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Endothelial Keratoplasty Update 2020

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Abstract: Endothelial keratoplasty has revolutionized the treatment of corneal endothelial dysfunction and lowered the threshold for treatment by providing rapid visual rehabilitation and setting a high standard for safety and efficacy. Over time, endothelial keratoplasty techniques have evolved toward the use of thinner tissue to optimize visual outcomes; refinements have facilitated donor tissue preparation, handling, and attachment; and adaptations have expanded utilization in eyes with challenging ocular anatomy. Despite early concerns about graft longevity, emerging 10-year endothelial cell loss and graft survival data have been encouraging. A shortage of human donor corneas restricts utilization in many areas of the world and is driving a search for keratoplasty alternatives. Further work is needed to expand the donor supply, minimize impediments to adoption, optimize graft survival, and improve refractive predictability.

Key Words: endothelial keratoplasty, penetrating keratoplasty, Fuchs endothelial corneal dystrophy, pseudophakic/aphakic corneal edema, corneal endothelial cell density

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Endothelial keratoplasty (EK) provides rapid visual rehabilitation and is the current standard of care for treatment of corneal endothelial dysfunction. When introduced clinically by Gerrit Melles in 1998,[1] selective endothelial replacement was significantly more challenging than the previous standard, penetrating keratoplasty (PK). Subsequent EK refinements with smaller incisions and thinner grafts have produced very favorable efficacy and safety profiles that have significantly lowered the threshold for treatment. Utilization is primarily constrained by limitations in eye banking capabilities and a shortage of human donor corneas in many parts of the world.

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EK ADOPTION

The 2 EK techniques in widespread use, Descemet stripping (automated) EK (DSEK or DSAEK) and Descemet membrane EK (DMEK), differ in the amount of donor tissue implanted, which affects preparation and handling characteristics. Whereas DMEK consists of donor endothelium and Descemet membrane, DSEK also includes some posterior donor stroma.

Introduced at an eye meeting in 2003,[2] DSEK underwent rapid adoption (Fig. 1) because of the significant safety and refractive advantages it offered relative to PK, which required a much larger incision and long-standing sutures to secure the donor tissue. DSEK provided faster visual recovery and more predictable refractive outcomes, and the small incision virtually eliminated the risk of losing the eye to intraoperative suprachoroidal hemorrhage or postoperative trauma.[3] Key developments that helped spur DSEK adoption were the use of a microkeratome to facilitate and improve the quality of the donor lamellar dissection relative to hand dissection,[4] eye bank preparation of the donor tissue for the surgeon,[5] and new devices to facilitate tissue delivery into the eye.[6]

Introduced in 2006,[7] DMEK was adopted more slowly (Fig. 1) because the benefits relative to DSEK were less dramatic than the safety and visual advantages of DSEK compared with PK, and the thinner DMEK tissue was more challenging to prepare and handle than DSEK. In addition, DMEK was harder to perform in eyes with significant comorbidities.

Developments in the past decade include the movement toward the use of thinner DSEK tissue to improve visual outcomes[8,9] and technique refinements to facilitate DMEK preparation, handling, and attachment.[10,11] The net result is that DSEK procedures still substantially outnumber DMEK procedures in the United States, although the margin is narrowing as DSEK usage peaked in 2013, whereas the use of DMEK continued to grow (Fig. 1).[12]

PURSUIT OF BETTER VISION

The pursuit of better vision is a central theme running throughout the EK narrative. The impetus to adopt DMEK was initially driven by the desire to optimize visual acuity. The earliest comparative case series found that DMEK provided better and faster visual recovery than DSEK,[13] and a fellow eye comparison of DMEK and DSEK found a preference for the vision in the DMEK eye.[14]

