· Letter to the Editor ·

Combine deep lamellar endothelial keratoplasty and anterior lamellar keratoplasty with limbal allograft for severe corneal injury: a case report

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Dear Editor,

I am Dr. Yi Liu from Department of Ophthalmology, Nanjing Hospital of Chinese Medicine Affiliated to Nanjing University of Chinese Medicine, Nanjing, China. I write to present a case of severe corneal acid-burn injury and describe a novel surgery namely, deep lamellar endothelial keratoplasty (DLEK) and anterior lamellar keratoplasty (ALK) with limbal allograft (LA).

Severe ocular surface injury by chemical and thermal burns may damage or even destroy ocular surface environment, which is critical in maintaining corneal transparency, and thus gives rise to a variety of pathological changes[1-4]. Ocular surface reconstruction and keratoplasty are effective in restoring the structure and function of injured ocular surface and cornea. However, current surgical options, *e.g.* partial penetrating keratoplasty (PK) or lamellar keratoplasty alone, are insufficient in tackling the simultaneous corneal limbal stem cell deficiency (CLSCD) and corneal endothelial cell decompensation (CECD) in the scenario of chemical or thermal injury. A novel surgical technique, posterior lamellar keratoplasty, has been applied in recent years[5]. However, the technique cannot be used with ocular surface disorders with stromal scarring without endothelial damage. We proposed a new surgical concept, combination of DLEK and ALK with LA, which may also be termed allogenic dual lamellar keratoplasty (ADLK) in short, for the treatment of high risk corneal transplantation patients with both CLSCD and CECD.

A 22-year-old man with severe corneal chemical injury presented with full-thickness corneal leukoma and conjunctivalization of the right eye 19mo after an acid burn accident. The vision was only light perception and there was no ectropion, trichiasis, eyelid defects or corneal perforation. Schemer test of the eye yielded 14 mm of wet strip at 5min. Intraocular pressure (IOP) was 21.7 mm Hg by non-contact tonometer (NCT). The anterior chamber angle was open at 3 quadrants on ultrasound biomicroscopy (UBM; Humphery, USA). Ultrasonography showed no intraocular abnormality. Past medical history was two amniotic membrane transplantations and long-term auto-serum and artificial tears, with no systemic disease. All procedures adhered to the tenets of the Declaration of Helsinki and were approved by the Institutional Review Board of Zhongshan Ophthalmic Centre, Sun Yat-sen University, China. Informed consent was obtained from the enrolled patient. In light of the devastating ocular surface environment with keratinization, neovascularization in the cornea and CLSCD, a novel surgical technique, ADLK was designed for ocular reconstruction of the patient. The procedure was reported as follows.

Preparation of the Allogeneic Dual Lamellar Grafts The donor cornea (endothelial density 2808 cell/mm^2) was demarcated with a microkeratome on the sclera 2 mm posterior to the limbus. An anterior lamellar corneal graft with limbus (13 mm in diameter and 350 μm in thickness) was created *via* horizontal resection by the Microlamellar Keratoplasty System (KN-5000, Wuxi Kangning Medical Electronic Equipment Development Co., Jiangsu, China). Intracameral ophthalmic viscoelastic device (OVD) was given to protect the corneal endothelium. The remaining posterior lamella with endothelium was placed on a cutting board and was cut by a trephine into a 7.5 mm diameter (Figures 1, 2).

