ARTICLE

Development of a nomogram to achieve ultrathin donor corneal disks for Descemet-stripping automated endothelial keratoplasty

Alberto Villarrubia, MD, Antonio Cano-Ortiz, MD

PURPOSE: To report the predictability of a nomogram for ultrathin donor lamella creation for Descemet-stripping automated endothelial keratoplasty (DSAEK) with an automated microkeratome.

SETTING: Instituto de Oftalmología La Arruzafa, Córdoba, Spain.

DESIGN: Prospective nonrandomized consecutive case series.

METHODS: This study enrolled eyes of consecutive patients in which DSAEK was performed to treat Fuchs dystrophy or bullous keratopathy. Patients with macular pathology or other vision-limiting pathology were included. The same surgeon performed all surgeries using an automated keratome (Amadeus II) linked to an artificial anterior chamber. The target donor lamella thickness was from 70 to 120 μm based on a nomogram that incorporates advancement speed, blade holder size, and corneal thickness. The decimal corrected distance visual acuity (CDVA) at 3 months postoperatively, graft thickness at 1 month, and complications were recorded.

RESULTS: Fifty-one patients (60 eyes) were enrolled. One month postoperatively, the mean donor lamella thickness was 99.33 μm $\pm$ 16.97 (SD) (range 67 to 130 μm). The target thickness range was achieved in 96.66% of cases (58 eyes). In 32 patients with a potential visual acuity of 20/20, the mean postoperative CDVA was 0.80 $\pm$ 0.16 (range 0.55 to 1.20). There were no complications during flap preparation, intraoperatively, or postoperatively and no events caused donor corneal tissue to be discarded.

CONCLUSIONS: The use of a nomogram with an automated microkeratome for DSAEK provided good visual outcomes with a thin donor lamella ($\leq$120 μm). The outcomes with the nomogram were similar to those reported for Descemet membrane endothelial keratoplasty.

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Endothelial keratoplasty is the preferred surgical option to treat corneal edema caused by endothelial dysfunction. Descemet membrane endothelial keratoplasty (DMEK) and Descemet-stripping automated endothelial keratoplasty (DSAEK) are 2 common procedures that remain under debate. In the past decade, studies[1,2] have shown that DMEK achieves better postoperative visual acuity and is an almost neutral refractive procedure. In addition, endothelial cell loss in the 2 procedures is similar.[2,3] Hence, DMEK could be the procedure of choice for endothelial dysfunction. However, an important drawback of DMEK over DSAEK is its steep learning curve, which increases the rate of donor graft dislocation and the potential that donor tissue will be discarded during dissection.[4,5]

Descemet-stripping automated endothelial keratoplasty involves transplantation of Descemet membrane, the endothelial layer, and a thin section of donor stroma. The safety and efficacy of DSAEK are

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well established.[6] However, vision tends to be worse after DSAEK than after DMEK likely because of interface problems, folds in the donor disk from maladaptation to the recipient stroma, decentration of the donor disk, and excess donor corneal thickness.[2,5,7,8,9]

Results in studies of the relationship between corneal thickness and visual outcomes after DSAEK are contradictory. For example, Terry et al.[9] report a weak correlation between preoperative graft thickness and visual outcomes. However, Maier et al.[8] report a statistically significantly better visual acuity when the donor lamella was 120 μm or thinner as opposed to thicker than 120 μm. Maier et al.[8] conclude that DSAEK with thinner donor lamellae (≤120 μm) might be a good alternative to DMEK. In a study by Busin et al.,[10] ultrathin DSAEK performed using a manual microkeratome yielded results similar to those of DMEK.

For 6 years, our clinic has performed DSAEK using an automated microkeratome (Amadeus II, Ziemer Ophthalmic Systems AG) linked to an artificial anterior chamber. We believe the automated advancement guarantees a consistent cutting speed, which should result in a higher quality stromal bed. In this prospective study, we developed a nomogram for DSAEK that incorporates translation (advancement) speed, blade holder size, and corneal thickness to consistently create endothelial donor lamellas of from 70 to 120 μm thick.