The subsequent discovery that thinner DSEK tissue was associated with better visual outcomes prompted a movement toward the use of thinner tissue and new nomenclature (ie, ultrathin and nanothin), albeit without a consensus regarding the thickness ranges denoted.[8,9,15] In a randomized trial that

compared standard DSAEK (median thickness, 209 μm; range, 147–289 μm) with ultrathin DSAEK (UT-DSAEK; median thickness, 101 μm; range, 40–145 μm), the mean corrected distance visual acuity (CDVA) was significantly better in the ultrathin group as compared with the standard group (20/30 vs. 20/40 at 3 mo and 20/25 vs. 20/30 at 12 mo, respectively).[9]

Of course, this prompted many to wonder how UT-DSAEK would compare with DMEK in a head-to-head trial. Chamberlain et al[15] conducted a randomized comparison of DMEK and UT-DSAEK (mean thickness, 73 μm; range, 37–88 μm) and found that CDVA was 1.5 lines better with DMEK at 3 months and 1.4 lines better with DMEK at 12 months in an analysis that corrected for baseline visual acuity. A secondary analysis of the same cohort found that posterior corneal higher order aberrations decreased after DMEK but increased after UT-DSAEK and were correlated with the 6-month and 12-month CDVA ($P < 0.001$) potentially accounting for the superior visual acuity with DMEK.[16]

Longer term DSEK and DMEK studies have shown that the early rapid improvement in vision was followed by further gradual improvement over time.[9,17] Vasiliauskaitė et al[17] found that between 1 and 10 years after DMEK, the proportion of eyes with CDVA ≥20/20 increased from 49% to 64%, the proportion with CDVA ≥20/25 increased from 81% to 89%, and the proportion with CDVA ≥20/40 improved from 96% to 98% in the absence of vision-limiting ocular comorbidity.

Given these impressive CDVA outcomes, the next frontier is optimization of uncorrected distance visual acuity (UDVA). Fuchs endothelial corneal dystrophy (FECD) is the leading indication for EK in the United States and Europe, and patients with FECD often present with concurrent lens changes because of the overlapping age demographic. The most common current treatment paradigms are to stage cataract surgery before EK or combine the procedures. However, the corneal changes in FECD distort the biometry measurements used to select the optimal intraocular lens (IOL) power, making it harder to hit the refractive target and thereby optimize UDVA. For example, the median UDVA was 20/40 after DMEK combined with cataract surgery in eyes without ocular comorbidity.[18] By contrast, staging cataract surgery and implantation of a presbyopia-correcting IOL after EK had cleared the corneal edema produced excellent UDVA and CDVA (median CDVA: 20/20, range: 20/15–20/25; median binocular UDVA: 20/25, range: 20/15–20/25; and median binocular uncorrected near vision: 20/20, range: 20/20-20/50.[19]

HITTING THE REFRACTIVE TARGET

Optimization of UDVA in patients with EK requires hitting the refractive target with staged or concurrent phacoemulsification and IOL implantation. The anticipated mean hyperopic shift [0.25–0.5 diopters (D) after DMEK and 0.5–1.0 D after DSEK] is routinely factored into the IOL power calculation when EK is combined with cataract surgery (EK triple). However, the refractive outcomes vary substantially among individual patients, ranging from −2.5 to +3.5 D after a DMEK triple,[18] with even wider ranges reported after DSEK triples. This is far less precise than the results of cataract surgery alone, which can achieve emmetropia (spherical equivalent ±0.5) in more than 80% of treated eyes.[20]

Patel et al[21] have shown that tomographic characteristics are indicative of subclinical edema in FECD and predictive of progression to keratoplasty. Retrospective analyses suggest that adjustment of the IOL power based on preoperative tomographic assessment could reduce the risk of a hyperopic surprise.[22] However, subtle changes in the anterior corneal surface have a more significant effect on refraction than changes in the posterior corneal surface because of the large difference in the index of refraction between air and the cornea. To our knowledge, no algorithms have been proposed to adjust for preoperative epithelial edema or bullae, which could significantly affect the apparent cylinder and corneal power measured with biometry. The location of epithelial edema can significantly affect keratometry measurements; central edema increases central keratometry, whereas epithelial edema offset from the center can flatten the preoperative central keratometry, resulting in a postoperative myopic surprise.

