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Outcomes of Descemet membrane endothelial keratoplasty, Descemet stripping automated endothelial keratoplasty and penetrating keratoplasty from a single centre study

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Abstract
Purpose According to some pioneer surgeons, lamellar endothelial keratoplasty techniques (EK), including Descemet membrane endothelial keratoplasty (DMEK) and Descemet stripping automated endothelial keratoplasty (DSAEK), yield excellent clinical results. However, there is a lack of studies with high levels of evidence and results of large national keratoplasty registers are contradictory. Therefore, two large cohorts of DMEK and DSAEK procedures are compared to a cohort of penetrating keratoplasty (PK).
Methods The study reports 868 keratoplasty procedures at a single centre (694 eyes with Fuchs endothelial dystrophy (FED) and 174 with bullous keratopathy (BK)). Patients underwent DMEK (450 eyes), DSAEK (89 eyes), or PK (329 eyes). Postoperative visual acuity, endothelial cell density (ECD), rate of regrafting, and rejections were recorded.
Results Visual acuity recovers faster and to a greater extent in EK compared to PK. DMEK performs better than DSAEK. ECD drops faster initially for EK compared to PK. In EK the rate of regrafting is higher than in PK (7 % in DMEK, 20 % in DSAEK and 2 % in PK in FED). The rejection rate is lowest following DMEK (7 % after DMEK, 21 % after DSAEK and 18 % after PK in FED).
Conclusions In contrast to recent reports from national keratoplasty registers, the overall clinical outcome of EK in FED and BK is superior to PK. Including ocular comorbidities and learning curves, these data reflect a realistic setting for comparing the different keratoplasty techniques. Corneal surgeons may be encouraged to preferentially use DMEK in FED and BK.

Keywords DMEK · DSAEK · PK · Keratoplasty · Cornea

Introduction

Excellent results have been reported for lamellar endothelial keratoplasty (EK) techniques, which include Descemet membrane endothelial keratoplasty (DMEK) and Descemet stripping automated endothelial keratoplasty (DSAEK) [1, 2]. Both techniques lead to refractive stability [3], especially compared to penetrating keratoplasty (PK) [4] as well as to a reduced risk of graft rejection [5]. They differ in terms of interface irregularities limiting visual acuity as seen following DSAEK [6–8], which is probably due to the transfer of corneal stroma in DSAEK.

Large national keratoplasty registers, including significant numbers of patients from various eye centres, do not currently reflect the beneficial results provided by single centre publications [9, 10]. This is especially true when considering graft survival. Moreover, no comparative study with established PK exists to date [9, 11, 12].

Therefore, it remains uncertain whether corneal surgeons should make the transition from PK to either DSAEK or DMEK [13, 14].

This study addresses this ambiguity by reporting an unbiased cohort under "real life" conditions including the learning curve of the surgeons as well as the ocular comorbidities of patients.

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Material and methods

Demography

The complete study cohort consists of 868 consecutive patients who underwent DMEK (450 patients), DSAEK (89 patients) or PK (329 patients) for Fuchs endothelial dystrophy (FED, 694 eyes) and bullous keratopathy (BK, 174 eyes, only pseudophakic BK or phakic BK because of glaucoma were included) between July 2011 and December 2014 at the Eye Center, Albert-Ludwigs-University Freiburg. Repeat keratoplasties were excluded as well as PK with trephines other than the guided trephine system. Patient characteristics are listed in table 1.

All grafts were stored under organ culture conditions according to the guidelines of the European Eye Bank Association (EEBA). These include the transfer of the graft to deswelling, dextran containing medium, before transplantation in DMEK, DSAEK, and PK.

The patients were included consecutively. No patients with comorbidities limiting visual acuity were excluded.

Phakic patients underwent DMEK or DSAEK in combination with cataract surgery (Triple-DMEK/Triple-DSAEK). In the phakic PK group, cataract was removed in a total of four eyes postoperatively because of reduction in BSCVA.

Surgical procedures

All surgeries were performed under general anesthesia by one out of three experienced surgeons.

Simultaneous cataract surgery was uniformly performed with a 2.2 mm microincision and capsular bag implantation. Special care was taken for removing all viscoelastic material. This was followed by administration of 1 % acetylcholine (Miochol®-E, Bausch & Lomb) into the anterior chamber.

DMEK

The surgeons prepared the grafts on the day of surgery in the operating theatre. The preparation technique has been described elsewhere [15]. The graft diameter was 8.0 or 7.5 mm.

