• Letter to the Editor •

Novel technique of penetrating keratoplasty in high-risk grafts with significant corneal neovascularization

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Received: 2021-10-18 Accepted: 2022-06-14

DOI:10.18240/ijo.2022.09.21

Citation: Soleimani M, Mohammadi N, Shahriari M, Karimi M, Alshaheeb A, Khalili A, Zamani MH, Cheraqpour K. Novel technique of penetrating keratoplasty in high-risk grafts with significant corneal neovascularization. *Int J Ophthalmol* 2022;15(9):1554-1556

Dear Editor,

We write to introduce a novel technique of penetrating keratoplasty (PK) with lower risk of graft rejection in high-risk grafts.

Corneal transplantation may be required in a variety of conditions such as keratoconus, pseudophakic bullous keratopathy (PBK), and corneal scars or dystrophies[1]. Anterior lamellar keratoplasty is considered an excellent option for the treatment of corneal stromal pathologies with normal endothelium. The main advantage of this method is prevention from endothelial graft rejection through preservation of the patient's endothelium. However, it is not effective in many cases such as full-thickness corneal scars or endothelial decompensation[1].

Descemet's stripping automated endothelial keratoplasty (DSAEK) and Descemet's membrane endothelial keratoplasty (DMEK) were described for the replacement of corneal endothelium in patients with endothelial problems. In comparison to PK, these methods preserved better visual outcome and lower rejection rate (5.0% for DSAEK and 1.7% for DMEK compared to 14.1% for PK)[2]. It seems recognition of donor antigens by the recipient's immune system may play a significant role in graft rejection. The collaborative corneal transplant study defined those recipients with vascularization of two or more quadrants are high-risk grafts[1].

Corneal graft rejection is the result of multiple immune reactions containing recognition of donor's histocompatibility antigens by the recipient's immune system. After the detection of foreign tissue, an immune response cascade is expected[1,3]. The most common and serious form of graft rejection is endothelial rejection. In the ocular immune processing systems, presented antigen to antigen processing cells (APCs) is transmitted to a central processing component (lymph node) *via* an afferent pathway followed by transmission of effector cells *via* an efferent pathway leading to endothelial and stromal cell damage by cytotoxic leukocytes of aqueous or limbal vessels. Several long-term studies reported that incidence of corneal graft rejection following DSAEK seems to be lower than PK[2]. Descemet graft could be associated with a stronger downregulation of the system, an immunologically deviant response known as "anterior chamber associated immune deviation" (ACAID). In ACAID, the presence of an antigen in the anterior chamber (AC) of the eye has been hypothesized to contribute to the ocular immune privilege through reduction of antigen-specific delayed hypersensitivity[1].

In our new technique, the donor is punched using routine punches. A minimal-depth punch with 0.5 mm size less than primary punch size is made by a trephine blade. After using trypan blue, a strip of Descemet's membrane (DM) is detached from the periphery of the donor. Hence, a 0.5 mm donut shape tissue is removed from the donor (Supplemental video 1). After preparing of donor in this novel manner, keratoplasty is followed by routine steps of conventional PK. Then, patients are treated with betamethasone 0.1% for eight times a day at first week that was tapered up to one drop per night indefinitely. A topical antibiotic is prescribed till healing of epithelial defect and also frequent lubrication is advised.

Four consecutive patients were included and scheduled for penetrating keratoplasty. Three patients were male and one patient was female. Preoperative (from the donor), first month and one-year central endothelial cell densities (ECDs) were measured by a non-contact specular microscope (TOPCON

SP-2000P, Topcon, Tokyo, Japan; Table 1). The underlying indication for keratoplasty was PBK and corneal scar due to previous keratitis. Corneal scars had depth of 85%-90% of corneal thickness occasionally involving DM. In this condition performing PKP was inevitable since lamellar keratoplasty was not possible. All patients had at least three quadrants of corneal neovascularization. Only one episode of graft rejection was found in one of the patients, which was managed using frequent topical steroid, one dose of sub Tenon injection of triamcinolone acetate and systemic steroid 1 mg/kg·d for 7d. All patients maintained a clear graft with an acceptable visual outcome at one-year follow-up. The mean of endothelial cell loss was 25.75% at one-year follow-up visit. Table 2 summarizes demographic data, preoperative, and visual outcome of the patients.

It has been shown that ACAID, which is a part of immune privilege contributes to corneal allograft survival. In corneal transplantation, the donor allografts are in direct contact with the AC and induce ACAID through provoking a series of immunological responses blocking normal delayed type hypersensitivity response[1,4-6]. In our method, direct contact between the host endothelium and donor is absent. Stimulation of ACAID through free endothelial edge of the donor may play a role in this situation. Several mechanisms are responsible for endothelial rejection such as presentation of donor's antigens and host-related immune response through mediator travel *via* the aqueous. Hence, it seems application of multiple strategies is required to decrease the risk of graft rejection. We believe our technique can target the first arm of rejection mechanisms (*e.g.* presentation of antigens), however it may be not so effective on the other arm (host-related immune response) and use of corticosteroids and immunosuppressive drugs can be helpful to suppress the circulating mediators. Our technique seems to induce the downregulation of hypersensitivity reactions in the anterior chamber in a manner like a DMEK (Figure 1).

