Outcomes of ultrathin Descemet stripping automated endothelial keratoplasty (UT-DSAEK) performed in eyes with failure of primary Descemet membrane endothelial keratoplasty (DMEK)

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Abstract Aim To evaluate the outcomes of ultrathin Descemet stripping automated endothelial keratoplasty (UT-DSAEK) performed in eyes after failure of primary Descemet membrane endothelial keratoplasty (DMEK).

Methods This was a retrospective, non-comparative interventional case series done in a tertiary care hospital. The study group included 21 eyes of patients which underwent UT-DSAEK following the failure of primary DMEK. Outcome measures included best spectaclecorrected visual acuity (BSCVA) and endothelial cell density (ECD) both recorded 6 and 12 months postoperatively as well as central graft thickness (CGT) measured 6 months after UT-DSAEK.

Results When considering only eyes without comorbidities (17 of 21), 12 months after UT-DSAEK, BSCVA was ≥20/25 in 12/13 (92%) eyes and ≥20/20 in 4/13 (30%) eyes. Mean ECD loss rate was 38.9% at 12 months postoperatively (range 8%–57%). Six months postoperatively, CGT averaged at 81±34 μm (range 34–131 μm). No intraoperative complications were recorded. Postoperatively, one patient (no. 8) had graft wrinkles that were fixed 2 days following UT-DSAEK. Four patients have developed intraocular lens (IOL) opacification, and two of them underwent IOL exchange. No other postoperative complications were recorded.

Conclusions UT-DSAEK is instrumental in the management of primary DMEK graft failure, allowing visual rehabilitation which is comparable with that of repeat DMEK.

Introduction

Descemet stripping automated endothelial keratoplasty (DSAEK) is to date the most popular procedure for the treatment of endothelial decompensation. It is easy to perform, yields results far superior to those of penetrating keratoplasty (PK) and is associated with a very low incidence of complications. Descemet membrane endothelial keratoplasty (DMEK) has been reported to further improve the visual outcomes and reduce the risk of immunologic allograft rejection recorded after DSAEK. However, although the number of DMEKs performed is constantly rising in most countries,1 2 the technical difficulty of the procedure (possibly accentuated by lack of access to training), the reported rates of graft detachment and primary failure are still deterring most surgeons from embracing this technique. In particular, primary failure averaged at 1.7% in a large literature search, ranging up to 12.5% of cases.3 Following DMEK, the cornea can remain oedematous because of primary graft failure, as well from other reasons such as graft dislocation unamenable to repeat anterior chamber re-bubbling attempts, or an upsidedown graft. In a recent large series of 1655 eyes operated on by an experienced DMEK surgeon, 2.9% of corneas did not clear following surgery.4 Failure of the cornea to clear following surgery, be it because of primary graft failure or because of unamenable graft detachment despite multiple AC re-bubbling attempts, is difficult to deal with, especially

in respect to the choice of further surgical treatment of these, often very disappointed, patients. The decision of technique for secondary transplant should consider the surgeon's experience, preferences and likelihood of success and further complications, considering also the availability of donor corneas and the willingness of the patient to undergo eventually additional procedures, if repeat DMEK will also result in primary graft failure. We report herein the results of UT-DSAEK performed after primary failure of DMEK in an attempt at optimising visual rehabilitation while minimising the possibility of repeat failure or other types of complications.

Methods

This retrospective, non-comparative interventional case series followed the tenets of the 1964 Declaration of Helsinki and was approved by the local ethics committee; a detailed informed consent form had been signed by all patients before surgery. All patients undergoing UT-DSAEK at Villa Igea Hospital (Forlì, Italy) for primarily failed DMEK, between January 2013 and December 2017, were included in this study. In all cases, UT-DSAEK was performed in a standardised fashion according to the technique described in detail elsewhere5 6 and included in brief following steps: (1) removal of the decompensated DMEK graft; (2) microkeratome-assisted preparation of an UT-DSAEK graft, aiming at a central thickness within 100 µm; (3) pull-through delivery of the graft using a Busin mini-glide inserted through a 3.2 mm clear-cornea incision.

We noted ocular comorbidities, time interval between DMEK and UT-DSAEK, as well as post-UT-DSAEK outcomes at 6 and 12 months, including best spectacle-corrected visual acuity (BSCVA) and endothelial cell density (ECD). Central graft thickness (CGT) was measured 6 months following UT-DSAEK. BSCVA was determined using Snellen projector charts; for comparison, the average value of BSCVA was expressed in logarithm of the minimum angle of resolution (LogMAR). ECD was evaluated by means of specular microscopy (EM-3000; Tomey, Erlangen, Germany) and CGT was measured by means of anterior segment optical coherence tomography (AS-OCT) (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany, till October 2014, then SS-1000 CASIA; Tomey, Tokyo, Japan). Intraoperative and postoperative complications of UT-DSAEK were recorded.