Postponing cataract surgery until after DMEK has cleared the corneal edema produces much more predictable refractive outcomes (spherical equivalent refraction within ±0.75 D) as compared with a DMEK triple (spherical equivalent range −2.5 to +3.5 D),[18,19] allowing more reliable screening for presbyopia-correcting IOL candidacy and improving the refractive predictability required for satisfactory use. Likewise, the predictability of toric IOL implantation for correction of astigmatism can be improved considerably by staging cataract surgery after DMEK has cleared the corneal edema.[18,19]

MINIMIZING COMPLICATIONS

Tissue Preparation

The most important challenge initially encountered with DMEK was to avoid damaging the extremely thin (<20 μm) donor tissue while preparing it. The original peeling technique entailed scoring the peripheral Descemet membrane

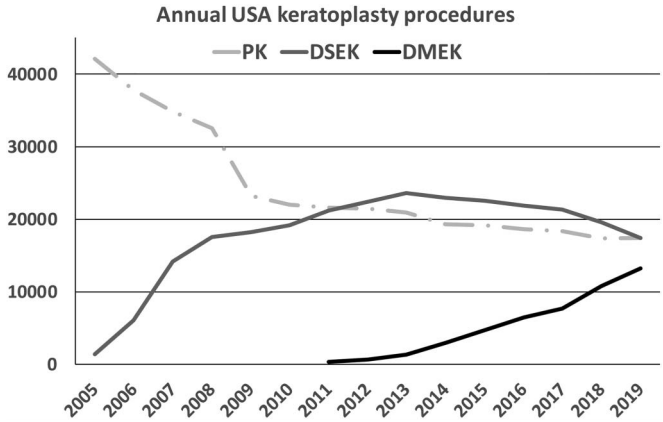

FIGURE 1. Annual domestic usage of corneas harvested by Eye Bank Association of America members for PK, DSEK, and DMEK from 2005 to 2019. DSEK and DMEK are specific for treating corneal endothelial dysfunction, whereas PK can be used to treat endothelial and/or stromal dysfunction.

and using forceps to carefully peel Descemet membrane and endothelium from the underlying stroma while the tissue was submerged in corneal storage solution.[13,23] Subsequent refinements included tactics to reduce the edge tension during peeling and techniques to recognize and rescue any tears that developed in the fragile tissue. In addition, eye banks made the crucial discovery that certain donor characteristics, especially advanced diabetes, were associated with an increased risk of tissue preparation failure and began assigning corneas from those types of donors to other types of keratoplasty procedures.[24,25]

An alternative to peeling is to inject air to produce a cleavage plane between the stroma and pre-Descemet layer forming a type 1 big bubble; this is known as pre-Descemet EK.[26] Inclusion of the pre-Descemet layer produces a somewhat thicker graft that unfolds more readily in the recipient eye. However, pneumatic dissection is potentially associated with more endothelial cell loss and higher risk of preparation failure, and the maximum graft diameter is restricted to 8 mm or less because of the pre-Descemet layer anatomy. One can also try to form peripheral type 2 bubbles creating the normal thinner graft produced with peeling techniques.

The net result is that US eye banks overwhelmingly use modified DMEK peeling techniques over pre-Descemet EK.[12] Although the rate of tissue loss in preparation was initially higher with DMEK than DSEK, this reversed over time, because improved techniques and donor selection criteria substantially reduced the risk of DMEK tissue loss, and the demand for ultrathin and nanothin tissue to improve visual outcomes increased the risk of tissue perforation with DSEK. Nevertheless, DSEK maintains an important advantage when attempting to place donors who are very young, have long-standing complicated diabetes, or are mates to corneas that failed DMEK preparation.