PATIENTS AND METHODS

This prospective single-center case series enrolled consecutive patients scheduled to have DSAEK performed to treat Fuchs dystrophy or bullous keratopathy at Instituto de Oftalmología La Arruzafa (Córdoba, Spain) from January 2012 to April 2013. The study adhered to the tenets of the Declaration of Helsinki. Research ethics approval was granted by the clinic's institutional ethics committee. Patients with ocular comorbidities that could affect vision, such as glaucoma, macular pathology, amblyopia, and corneal scarring, were not excluded from the study.

Patients had a thorough preoperative ophthalmic examination that included decimal uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), manifest refraction, slitlamp biomicroscopy, Goldmann applanation tonometry, dilated retinal evaluation, and optical coherence tomography (OCT) (Visante, Carl Zeiss Meditec AG). Donor endothelial cell density was measured by the eye bank using a Konan specular microscope (Cellchek EB-10, Konan Medical).

Postoperative examinations were performed at 1 month and 3 months and included UDVA, CDVA, manifest refraction, slitlamp biomicroscopy, and Goldmann applanation tonometry. One month postoperatively, the donor thickness was measured with OCT. Postoperative corneal thickness was measured at the center of the corneal apex by 3 independent observers, and the mean value was calculated.

Surgical Technique

All DSAEK procedures were performed by the same surgeon (A.V.). All donor corneas were delivered by the eye bank in cold storage media (Eusol–C, Alchimia srl). After the donor cornea was prepared, sclerocorneal disks 14.0 to 16.0 mm in diameter and with a white-to-white distance of 11.0 mm or more were obtained. The donor tissue was mounted on an artificial anterior chamber (Ziemer Ophthalmic Systems AG). The artificial chamber was linked to a phacoemulsification unit with a venturi pump preset at 65 mm Hg, and the pressure inside the chamber was maintained under the same conditions. The pump pressure was checked with a Barraquer tonometer before the cut. The donor graft thickness was measured using an ultrasonic pachymeter (DGH-550 Pachette 2, DGH Technology, Inc.).

A free cap was created with the Amadeus II microkeratome. Under the principle that with the same conditions, the slower the translational speed of the microkeratome blade, the thicker the anterior lamella produced, the donor cut was performed with the 450 μm or 500 μm blade holder of the microkeratome with different translational speed according to the corneal thickness. The translational speed can be preset in the control panel of the automated microkeratome. Ultrathin DSAEK is defined here as a donor lamella thickness of 120 μm or less. The target donor lamella thickness was from 70 to 120 μm. Table 1 shows the nomogram used.

For donor corneal disk thicknesses through 550 μm, the 450 μm blade holder was used and the translational speed diminished when the donor thickness increased. When the thickness was 551 to 650 μm, the 500 blade holder was used under the same rationale. For thicknesses 651 μm and higher, a double-pass technique was used; the second cut was made starting from the end of the initial cut. In these cases, the 140 μm blade holder was used first. Then, depending on the residual thickness, the 450 μm or the 500 μm blade holder was used under the same rationale as for cases in which the donor thickness was 650 μm or less. The epithelium was left in place before the cut in cases in which the final thickness of the donor cornea would be less than 500 μm if the epithelium were removed. During the whole procedure, the same assistant operated the control panel.

Once the free cap was created, the anterior and posterior lamellae were placed over the Hessburg-Barron punch system with the endothelial layer facing up, and trephination was performed. The donor disk with the posterior stroma, Descemet membrane, and endothelial cells remained on the Hessburg-Barron system covered with the cold storage media. The diameter of the donor disk was between 8.0 mm and 9.0 mm in all cases.

After the graft was prepared, surgery was performed with peribulbar anesthesia (10 mL L-bupivacaine 0.75% combined with hyaluronidase 100 IU) using a standardized

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From the Instituto de Oftalmología La Arruzafa, Córdoba, Spain.

Corresponding author: Alberto Villarrubia, MD, Instituto de Oftalmología La Arruzafa, Avenida de la Arruzafa 9, 14012 Córdoba, Spain. E-mail: alvillarrubia@yahoo.com.

Table 1. Nomogram for thin donor corneal disks for DSAEK performed using an automated microkeratome.