Results

In the study period, 254 DMEK surgeries were performed at our institution. Out of these, 29 eyes were operated with the indication of failed prior DMEK (11.8%) of which in six cases (6/254%–2.4%) the primary DMEK was performed in our institution while in all other 23 cases, primary DMEK was done elsewhere. Eight eyes were excluded from the study because of lack of follow-up data, resulting in a total of 21 eyes being included in the study. In 6 of these eyes, successful re-bubbling was performed following primary DMEK, and in all 21 eyes AS-OCT showed correctly oriented and fully attached graft, following which primary graft failure was declared. Table 1 describes the demographic details and clinical outcomes of the eyes included in this study. Briefly, there were 11 women and 10 men; their age ranged from 52 to 78 years (average±SD=69.2±7.2). The indication for DMEK was pseudophakic bullous keratopathy in 3 eyes and Fuchs endothelial dystrophy in 18 eyes, 1 of which underwent a combined procedure (patient 20 in table 1) including DMEK and phacoemulsification with intraocular lens (IOL) implantation in the capsular bag. All eyes had primary DMEK failure, with persistence of intense corneal oedema starting from the first postoperative day and remaining unchanged over time (eg, figure 1). All UT-DSAEK procedures were

uneventful. No intraoperative complications were recorded. Postoperatively, one patient (patient 8) had graft wrinkles that were fixed 2 days following UT-DSAEK. Four patients have developed IOL opacification, and two of them underwent IOL exchange. No other postoperative complications were recorded. When excluding four eyes which had significant comorbidities (two eyes with age-related macular degeneration, one with previous retinal detachment and one with advanced glaucoma), mean BSCVA was 0.11±0.09 LogMAR and 0.06±0.05 LogMAR, respectively, 6 and 12 months after UT-DSAEK. When excluding these eyes, at 6 months after UT-DSAEK, BSCVA was ≥20/40 in 15/15 (100%) eyes, ≥20/25 in 8/15 (53.3%) eyes and 20/20 in 4/15 (26%) eyes; 12 months after UT-DSAEK, BSCVA was ≥20/25 in 12/13 (92%) eyes and ≥20/20 in 4/13 (31%) eyes. The average preoperative donor ECD (measured at three eye banks) was 2514±149 cells/mm2 and decreased to 1704±319 cells/mm2 (32.2% cell loss rate, range 1143–2230 cells/mm2) and 1534±369 cells/ mm2 (38.9% cell loss rate, range 1030– 2205 cells/mm2), respectively, 6 and 12 months postoperatively. Six months after UT-DSAEK, CGT averaged 81±34 µm (range 34–131 µm).

DISCUSSION

After graft detachment and intraocular pressure elevation, primary failure represents the most frequent vision-threatening complication of DMEK.3 Several modifications of the technique have been introduced in order to minimise endothelial damage during graft preparation and/or surgical manipulation as well as properly identifying the endothelial and Descemetic sides of the graft. Nevertheless primary failure still occurs in a relatively high number of DMEK procedures even in the hands of very experienced surgeons.4 When making a decision about secondary surgery, surgeons are likely to favour a procedure that minimises further complications to patients who are very disappointed by the initial result. In addition, for the specific case of DMEK, secondary surgery must provide a visual outcome as close as possible to the visual potential in a relatively short time. In the largest series published to date, Price et al4 reported recently that 43% of 55 eyes with primarily failed DMEKs could reach ≥20/20 corrected distance visual acuity 1 year after repeat DMEK in the absence of comorbidities. This result was comparable to that achieved by the same group after primarily successful DMEK (n=1600). However, re-bubbling was necessary once in 7 of 55 (13%) eyes and twice in 1 of 55 (2%) eyes. Instead, another study by Baydoun et al7 has shown that visual outcomes of repeat DMEK are worse than those of primary DMEK, with an overall complication rate of 76.5% (n=13 of 17), including a repeat failure rate of 17.6% (n=3 of 17) and a re-bubbling rate of 5.8% (n=1 of 17). The authors also noticed that the detachments tended to recur in the same corneal quadrant, thus stressing the possibility of recipient abnormalities at the base of some types of graft detachment. Also Ćirković et al8 in a recent publication reported that repeating DMEK is safe but yields results worse than those recorded after primary DMEK. In this series, 1 year after surgery no eye without comorbidity could see 20/20 and only 2 of 15 (13.3%) eyes could see 20/25. These authors also describe a number of re-bubbling procedures necessary after repeat DMEK are higher than that of the procedures required after primary DMEK (range 0–3 vs 0–2). Finally, 1 of the 18 (5.5%) repeat DMEK failed again and a penetrating keratoplasty was performed. The differences in visual outcomes among these studies may be explained by the various length of time elapsed between primary and repeat DMEK, with irreversible stromal changes developing if oedema had persisted for too long. In the paired analysis made by Price et al, the interval between primary and repeat DMEK ranged between 2 and 133 days (median=21 days), whereas both in the study by Baydoun et al7 and in that by Ćirković et al,8 the interval was much longer, ranging in the former series between 4 and 33 months, and in the latter series between 7 and 497 days. As early reintervention is crucial in order to optimise visual recovery, waiting for the cornea to clear does not seem to be justified beyond few weeks, even if late recovery of transparency may occasionally occur even in the presence of graft detachment.9