All surgeries were performed according to the technique described by Melles et al. [16] including some minor modifications: briefly, the graft was stained with trypan blue 0.6 mg/ml for a few seconds and inserted through a conventional intraocular lens cartridge (CT Asphina 409 M, Zeiss, Germany). This cartridge was filled with balanced salt solution (BSS, Alcon, Freiburg, Germany). Before graft implantation a peripheral iridectomy was performed. Following descemetorhexis (9 mm) and graft implantation, the graft was unfolded by gentle manipulation with the aid of an air bubble in between the host stroma and the graft. After unfolding the graft centrally on the iris, intracameral air was withdrawn. Thereafter, an air bubble was placed underneath the graft to attach it to the stroma of the host. Here, no air-fluid exchange was performed, and the pupil was left miotic.

DSAEK

The DSAEK technique used has been described previously [8]. Following the preparation of the graft by microkeratome (7.5 or 8 mm diameter), stripping of Descemet's membrane (9 mm diameter), and a peripheral iridectomy were performed. Using a Busin glide, the graft was pulled into the anterior chamber, which was

Table 1 Baseline characteristics of the three study groups (means with SD)

	DMEK (450)	DSAEK (89)	PK (329)
Proportion of total cohort	45 %	14 %	41 %
Male:female	43 %:57 %	54 %:46 %	43 %:57 %
Mean age (years) at time of surgery	69+/−12	70+/−9	71+/−9
Indication for keratoplasty	409:41	71:18	214:115
FED:BK	91 %:9 %	80 %:20 %	65 %:35 %
Triple:Non-Triple	237:213	34:55	59:270
	53 %:47 %	38 %:62 %	18 %:72 %
Follow-up (months)	42+/−31	9+/−8	24+/−17
Postmortem time at retrieval (hours)	22+/−14	24+/−15	26+/−14
Donor age (years)	69+/−13	72+/−12	68+/−13
Preservation time in organ culture (days)	21+/−5	24+/−5	21+/−5
Preoperative ECD	2409+/−208	2423+/−247	2480+/−261

DMEK Descemet membrane endothelial keratoplasty, *DSAEK* Descemet stripping automated endothelial keratoplasty, *PK* penetrating keratoplasty, *FED* Fuchs endothelial dystrophy, *BK* bullous keratopathy, *BSCVA* best spectacle-corrected visual acuity, *Triple* combination of keratoplasty with phacoemulsification, *Non-Triple* existing pseudophakia at time of keratoplasty, *ECD* endothelial cell density

completely filled with air after centralising manipulations of the graft from the surface of the cornea.

PK

In all cases, penetration of the graft and host cornea was performed by a guided trephine system (GTS, Polytech, Germany, diameter 8 mm). Peripheral iridectomy was performed after administration of 1 % acetylcholine (Miochol®-E, Bausch & Lomb). The graft was sutured with a double-running cross-stitch nylon suture according to the procedure described by Hoffmann et al. [17]. In case of lens opacities limiting visual acuity, cataract surgery was performed simultaneously to the PK (Triple-PK, 18 %, Table 1) or during the postoperative period in case of newly developed opacities reducing visual acuity. Suture removal was performed between 6 and 18 months postoperatively.

Postoperative treatment

In all keratoplasty procedures, medical aftercare included topical dexamethasone (Dexa EDO, Dr. Gerhard Mann GmbH) five times per day and preservative-free artificial tears (Vismed, TRB Chemedica AG). Topical steroids were tapered over 5 months. Dexpanthenol (Bepanthen®, Bayer HealthCare) and ofloxacin (Floxal, Dr. Gerhard Mann GmbH) ointment were administered to treat epithelial defects by coating and preventing infections until reepithelialisation was achieved.

Postoperative parameters

Postoperatively, best spectacle-corrected visual acuity (BSCVA), endothelial cell density (ECD), rate of regrafting, and episodes of rejection were determined (Figs. 1, 2, 3 and 4).

Graft rejection was diagnosed in the case of new endothelial precipitates on the graft but not on the host cornea (with or without edema and with or without flare or cells inside the anterior chamber and independent of reduction in BSCVA). In case of otherwise unexplained graft oedema, rejection also was presumed. Without being able to perform histologic examination, it may be difficult to just morphologically discriminate between graft failure caused by immunologic rejection in contrast to graft failure caused by graft detachment or by nonimmunologic endothelial insufficiency (e.g., caused by mechanical stress intraoperatively). There even may be combinations of different causes. If graft-related immunologic precipitates were found and no signs of endothelial dysfunction or graft dislocation were present, rejection was postulated.

