Descemet's stripping with automated endothelial keratoplasty and glaucoma

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Purpose of review

Descemet's stripping with automated endothelial keratoplasty (DSAEK) has recently become the preferred surgical procedure replacing penetrating keratoplasty (PKP) for corneal endothelial disorders. However, DSAEK may also be associated with postprocedure intraocular pressure elevation and secondary glaucoma, and presents unique surgical challenges in patients with preexisting glaucoma surgeries.

Recent findings

The relatively high rate of glaucoma induction or worsening after PKP has significant implications leading to corneal graft failure and irreversible vision loss from glaucomatous optic neuropathy. In contrast, DSAEK, in addition to providing excellent visual outcomes with faster recovery, may provide advantages over PKP with lower risk of serious, vision-threatening glaucoma-related complications. Pupillary block glaucoma, steroid-induced intraocular pressure elevation, and less commonly peripheral anterior synechiae development have been reported after DSAEK. In patients with preexisting glaucoma surgical procedures (trabeculectomy or tube shunts), special attention to techniques (which continue to evolve) are required to perform DSAEK safely and effectively.

Summary

As DSAEK continues to gain popularity and advance with more studies performed, our understanding of DSAEK-associated intraocular pressure elevation and secondary glaucoma-related complications will become more complete. Current limited data suggest that DSAEK may be a suitable surgical alternative to PKP in patients with corneal endothelial disease and coexistent glaucoma with or without prior glaucoma procedures with faster recovery and good visual outcomes.

Keywords

Descemet's stripping with automated endothelial keratoplasty, Descemet's stripping with endothelial keratoplasty, glaucoma, intraocular pressure, penetrating keratoplasty

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Introduction

Human corneal transplantation was first successfully performed by Zirm in 1905 [1]. Since the first penetrating keratoplasty (PKP) was performed, there have been many changes in the technique of and indications for corneal transplantation. Fresh tissue was used until the mid-1970s when McCarey–Kaufman medium allowed for tissue to be stored for up to 4 days at 4°C. Prior to 1980, the primary indications for PKP were aphakic bullous keratopathy and regrafting [2]. During the 1980s, the number of transplants being performed doubled to 36 037 in 1990s. The leading indication for transplantation became pseudophakic bullous keratopathy related to the use of closed-loop anterior chamber intraocular lenses. Currently, the rate of PKP for pseudophakic bullous keratopathy is on the decline. In 2008, keratoconus was the single leading indication for PKP instead of pseudophakic bullous keratopathy. When bullous keratopathy and Fuchs' endothelial dystrophy are taken together, patients with endothelial dysfunction make up the largest indication for corneal transplantation.

The thought of selectively replacing diseased layers of the cornea had its origin many years ago; it was Von Hippel [3] who is credited with performing the first successful human lamellar corneal transplant in 1886. Tillett [4] later described selectively transplanting only the posterior layers of the cornea. Using a similar technique, Melles *et al.* [5–8] are credited with the re-emergence of posterior lamellar keratoplasty. Although Terry and Ousley [9,10] later modified and changed the name of the procedure, the technique of 'descemetorhexis' described by Melles *et al.* [5–8] has led to what we now call Descemet's stripping with endothelial keratoplasty (DSEK) or Descemet's stripping with automated endothelial keratoplasty (DSAEK); terms that are now used interchangeably [5–11]. From 2005 to 2008, the Eye Bank Association of America reported an increase in the number of endothelial transplants from 1429 to 17 468 [12]. During this same time period, the number of PKP decreased from 45 821 to 32 524.

Limitations of penetrating keratoplasty

The goal of PKP is to restore an optically clear anterior visual axis. Although mostly successful, the technique does have its limitations. Optimal visual recovery typically takes several months to 1 year, as astigmatism is reduced to the point wherein patients are stable enough for refractive correction. Induced astigmatism typically measures from three to six diopters [13–16]. When the residual astigmatism is irregular, the use of a rigid gas permeable lens may be required. This can be difficult to manage, particularly for patients in older age groups.

An additional limitation of PKP is the comprised strength of the healed wound, which can lead to wound dehiscence with even minor trauma. Obviously, graft dehiscence can result in disastrous consequences.

The sutures used to secure the graft frequently loosen or break during the postoperative period. Presenting as discomfort or a red eye, broken sutures can result in wound infection, suture-related infiltrates, and dehiscence.