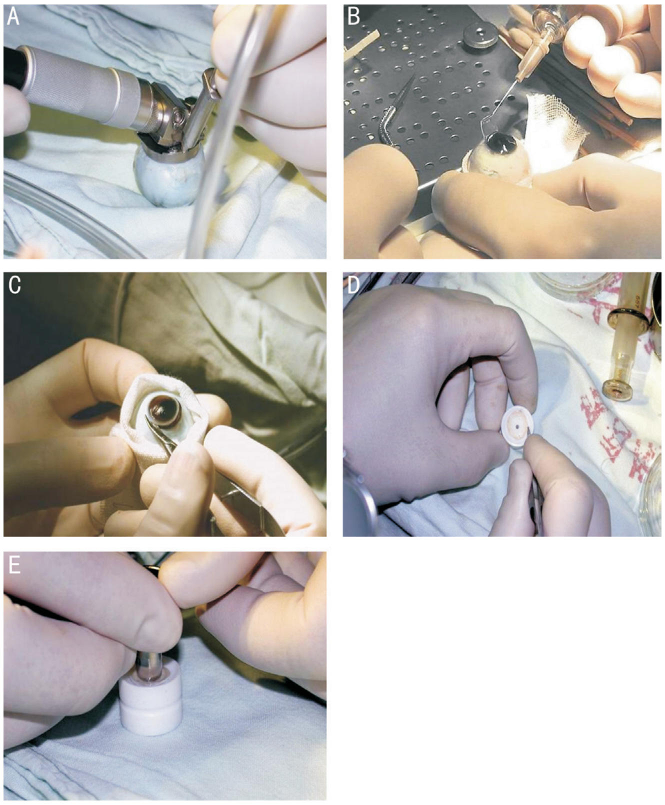

Figure 1 Preparation of allogenic dual lamellar graft A: The eye donor is fixed with the negative pressure suction device of the Microlamellar Keratoplasty System; B: Separation of the anterior lamellar corneal graft with the limbus; C: The posterior lamellar corneal graft with corneal endothelial cells; D: The posterior lamellar corneal graft is put on the corneal cutting pillow and the viscoelastic agent is injected onto the endothelium; E: The small diameter posterior lamellar corneal graft is trephined with the endothelium by the cornea trephine.

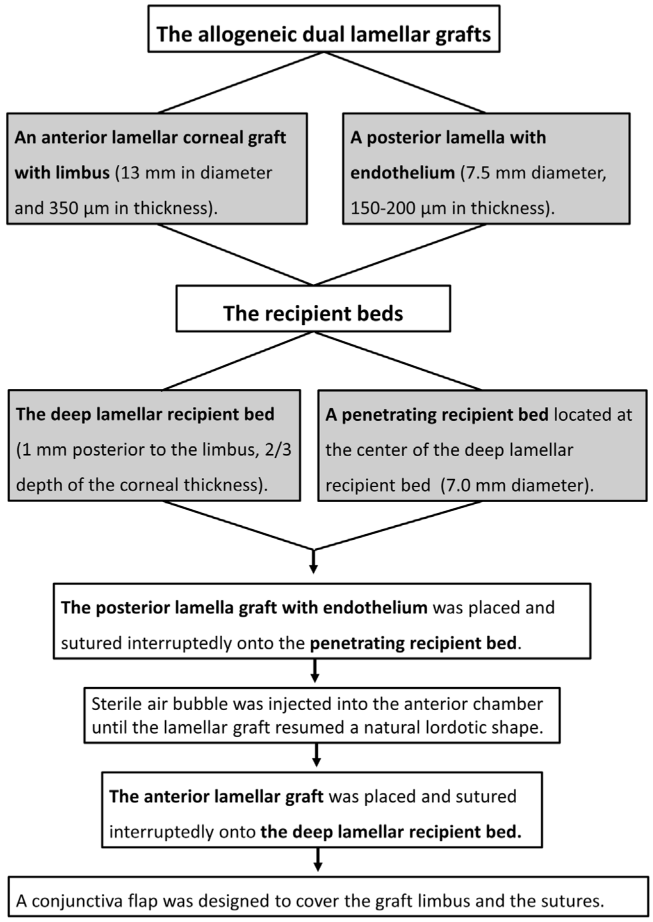

Figure 2 A diagram showing the procedure of the ADLK.

Preparation of the Recipient Beds The diseased region of cornea was demarcated by a blade at 1 mm posterior to the limbus into a depth of about 2/3 of the corneal thickness using techniques similar to conventional lamellar keratoplasty. The penetrating recipient bed was finally designed in the center with a trephine at a diameter 0.25 mm smaller than the donor button before its creation using castrovejo scissors. Great care was taken to avoid cutting through the iris and damaging the iris and lens and OVD was injected into the anterior chamber as additional protection (Figures 2, 3A-3C).

Transplantation Donor graft with endothelium was placed onto the penetrating recipient bed. Four conventional sutures were placed with 10-0 micro-suture at the 12, 6, 3 and 9 o'clock positions and additional 16 interrupted sutures were made in the four quadrants gently. Each step was carefully performed to avoid sewing through the graft. Fixing only a small amount of the stroma on the recipient bed is sufficient to secure the implant. Additional suturing might be required to keep the graft edge from folding and becoming misaligned with the anterior lamellar graft. After suturing, sterile air bubble was injected into the anterior chamber until the lamellar graft resumed a natural lordotic shape. After checking for incision leaks, the anterior lamellar graft was placed on the whole corneal recipient bed and sutured with 20 interrupted sutures with greater tension to keep the two layers of graft tightly together. Finally, a conjunctiva flap was designed to cover the graft limbus and the sutures (Figures 2, 3D-3F).

