Descemet's Stripping Endothelial Keratoplasty: Safety and Outcomes

A Report by the American Academy of Ophthalmology

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Objective: To review the published literature on safety and outcomes of Descemet's stripping endothelial keratoplasty (DSEK) for the surgical treatment of endothelial diseases of the cornea.

Design: Peer-reviewed literature searches were conducted in PubMed and the Cochrane Library with the most recent search in February 2009. The searches yielded 2118 citations in English-language journals. The abstracts of these articles were reviewed and 131 articles were selected for possible clinical relevance, of which 34 were determined to be relevant to the assessment objectives.

Results: The most common complications from DSEK among reviewed reports included posterior graft dislocations (mean, 14%; range, 0%–82%), followed by endothelial graft rejection (mean, 10%; range, 0%–45%), primary graft failure (mean, 5%; range, 0%–29%), and iatrogenic glaucoma (mean, 3%; range, 0%–15%). Average endothelial cell loss as measured by specular microscopy ranged from 25% to 54%, with an average cell loss of 37% at 6 months, and from 24% to 61%, with an average cell loss of 42% at 12 months. The average best-corrected Snellen visual acuity (mean, 9 months; range, 3–21 months) ranged from 20/34 to 20/66. A review of postoperative refractive results found induced hyperopia ranging from 0.7 to 1.5 diopters (D; mean, 1.1 D), with minimal induced astigmatism ranging from −0.4 to 0.6 D and a mean refractive shift of 0.11 D. A review of graft survival found that clear grafts at 1 year ranged from 55% to 100% (mean, 94%).

Conclusions: The evidence reviewed is supportive of DSEK being a safe and effective treatment for endothelial diseases of the cornea. In terms of surgical risks, complication rates, graft survival (clarity), visual acuity, and endothelial cell loss, DSEK appears similar to penetrating keratoplasty (PK). It seems to be superior to PK in terms of earlier visual recovery, refractive stability, postoperative refractive outcomes, wound and suture-related complications, and intraoperative and late suprachoroidal hemorrhage risk. The most common complications of DSEK do not appear to be detrimental to the ultimate vision recovery in most cases. Long-term endothelial cell survival and the risk of late endothelial rejection are beyond the scope of this assessment.

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Background

Endothelial keratoplasty (EK), also referred to as *posterior lamellar keratoplasty*, is a form of corneal transplantation in which a donor posterior corneal button, including donor corneal endothelium, Descemet's membrane, and posterior corneal stroma, is used for selective replacement of diseased corneal endothelium in conditions characterized by corneal endothelial dysfunction. According to the Eye Bank of America Association 2007 Statistical Report, 85% of all grafts performed in the United States for endothelial disease were EK surgical procedures, approximating 14 159 corneal transplantation procedures in 2007.

Nomenclature in EK remains in evolution. This Ophthalmic Technology Assessment panel opted not to address method of donor tissue preparation (manual vs. automated, as detailed below) as a significant endothelial variable regarding safety and outcomes in this procedure. For the remainder of the report, the acronym DSEK is used to refer to Descemet's stripping endothelial keratoplasty, regardless of method of donor tissue preparation, and reports on either or both of these approaches are included in this analysis.

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Descemet's stripping (automated) endothelial keratoplasty (DSEK) has become the most widespread variation of EK surgery performed by corneal surgeons across the world because of the straightforward automated preparation of the donor tissue performed increasingly by eye banks, extensive DSEK educational courses and scientific meeting presentations, and a growing body of peer-reviewed DSEK literature. Descemet's stripping (automated) endothelial keratoplasty is purported to have several advantages over penetrating keratoplasty (PK), including the following: (1) it avoids an open-sky procedure; (2) there are fewer sutures, which results in minimal induced astigmatism and a smoother anterior corneal surface, and prevents suture-related graft complications; (3) it promotes better tectonic stability (a 5-mm or less beveled incision versus a longer full-thickness vertical incision with PK); (4) it allows avoidance of an anesthetic donor cornea in the early postoperative period; (5) it results in reduced graft failure from ocular surface disease; and (6) it allows an earlier return of refractive stability and good visual acuity. Descemet's stripping (automated) endothelial keratoplasty has generated successful outcomes in many patients who have endothelial disease as well as concerns for a new set of potential complications that did not exist with PK. These include dislocations from poor posterior donor–recipient adherence and donor endothelial trauma leading to earlier graft failure or increased primary graft failures. The purpose of this assessment was to address safety and outcomes in DSEK.