Orientation and Positioning

It can be challenging to discern whether DSEK or DMEK tissue is correctly oriented in the eye with the donor endothelium facing the recipient iris. DMEK orientation can be assessed with a handheld slit beam or intraoperative optical coherence tomography, knowing that the tissue naturally curls endothelium outward. Many surgeons prefer to have an orientation mark placed on the tissue, and eye banks now provide tissue that is prepeeled, precut, premarked, and preloaded inside a tissue insertion device (Fig. 2). Studies have demonstrated that eye bank-prepared/preloaded tissue matches the clinical outcomes obtained with surgeon-prepared tissue.[27]

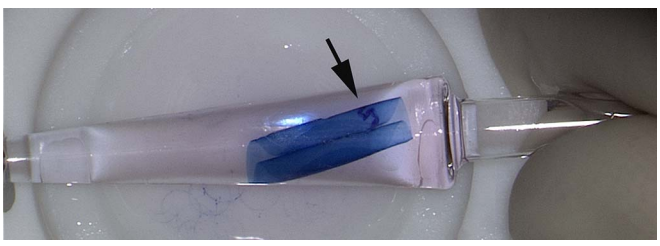

FIGURE 2. Full service: eye bank-prepared Descemet membrane EK tissue, prestained with trypan blue, prestamped with an orientation mark (indicated with an arrow), and preloaded into a glass tissue insertion device for shipment to the surgeon. The tissue is curled in a double-scroll configuration, endothelium facing outward. (The full color version of this figure is available at www.corneajrnl.com.)

DMEK tissue is typically inserted in its natural curled configuration, but it can also be folded into a trifold configuration with the endothelium facing inward.[28] The trifold can be useful in eyes with narrow angles and minimal space in the anterior chamber for tissue manipulation. Conversely, it can be helpful in eyes with a very deep anterior chamber because, after being pulled into the eye, it spontaneously unfolds and air can be immediately injected underneath to maintain the correct orientation.

Graft Detachment: Prevention and Treatment

Graft detachment is the most frequent EK complication in the early postoperative period. Strategies to promote EK attachment include careful wound construction to avoid postoperative leaks, meticulous removal of any viscoelastic from the anterior chamber, obtaining a firm air or gas fill to press the graft against the host cornea, and cautioning patients against eye rubbing in the early postoperative period.

DMEK does not adhere as readily to the retained host endothelium as DSEK,[29] so many surgeons prefer to strip the host Descemet membrane and endothelium from an area slightly larger than the planned graft diameter. Interestingly, Sorkin et al[30] found that use of a femtosecond laser to exactly match the host and donor descemetorhexis incisions significantly improved DMEK adherence, although the added time and expense could be a significant deterrent.

With DSEK, a full air fill can be maintained for as little as 5 minutes, whereas longer bubble retention facilitates DMEK adherence, so it is more common to create a peripheral iridotomy with DMEK so that the eye can remain nearly full of air at the end of the case.[13] To prevent pupillary block, the intraocular pressure (IOP) should be checked an hour or 2 later. Longer-acting gases, such as 20% sulfur hexafluoride or 10% perfluoropropane, can be used instead of air for even longer bubble retention.[11]

The postoperative graft detachment rate varies widely between studies and was 8% with DSEK in the multicenter, prospective Cornea Preservation Time Study.[31] DSEK tends to naturally adhere better than DMEK, and partial DSEK detachments will often seal down spontaneously over time, so rebubbling can be usually reserved for treating total DSEK detachment. On the other hand, it is preferable to intervene before total detachment with DMEK because fully detached DMEK tissue spontaneously curls up, requiring a return to the operating room to uncurl and reposition the tissue.

Criteria vary regarding whether and when to intervene with rebubbling. Some rebubble if more than one-third of a DMEK graft is detached, whereas others rebubble if the detachment affects the pupillary area or appears to be increasing from one examination to the next. Prompt treatment of a large DMEK detachment helps minimize

endothelial cell loss and prevent fibrosis that can limit visual acuity.[17]

Some studies have found that even a single air reinjection is associated with endothelial cell loss, whereas others have not.[32,33] The disparate findings may reflect differences in rebubbling technique because injection of multiple small bubbles may cause cavitation damage as the bubbles pop and coalesce against the endothelium, whereas careful injection of a single large bubble may not.