Secondary glaucoma occurs after PKP at varying rates. Preexisting glaucoma has been reported to increase the relative risk of developing postkeratoplasty glaucoma four-fold [17]. The indication for PKP has a large impact on developing postkeratoplasty glaucoma [17–21]. Development of postkeratoplasty glaucoma is significant because it is a leading risk factor for graft failure and irreversible vision loss [22,23•].

Graft rejection and graft failure remain significant challenges to successful PKP surgery. In a landmark study [24••], the graft survival rate after 5 years in patients primarily with endothelial disease was found to be 86%. The survival rate declined significantly with preexisting glaucoma. Other risk factors, such as aphakic bullous keratopathy, vitrectomy, and smaller graft size, likely contribute to lower survival rates.

Glaucoma after penetrating keratoplasty

Postkeratoplasty glaucoma develops at varying rates but is typically within the range of 15–30% [18,19,25–28]. Development of postkeratoplasty glaucoma is significant because it is a leading risk factor for graft failure and irreversible vision loss [22,23•]. One of the main risk factors for developing glaucoma postkeratoplasty is the indication for surgery. Keratoconus is reported to have a 1% incidence of induced glaucoma, whereas the incidence rises to 29–44% in patients undergoing surgery for aphakic bullous keratopathy [19,20,26].

The mechanisms of induced glaucoma include both open and closed-angle glaucoma. Closed-angle glaucoma with the formation of peripheral anterior synechiae is by far the most commonly observed. Less commonly, open-angle glaucoma can be caused by inflammation or steroid use. Open-angle glaucoma can also occur from distortion of the angle anatomy from long or tight sutures. Corneal donor size may affect intraocular pressure (IOP) but there are limited data to support this.

Departure from penetrating keratoplasty and evolution of lamellar keratoplasty

The many forms of endothelial keratoplasty have exploded in popularity in the last several years. Melles *et al.* [5] started the recent trend in endothelial lamellar keratoplasty when they described posterior lamellar keratoplasty in 1998. Several years later, it was Terry and Ousley [9,10] who modified the technique and renamed it deep lamellar endothelial keratoplasty (DLEK). Melles *et al.* [7] described the technique of 'descemetorhexis', but it was Price and Price [29] who first published a series of patients using this technique by replacing diseased corneal endothelium with donor corneal endothelium, Descemet's membrane and a small amount of posterior stroma. Several months later, Gorovoy [11] 'automated' the procedure by using a microkeratome to cut the donor tissue, DSAEK. Now the procedure of choice for endothelial dysfunction, most authors use the terms DSEK and DSAEK interchangeably. Most recently, Melles *et al.* have [30] described transplantation of a thinner graft composed of endothelial cells and Descemet's membrane (and lacking the thin layer of donor stroma that is transplanted during DSEK). They have termed this procedure, Descemet's membrane endothelial keratoplasty (DMEK).

In its current form, there are several advantages of DSAEK over conventional PKP. Likely, the most impressive is rapid healing and early visual rehabilitation. The surgery requires few, if any, corneal sutures allowing for an astigmatically neutral procedure. Another major advantage is that the structural integrity of the recipient eye is maintained. Instead of making a circular 7–8 mm full thickness penetrating vertical incision as with PKP, DSEK utilizes a tunnel 4–6 mm incision through the cornea or sclera. If the epithelium is healthy, the ocular surface undergoes minimal disturbance during the surgery and the postoperative course. Taken together, these factors allow for rapid recovery of a good visual outcome (although not always 20/20 vision). The operation is easily performed in combination with cataract extraction.

A main limitation of DSEK, however, is the initial learning that occurs with acquiring a new skill set. Graft detachment rates, while learning the procedure, can be very high (>30%). As with PKP, there is a risk of graft rejection and failure. The risk of iatrogenic primary graft failure is much higher during the initial learning curve than with PKP, which is most likely due to direct manipulation of the graft during surgery. The rate of primary graft failure with an experienced surgeon is similar to PKP [31•]. Epithelial downgrowth can occur especially when venting slits are used. Sandwich infectious keratitis has been termed for infections in the graft–host interface. Graft and intraocular lens dislocation into the vitreous have both been reported. Finally, visual acuity is often reported to be better than 20/40, but the presence of mild interface irregularity and increased corneal thickness may preclude 20/20 vision. The DMEK procedure with its Descemet's membrane to stroma interface instead of a stroma-to-stroma interface and thinner final corneal thickness may improve visual outcomes.