History

The concept of EK is not a novel idea and actually was postulated in the mid-1900s. The first successful case was published in 1956 and was described as *posterior lamellar keratoplasty*.[1] The technique involved creating an anterior lamellar corneal flap from a 180-degree incision through which access to the posterior recipient cornea was established followed by trephination. The donor tissue was inserted through the large corneal incision and was fixated to the recipient with mattress sutures, and the anterior corneal flap was closed with sutures.[1] After the 1956 report, the idea fell into relative obscurity and reappeared in animal studies later in the twentieth century.[2] After several promising laboratory and animal studies in the 1990s, posterior lamellar keratoplasty was reintroduced to the published literature in 1998 by Melles et al.[3,4] Melles et al deviated from the anterior corneal flap approach and created a corneoscleral pocket incision of 9 mm, through which they trephinated and removed the posterior cornea using air as an adjunct. After creating a similar dissection and trephination on the donor cornea of an entire globe, the posterior donor lenticule was inserted carefully through the pocket incision and was held in place with an air bubble rather than fixation sutures. Various authors have proposed a variety of alterations to this technique, and subsequent changes in nomenclature as the concept of posterior corneal replacement evolved; these include endothelial lamellar keratoplasty, endokeratoplasty, posterior corneal grafting, and microkeratome-assisted posterior keratoplasty.[5–8] After additional laboratory research, Terry[9] and Terry and Ousley[10–12] popularized and reported on deep lamellar endothelial keratoplasty, a variation of the Melles et al technique that used new instruments and hand dissection of donor tissue on an artificial anterior chamber as well as removal of recipient tissue under viscoelastic rather than air. The hand-dissection techniques described by Melles et al and Terry and Ousley were technically difficult, and many surgeons failed to produce similar results, which led to the exploration of new techniques. After the original description of removing recipient Descemet's membrane using a technique referred to as *descemetorhexis* by Melles et al,[13] Price and Price[14,15] popularized the technique in the United States, referring to the procedure as *Descemet's stripping with endothelial keratoplasty*, or DSEK. Continued modification of the procedure included abandoning challenging hand-dissected donor tissue preparations and using an automated microkeratome-assisted donor tissue dissection. This spawned the name *Descemet's stripping automated endothelial keratoplasty* (DSAEK), as described by Gorovoy.[16]

The most widely performed and reported form of EK surgery today is DSEK. The procedure involves removing the diseased host endothelium and Descemet's membrane with special instruments through a scleral tunnel, limbal, or corneal incision similar to cataract surgery. After removal of the diseased host tissue, the donor corneoscleral tissue is placed on an artificial anterior chamber, and a donor posterior cornea (endothelium, Descemet's membrane, and a portion of posterior stroma) is created by either hand dissection (DSEK) or by automated keratome (DSAEK). Most surgeons now prefer automated preparation because it significantly reduces the risk of donor perforation compared with hand dissection. Donor tissue preparation, whether manual or automated, can be performed by the surgeon in the operating room, or the tissue may be prepared by eye bank technical staff using an automated microkeratome and returned to corneal storage medium before distribution. Again, for the remainder of the report, the acronym DSEK is used to refer to Descemet's stripping endothelial keratoplasty, regardless of method of donor tissue preparation, and studies on either or both of these approaches were included in this analysis.

After the donor tissue is prepared, it is trephinated to a desired diameter, separated from the anterior lamellae, and placed in the anterior chamber using one of a variety of insertion techniques. After tissue insertion, the corneal or limbal incision typically is closed with 1 or more sutures. The tissue is positioned and centered with respect to the pupil within the anterior chamber, after which an air bubble is used to create apposition between the stromal side of the donor lenticule and the host posterior corneal stroma.

Question for Assessment

This assessment addresses the following question: Is Descemet's stripping endothelial keratoplasty effective for treatment of corneal endothelial diseases?

Table 1. Outcomes and Complications after

Author,[Ref. No.] Year	Country	Level of Evidence	Eyes (No.)	Follow-up (Mos)	Study Type
Terry et al,[113] 2009	USA	III	315	6	Retrospective comparative series
Terry et al,[112] 2009	USA	III	100	12	Retrospective comparative series
Bahar et al,[91] 2009	Canada	III	12	21 (mean)	Retrospective comparative series
O'Brien et al,[104] 2008	UK	III	89 (DSEK/DSAEK)	—	Retrospective case series
Terry et al,[111] 2008	USA	III	350	12	Retrospective comparative series
Bahar et al,[90] 2009	Canada	III	26, 37	6	Retrospective comparative series
Kobayashi et al,[99] 2008	Japan	III	14	6	Retrospective case series
Wylegala, Tarnawska,[114] 2008	Poland	III	11	19 (mean)	Retrospective case series
Busin et al,[93] 2008	Italy	III	10	12	Retrospective case series
Yoo et al,[115] 2008	USA	III	12	12	Retrospective case series
Sarnicola and Toro,[107] 2008	Italy	III	16	12	Retrospective case series
Basak,[92] 2008	India	III	75 (DSEK)	3	Retrospective series
Chen et al,[94] 2008	USA	III	100	6	Retrospective series
Bahar et al,[89] 2008	Canada	III	61 (DSEK/DSAEK)	12	Retrospective comparative series
Price et al,[88] 2008	USA	I	40	12	Randomized clinical trial
Kaiserman et al,[98] 2008	Canada	III	28 total (20 with forceps insertion)	6	Retrospective comparative series
Suh et al,[108] 2008	USA	III	118	—	Retrospective case series
Chen et al,[95] 2008	USA	III	100	—	Retrospective case series
Terry et al,[109] 2008	USA	III	80 (DSEK/DSAEK)	12	Retrospective comparative series
Terry et al,[110] 2008	USA	III	200	All ≥4	Retrospective case series
Mehta et al,[103] 2008	Singapore	III	10	6	Retrospective case series
Price and Price,[106] 2008	USA	III	263 (DSEK/DSAEK)	24	Retrospective cross-sectional case series
Koenig et al,[101] 2007	USA	III	34	6	Retrospective case series
Covert and Koenig,[96] 2007	USA	III	7	13	Retrospective case series
Covert and Koenig,[97] 2007	USA	III	21	6	Retrospective case series
Mearza et al,[102] 2007	UK	III	11 (DSEK)	12	Retrospective case series
Koenig and Covert,[100] 2007	USA	III	26	3	Retrospective case series
Gorovoy,[16] 2006	USA	III	16	12	Retrospective case series
Price and Price,[105] 2006	USA	III	330 (DSEK/DSAEK)	6	Retrospective case series
Price and Price,[15] 2006	USA	III	200 (DSEK/DSAEK)	7–20	Retrospective case series
Price and Price,[14] 2005	USA	III	50 (DSEK)	6	Retrospective case series

DSAEK = Descemet's stripping automated endothelial keratoplasty; DSEK = Descemet's stripping endothelial keratoplasty; — = no data reported.
*Tissue insertion with glide.
†Tissue insertion with forceps.
‡Two eyes underwent repeat DSAEK for decentration.