Postoperative Management Considering the high risk of acute graft rejection in our study, anti-rejection treatment based on ordinary postoperative care for PK was intensified postoperatively for 5d, including betamethasone acetate injection (10 mg/d, intravenous drip). After removal of patching in the surgical eye, 0.1% tobramycin-dexamethasone eye drops four times a day were administered for 4wk before gradually reduced to three times a day for two weeks and eventually replaced by 0.05% FK-506 eye drops four times a day with 0.02% fluorometholone eye drops (Santen, Japan) twice a day. The sutures could be selectively removed 6mo after the surgery if any suture exposure or graft neovascularization were found on the anterior lamellar graft. For the sutures on posterior graft, we suggest to keep them until self-degradation.

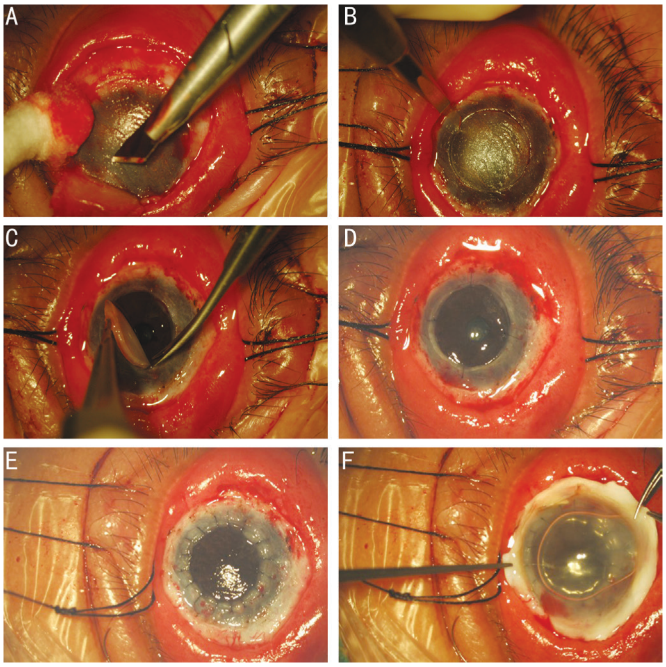

Figure 3 The process of transplantation A: The corneal tissue lesion of pseudo corneal pterygium and the corneal stroma opacity is cut to prepared for the whole corneal recipient bed; B: The ring of deep lamellar endothelial recipient bed is grooved by corneal trephined; C: The posterior lamella is cut with corneal scissors; D: The posterior lamellar graft with endothelial cells from donor is sutured at the 12, 6, 3 and 9 o'clock positions to recipient bed; E: The posterior lamellar graft is secured with interrupted sutures; F: The anterior lamellar graft is placed on the partial penetrating graft.

The patient was followed up for 12mo. Double anterior chambers between the host and donor occurred one day after surgery. We subsequently injected air bubbles into the chamber to facilitate apposition between the posterior and the anterior grafts. The additional anterior chamber disappeared with absorption of the effusion on postoperative day 7 (Figure 4). At the last 6-month follow-up, the corrected visual acuity of patient improved from 0.5 (20/40) in 3mo to 0.6 (20/32) and stabilized at 0.6 (20/32) within 12mo. IOP, corneal thickness and endothelial cell density were monitored and within normal range (Table 1). The lens appeared transparent during the 12-month follow-up period.

Existing surgical options such as total keratoplasty, PK and deep anterior lamellar keratoplasty (DALK), have all been widely used for restoration of visual acuity in severe corneal injuries. Since viable limbal stem cells are not transplanted in PK, it is difficult to rebuild healthy endothelium in recipients, which may cause corneal flap melting and failure of the surgery. Total keratoplasty, which replaces the whole cornea as well as the limbus and endothelium, suffers a 70%-80% risk of graft rejection due to excessive alloantigens from the donor graft, the inflammatory microenvironment and neovascularization of the recipient induced by chemical injury[6]. In addition,