Corneal Thickness (μm)	Blade Holder Size (μm)	Advancement Speed (mm/s)	Eyes (n)	Thickness (μm)	
				Mean ± SD	Range
475 to 500	450	3.0	3	97.00 ± 13.11	85, 111
501 to 525	450	2.0	3	96.20 ± 19.56	67, 117
526 to 550	450	1.5	5	99.11 ± 9.03	86, 112
551 to 575	500	3.0	9	97.06 ± 13.72	74, 117
576 to 600	500	2.0	15	97.00 ± 13.11	85, 111
601 to 650	500	1.5	18	98.44 ± 13.56	73, 119
≥651	Two passes: 140, then same nomogram for the RSB	1.5 for 140 μm blade handle	7	110.57 ± 15.61	88, 130

RSB = residual stromal bed

DSAEK technique. Three 23-gauge paracenteses were created, and an anterior chamber maintainer (ACM) (25 gauge, Manic, Asico, LLC) was introduced through 1 of the paracenteses. The ACM was linked to a phacoemulsification unit with a venturi pump. This system enabled pressurization of the anterior chamber using a balanced salt solution and maintenance of constant intraocular pressure (IOP) intraoperatively. Subsequently, air–fluid exchange was performed to fill the anterior chamber with air. Through a second paracentesis, the Descemet membrane was stripped with a reverse Sinskey hook, a second air–fluid exchange was performed, and a 5.0 mm corneal incision was made at the 6 o'clock position. The donor disk was left over a Busin glide (Moria SA) and positioned in the inferior corneal incision. A forceps (AE – 4219, Asico LLC) was introduced through the superior paracentesis, and the donor disk was delivered into the anterior chamber using a pull-through technique. Air–fluid exchange was performed and an air bubble delivered into the anterior chamber to unfold the donor disk to the posterior recipient stroma. One 10-0 nylon suture was placed at the main inferior incision, and the patient was left supine in the operating room with the anterior chamber filled with air for 30 minutes and with an IOP of 30 to 40 mm Hg. Subsequently, the air bubble was removed from the anterior chamber, leaving a small mobile air bubble within the anterior chamber.

Postoperatively, the patients lay supine for 3 hours, after which a slitlamp examination was performed. Patients were instructed to instill topical dexamethasone and topical moxifloxacin 4 times a day for 2 weeks, then 3 times a day for another 2 weeks. Topical fluorometholone was continued 4 times a day for the first month and then reduced by 1 drop each subsequent month until the dosage reached 1 drop once a day; this dosage was maintained indefinitely in the absence of an IOP spike. All sutures were removed between 1 month and 2 months postoperatively.

Data Analysis

Data were collected on the CDVA 3 months postoperatively and on donor graft thickness at 1 month. The CDVA values were converted to logMAR values for analysis. Data are reported here in decimal notation. The frequency of intraoperative and postoperative complications was recorded. Data are presented as mean ± standard deviation (SD).

RESULTS

The study enrolled 60 eyes of 51 patients. The mean precut donor tissue thickness was 572 ± 24.12 μm (range 491 to 752 μm).

One month postoperatively, the mean donor lamella thickness was 99.33 ± 16.97 μm (range 67 to 130 μm). In 2 cases (3.33%) the donor lamella was thicker than 120 μm. (Both cases were in the group of corneas thicker than 650 μm, in which a double pass was needed.) All remaining cases (96.66%) were within the targeted thickness, with 32 cases (53.33%) targeted for 100 μm or less. Table 1 shows the number of eyes and the mean thickness.

In 32 patients without ocular comorbidities and with a potential visual acuity of 20/20, the mean postoperative CDVA was 0.80 ± 0.16 (range 0.55 to 1.20); in 25 of these patients (78.12%), CDVA was 0.7 or better.

All surgeries were uneventful. In addition, there were no other events that led to donor corneal tissue being discarded. Four eyes (6.6%) needed air reinjection in the immediate postoperative period to reattach a dislocated corneal lamella.

In all cases, the shape of the donor graft was thicker in the periphery and thinner in the center. Figure 1 shows 3 examples of the thin donor grafts from this study.