Graft failure was defined as persistent dislocation and/or missing transparency of the cornea/graft or in case of otherwise unexplained, unsatisfying visual results. As it was impossible to clearly discriminate between surgery-related and/or graft or patient- (respectively treatment-) related endothelial failure, all cases of graft failure were summarized.

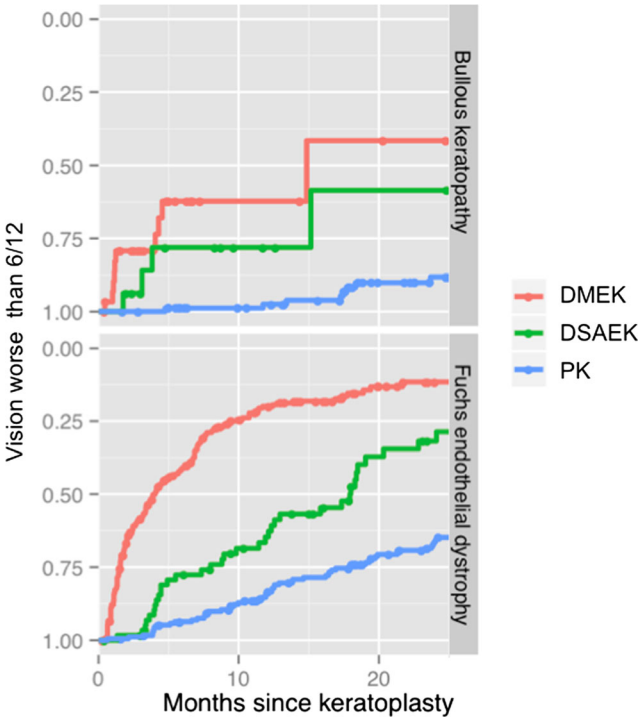

Fig. 1 Kaplan-Meier estimation of visual rehabilitation following keratoplasty. BSCVA of 6/12 is achieved faster following DMEK compared to DSAEK, and then PK. Abbr.: *DMEK* Descemet membrane endothelial keratoplasty, *DSAEK* Descemet stripping automated endothelial keratoplasty, *PK* penetrating keratoplasty

ECD was determined using noncontact specular microscopy (in hypotonic salt solution) and automated counting by Noncon ROBO-CA SP-8000, Japan.

Statistics

Survival analysis was used to compare improvement in visual acuity, endothelial cell loss, graft survival, and rejection between EK and PK. The log rank test was used to compare two survival curves as well as the Cox proportional hazards model for multifactorial analysis. All computations were performed with the software "R" (http://www.R-project.org). Statistical significance was defined as $p</= 0.05$.

Results

Visual acuity

The postoperative visual improvement was fastest in the DMEK group, followed by the DSAEK group for both FED and BK. In the FED group, 50 % of patients reached a BSCVA of Snellen 6/12 or more after 4 months following DMEK, 18 months following DSAEK, and more than 24 months