Description of Evidence

The peer-reviewed English literature was searched in June and December 2008 and February 2009 without date restrictions in PubMed and the Cochrane Library. Key words in the search were *endothelial keratoplasty*, *Descemet's stripping endothelial keratoplasty*, *DSAEK*, and *posterior lamellar keratoplasty*. The authors assessed the abstracts of the 2118 citations resulting from the electronic searches, and they selected 131 studies of possible clinical relevance to review in full text. Of these studies, 34 were determined to be relevant to the assessment objective. Publications included large case series, observational studies, and 1 randomized controlled trial with reporting on outcomes, adverse events, or complications for individuals of any country who underwent treatment with DSEK and met the inclusion criteria. Articles not included for the purpose of this review include letters, editorials, or case reports (n = 53)[17–69]; reviews (n = 4)[70–73]; and reports on histopathologic or laboratory studies (n = 14).[74–87] Case reports and small case series represent observations from an undefined population, and data often are not collected in a standardized manner. The remaining articles excluded from this review pertained to types of EK procedures other than DSEK or DSAEK. The reviewers were not masked to the publication or authors' names. Abstracts of meeting presentations were not included in the review.

The panel methodologist assigned one of the following ratings of level of evidence to each of the 34 selected studies. The rating scale is based on that developed by the British Centre for Evidence-Based Medicine. A level I rating was assigned to well-designed and well-conducted randomized clinical trials; a level II rating was assigned to well-designed case-control and cohort studies and randomized clinical trials with substantial methodological deficits; and a level III rating was assigned to case series, case reports, and poor-quality cohort and case-control studies. Of the studies reviewed, 33 met level III evidence and most commonly included retrospective case series. Among these 33 articles was the variation in size of the series, ranging from reports dealing with 7 to more than 600 procedures, and the comparative nature of some case series, which reported on different approaches to EK. One study met the criteria for level I evidence.[88]

Descemet's Stripping Endothelial Keratoplasty

Average Postoperative Best-Corrected Visual Acuity (Snellen)	Dislocation Rate	Primary Graft Failure	Iatrogenic Glaucoma	% Mean Endothelial Cell Loss
20/33; ≥20/40 (80%)	8 (3%)	1 (0.3%)	1 (0.3%)	31 (includes 173 eyes)
20/38; ≥20/40 (90%)	—	—	—	29
20/66; ≥20/40 (50%)	1 (8%)	0	0	—
≥20/40 (89%)	23 (26%)	10 (11%)	—	—
—	9 (3%)	0	0	36
20/37*; 20/42†	2 (8%)*; 7 (19%)†	0*; 1 (3%)†	3 (12%)*; 3 (8%)†	25*; 34†
≥20/40 (100%)	2 (14%)	0	0	54
20/50	3 (27%)	0	0	36
20/38	0	0	0	24
—	1 (8%)	0	1 (8%)	—
≥20/40 (38%)	1 (6%)	0	0	30
≥20/60 (82.7%)	6 (8%)	1 (1%)	2 (3%)	27
20/38 with ≥20/40 (81%)	3 (3%)	0	—	—
20/44	9 (15%)	1 (2%)	5 (8%)	40
≥20/40 (80%)	4 (10%)	0	0	34
20/40 (suture-assisted); 20/36 (forceps)	1 (12.5%); 2 (10%)	1 (12.5%); 0	0; 3 (15%)	39; 38
—	27 (23%)	21 (17%)	2 (2%)	—
—	1 (1%)	0	0	—
—	4 (5%)	0 but 6 late rejections	0	35
—	3 (1.5%)	0‡	0	—
20/48	0	0	0	25
—	17 (6.5%)	—	—	34 (6 mos); 41 (24 mos in 34 eyes)
20/42	9 (26.5%)	3 (9%)	—	50
20/65	2 (29%)	2 (29%)	0	57
20/34	3 (14%)	3 (14%)	2 (9.5%)	—
≥20/40 (65%)	9 (82%)	1 (11%)	—	61
20/45	9 (35%)	3 (11.5%)	1 (4%)	—
20/54	4 (25%)	1 (6%)	0	40
≥20/40 (69%)	26 (8%)	7 (2%)	—	—
≥20/40 (62%)	24 (12%)	7 (3.5%)	1 (0.5%)	—
20/50; ≥20/40 (62%)	—	3 (6%)	—	—