Balancing the Risks of Immunologic Rejection and IOP Elevation

The risk of experiencing an immunologic rejection episode is significantly lower with EK than PK, and EK rejection episodes tend to be milder and less likely to progress to graft failure than PK rejection episodes.[34] An early comparative study found that the 2-year cumulative risk of experiencing a possible or probable rejection episode was 2% with DMEK, 12% with DSEK, and 18% with PK when performed for similar indications.[34] In a 5-year study of patients treated for FECD, the rate of possible or probable immunologic rejection episodes was 2.6% with DMEK versus 7.9% with DSEK; most of the rejection episodes were mild and resolved successfully with increased topical corticosteroids, and few led to graft failure within 5 years.[35] Another 5-year study reported cumulative graft rejection rates of 1.7% with DMEK, 5% with DSEK, and 14% with PK performed for similar indications.[36] In the prospective Cornea Preservation Time Study, the cumulative 3-year probability of definite graft rejection was 3.6% with DSEK and rejection was not a leading cause of graft failure.[37]

Topical corticosteroids have long been used off label to prevent transplant rejection with no consensus regarding dosing strength and duration. Given the very low risk of rejection with DMEK, prospective, randomized studies showed that topical corticosteroid strength could be reduced as early as 1 month after DMEK (from prednisolone acetate 1% to fluorometholone 0.1% or loteprednol etabonate 0.5%), without significantly increasing the risk of immunologic rejection in a study population that was primarily White. Early reduction of steroid strength significantly reduced the risk of the main topical corticosteroid side effect, IOP elevation, from 22% to 11%.[38] Data from the Singapore Cornea Transplant Study confirmed a comparable drop in the risk of IOP elevation with early steroid reduction after DMEK as compared with the use of a standard steroid regimen after DSEK and PK.[36]

No consensus exists regarding whether or when to discontinue topical corticosteroid use after EK. A prospective DMEK study found that the risk of experiencing an immunologic rejection episode was 6% within 1 year if topical corticosteroid use was discontinued versus 0% with continued once daily use of a weak topical corticosteroid.[39]

DONOR FUNGAL CONTAMINATION

Fungal infection from contaminated donor tissue is a rare but vision-threatening complication and may be more common with EK than PK because of the potentially longer storage time and warming associated with tissue preparation and the lamellar interface.[40,41] Unfortunately, the incidence of fungal infections is increasing among hospitalized patients worldwide. Actions that can potentially reduce the risk of postkeratoplasty infection include increasing the povidone–iodine exposure time during corneal tissue recovery, careful consideration of donors who have had long-term care with infusion lines or time in intensive care units, use of antifungals in storage solutions, replacement of the storage solution after EK preparation, and culturing the donor rim at the end of surgery.[40,41] The cold storage conditions used in the United States do not allow sufficient time to culture and discard fungal-positive tissue before distribution and use, whereas the culture storage conditions used in many other parts of the world do allow this. Should an infection develop, EK can be removed and/or replaced more easily than PK.

MID-TERM TO LONG-TERM ENDOTHELIAL CELL LOSS AND GRAFT SURVIVAL

Despite early concerns that EK might suffer from poorer long-term endothelial cell loss and graft survival than PK, the longer term data so far have been reassuring. The cumulative 10-year endothelial cell loss with DSEK was similar to that with PK (71% vs. 78%, respectively) although the cell loss trends differed.[42] With DSEK, endothelial cell density declined linearly between 6 months and 10 years, whereas PK exhibited a rapid decline of 71% within the first 5 years, followed by a much slower decline thereafter. Interestingly, the median DSEK cell density at 10 years substantially exceeded the median PK cell density at 5 years, although the cumulative cell loss was equivalent (71%), because the median baseline donor cell density was higher in the DSEK cases. Therefore, 15- to 20-year follow-up will be necessary to determine whether the rate of decline slows as the median DSEK cell density falls further, as observed with PK.