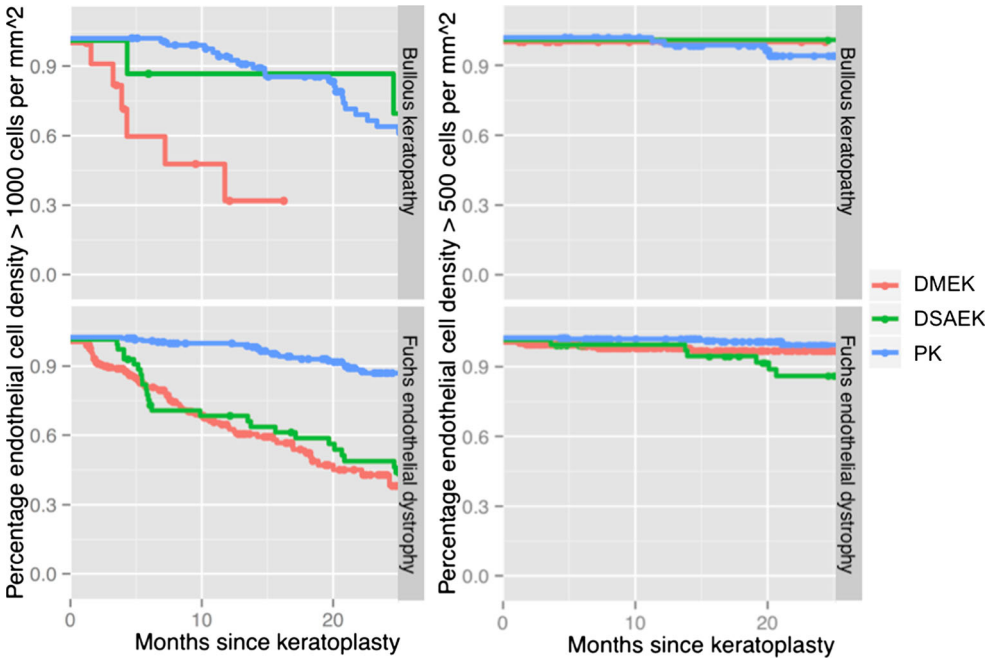

Fig. 2 Kaplan-Meier estimation of the percentage with ECD dropping below 500 (right) and 1000 (left) cells/mm^2. Abbr.: *DMEK* Descemet membrane endothelial keratoplasty, *DSAEK* Descemet stripping automated endothelial keratoplasty, *PK* penetrating keratoplasty

following PK. Visual rehabilitation took significantly longer in patients with BK (Fig. 1). In general, the FED group showed more successful outcomes compared to the BK group.

In patients with FED, the criteria of a BSCVA of Snellen 6/7.5 or better at 24 months postoperatively was reached in 53 % after DMEK, 15 % after DSAEK, and 10 % after PK. The overall BSCVA was significantly higher in DMEK than in PK and DSAEK, the latter reaching a slightly better maximum than PK (data not shown).

In the Cox model, risk factors for reaching BSCVA of 0.5 or more in comparison to PK are ($p < 0.001$): DSAEK (2.6

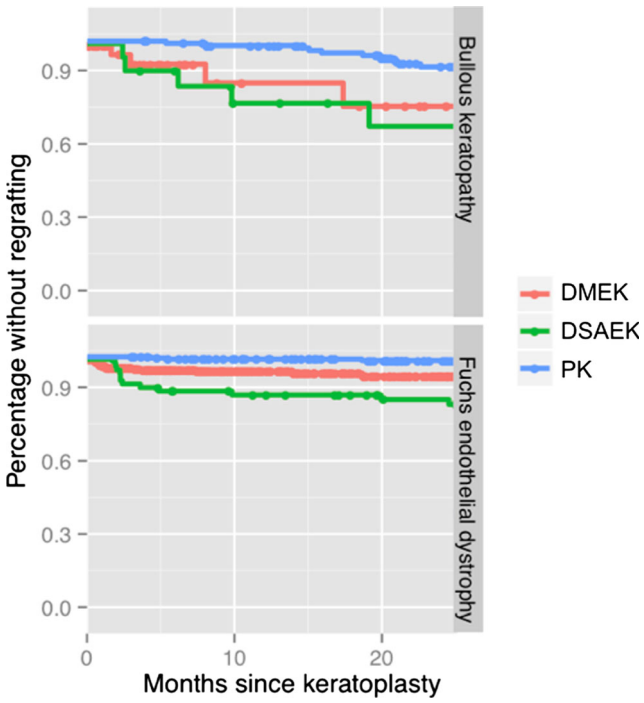

Fig. 3 Kaplan-Meier estimation of graft survival following DMEK, DSAEK and PK. Abbr.: *DMEK* Descemet membrane endothelial keratoplasty, *DSAEK* Descemet stripping automated endothelial keratoplasty, *PK* penetrating keratoplasty

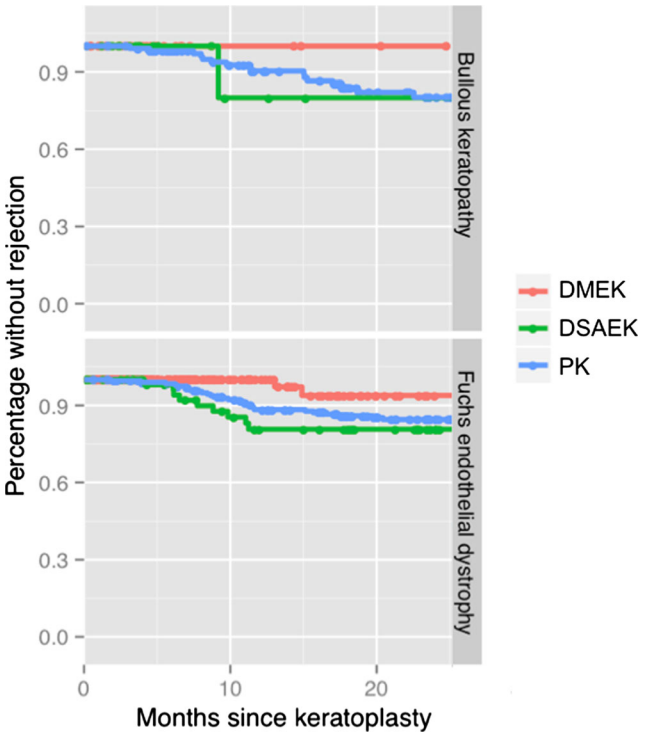

Fig. 4 Kaplan-Meier estimation of the rejection rate following DMEK, DSAEK, and PK. Abbr.: *DMEK* Descemet membrane endothelial keratoplasty *DSAEK* Descemet stripping automated endothelial keratoplasty, *PK* penetrating keratoplasty

times), DMEK (7.5 times), FED (2.7 times), every year of age of the recipient and Triple procedure are also protective factors. ECD and age of the donor were not statistically significant ($p = 0.9$).