Published Results

Table 1 lists the most common adverse events cited in the various retrospective and prospective studies that discuss DSEK outcomes.[14–16,88–115] The most common adverse events include dislocation of posterior donor corneal grafts, endothelial rejection, primary graft failure, and iatrogenic glaucoma from either air bubble-induced pupillary block or steroid-induced intraocular pressure elevation. The average endothelial cell losses are presented within Table 1 as well. Anecdotal reports of additional rare complications include epithelial downgrowth, interface abnormalities, dislocation of the posterior lenticule or intraocular lens into the vitreous cavity, retinal complications including cystoid macular edema and limited choroidal hemorrhage, and late traumatic wound dehiscence.[38,40,61,62,69,82,108]

Table 2 lists the reports of large case series outlining the rate of endothelial graft rejection.[88–92,96,97,100–102,106,108,109,114,116,117] This table excludes cases of primary graft failure. Few reports discuss endothelial graft rejection, likely because most DSEK case series lack long-term follow-up results because of the procedure's limited history. Most endothelial graft rejection cases were treated effectively with topical or oral immunosuppression, or both. Graft failure after endothelial rejection led to a repeat DSEK or, in rare instances, to a conversion to PK.

Table 3 shows the refractive results after DSEK cases obtained from 18 studies, which discuss spherical equivalent and astigmatism results and postoperative changes in refractive astigmatism after DSEK.[14,16,88–90,92–94,97,99–102,105,113–115,118] All studies that included data on spherical equivalent changes showed a hyperopic shift after DSEK ranging from 0.7 to 1.5 diopters (D), with a mean hyperopic shift of 1.1 D.[88,97,100,101,105,115] Postoperative change in refractive cylinder ranged from −0.4 to 0.6 D, with a mean refractive shift of 0.11 D. This demonstrates that DSEK is a relatively astigmatism-neutral surgery, as would be expected from the cataractlike incision.

Table 4 describes the mean endothelial cell loss in published series of 11 eyes or more after both PK and DSEK.[16,89,90,99,101,102,106,109,111–113,119–125] Mean percent endothelial cell loss in PK ranged from 11% to 29% at 2 to 6 months, 16% to 45% at 12 months, and 29% to 54% at 24 months. Mean percent endothelial cell loss in DSEK reports of 11 or more eyes ranged from 25% to 54% at 6 months

Table 2. Endothelial Graft Rejection in Descemet's Stripping Endothelial Keratoplasty and Descemet's Stripping Automated Endothelial Keratoplasty Cases

Author,[Ref. No.] Year	Eyes (No.)	Follow-up (mos)	Graft Rejection
Jordan et al,[117] 2009	598	—	54 (9%)
Bahar et al,[90] 2009	63	6	2 (3%)
Bahar et al,[91] 2009	12	21	1 (8%)
Wylegala and Tarnawska,[114] 2008	11	19.3	1 (9%)
Basak,[92] 2008	75	3	1 (1%)
Bahar et al,[89] 2008	16	12	1 (2%)
Price et al,[88] 2008	40	12	2 (5%)
Suh et al,[108] 2008	118	—	7 (6%)
Terry et al,[109] 2008	80	12	6 (7.5%)
Allan et al,[116] 2007	199	24	15 (7.5%)
Price and Price,[106] 2008	263; 34*	24	2 (6%)†
Covert and Koenig,[96] 2007	7	13.3	1 (14%)
Koenig et al,[101] 2007	34	6	6 (18%)
Covert and Koenig,[97] 2007	21	6	3 (14%)
Mearza et al,[102] 2007	11	12	5 (45.5%)
Koenig and Covert,[100] 2007	26	3	3 (11.5%)

— = no data reported.
Table excludes iatrogenic primary graft failure cases and 18 studies with no rejections reported.
*Subset of patients for longitudinal analysis over 2 years.
†Rejection rates only reported for subset of 34 eyes followed up out to 2 years.

and 29% to 61% at 12 months, and 1 study reported 41% cell loss at 24 months.

Table 5 describes graft clarity in DSEK cases at 12 months or more.[16,88–90,93,96,102,106,107,109,111,114,115] Follow-up ranged from 12 to 24 months, with clear grafts ranging from 55% to 100%.

Posterior Graft Dislocation

Dislocation rates were reported in nearly all (29 of 34) publications included in this review. A dislocation represents lack of adherence of the donor posterior lenticule to the recipient stroma, and it is typically evident within the initial week, although reports of late dislocations exist.[21,30] Dislocations may represent either fluid in the interface of an otherwise well-positioned graft or complete dislocation into the anterior chamber. Dislocation rates varied from 0% to 82%, with an average dislocation rate of 14.5%; 8 studies reported dislocation rates of 5% or less and 8 studies reported dislocation rates of 20% or more.[15,16,88–111,113–115] Sample size was small and limiting in some of the reports, yet dislocations remained the most common complication of DSEK. In addition, average dislocation rates may be skewed falsely because 1 group authored multiple publications reporting on dislocation rates that were the lowest of all studies reviewed. Exclusion of these studies increased the average dislocation rate.[94,95,109–111,113]

Endothelial Rejection

Endothelial rejection develops in grafts that previously were clear after DSEK surgery, unlike primary graft failure. They represent the host's immunologic reaction directed against the foreign antigen of the donor corneal tissue. Sixteen of the 34 studies reported cases of endothelial rejection, as shown in Table 2.[88–92,96,97,100–102,106,108,109,114,116,117] The remaining 18 studies did not report any cases of endothelial rejection. Rejection rates varied from 0% to 45.5%, with an average rejection rate of 10% among reviewed studies with follow-up ranging from 3 to 24 months. Most cases were reversed with topical or oral immunosuppression, with some cases progressing to graft failure. Underreporting of endothelial rejection may occur because not all studies reporting rejection rates had 100% follow-up from the initial patient study numbers and no studies followed up patients beyond 24 months.