DISCUSSION

The outcomes in this study using a nomogram for DSAEK indicate that a target donor lamella thickness is achievable in most cases; the target was achieved in 96.66% of cases (58 eyes). Graft thickness has been implicated as a factor in final postoperative vision. In a study of ultrathin DSAEK, the mean graft thickness in 285 eyes was 78.28 ± 28.89 μm[10]; the visual outcomes were similar to those reported for DMEK. In a

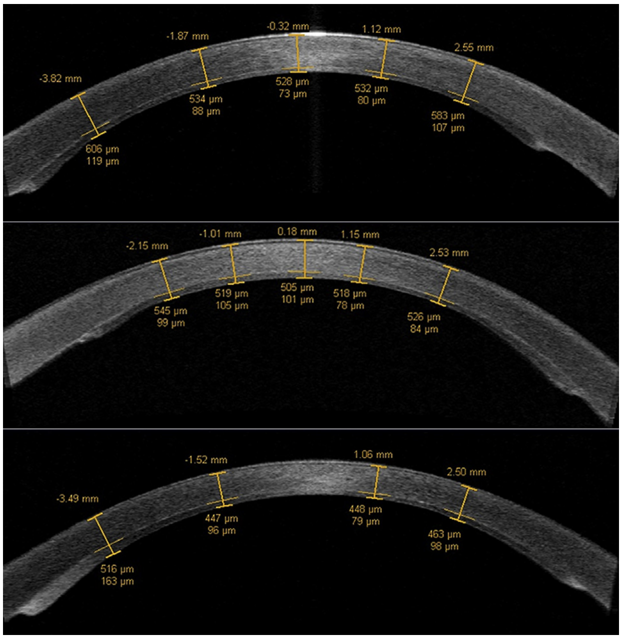

Figure 1. Three examples of an ultrathin donor lamella.

study of the relationship between donor thickness and postoperative vision, Terry et al.[9] conclude that for the standard range of graft thickness (100 to 200 µm), there was no effect on visual outcomes after DSAEK. The mean graft thickness for ultrathin DSAEK (78.28 ± 28.89 µm)[10] and the mean thickness in the current study (99.33 ± 16.97 µm) are well below that reported by Terry et al.[9] (162.9 ± 29.0 µm), which might explain the different outcomes between studies. Studies comparing DSAEK and DMEK that report better vision outcomes with DMEK[1,9] have generally targeted graft thicknesses of more than 120 µm.

We opted not to measure the donor thickness intraoperatively to avoid manipulating the donor tissue and because it is difficult to obtain a reliable result with ultrasound pachymetry of such a thin surface. Although it might take 3 to 6 months for postoperative swelling to resolve, we preferred to measure the donor graft thickness with OCT at 1 month because many of the patients were not local to the clinic and some could not return for an appointment at 6 months.

A decrease in donor graft thickness over time might be beneficial. A continuous decrease in thickness of the grafted lenticule from 191 ± 56 µm to 100 ± 38 µm over 6 months after DSAEK has been statistically correlated with better vision.[11] This observation, considered in light of results in studies of thinner grafts for DSAEK, indicates that vision is affected by a thinner lenticule. Terry et al.[9] report that the best visual outcomes after DSAEK were in the decile group with the thinnest grafts, 80 to 124 µm. However, the surgical conundrum is how to reproduce a standardized thin donor lamella. In a study by Busin et al.[10] in which a manual microkeratome was used, the flaps were less than perfect in 7.2% of ultrathin cases, with 2.1% being discarded. We believe that using a nomogram and an automated microkeratome to create a donor lamella rather than a microkeratome that requires manual translation allows standardization of donor lamella thickness. Also, using blade holders of 200 to 500 µm might allow reproducible creation of thin donor disks.

In the current study, only 2 of the 60 lamellae were thicker than 120 µm, indicating the reproducibility of the procedure. The procedure was uneventful in all 60 eyes. The reproducibility of the flap thickness is also indicated by the low SD in our cohort (±16.97 µm). The SD is lower than that reported in studies of DSAEK with manual microkeratomes. Terry et al.[9] report an SD of ±29 µm for 419 eyes in which DSAEK was performed with a manual microkeratome. Theil et al.[12] studied 60 consecutive DSAEK procedures that used 4 different manual microkeratomes and report an SD that varied from ±45 µm to ±94 µm. In a study by Busin et al.[10] of ultrathin DSAEK with a manual keratome, the SD was ±28.89 µm. Thomas et al.[13] used a microthin DSAEK technique with a manual keratome; the SD was ±32 µm. In all these studies, the surgeries were performed by highly experienced DSAEK surgeons. Hence, it is likely that the automated microkeratome and use of a well-defined nomogram contributed to the lower SD in the current study. Although a prospective contralateral randomized study could definitively address this observation, convincing patients to have or surgeons to perform a procedure that is likely to result in worse than expected outcomes (eg, DSAEK with a nomogram) would be difficult.