Chronic endothelial cell loss

During the early postoperative period, there was no significant difference in loss of endothelial cells between the cohorts. In patients with FED, after 15 months, 99 % of grafts had ECD >500 cells/mm^2 in PK, 95 % in DMEK, and 93 % in DSAEK (Fig. 2, right). However, 24 months postoperatively endothelial cell count seemed to stabilise in DMEK and DSAEK after an early decrease, whereas following PK, there was a continuous decrease in endothelial cell count during the entire follow-up period.

In the smaller BK group, DSAEK and DMEK also yielded stable endothelial cell density after the high early postoperative decrease (Fig. 2). In comparison, there was a continuous decrease in ECD following PK during the first 24 months, approaching 90 % above the critical level of ECD > 500cells/mm^2.

Looking at a higher level of ECD loss of >1000 cells/mm^2 (Fig. 2, left), a difference in velocity between DMEK/DSAEK (fast early loss) and PK (more slow loss) is detectable for FED. In BK, DSAEK seems to resemble more PK.

Graft survival

In FED, both EK techniques showed a slightly increased risk of late endothelial failure during the first 2 years compared to PK (Fig. 3). However, graft survival was lower in BK compared to FED (Fig. 3). For FED, a higher regrafting rate was observed after DMEK (7 %) and DSAEK (20 %) compared to PK (2 %). However, the graft failure rate following DMEK was significantly lower than following DSAEK.

The significant risk factors ($p < 0.05$) for graft failure from the Cox model are the following: method (DSAEK is 6.5 times more likely to fail in comparison to PK, DMEK still 3.7 times. FED is protective (3.2 times less likely to fail than BK). Donor and recipient age are protective (2 % less risk per year of donor age, 3 % per year recipient age). Graft ECD and triple missed statistical significance.

Complications

The rate of reoperations was highest in the DMEK cohort because of the rebubbling rate of about 20 % (data not shown). Among all patients, no serious complications, such as exogenous endophthalmitis or expulsive choroidal hemorrhage, were observed.

Immunologic graft rejection

Endothelial graft rejections were observed in each cohort (Fig. 4). In patients with FED, DMEK grafts showed the lowest rejection rate, at 7 % after 2 years, followed by 18 % in PK and 21 % in DSAEK. Patients with BK show similar results despite the smaller group size.

Discussion

The aim of this study was to assess the long-term outcome of DMEK and DSAEK compared with PK when used in a clinical setting rather than in a controlled trial. We report a large consecutive case series from a single centre comparing the clinical results of DMEK, DSAEK, and PK for FED and BK. The series includes all learning curves as well as ocular comorbidities.

The data reveal the superior clinical outcome (BSCVA, ECD loss, and rejection rate) of DMEK, and even of DSAEK, compared to PK. This finding is evident even if graft survival seems not to be significantly reduced in EK during the first two postoperative years.

This contradicts the two existing studies with evidence level II (studies with evidence based on at least one well-designed and controlled trial without randomization) based on national keratoplasty registers from Australia and the United Kingdom [9, 10, 18]. This contradiction has been attributed to the heterogeneity of centres that report to a national registry. The data in this study are thought to represent the “real life” situation in contrast to any “controlled study” conditions with highly selected patients and without learning curves. From the literature, as well as from the experiences of the authors, it is known that the results following DMEK and DSAEK become better with increasing knowledge and skills in these techniques [19].

Visual acuity

In the current literature, there are a few studies of evidence level III (evidence based on well-designed, nonexperimental and descriptive trials) investigating more than 100 eyes following DMEK [19–25]. In contrast to this report, it only included eyes with good visual potential and excluded eyes with reoperations. As a result, it reports a mean BSCVA of 6/7.5 or better in 50–80 % of the patients after 6 months. These results in otherwise healthy eyes clearly exceed the results of this nonselective cohort. In addition, they are noncomparative.