Primary Graft Failure

Primary graft failure deserves special mention because as a term, it is used by corneal surgeons and the eye banking community to characterize the clinical situation in which a corneal graft does not clear as expected after surgery. Corneal grafts that have not cleared after 2 months are classified as primary graft failures. Primary graft failures do not represent a rejection, but rather a lack of endothelial function from unhealthy tissue, unhealthy recipient circumstances (blood, interface foreign bodies, infection, flat chamber), or surgical technique. Primary graft failure in DSEK also can occur because of primary donor endothelial failure, but it more often is considered because of excessive endothelial cell trauma and subsequent damage during the surgical procedure. Poor surgical technique has been linked to primary graft failure in DSEK, with surgeon inexperience and related excessive iatrogenic intraoperative donor endothelial trauma as a main factor. In fact, some studies in this assessment refer to this entity as iatrogenic primary graft failure.[23,64,95,109,110] The published studies showed rates from 0% to 29%, with an average primary graft failure rate of 5%.[14–16,88–105,107–111,113–115] Fifteen studies found no primary graft failures, whereas 9 studies found rates of less than 10%.[14–16,88–95,98,99,101,103,105,107,109–111,113–115]

Iatrogenic Glaucoma

Glaucoma after DSEK occurred by 2 mechanisms. The first mechanism involved a pupil block induced from the air bubble in the immediate postoperative period. The air bubble prevented flow of aqueous into the anterior chamber and created obstruction of the trabecular meshwork similar to acute angle-closure glaucoma. The second mechanism was delayed glaucoma induced by topical corticosteroids. Published reports in this review included an iatrogenic rate of glaucoma from 0% to 15%, with an average of 3%.[15,16,88–93,95–100,103,107–111,113–115] Fourteen studies had no cases of iatrogenic glaucoma.[16,88,91,93,95,96,98,99,103,107,109–111,114] Management of the glaucomatous cases involved topical or oral intraocular pressure-lowering medications, release of air from a paracentesis site, or both, without reported sight-threatening complications, although visual field and optic nerve head studies were not documented or discussed in most of the reviewed studies. A differentiation between the 2 types of glaucoma was not made in all studies.

Table 3. Review of Refractive Changes after Descemet's Stripping Endothelial Keratoplasty and Descemet's Stripping Automated Endothelial Keratoplasty

Author,[Ref. No.] Year	Eyes (No.)	Mean Change in Spherical Equivalent (D)	Final Refractive Astigmatism (D)	Mean Change in Refractive Astigmatism (D)
Jun et al,[118] 2009	45	0.9	—	—
Terry et al,[113] 2009	85	—	1.1	0.1
Bahar et al,[90] 2009	26	—	2.2*; 1.3†	—
Kobayashi et al,[99] 2008	14	—	1.2	0.5
Wylegala, Tarnawska,[114] 2008	11	—	2.2	—
Busin et al,[93] 2008	10	—	0.8	—
Basak,[92] 2008	75	—	1.1	—
Chen et al,[94] 2008	100	—	1.2	0.1
Bahar et al,[89] 2008	16; 48	—	1.4‡; 3.8§	—
Price et al,[88] 2008	40	0.9	—	0.1
Yoo et al,[115] 2008	12	1.5	—	—
Koenig et al,[101] 2007	34	1.2	—	0
Covert and Koenig,[97] 2007	21	1.1	1.6	0.1
Mearza et al,[102] 2007	11	—	1.5	−0.4
Koenig and Covert,[100] 2007	26	1.2	—	0.1
Gorovoy,[16] 2006	16	—	1.4	0.6
Price and Price,[105] 2006	216	0.7	1.5	0
Price and Price,[14] 2005	50	—	1.5	0

D = diopter; — = no data reported.
*Tissue insertion with glide.
†Tissue insertion with forceps.
‡DSAEK cases.
§Penetrating keratoplasty cases.

Endothelial Cell Loss

Although endothelial cell loss is not a complication, acceleration of cell loss can lead to earlier onset of late endothelial failure and ultimate graft decompensation. Late endothelial failure is difficult to assess because DSEK reports are based on lower numbers and shorter follow-up times compared with studies of PK; however, retrospective measurements of endothelial cell loss were found in 19 studies in the assessment. Endothelial cell loss at 6 months ranged from 25% to 54%, with an average of 37% cell loss. Endothelial cell loss at 1 year ranged from 24% to 61%, with an average of 41% cell loss.[16,88–90,92,93,96,98,99,101–103,106,107,109,111–114] Price and Price[106] described cell loss in a longitudinal analysis of a subset of 34 patients that showed 34% cell loss at 6 months, 36% at 12 months, and 41% at 24 months.

Infection

No cases of endophthalmitis were reported. Although endophthalmitis is a potential complication of DSEK, the absence of reports may reflect underreporting by surgeons, unwillingness of journals to publish single cases of endophthalmitis, or an absence of this complication to date.