Descemet stripping endothelial keratoplasty (DSEK) and DSAEK have also been used to treat primarily failed DMEK. In 2010, Dapena and associates10 proposed hand-dissected DSEK as a suitable and safe backup procedure after primarily failed DMEK. Six months postoperatively, all but one of the eyes without comorbidities (n=8) reached a best-corrected visual acuity (BCVA) of 20/40 or better; however, no eye could see 20/20 and only one eye could see 20/25. In addition, three of eight eyes (37%) needed re-bubbling to treat graft detachment. These results line up with other observations that, in comparison with DSAEK grafts, manually prepared DSEK grafts provide suboptimal visual outcomes and are associated with a higher rate of intraoperative and postoperative complications.11 12 In a recent study by Arnalich-Montiel et al,13 primary DSAEK was compared with secondary DSAEK performed on failed DMEK eyes. Six months after surgery, relatively poor visual outcomes were recorded in both groups. BCVA of ≥20/25 was achieved only by 60% of the primary DSAEK eyes and by none of the eyes in the secondary DSAEK group. However, DSAEK grafts were prepared using in all cases a 350 µm microkeratome head with a technique that yielded donor tissues with a very variable thickness ranging from 130 µm to 268 µm (median CGT=161.6 µm) in primary DSAEK eyes, and from 90 µm to 229.6 µm (median CGT=149.4 µm) in the secondary DSAEK eyes. Recently, Dickman et al14 have shown in a multicentric, randomised controlled study that CGT of DSAEK grafts correlates with both speed of visual recovery and final level of visual acuity achieved. The same group had also shown in a previous publication that thinner DSAEK grafts had less irregularities and induced less optical aberrations.15 This evidence confirmed our previous observation that ultrathin grafts produce excellent visual results, improving over time to levels very close to those recorded by other authors after DMEK.5 In our series, all DSAEK grafts were intended to have a CGT within 100 µm and were prepared according to standardised techniques described in detail elsewhere.5 6 As a result, 15 out of 21 grafts (71.4%) had a CGT≤100 µm with a maximal thickness within 131 µm in all cases. The interval between DMEK and UT-DSAEK surgery averaged 3±2.1 months and did not exceed in any case 7 months. Performing UT-DSAEK very promptly probably prevented the recipient cornea from developing changes that may have affected the outcomes of subsequent surgery and yielded 1 year outcomes that are comparable with those reported by Price et al with repeat DMEK4 as described in table 2. Our results show a rate of 19% (4/21) of IOL opacification following repeat surgery. IOL opacification following primary DSAEK was reported to be as high as 9.7%.16 Risk factors for this complication included AC re-bubbling, repeat surgery and the use of hydrophilic lenses.17 18 We found no previous reports describing the rate of this complication exclusively in repeat DSAEK patients. In our series, the apparently high rate of IOL opacification is probably the result of repeat air filling required by repeat endothelial keratoplasty (UT-DSAEK after DMEK) which was performed in 100% of cases. In all our cases of primary DMEK failure, as well as UT-DSEK postDMEK, a complete air fill was used in the first 2–3 postoperative hours. Instead, some surgeons use a partial air fill, especially after DMEK and this may possibly affect the rate of IOL opacification. This study was limited by a high number (8/29) of patients excluded because of unavailability of follow-up data. We could not identify any specific factor that was associated with being lost-to-follow-up, except for the fact that all these patients were referred to us from distant centres/colleagues. It is worth mentioning that the study period spanned 5 years in which gradual modifications to our DMEK technique were done. Later cases (from June 2014 and on) were done using the contact lens-assisted pull-through technique previously described.19 In conclusion, this study demonstrates that UT-DSAEK can provide excellent visual results, comparable to those of repeat DMEK, and low risk of complications, after failure of a primary DMEK. Surgeons may prefer UT-DSAEK in this situation, especially if they are at the beginning of their DMEK learning curve or if they are more comfortable with UT-DSAEK.