As in all groups, lens-related reduction in BSCVA was not tolerated (EK in phakic eyes always was combined with cataract surgery and cataract following PK was removed when limiting visual acuity), only other comorbidities could limit the visual potential. By comparing large numbers of patients

and differing FED from BK, the groups should be comparable and represent a "real life setting."

According to this study, BSCVA rises faster and to a higher maximum in DMEK compared to DSAEK patients for both FED and BK (Fig. 1). In PK visual rehabilitation is slower compared to DMEK and DSAEK. DMEK clearly differs from DSAEK in that no stromal tissue is transferred with the graft. Stroma-to-stroma interactions are thought to cause posterior surface irregularities as well as interface disturbances, leading to reduced BSCVA [7, 8] following DSAEK. In PK, visual rehabilitation is known to progress slowly because of the graft sutures and the resulting refractive changes [26, 27].

Chronic endothelial cell loss

During the early postoperative phase, ECD decreases faster in DMEK and DSAEK compared to PK and faster in BK than in FED (Fig. 2). This may be due to the amount of manipulation needed during preparation and unfolding of the graft compared to PK, where chronic processes are assumed to cause the decrease [28]. Following DMEK, migration of endothelial cells in the region of the gap surrounding the graft was detected [29], which may also explain the greater decrease in central ECD. Additionally, the peripheral reservoir of endothelial cells may be reduced in BK compared to FED, which may also explain the faster loss of ECD. Moreover, in patients with BK, the rapid loss of endothelial cells following PK is attributed to subclinical inflammation and rejection processes beyond the migration theory [28]. Inflammation and rejection might also be present in EK. It could be speculated, however, that with the less tissue transferred, fewer of these processes may occur.

Graft survival

DMEK and DSAEK require more reoperations compared to PK for both FED and BK. For DMEK this is mainly due to postoperative adherence problems of the lamellar grafts that need surgical intervention leading to a further decrease of endothelial cells. Although the current data cannot provide the long-term prognosis of regrafting, there is a tendency of stabilisation of the regrafting rate following DMEK after 24 months (Fig. 3). Especially during the learning phase of a corneal surgeon, it is recommended to choose older donors with high preoperative ECD of the graft [30] for easier unfolding, as older grafts form broader and less tight rolls. Following DSAEK, regrafting was often performed because of unsatisfactory visual results [8]. Besides insufficient function, acute or chronic rejection may be a reason for regrafting in DSAEK and PK leading to low ECD and increased corneal thickness [31], but not in DMEK. This is because the observed episodes of rejection in DMEK were very mild and occurred in only a few endothelial precipitates without oedema and/or endothelial decompensation and without flare.

The difference in regrafting between patients with BK and FED for DMEK, DSAEK, and PK may be explained by unfavorable points of departure with previous endothelial cell damage due to surgical trauma or inflammation processes, for example, in BK. This results in a lower peripheral endothelial reservoir in BK compared to FED, which contributes to more rapid graft failure [28]. Additionally, because of the low initial BSCVA, patients may not be able to perceive their own complications, which include macular or corneal oedema and thus, adequate treatment may be delayed at the expense of the graft's life span.

Immunologic graft rejection

Following DMEK, fewer rejection episodes occurred compared with DSAEK and PK. The incidence of rejection was similar for DSAEK and PK (Fig. 4). This may be due to the fact that in DMEK, no stromal tissue is transferred containing any antigen-presenting cells [32]. But, ultimately, the available data from this study and the literature are not yet sufficient to draw any definite conclusions to explain the low rejection rate following DMEK. Due to the different group sizes, no direct comparison can be drawn to explain the different graft rejection rates of PK and DSAEK. Underlying diagnosis FED or BK does not have any impact on graft survival (Fig. 4).

Guerra et al. report a 5 % rejection rate during the first 12 months [23]. The first rejection in that study occurred in the second postoperative year, and the overall rejection rate was lower.

Conclusion

DSAEK and, especially DMEK, lead to higher regrafting rates compared to PK. At first, this seems to be disadvantageous in terms of a higher long-term need for grafts in times of shortage of corneas. However, these methods provide faster and more complete visual rehabilitation. Together with the considerably lower rejection risk and acceptable ECD loss, clinical outcomes of DMEK are clearly beneficial for patients. Because of the evident advantages, corneal surgeons are encouraged to change from PK to EK and, furthermore, from DSAEK to DMEK. Finally, more experienced centres may serve as the basis for studies with stronger levels of evidence and may lead to the promotion of more standardised DMEK procedures.

Compliance with ethical standards

Funding No funding was received for this research.

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethical board Freiburg, AZ 88/12) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study formal consent is not required.