Postoperative Ametropia

Descemet's stripping (automated) endothelial keratoplasty surgery induced 0.7 to 1.5 D of hyperopia in the reviewed studies, with an average induced hyperopia of 1.1 D.[88,97,100,101,105,115,118] With the aid of arc-scanning ultrasound, Dupps et al[26] found that the hyperopic refractive result occurred from nonuniform thickness profiles of donor lenticules. Donor lenticules prepared with the microkeratome were thinner centrally and thicker in the graft periphery, resulting in a reduced radius of curvature of the posterior corneal surface and reduced effective corneal power. This effect created a clinical shift toward hyperopia.[26,58,65]

The most common complication of PK is postkeratoplasty ametropia, most commonly manifested as astigmatism or myopia. The ametropia often can lead to troublesome anisometropia. The average postoperative astigmatism after DSEK was 1.5 D, with surgically induced astigmatism ranging from −0.4 to 0.6 D, with a mean of 0.11 D of induced astigmatism.[14,16,88,94,97,99–102,105,113] The limbal insertion incision for DSEK is created in a manner similar to the standard phacoemulsification cataract surgical incision, except that it is typically 1 to 2 mm wider. Incisions can vary among surgeons and range from creation of a scleral tunnel to a near-clear or peripheral clear corneal incision, as with cataract surgery. A 5-mm scleral incision has been found to induce only 0.10 D of astigmatism.[94] This astigmatism neutrality affords quicker vision recovery and better uncorrected and best-corrected postoperative visual acuity compared with PK. The lack of induced astigmatism with DSEK likely was the reason why patients preferred vision with DSEK over that with PK.[90,91]

Visual Acuity

Visual acuity reporting was not standardized among studies reviewed (Table 1). Eleven studies reported an aver-

Table 4. Mean Endothelial Cell Loss after Keratoplasty in Large Series (≥11 Eyes)

Surgical Technique[Ref. No.]	Study Year	Eyes (No.)	Mean Percent Endothelial Cell Loss (2–6 Mos)	Mean Percent Endothelial Cell Loss (12 Mos)	Mean Percent Endothelial Cell Loss (24 Mos)
PK[120]	1980	34	24	45	—
PK[122]	1982	39	18	34	—
PK[124]	1992	62	—	18	—
PK[123]	2000	24	—	16	29
PK[121]	2001	17 (Optisol storage only)	11	17	—
PK[125]	2004	329	—	34	54*
PK[119]	2006	293	29	40	49
DSAEK[16]	2006	16	—	40	—
DSAEK[102]	2007	11	—	61	—
DSAEK[101]	2007	34	50	—	—
DSAEK[106]	2008	263	34	36†	41†
DSAEK[109]	2008	80	34	39	—
DSEK[89]	2008	61	—	40	—
DSAEK[99]	2008	14	54	—	—
DSEK/DSAEK[90]	2009	26‡	25	—	—
		37§	34		
DSAEK[111]	2008	350	—	36	—
DSAEK[113]	2009	173	31	—	—
DSAEK[112]	2009	100	31	29	—

DSAEK = Descemet's stripping automated endothelial keratoplasty; DSEK = Descemet's stripping endothelial keratoplasty; PK = penetrating keratoplasty; — = no data reported.
*Thirty-six–month data.
†Subset of 34 eyes.
‡DSAEK cases with glide insertion of tissue.
§DSAEK cases with forceps insertion of tissue.

age Snellen visual acuity,[16,89,90,93,96–98,100,101,103,114] 8 reported the percentage of patients seeing at a specific Snellen acuity level,[15,88,92,99,102,104,105,107] and 4 reported on both.[14,91,112,113] Seven reviewed studies did not report visual acuity results.[95,106,108–111,115] Studies reporting on the percentage of Snellen acuity at a specific level typically reported on the percentage of patients seeing 20/40 or better, with 1 article reporting the percentage of patients seeing 20/60 or better. In studies reporting average Snellen visual acuities with follow-ups from 3 to 21 months, vision ranged from 20/34 to 20/66. Studies reporting on the percentage of subjects whose visual acuity was 20/40 or better yielded a range of 38% to 100% from 3 to 20 months.

Table 5. Graft Survival (Clarity) with Descemet's Stripping Endothelial Keratoplasty

Author,[Ref. No.] Year	Postoperative Follow-up (Mos)	Percent Graft Survival (Clarity)
Bahar et al,[91] 2009	21	100
Terry et al,[111] 2008	12	100
Wylegala and Tarnawska,[114] 2008	19	100
Busin et al,[93] 2008	12	100
Yoo et al,[115] 2008	12	100
Sarnicola and Toro,[107] 2008	12	100
Bahar et al,[89] 2008	12	98
Price et al,[88] 2008	12	100
Terry et al,[109] 2008	12	100
Price and Price,[106] 2008	24	99
Covert and Koenig,[96] 2007	13	71
Mearza et al,[102] 2007	12	55
Gorovoy,[16] 2006	12	94

Graft Survival

Graft clarity or graft survival was not typically reported for DSEK, as it often is for PK, for a number of likely reasons. The visual acuity after EK improves and stabilizes much faster than that after PK, so visual acuity data appear early, eliminating the need to report graft clarity or survival that may be used as a proxy for graft function in the absence of meaningful acuity data. The absence of significant postkeratoplasty astigmatism, fewer corneal surface issues, and no corneal suture issues with DSEK, compared with PK, all contribute to early emergence of data on visual acuity and refractive error in DSEK. Also, published reports of DSEK beyond 2 years do not exist as with PK studies, so long-term graft clarity with DSEK has yet to be determined. Regardless, graft survival can be extrapolated from 13 reviewed studies at 1 year or beyond and shows clear grafts ranging from 55% to 100%, with an average of 94% graft survival at 1 year (Table 5).[16,88,89,91,93,96,102,106,107,109,111,114,115] Excluding the 2 studies with low patient numbers (also the lowest graft clarity percentages),[96,102] the range of clear grafts at 1 year improved from 94% to 100%, with a graft survival average of 99%. One study reported 2-year graft survival of 99%.[106]