Glaucoma after Descemet's stripping with endothelial keratoplasty

As DSEK is a relatively new procedure, the true incidence of glaucoma after DSEK is not clearly known. In early reports [10,11,31•,32•,33,34,35••,36••,37,38•,39••], the incidence of induced glaucoma has been reported to be from zero to 18%. Recently, Vajaranant *et al.* [39••] reported a relatively high incidence of IOP elevation after DSEK in 35% of patients with no prior glaucoma, 45% of patients with prior glaucoma, and 43% of patients with prior glaucoma with preexisting glaucoma surgery, but no adverse visual outcomes related to IOP elevation in any group. Glaucoma medications were started during the first year after DSEK in 18% of patients without preexisting glaucoma and were increased in 33% of patients with preexisting glaucoma. Although these rates appear high, only one out of 315 (0.3%) patients without preexisting glaucoma went on to need glaucoma surgery, seven of 85 (8%) patients with preexisting glaucoma needed glaucoma surgery. Lee *et al.* [35••] reported an IOP rise to greater than 30 mmHg during the first 6 months following DSEK surgery in 13 of 100 patients.

The mechanisms of glaucoma after DSEK may include development of anterior synechiae and prolonged steroid use. In the study by Vajaranant *et al.* [39••], their standard practice was to use topical steroids four times daily for 4 months unless there was an increase in IOP. They report their median IOP peaked 3 months postoperatively leading them to conclude that the mechanism of increased IOP was steroid-induced. Another mechanism of glaucoma after DSEK could be distortion of the angle leading to increased IOP. However, this seems less likely as the incision is much smaller than with traditional PKP. Inflammatory glaucoma is also possible but less likely, as a previous report [40] demonstrates a lower rate of rejection than with traditional PKP.

DSEK involves injecting air into the anterior chamber and positioning the patient supine to assist in graft attachment. The procedure typically involves an anterior chamber air fill of 10 min to an hour followed by an exchange of approximately half of the air for balanced salt solution. Although necessary, injection of the air bubble can lead to complications. If the air bubble extends beyond the inferior pupillary border when the patient is upright, pupillary block glaucoma can occur [33,35••,37,38•,41]. To avoid pupillary block, the pupil should be dilated with a longer acting medication at the conclusion of the procedure. Many surgeons evaluate the patient 1 h postoperatively in an upright position prior to discharge to confirm that the graft is attached and that the air bubble does not cover the pupil. If there is too much air or signs of pupillary block, the air can easily be removed while at the slit lamp. Some surgeons create a preoperative inferior iridotomy or intraoperative iridectomy to avoid this complication routinely or in special high-risk circumstances.

Pupillary block, although uncommon, often leads to significant complications such as graft failure and chronic glaucoma [4,33,35••,37,38•,41]. In Tillett's [4] original description of posterior lamellar keratoplasty, air was trapped behind the iris with a clear postoperative day one cornea. The iris was pushed forward against the graft creating anterior synechiae and increased IOP.

Peripheral anterior synechiae can be formed if pupillary block occurs. Peripheral anterior synechiae may also be formed if air enters the posterior chamber during the procedure and remains behind the iris while the patient remains supine. Air behind the iris pushes anteriorly which closes areas of the angle leading to peripheral anterior synechiae. Lee *et al.* [35••] described a patient of pupillary block glaucoma and six patients of air in the posterior chamber leading to iridocorneal adhesions and increased IOP. Only two of the seven patients had clear grafts 6 months after surgery; all of the others failed.

Concerns regarding Descemet's stripping with endothelial keratoplasty and glaucoma

Patients with glaucoma who have had an iridotomy are at low risk for pupillary block after DSEK. Those patients who have had a large iridectomy are at risk for passage of air through the iridectomy into the posterior chamber. In the supine position, air behind the iris produces a shallow anterior chamber mimicking positive vitreous pressure. Movement of the iris anteriorly makes instrumentation and tissue manipulation inside the anterior chamber difficult. It also may cause the iris to come into contact with the transplanted tissue. Excess manipulation and damage to the endothelium can lead to graft dislocation and primary graft failure.

Superior iridotomies and iridectomies can be particularly challenging in the setting of a unicameral eye, as air escapes from the anterior chamber into the vitreous cavity. Once air enters the vitreous space, repositioning the patient may not fully correct the situation. In these cases, Peng *et al.* [42] advocate the placement viscoelastic between the graft and the iris to block the escape of air from the anterior chamber, thereby helping to maintain the bubble in the anterior chamber.