References

1. Melles GR (2006) Posterior lamellar keratoplasty: DLEK to DSEK to DMEK. Cornea 25:879–881. doi:10.1097/01.ico.0000243962.60392.4f
2. Dapena I, Ham L, Melles GR (2009) Endothelial keratoplasty: DSEK/DSAEK or DMEK–the thinner the better? Curr Opin Ophthalmol 20:299–307. doi:10.1097/ICU.0b013e32832b8d18
3. Kwon RO, Price MO, Price FW Jr, Ambrosio R Jr, Belin MW (2010) Pentacam characterization of corneas with Fuchs dystrophy treated with Descemet membrane endothelial keratoplasty. J Refract Surg 26:972–979. doi:10.3928/1081597X-20100212-08
4. Maier AK, Gundlach E, Gonnermann J, Klamann MK, Eulufi C, Bertelmann E, Joussen AM, Torun N (2013) Fellow eye comparison of descemet membrane endothelial keratoplasty and penetrating keratoplasty. Cornea doi. doi:10.1097/ICO.0b013e31829dd816
5. Anshu A, Price MO, Price FW Jr (2012) Risk of corneal transplant rejection significantly reduced with Descemet's membrane endothelial keratoplasty. Ophthalmology 119:536–540. doi:10.1016/j.ophtha.2011.09.019
6. Price MO, Price FW Jr (2013) Descemet's membrane endothelial keratoplasty surgery: update on the evidence and hurdles to acceptance. Curr Opin Ophthalmol 24:329–335. doi:10.1097/ICU.0b013e32836229ab
7. Heinzelmann S, Bohringer D, Maier PC, Reinhard T (2014) Correlation between visual acuity and interface reflectivity measured by pentacam following DSAEK. Acta Ophthalmol 92:e1–e4. doi:10.1111/aos.12217
8. Heinzelmann S, Maier P, Bohringer D, Auw-Hadrich C, Reinhard T (2013) Visual outcome and histological findings following femtosecond laser-assisted versus microkeratome-assisted DSAEK. Graefes Arch Clin Exp Ophthalmol 251:1979–1985. doi:10.1007/s00417-013-2359-7
9. Patel SV, Armitage WJ, Claesson M (2014) Keratoplasty outcomes: are we making advances? Ophthalmology 121:977–978. doi:10.1016/j.ophtha.2014.01.029
10. Greenrod EB, Jones MN, Kaye S, Larkin DF (2014) Center and surgeon effect on outcomes of endothelial keratoplasty versus penetrating keratoplasty in the United Kingdom. Am J Ophthalmol 158:957–966. doi:10.1016/j.ajo.2014.07.037
11. Nanavaty MA, Wang X, Shortt AJ (2014) Endothelial keratoplasty versus penetrating keratoplasty for Fuchs endothelial dystrophy. Cochrane Database Syst Rev 2, CD008420. doi:10.1002/14651858.CD008420.pub3
12. Heinzelmann S, Maier P, Reinhard T (2011) Perspectives of posterior lamellar keratoplasty. In search of the perfect lamella. Ophthalmologe 108:825–832. doi:10.1007/s00347-011-2330-0
13. Maier P, Reinhard T, Cursiefen C (2013) Descemet stripping endothelial keratoplasty–rapid recovery of visual acuity. Dtsch Arztebl Int 110:365–371. doi:10.3238/arztebl.2013.0365
14. Parekh M, Salvalaio G, Ruzza A, Camposampiero D, Griffoni C, Zampini A, Ponzin D, Ferrari S (2013) Posterior lamellar graft preparation: a prospective review from an eye bank on current and future aspects. J Ophthalmol 2013:769860. doi:10.1155/2013/769860
15. Kruse FE, Laaser K, Cursiefen C, Heindl LM, Schlotzer-Schrehardt U, Riss S, Bachmann BO (2011) A stepwise approach to donor preparation and insertion increases safety and outcome of Descemet membrane endothelial keratoplasty. Cornea 30:580–587
16. Melles GR, Ong TS, Ververs B, van der Wees J (2006) Descemet membrane endothelial keratoplasty (DMEK). Cornea 25:987–990. doi:10.1097/01.ico.0000248385.16896.34
17. Hoffmann F (1976) Suture technique for perforating keratoplasty (author's transl). Klin Monbl Augenheilkd 169:584–590
18. Coster DJ, Lowe MT, Keane MC, Williams KA (2014) A comparison of lamellar and penetrating keratoplasty outcomes: a registry study. Ophthalmology 121:979–987. doi:10.1016/j.ophtha.2013.12.017
19. Dapena I, Ham L, Droutsas K, van Dijk K, Moutsouris K, Melles GR (2011) Learning curve in Descemet's membrane endothelial keratoplasty: first series of 135 consecutive cases. Ophthalmology 118:2147–2154. doi:10.1016/j.ophtha.2011.03.037
20. Monnereau C, Quilendrino R, Dapena I, Liarakos VS, Alfonso JF, Arnalich-Montiel F, Bohnke M, Pereira NC, Dirisamer M, Parker J, Droutsas K, Geerling G, Gerten G, Hashemi H, Kobayashi A, Naveiras M, Oganesyan O, Orduna Domingo E, Priglinger S, Stodulka P, Torrano Silva J Jr, Venzano D, Vetter JM, Yiu E, Melles GR (2014) Multicenter study of descemet membrane endothelial keratoplasty: first case series of 18 surgeons. JAMA Ophthalmol 132:1192–1198. doi:10.1001/jamaophthalmol.2014.1710
21. Chaurasia S, Price FW Jr, Gunderson L, Price MO (2014) Descemet's membrane endothelial keratoplasty: clinical results of single versus triple procedures (combined with cataract surgery). Ophthalmology 121:454–458. doi:10.1016/j.ophtha.2013.09.032
22. Heindl LM, Riss S, Adler W, Bucher F, Hos D, Cursiefen C (2013) Split cornea transplantation: relationship between storage time of split donor tissue and outcome. Ophthalmology DOI. doi:10.1016/j.ophtha.2012.11.012
23. Guerra FP, Anshu A, Price MO, Giebel AW, Price FW (2011) Descemet's membrane endothelial keratoplasty: prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology 118:2368–2373. doi:10.1016/j.ophtha.2011.06.002
24. Ciechanowski PP, Droutsas K, Baydoun L, Dirisamer M, Oellerich S, Melles GR (2014) Standardized Descemet membrane endothelial keratoplasty (DMEK): technique and latest results. Ophthalmologe 111:1041–1049. doi:10.1007/s00347-013-3014-8
25. Rodriguez-Calvo-de-Mora M, Quilendrino R, Ham L, Liarakos VS, van Dijk K, Baydoun L, Dapena I, Oellerich S, Melles GR (2015) Clinical outcome of 500 consecutive cases undergoing Descemet's membrane endothelial keratoplasty. Ophthalmology 122:464–470. doi:10.1016/j.ophtha.2014.09.004