Discussion

For many years, PK has been used for surgical treatment of endothelial diseases of the cornea. Several reports have suggested that DSEK should replace PK for surgical treatment of endothelial corneal disease.[90,91,93] With this in

mind, this study's objective was to assess safety and outcomes of EK for the treatment of endothelial diseases of the cornea. Although systematic comparison with PK was not the design of this report, some comparisons can be drawn. The most common complications of PK are postkeratoplasty astigmatism and unpredictable anisometropia.[126–128] Analysis of post-EK astigmatism found that induced astigmatism with DSAEK ranges from −0.4 to 0.6 D, with an average induced astigmatism of 0.11 D. This indicates that the procedure results in minimal astigmatic change, unlike PK. However, the most common complication of DSEK was graft dislocation. Although not directly comparable, traumatic dislocation of a PK graft or PK wound dehiscence resulting from trauma or suture-related complications is a sight-threatening situation, whereas a DSEK graft dislocation is not immediately sight threatening and does not require emergent correction in attempting vision preservation.[129–133] In fact, wound dehiscence or graft dislocation in PK often can lead to loss of the eye.[130] Late graft dislocation with PK can occur with suture removal or with suture breakage or can occur spontaneously.[130,134,135] Descemet's stripping (automated) endothelial keratoplasty graft dislocation required additional surgical procedures (rebubble procedures) in all cases, but repair did not lead to irreversible vision loss in the studies reviewed. Rebubble procedures have the potential to increase endothelial cell damage in the early postoperative period and also may increase the risk of primary graft failure, but the risk of primary graft failure after dislocation and rebubble could not be determined from this review.

There are additional differences in complications between PK and DSEK. Interface abnormalities do not develop in patients who undergo PK because there is no interface. Abnormalities of the interface in lamellar keratoplasty procedures such as DSEK remain a risk. Interface contaminants may include blood, inflammatory cells, debris, retained Descemet's membrane fragments, infectious agents, and epithelial cells. Although retained Descemet's membrane fragments or trapped epithelial cells in the interface may be innocuous, the presence of both in the interface has been linked to primary graft failure in some cases, leading to subsequent repeat DSEK.[82,83] Decentered trephination of donor tissue after DSEK donor tissue preparation also has been linked to primary graft failure from trapped epithelial cells in the interface.[108] In a study of complications of DSAEK, Suh et al[108] found 2 (2%) of 118 cases with interface opacities, 1 with blood and 1 with epithelial cells. Neither led to sight-threatening problems. Busin et al[93] found a similar rate of interface opacities in 1 (2.7%) of 37 eyes undergoing DSEK with forceps introduction of the donor tissue. Although interface opacities such as haze and debris may decrease visual acuity initially, most reports document improved vision over time with ultimate reduction in interface haze.[93,108]

Corneal suture complications, although not encountered in DSEK, represent one of the main postoperative complications of PK. Suture-related complications after PK include suture erosions, suture infections, premature suture breakage, or suture-related astigmatism.[136]

A rare, acute complication that can be sight-threatening in both PK and DSEK is a suprachoroidal hemorrhage. Suprachoroidal hemorrhage occurs during surgery or after surgery after eyes that undergo keratoplasty sustain trauma; however, the risk of vision loss with suprachoroidal hemorrhage is high in PK because of the open sky and large incision that must be closed.[137–139] A DSEK procedure avoids the large open-sky wound, providing more tectonic stability for the eye both during and after surgery. Suh et al[108] described 1 intraoperative suprachoroidal hemorrhage in their retrospective review of DSEK complications in 118 eyes. The hemorrhage remained limited according to the report and the eye was saved, with eventual resolution of subretinal fluid and hemorrhage. Intuitively, a smaller incision would be expected to have a lower incidence of significant choroidal hemorrhage as is true of cataract surgery. However, long-term data on both intraoperative and postoperative suprachoroidal hemorrhage in DSEK are lacking, likely because of the limited history of the procedure, lower surgical volume compared with PK, reporting bias, or a combination thereof.

The short-term and long-term health and viability of the donor corneal endothelium in the surgical management of corneal endothelial disease remain important considerations. Primary graft failure rates reflect the short-term health of donor corneal tissue. Primary graft failure in PK is not a common complication.[140] However, primary graft failure was the third most common DSEK complication in the reviewed literature, with a range of 0% to 29% and an average primary graft failure rate of 5% among all published studies. In comparison, Mead et al[141] found a primary failure rate of 2.7% in 778 PK eyes, whereas Wilhelmus et al[142] found a 2% primary graft failure rate in a review of the Adverse Reaction Registry of the Eye Bank Association of America, which included 7240 donor corneas undergoing PK. de Freitas et al[143] found a 17% primary graft failure rate in 213 eyes that underwent PK performed by cornea fellows, likely reflecting increased endothelial trauma from surgeon inexperience with technique and tissue handling. Terry,[64] Chen et al,[95] and Terry et al[109,110] propose that the same scenario may occur in DSEK and caution that poor surgical technique, excessive tissue handling from surgeon inexperience, and use of specific surgical steps that are inherently more traumatic are all associated with a higher risk of primary graft failure. The implications of higher rate of primary graft failure in DSEK, compared with PK, on eye banking and tissue availability are worthy of consideration, but beyond the scope of this assessment.