It should be reminding only a peripheral rim with 0.5 mm diameter was removed from donor. Although ECD is more in the periphery, we believe enough endothelial cells remain to guarantee long-term survival of graft. As mentioned in Table 1, less than 30% endothelial cell loss was occurred in our cases at the one-year follow-up. Also, it could be mentioned

Table 1 Endothelial cell density at different time points cells/mm^2

Patient	Preoperative	First month	One-year after operation
1	2963	2624	2103
2	3141	2711	2450
3	2770	2519	2105
4	2632	2380	1895

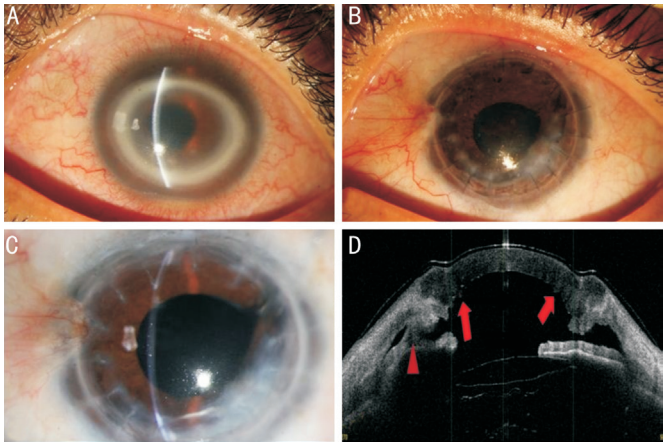

Figure 1 Preoperative and postoperative photos of one of our cases A: Pre-operative slit photo showing significant corneal opacity, haziness, and neovascularization; B: Early post-operative photo showing progression of pterygium, mild corneal edema, iris pigments on lens, and fixed sutures; C: Slit-photo of the one-year follow-up visit showing clear central cornea and pseudophakia; D: Anterior segment optical coherence tomography (AS-OCT), one week after penetrating keratoplasty, shows two demarcations (red arrows) of removed donut in the periphery of the donor and peripheral anterior synechia (arrowhead), a bandage contact lens is in place.

over 3y has been passed from the surgery of the first patient without any signs of graft failure on the neither slit-lamp examination nor specular microscopy. Moreover, although there are logically concerns regarding entering of aqueous humor into the corneal stroma from areas without endothelial cells, remained healthy endothelium can easily compensate the probable entered aqueous from the removed donor. The possibility of endothelial cell migration over the time cannot be rejected. However, this event was not occurred in our patients during 3-year period of follow-up. Further studies and longer observations are required to address this issue. We believe that our technique can be used, safe, and effective to reduce chance of endothelial rejection in patients with high-

Table 2 Descriptive data of patients underwent penetrating keratoplasty

Patient, y/sex	Underlying disease	Preoperative BCVA	Quadrants of vascularization	Rejection episode	Status of clarity at one year	Postoperative BCVA	Endothelial cell loss at one year
35/M	Corneal scar (previous keratitis)	HM	4	1	Clear	20/30	29%
47/M	Corneal scar (previous keratitis)	HM	4	0	Clear	20/30	22%
63/M	PBK	CF at 2 m	3	0	Clear	20/40	24%
76/F	PBK	HM	4	0	Clear	20/60	28%

M: Male; F: Female; PBK: Pseudophakic bullous keratopathy; BCVA: Best-corrected visual acuity; CF: Counting finger; HM: Hand motions.

risk grafts who are not suitable for lamellar keratoplasty. Future research should focus on the efficacy and safety of this technique; a randomized clinical trial comparing this method with conventional PK in high-risk patients can be useful.

ACKNOWLEDGEMENTS

Conflicts of Interest: Soleimani M, None; **Mohammadi N,** None; **Shahriari M,** None; **Karimi M,** None; **Alshaheeb A,** None; **Khalili A,** None; **Zamani MH,** None; **Cheraqpour K,** None.

REFERENCES

1 Hos D, Matthaei M, Bock F, Maruyama K, Notara M, Clahsen T, Hou YH, Le VNH, Salabarria AC, Horstmann J, Bachmann BO, Cursiefen C. Immune reactions after modern lamellar (DALK, DSAEK, DMEK) versus conventional penetrating corneal transplantation. *Prog Retin Eye Res* 2019;73:100768.

2 Tourtas T, Laaser K, Bachmann BO, Cursiefen C, Kruse FE. Descemet membrane endothelial keratoplasty versus descemet stripping automated endothelial keratoplasty. *Am J Ophthalmol* 2012;153(6):1082-1090.e2.

3 Alldredge OC, Krachmer JH. Clinical types of corneal transplant rejection. Their manifestations, frequency, preoperative correlates, and treatment. *Arch Ophthalmol* 1981;99(4):599-604.

4. Hori J, Yamaguchi T, Keino H, Hamrah P, Maruyama K. Immune privilege in corneal transplantation. *Prog Retin Eye Res* 2019;72:100758.

5 Keino H, Horie S, Sugita S. Immune privilege and eye-derived T-regulatory cells. *J Immunol Res* 2018;2018:1679197.

6 Sakowska J, Glasner P, Zieliński M, Trzonkowski P, Glasner L. Corneal allografts: factors for and against acceptance. *J Immunol Res* 2021;2021:5372090.