Similar to DSEK, DMEK exhibits a linear decline in endothelial cell density from 6 months to 10 years. In a series of >2000 EK procedures performed for FECD at a single center, the cumulative mean endothelial cell loss was similar with DMEK and DSEK at 1 year (32% with both) through 5 years (48% vs. 47%, respectively).[35] In a separate cohort of 100 consecutive DMEK cases, the endothelial cell loss was 59% at 5 years and 68% at 10 years, similar to the 10-year cell loss reported with DSEK.[17,42]

Longer term EK survival seems to equal or exceed that of PK when performed by experienced surgeons, although the EK learning curve is undoubtedly characterized by an increased risk of early graft failure. In prospective, multicenter US clinical trials with experienced surgeons, the overall graft success rate at 3 years was 94% with DSEK versus 92% with PK for treatment of similar indications.[43]

The 5-year survival rates were 93% with both DSEK and DMEK in a single-center study of more than 2000 EK procedures performed for FECD.[35] These survival rates were similar to the 95% PK survival rate for FECD reported

25 years earlier by the same center. Interestingly, most of the EK failures happened within the first year and were associated with early technique challenges that subsequently have been addressed, for example, adherence with DMEK and unsatisfactory vision because of uneven thickness or wrinkling with DSEK. The cumulative rate of late graft failures between 1 and 5 years was only 2% with both DMEK and DSEK.[35]

Data collected prospectively in the Singapore Corneal Transplant Registry also showed excellent 5-year survival with EK as compared with poorer 5-year survival with PK.[36] The overall 5-year survival was 97% with DMEK, 96% with DSEK, and 73% with PK in patients treated for FECD, whereas in patients treated for bullous keratopathy, the 5-year survival was 65% with DSEK versus 47% with PK.

Endothelial cell loss and graft survival are more profoundly affected by the surgical technique and recipient characteristics than by donor characteristics, which are strictly regulated by the eye banks.[44] The principal recipient characteristics that influence endothelial cell loss and EK survival are the indication for grafting and prior glaucoma filtration surgery. Keratoplasty recipients with relatively functional peripheral endothelium, for example, patients with FECD, generally have a lower median rate of chronic endothelial cell loss and longer median graft survival than those with dysfunctional peripheral endothelium, for example, patients with pseudophakic or aphakic corneal edema.[42,44]

Differing rates of prior glaucoma filtration surgery in patients with FECD versus pseudophakic/aphakic corneal edema contribute to the disparity in chronic endothelial cell loss and graft survival.[45] In addition, the composition of the aqueous humor is substantially altered in eyes with a prior trabeculectomy or aqueous shunt and may no longer provide a hospitable environment for the corneal endothelium.[46] Finally, aqueous shunts that are not properly positioned can directly damage the corneal endothelium.[47]

Given the substantial perioperative decline in the donor endothelial cell density, strategies to improve donor tissue resilience could potentially enhance long-term graft survival. Cellular apoptosis is a key factor in endothelial cell loss during corneal tissue storage. Gene transfer and pharmacologic modulation approaches both have shown potential to reduce endothelial apoptosis when evaluated in corneal storage conditions, although they have not yet been evaluated clinically.[48,49]

A substantial portion of the EK perioperative cell loss may be associated with the surgical procedure itself because studies suggest that the cell loss associated with graft preparation is modest. Therefore, more effective surgical simulators and imaging methods to provide keratoplasty surgeons with immediate feedback on perioperative cell loss could potentially help surgeons further refine techniques to minimize cell loss. A study that evaluated the use of a fluorescent dye with a currently available clinical imaging system found that it provided highly sensitive feedback regarding the global endothelial cell loss after DMEK in an animal eye model; additional work is underway to adapt this technique for clinical use.[50] Another potential source of initial cell "loss" could be disparity in the counting methods used by eye banks versus methods used in clinical practice, resulting in some systematic overestimation of the preoperative baseline cell density.[51]

ADDRESSING IMPEDIMENTS TO EK ADOPTION

The safety and visual advantages of EK relative to PK have led to increasing the use of EK in eyes with anterior chamber, iris, and/or lens abnormalities; previous glaucoma filtration surgery; and previous failed PK, using technique modifications appropriate for each condition.[52] When deciding which EK technique to use, the degree of patient and ocular complexity and the extent of surgeon experience are key considerations. DMEK has well-documented visual and immune advantages, whereas DSEK tissue is easier to discern and maneuver inside the recipient eye, adheres more readily, can be suture-fixated to the host cornea, and is less likely to escape to the back of the eye.