An additional concern in patients who have previously undergone trabeculectomy or implantation of a glaucoma drainage implant is the possibility of air escaping through the trabeculectomy sclerostomy or tube [43•]. As air is injected into the anterior chamber, it may escape into the subconjunctival space. However, once equilibrium between the pressure in the subconjunctival space and anterior chamber has been reached, it should be possible to increase the IOP to the level required to achieve successful tissue attachment. As these eyes almost always have iridotomies, the DSEK surgeon can leave more air than usual at the end of procedure without risking pupillary block.

There are published reports [35••,39••,43•,44,45•,46•,47,48•] of successful DSEK in eyes with both functioning trabeculectomies and glaucoma drainage implants including an eye with two-tube implants. At the 2009 Annual Meeting of the American Association of Cataract and Refractive Surgery, there were two reports of DSAEK in eyes with prior glaucoma surgery. One series of 18 patients who underwent DSEK (nine eyes had trabeculectomies and nine eyes had tube shunts) was compared with 58 control eyes (Aldave A, Yu F, 2009 Annual Meeting of the American Association of Cataract and Refractive Surgery, unpublished data). The report found no statistical difference between the dislocation rates of the study and control eyes (22.2 vs. 24.1%, respectively). Rates of primary graft failure were also similar between the two groups; 5.6% in eyes that had undergone glaucoma surgery and 5.2% in control eyes. In two of the 18 patients, the tubes were trimmed at the time of surgery. The second series compared 19 eyes with trabeculectomies and nine with tube shunts with 431 time-matched controls (Phillips P, Terry M, Shamie N, *et al.*, 2009 Annual Meeting of the American Association of Cataract and Refractive Surgery, unpublished data). There was one case of dislocation (3.6%) and one case of decentered graft (3.6%) in the eyes that had previously undergone glaucoma surgery. There was no significant difference between the rate of dislocation or decentered grafts between the two groups. There were no cases of primary graft failure in the eyes with previous glaucoma surgery.

The length and location of glaucoma drainage implant tubes is of concern. It is possible that tube position is a contributing factor to corneal decompensation. A tube within the anterior chamber, which extends centrally into the 8–9-mm DSEK graft, should be trimmed or relocated. Alternatively, Sansanayudh *et al.* [49•] described one case of a successful DSEK procedure using a novel technique to cut the edge of the donor graft to accommodate a preexisting glaucoma tube shunt in the anterior chamber that could not be repositioned. If the tube is peripherally located or closer to the iris, the tube may be left alone. Tube placement in the posterior chamber (through the ciliary sulcus) or into the vitreous cavity should not prevent successful DSEK surgery and may provide greater protection to the endothelium. Although the optimal tube location for DSEK patients is not known, primary tube insertion into the posterior chamber may become the preferred option.

A factor to consider postoperatively is the measurement of IOP in eyes that have undergone DSAEK. The graft inserted typically has a preoperative thickness of 100–200 μm. After the cornea has cleared, most DSAEK eyes have a corneal thickness near 700 μm [11,33,50,51••,52•]. Corneal thickness typically affects the accuracy of the Goldmann applanation tonometry reading. Dynamic contour tonometry has been shown to be less dependent on corneal thickness and its shape. Two studies [51••,52•] have assessed the effect of increased corneal thickness on IOP measurements from both Goldmann and dynamic contour tonometry. These studies suggest good correlation between Goldmann applanation and dynamic contour tonometry in eyes following DSAEK surgery. It also suggests that Goldmann tonometry performed in corneas thickened after DSAEK does not provide artificially elevated measurements. Therefore, IOPs measured by Goldmann tonometry should not be corrected for a postoperative increase in corneal thickness, as this could miss a truly elevated IOP.

Finally, eyes with advanced glaucomatous damage especially with vision loss into the four central visual field points may be at particular risk. An elevation in IOP during surgery or shortly after surgery could cause loss of vision to these patients. During the surgery, it is common to raise the IOP with air to aid graft attachment. This concern may be compounded by the fact that these patients typically receive a retrobulbar block, which may also raise the IOP for a short period of time and when patients do not take regular topical glaucoma medications while the eye is patched. These perioperative concerns should be included in the perioperative discussion of the risks and benefits of the procedure.

Conclusion

In summary, DSEK is quickly becoming the standard of care for the management of corneal endothelial disorders. It allows for quick recovery of good visual outcomes with a lower complication profile when compared with traditional PKP. Although the glaucoma-related complications from DSAEK may be less frequent, less severe or both as compared with those following PKP, additional studies and longer follow-up are needed. Although the procedure may be technically more challenging in eyes that have undergone glaucoma surgery, DSAEK remains an option. As these cases continue to be performed, techniques will evolve to minimize the intraoperative difficulties induced by prior glaucoma surgery.

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