References

1 Eye Bank Association of America (EBAA). 2015. 2015 Eye Banking Statistical. Washington, DC: Eye Bank Association of America. http://restoresight.org/wp-content/ uploads/2016/03/2015-Statistical-Report.pdf (accessed 27 Dec 2017).

2 Williams K, Lowe M. K, et al. The Australian Graft Registry 2015 Report. 2015. Available at https://dspace.flinders.edu.au/xmlui/handle/2328/35402 (accessed 27 Dec 2017).

3 Deng SX, Lee WB, Hammersmith KM, et al. Descemet membrane endothelial keratoplasty: safety and outcomes: a report by the American Academy of Ophthalmology. Ophthalmology 2018;125:295–310.

4 Price MO, Feng MT, McKee Y, et al. Repeat Descemet membrane endothelial keratoplasty: secondary grafts with early intervention are comparable with fellow-eye primary grafts. Ophthalmology 2015;122:1639–44.

5 Busin M, Madi S, Santorum P, et al. Ultrathin Descemet's stripping automated endothelial keratoplasty with the microkeratome double-pass technique: two-year outcomes. Ophthalmology 2013;120:1186–94.

6 Nahum Y, Leon P, Busin M. Postoperative Graft Thickness Obtained With SinglePass Microkeratome-Assisted Ultrathin Descemet Stripping Automated Endothelial Keratoplasty. Cornea 2015;34:1362–4.

7 Baydoun L, van Dijk K, Dapena I, et al. Repeat Descemet membrane endothelial keratoplasty after complicated primary Descemet membrane endothelial keratoplasty. Ophthalmology 2015;122:8–16.

8 Ćirković A, Schlötzer-Schrehardt U, Weller JM, et al. Clinical and ultrastructural characteristics of graft failure in DMEK: 1-year results after repeat DMEK. Cornea 2015;34:11–17.

9 Dirisamer M, Dapena I, Ham L, et al. Patterns of corneal endothelialization and corneal clearance after descemet membrane endothelial keratoplasty for fuchs endothelial dystrophy. Am J Ophthalmol 2011;152:543–55.

10 Dapena I, Ham L, van Luijk C, et al. Back-up procedure for graft failure in Descemet membrane endothelial keratoplasty (DMEK). Br J Ophthalmol 2010;94:241–4.

11 Price MO, Price FW. Descemet's stripping with endothelial keratoplasty: comparative outcomes with microkeratome-dissected and manually dissected donor tissue. Ophthalmology 2006;113:1936–42.

12 Unterlauft JD, Elsässer K, Haigis W, et al. Corneal back surface radius after DSEK and DSAEK: a comparative single surgeon case control study. Int Ophthalmol 2015;35:533–40.

13 Arnalich-Montiel F, Hernández-Verdejo JL, Oblanca N, et al. Comparison of corneal haze and visual outcome in primary DSAEK versus DSAEK following failed DMEK. Graefes Arch Clin Exp Ophthalmol 2013;251:2575–84.

14 Dickman MM, Kruit PJ, Remeijer L, et al. A randomized multicenter clinical trial of ultrathin Descemet stripping automated endothelial keratoplasty (DSAEK) versus DSAEK. Ophthalmology 2016;123:2276–84.

15 Dickman MM, Cheng YY, Berendschot TT, et al. Effects of graft thickness and asymmetry on visual gain and aberrations after descemet stripping automated endothelial keratoplasty. JAMA Ophthalmol 2013;131:737–44.

16 Ahad MA, Darcy K, Cook SD, et al. Intraocular lens opacification after descemet stripping automated endothelial keratoplasty. Cornea 2014;33:1307–11.

17 Morgan-Warren PJ, Andreatta W, Patel AK. Opacification of hydrophilic intraocular lenses after Descemet stripping automated endothelial keratoplasty. Clin Ophthalmol 2015;9:277–83.

18 Maier PC, Heinzelmann S, Böhringer D, et al. [Intraocular lens opacification following posterior lamellar keratoplasty]. Klin Monbl Augenheilkd 2015;232:976–81.

19 Busin M, Leon P, Scorcia V, et al. Contact Lens-Assisted Pull-Through Technique for Delivery of Tri-Folded (Endothelium in) DMEK Grafts Minimizes Surgical Time and Cell Loss. Ophthalmology 2016;123:476–83.