DMEK tissue can be prepared with inexpensive instruments, making it readily adaptable anywhere in the world, whereas DSEK tissue preparation requires use of a relatively expensive microkeratome for best visual outcomes. DSEK was adopted fairly rapidly in the United States (Fig. 1), where eye banks were quick to purchase microkeratomes, validate tissue preparation processes, and provide precut tissue for the surgeons, whereas in many other countries the reimbursement systems and lack of confidence from surgeons have hindered widespread acceptance of eye bank-prepared tissue. However, a recent economic analysis conducted in Asia found that depending on the volume of transplants performed, adopting an eye bank tissue preparation strategy could be cost-effective at the regional or national level.[53]

In many parts of the world, EK adoption has been impeded by a shortage of donor tissue and lack of mentors to provide real-time support and advice. Although surgeons can attend EK training courses and watch EK surgical videos online, practice tissue is essential for honing techniques in a wet laboratory environment before operating on patients and transplant-grade backup corneas are necessary to replace any tissue that is inadvertently damaged during preparation or to treat early graft failures.

EXTENDING THE DONOR SUPPLY

Treatment of corneal blindness is currently limited by a global shortage of human donor corneas. The United States is unique in having a plentiful supply of donor corneas because it has the required combination of favorable attitudes toward donation, a clear legal framework, a well-organized eye banking system, and adequate reimbursement. The US eye banks currently export more than one-third of their transplantable corneas for international use and have partnered with eye banks in developing countries to help increase the donor supply,[12] yet there is still a significant shortfall.

Splitting a single donor cornea among multiple recipients could help extend the existing donor supply. For example, the endothelium and Descemet membrane can be used for DMEK, whereas the stromal tissue is used for deep anterior lamellar

keratoplasty.[54] The main limitation to this approach is that the need for corneal endothelial tissue far outstrips the need for corneal stromal tissue.[12]

Alternatively, the corneal endothelium and Descemet membrane could be divided among 2 to 4 DMEK recipients. Compared with standard DMEK, initial series of hemi-DMEK and quarter-DMEK were characterized by substantially higher rates of graft detachment and relatively low postoperative endothelial cell density,[55] suggesting an opportunity for further optimization and need for longer follow-up to more fully assess the long-term cost/benefit ratio.

Ex vivo expansion of donor-derived human corneal endothelial cells could allow hundreds or possibly 1000 patients to benefit from a single donor cornea. Several clinical trials are underway evaluating various approaches to using cultured human corneal endothelial cells, including a "tissue-engineered EK" trial in Singapore using tissue-engineered cells delivered on a biological carrier (personal communication Jod Mehta, June 2020) and a trial in Mexico injecting human corneal endothelial cells loaded with magnetic particles.[56] The longest-running trial used cell injection delivery and has enrolled more than 60 participants in Japan with over 5-year follow-up on the earliest cases.[57]

CONCLUSIONS AND FUTURE DIRECTIONS

EK has revolutionized the treatment of corneal endothelial dysfunction, setting a high standard for safety and efficacy. EK provides rapid visual rehabilitation, and adaptations have facilitated its use even in eyes with challenging ocular anatomy and comorbidity. Further work is needed to expand the donor supply, minimize impediments to adoption, reduce perioperative and postoperative endothelial cell loss, and improve refractive predictability.

A shortage of human donor corneas has prompted investigation into keratoplasty alternatives, including cultured human corneal endothelial cells and Descemet stripping only without implantation of donor tissue.[58,59] In addition, a deepening understanding of FECD etiology may lead to biologic or pharmacologic treatment modalities. Yet, when patients ask whether they should wait for newer options to become available, we do not advise waiting if symptomatic because EK provides such excellent outcomes.

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