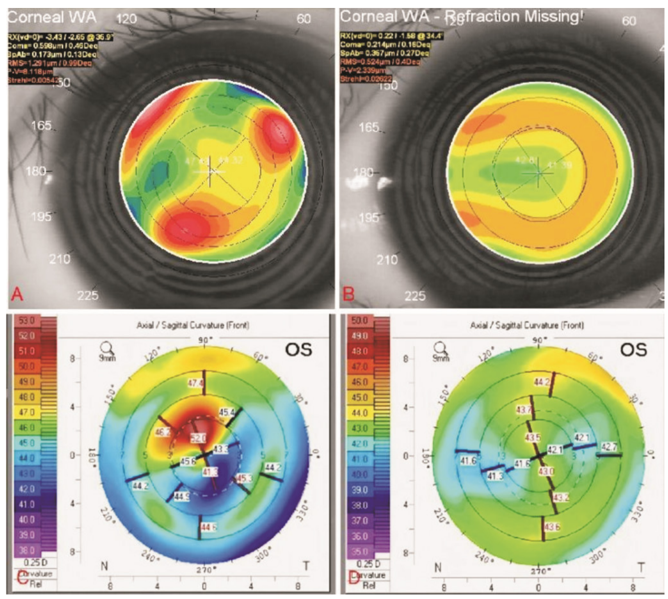

Figure 2 Corneal topography of the left eye A: Before transepithelial photorefractive keratectomy, but after the removal of epithelial ingrowth; B: One year following the transepithelial photorefractive keratectomy procedure; C: Irregular astigmatism of the cornea after removal of epithelial ingrowth; D: One year after transepithelial photorefractive keratectomy.

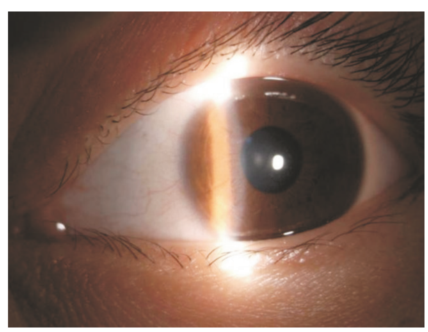

Figure 3 The anterior segment of the left eye a year after transepithelial photorefractive keratectomy.

MMC also reduced keratinocytes, abnormal collagen and extracellular matrix deposition. Due to its effectiveness in preserving corneal transparency and preventing the formation of opacity, it is currently used as a preventive agent for haze following high-risk PRK[7-8]. Several studies have demonstrated the potential of MMC in suppressing haze formation, but its application is also risky[9]. Research findings suggest that MMC may exert an impact on the cellularity of the anterior stroma, corneal nerves, and corneal endothelium. The potential cytotoxicity of MMC on the corneal endothelium has been identified *in vitro* and animal experiments, indicating that surgeons should approach its use with greater caution[10].

Currently, the use of MMC in PRK for mild myopia remains controversial. Some reports suggest that lower depth ablation is less likely to cause postoperative haze. Some scholars argue that the use of MMC in treating mild to moderate myopia may be unnecessary or that its dosage and duration could potentially be reduced[10-11]. The study conducted by Adib-Moghaddam *et al*[11] also demonstrated a higher degree of endothelial loss in patients with mild to moderate myopia who underwent TPRK with MMC compared to those who received treatment without MMC.

Furthermore, the investigation conducted by Thomas *et al*[12] revealed a noteworthy correlation between postoperative corneal haze and preoperative astigmatism. Kaiserman *et al*[13] also reported a higher risk of haze for large myopia or astigmatism correction. Adib-Moghaddam *et al*[11] proposed that a myopia exceeding 5.25 D and an astigmatism surpassing 1.50 D serve as threshold values for the induction of corneal haze.

Our case showed that TPRK without MMC was successfully used for retreatment in a post-LASIK patient with irregular astigmatism and myopia and no corneal haze had appeared. Further investigations are warranted to ascertain the safety and efficacy of TPRK without MMC in treating low to moderate myopia or low astigmatism, thereby providing valuable insights for potential clinical applications.

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