Long-term health of donor corneal grafts is measured by overall endothelial cell density and cell loss. The Cornea Donor Study reported on mean endothelial cell loss in 340 PK eyes and found an overall cell loss of 69% (12- to 65-year-old donors) and 75% (66- to 75-year-old donors) at 5 years.[144] It is difficult to assess long-term endothelial survival with DSEK, because only 1 published study to date discussed endothelial cell density and overall cell loss at 2 years in 34 eyes after DSEK.[106] A better comparison can be made between both procedures at 6 months and 12 months (Table 4), but a large randomized controlled trial between the 2 procedures is necessary to confirm whether one technique was accompanied by more cell loss than the other. Neverthe-

less, endothelial cell loss with DSEK seems higher than with PK at 6 months, but equivalent to PK at 12 months.

Graft survival is another outcome for comparison between PK and DSEK. Several studies of PK survival exist in the literature. The Cornea Donor Study found a graft survival of 86% in donors 12 to 65 years of age and 75% in donors 66 to 75 years of age at 5 years.[145] The Swedish Corneal Transplant Register found a graft survival of 90% at 2 years,[146] as did a study by Thompson et al[147] reporting on 90% graft clarity at 5 years. Guerin et al[148] found a graft survival of 93% at 1 year in Ireland. Although some studies in this review of graft clarity for DSEK found lower percentages, the numbers of patients reported were very low in most cases reviewed. Most of the PK graft survival studies included more than 1000 patients, whereas most of the DSEK studies included 100 patients or fewer. Regardless, the average graft survival of DSEK was 94% at 1 year, with 1 study finding 99% graft survival at 2 years. Certainly, early endothelial keratoplasty graft survival seems at least equivalent to PK in terms of average overall percent graft survival.

In conclusion, the evidence on safety and outcomes reviewed here suggests that DSEK appears effective for the treatment of endothelial diseases of the cornea. Descemet's stripping (automated) endothelial keratoplasty seems to be similar to PK in terms of surgical risks and complication rates, graft survival (clarity) and acuity, and endothelial cell loss, and superior to PK in terms of early visual recovery and refractive stability, postoperative refractive outcomes, wound and suture-related complications, and intraoperative and late choroidal hemorrhage risk. The evidence reveals that the 4 most common complications of DSEK are graft dislocation, endothelial rejection, graft failure, and glaucoma. Despite these findings, a reliable estimate of the incidence and ranking of complications associated with DSEK remains to be determined because of its recent adoption as a surgical alternative to PK. Complication rates have been described in case reports, letters, and retrospective and prospective cases series, as outlined in Tables 1, 2, and 3. Furthermore, although some facilities have established well-designed studies, data collection and reporting remains limited by relatively low surgical numbers and nonstandard reporting of outcomes. In addition, assessment of risk factors for various complications is complicated by variation in patient characteristics, donor tissue characteristics, differing surgical techniques, surgeon training and experience level, and absence of long-term follow-up among the various case reports and case series.

Surgeon training, skill, and experience deserve special mention because this factor can affect DSEK outcomes and subsequent reporting of complication rates. With the relative novelty of DSEK, teaching of the procedure at residency and fellowship training programs remains limited. Most surgeons performing the procedure have learned techniques in 1- to 2-day courses rather than as part of cornea fellowship training, which is the traditional standard for training in PK. As more surgeons complete formal training in DSEK within their residency and fellowship training, the surgeon variable should become less important over time.

Despite the complications enumerated above, there is no evidence that DSEK carries unacceptable risks for the surgical treatment of endothelial corneal disease. Evidence from retrospective and prospective DSEK and DSAEK studies described a variety of complications associated with the procedure, but these complications do not seem to be detrimental to the ultimate vision recovery in most cases. Descemet's stripping endothelial automated keratoplasty should not be used in lieu of PK for conditions with concurrent endothelial disease and stromal corneal disease. These situations include concurrent stromal corneal dystrophies, anterior corneal scars from trauma or prior infection, and ectatic conditions of the cornea such as keratoconus, pellucid marginal degeneration, and ectasia after previous laser vision correction surgery. Assessment of evidence regarding long-term endothelial cell survival and the risk of late endothelial rejection in DSEK is beyond the scope of this review.

Future Research

Future research in EK should be directed at enhancing endothelial cell survival. Continued laboratory and animal research is needed to study different tissue preparation techniques, including adjunct use of femtosecond lasers, optimal tissue preservation for precut tissue, and new insertion techniques, including the development of donor tissue insertion devices or new techniques to limit intraoperative endothelial cell loss. Innovative techniques such as Descemet's membrane endothelial keratoplasty (DMEK), femtosecond laser-assisted DSAEK, and new insertion techniques and instruments must be validated by basic laboratory animal and ex vivo studies and large, well-designed cohort or randomized controlled studies between the various endothelial keratoplasty techniques. Long-term prospective studies demonstrating acceptable complication rates and long-term endothelial cell survival remain of utmost importance for continued improvement of EK and patient outcomes.

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