26. Birnbaum F, Wiggermann A, Maier PC, Bohringer D, Reinhard T (2013) Clinical results of 123 femtosecond laser-assisted penetrating keratoplasties. Graefes Arch Clin Exp Ophthalmol 251:95–103. doi:10.1007/s00417-012-2054-0
27. Ruhswurm I, Scholz U, Pfleger T, Zehetmayer M, Hanselmayer G, Skorpik C (1999) Three-year clinical outcome after penetrating keratoplasty for keratoconus with the guided trephine system. Am J Ophthalmol 127:666–673
28. Reinhard T, Bohringer D, Huschen D, Sundmacher R (2002) Chronic endothelial cell loss of the graft after penetrating keratoplasty: influence of endothelial cell migration from graft to host. Klin Monbl Augenheilkd 219:410–416. doi:10.1055/s-2002-32876
29. Dirisamer M, Dapena I, Ham L, van Dijk K, Oganes O, Frank LE, van der Wees J, Melles GR (2011) Patterns of corneal endothelialization and corneal clearance after descemet membrane endothelial keratoplasty for fuchs endothelial dystrophy. Am J Ophthalmol 152(543–555), e541. doi:10.1016/j.ajo.2011.03.031
30. Heinzelmann S, Huther S, Bohringer D, Eberwein P, Reinhard T, Maier P (2014) Influence of donor characteristics on descemet membrane endothelial keratoplasty. Cornea 33:644–648. doi:10.1097/ICO.0000000000000106
31. Writing Committee for the Cornea Donor Study Research Group, Sugar A, Gal RL, Kollman C, Raghinaru D, Dontchev M, Croasdale CR, Feder RS, Holland EJ, Lass JH, Macy JI, Mannis MJ, Smith PW, Soukiasian SH, Beck RW (2015) Factors associated with corneal graft survival in the cornea donor study. JAMA Ophthalmol 133:246–254. doi:10.1001/jamaophthalmol.2014.3923
32. Yamagami S, Ebihara N, Usui T, Yokoo S, Amano S (2006) Bone marrow-derived cells in normal human corneal stroma. Arch Ophthalmol 124:62–69. doi:10.1001/archopht.124.1.62