We did not perform a study of eye-bank corneas before conceiving the nomogram because from our experience using the automated microkeratome in laser in situ keratomileusis surgery over more than 12 years, we know that the lower the translation speed we use, the thicker the anterior cap.

A potential advantage of performing ultrathin DSAEK with an automated microkeratome is that the quality of the stromal bed might be better than for manual microkeratome translation across the cornea. The better stromal quality might result in better visual outcomes.[14] Vision recovery is faster, and more patients achieve 20/20 CDVA with ultrathin DSAEK than with conventional DSAEK.[10] In addition, the visual outcomes of ultrathin DSAEK rival those of DMEK.[10]

Descemet membrane endothelial keratoplasty is technically more challenging than DSAEK; it also has higher surgical complication rates and takes more time. A prospective case series study of DMEK with the same sample size as our study reports more complications.[5] For example, the Descemet membrane was stripped successfully in 60 of 72 donor corneas, the procedure was converted to DSAEK in 6 donor corneas, and the donor tissue was discarded in 6 eyes (8%).[5] Five corneas (8%) that had DMEK failed to clear and a second surgery (DMEK or DSAEK) was performed. Secondary interventions included reinjection in 38 eyes (63%), generally for partial detachments. In contrast, in the current study there were no complications intraoperatively or during donor lamella preparation. Only 6.6% of cases required air reinjection in the immediate postoperative period to reattach a dislocated corneal lamella.

The current study's limitations include its short follow-up, the small sample size, and that only one surgeon performed the procedures. The short follow-up was unavoidable; in our experience, satisfied patients tend to present for follow-up after 3 to 4 months, and we did not extend the follow-up period because we did not want to risk a significant dropout rate. Nonetheless, longer follow-up is needed to verify the observations in our study. We did not measure the endothelial cell loss over time, and this warrants study. However, an earlier study shows equivalent cell loss between DMEK, DSAEK, and ultrathin DSAEK.[10] Furthermore, the indication for surgery (ie, the recipient's diagnosis) might affect the rate of long-term cell loss after DSAEK, and this requires further study.[10,15] All surgeries in the current study were performed by a surgeon experienced in the use of a microkeratome for more than 6 years; thus, the outcomes may not be indicative of surgeons who do not regularly perform DSAEK or do not regularly use an automated microkeratome. Regarding the reproducibility of the translation speed, Vajpayee et al.[16] deliberately moved a manual microkeratome slowly across the donor corneal surface; their results were similar to ours, but the study involved only 15 cases. Presetting the translation speed with the control panel of an automated microkeratome should yield more reproducible results.

In summary, using an automated microkeratome with a well-developed nomogram provided better visual outcomes for DSAEK when the donor lamella thickness was 120 μm or less. There were no complications during flap preparation with this technique. The effect of a thinner lamella on endothelial cell loss remains unknown. The outcomes when using the nomogram were close to those in published studies of DMEK; however, more studies are needed to confirm that the thinner the donor lamella, the better the postoperative CDVA.

WHAT WAS KNOWN

- Studies comparing DSAEK and DMEK that report better vision outcomes with DMEK have generally used a target graft thickness of 120 μm or more.
- Several studies report better visual outcomes after DSAEK in which the donor lamella thickness is less than 120 μm.
- A double-pass technique for ultrathin DSAEK yields results comparable to those of DMEK.

WHAT THIS PAPER ADDS

- The automated microkeratome provided a consistent cutting speed. This, combined with a nomogram that incorporates translation (advancement) speed, blade holder size, and corneal thickness, achieved a donor lamella thickness of 70 to 120 μm in more than 90% of cases in which a 1-pass technique was used.

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First author:
Alberto Villarrubia, MD

Instituto de Oftalmología La Arruzafa, Córdoba, Spain