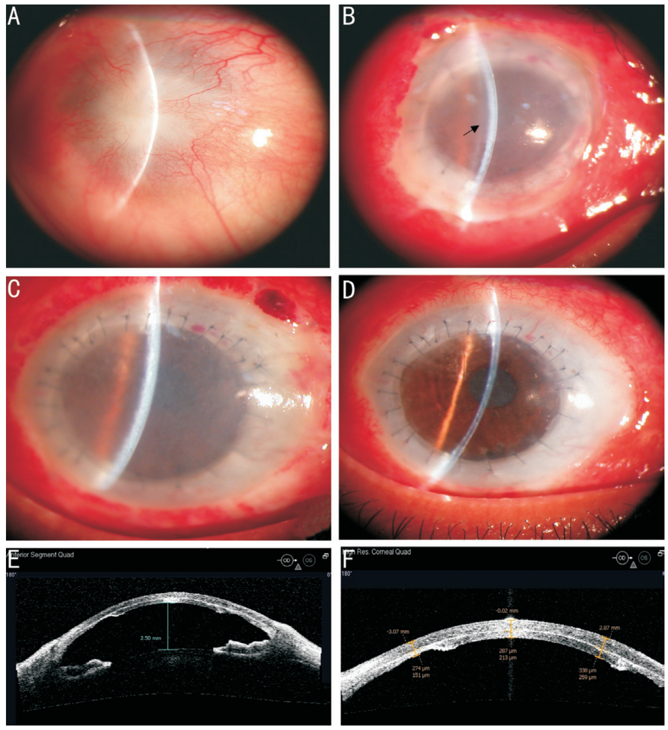

Figure 4 The gross appearance of one typical case A: Before surgery; B: One day after the operation, the anterior lamellar corneal graft edema and double anterior chamber with slit lamp; C: At 2wk, the double anterior chamber disappeared and the corneal graft edema reduced; D: At 6mo after operation, both lamellar cornel grafts gained transparency; E: Depth of anterior chamber is 2.5 mm measured through the picture from AS-OCT in 12th month; F: Thickness of center cornea is 500 μm from AS-OCT in 12th month. AS-OCT: Anterior segment optical coherence tomography.

Table 1 Clinical parameter at preoperation, 3, 6, and 12mo follow-up

Parameters	Preop.	3mo	6mo	12mo
Corrected VA (logMAR)	LP	0.5	0.6	0.6
IOP (mm Hg)	21.7	20.0	19.7	20.7
Corneal thickness (μm)	-/-	545	541	542
Endothelial density (cell/mm^2)	-/-	2568	2448	2354

VA: Visual acuity; IOP: Intraocular pressure; LP: Light perception.

complete removal of the cornea may bring about fluctuations to IOP, predispose patients to expulsive choroidal hemorrhage, or even result in enucleation or evisceration. Over the recent years, a novel surgical technique, descemets stripping automated endothelial keratoplasty (DSAEK), has been introduced, in which the anterior lamellar tissue of the cornea is preserved while the posterior lamellar tissue is replaced[7]. The main indications of this type of surgery are bullous cornea lesions and Fuchs cornea endothelial dystrophy without substantial changes in the anterior stroma. Currently, a two-step surgical strategy is being proposed that before elective PK, a modified lamellar keratoplasty has advantage for reconstruction of normal corneal limbus and stroma so as to improve vision[8-9]. However, it cannot be applied to patients with decompensated corneal endothelia. Due to corneal endothelial dysfunction, lamellar graft edema induces growth of new blood vessels into the cornea. Meanwhile, excessive water enters the subendothelial layer, causing bullous keratopathy and repeated exfoliations. Moreover, patients have to undergo two surgeries, increasing surgical risk and operative cost and greatly prolonging the treatment cycle. Therefore, it is difficult to tackle the challenges raised by simultaneous CLSCD and CECD, so called "refractory ocular surface and cornea diseases", through currently available surgical methods.

Compared with conventional keratoplasties, our surgical approach avoids additional damage to the anterior chamber angle. Reduction in the use of graft tissues means fewer antigens. The residual autologous peripheral lamellar cornea also provides physical support for donor graft to reconstruct a normal chamber depth, thereby reducing the incidence of postoperative refractory intraocular hypertension. To improve the patient's refractive status, the surface sutures were performed far from the visual axis to decrease the risk of irregular astigmatism. With limbus reconstruction, the risk of postoperative corneal endothelial dysfunction and corneal edema is minimized compared with partial PK.

During follow-up, the density of corneal endothelial cells gradually declined but is still sufficient to meet physiological needs, which may be ascribed to the damage caused by intraoperative and postoperative inflammatory reactions, as well as expansion and migration of endothelial cells from the graft into the surrounding tissues, which could also lower their density within the cornea[10]. Following the operation, the occurrence of double anterior chambers may be due to aqueous leakage into the space between the endothelial graft and the recipient bed or leakage from tissue infiltrating the surgical wound. As the edema gradually eliminated, the gap between the two grafts became smaller. At the same time, the compliance of the endothelial graft, which became "rigid" or "variant" due to suture banding, improved, forcing it to bulge outward until the two layers of graft met. As a result, the gap disappeared over time and corneal edema went down to the semi-dehydrated normal cornea within two weeks.

In short, combination of deep lamellar corneal endothelial transplantation and ALK with LA can be a good choice for full-thickness corneal injury that provides lower risk of failure and higher refractive quality in postoperative outcomes. However, its long-term effects and complications require further investigation.

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Conflicts of Interest: Liu Y, None; **Deng YQ,** None; **Yuan J,** None.

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