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Real-World Outcomes of DMEK: A Prospective Dutch Registry Study

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ABSTRACT

Purpose: To analyze real-world practice patterns, graft survival, and outcomes of Descemet membrane endothelial keratoplasty (DMEK) in the Netherlands.

Design: Population-based interventional clinical study.

Methods: In this prospective registry study, all consecutive primary DMEK procedures registered in the Netherlands Organ Transplant Registry were identified. Short-term graft survival and outcomes of primary transplants for Fuchs endothelial dystrophy (FED) were analyzed using Kaplan-Meier survival curves with log-rank test and Cox regression. Linear mixed model analyses were used for best spectacle-corrected visual acuity (BSCVA), spherical equivalent, hyperopic shift, and endothelial cell density.

Results: 752 DMEKs were identified between 2011 and 2018. In 90% of cases, the indication for DMEK was FED. Graft survival measured 87% at 3 months, 85% at 6 months, 85% at 1 year, and 78% at 2 years. DMEK procedures after 2015 showed better survival compared to previous years (Hazard ratio = 0.4; P<0.001). Baseline BSCVA in primary transplants with FED measured on average 0.45 logarithm of the minimum angle of resolution (logMAR) (95% CI 0.41 – 0.49), and significantly improved (overall P<0.001) to 0.17 logMAR (95% CI 0.14 – 0.21) at 3 months, 0.15 logMAR (95% CI 0.11 – 0.18) at 6 months, 0.12 logMAR (95% CI 0.08 – 0.16) at 1 year, and 0.08 (95% CI 0.05 – 0.12) at 2 years. At 3 months, a hyperopic shift of +0.36 diopters (P<0.001) was observed and endothelial cell loss measured 33%.

Conclusion: Our findings provide real-world support that DMEK is an effective treatment for FED with respect to vision restoration, inducing a small hyperopic shift with an acceptable endothelial cell loss. Graft survival improved over time, suggesting a learning curve on a national level.

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INTRODUCTION

National quality registries are increasingly recognized in recent years as a valuable tool for improving healthcare via the use of real-world data.[1]The primary attribute that distinguishes "real-world" evidence is related to the context in which the evidence is gathered – in other words, in clinical care settings. Key to understanding the usefulness of real-world evidence is an appreciation of its potential for complementing the knowledge gained from traditional clinical trials, whose well-known limitations make it difficult to generalize findings to larger, more inclusive populations of patients and settings that reflect actual use in practice.[2]

Much of our knowledge on the outcomes of corneal transplantation originates from such registries. Using the Netherlands Organ Transplant Registry (NOTR), our group previously reported on the long-term real-world outcomes of penetrating keratoplasty (PK) and Descemet stripping automated endothelial keratoplasty (DSAEK).[3,4]

Descemet membrane endothelial keratoplasty (DMEK), the latest iteration in endothelial keratoplasty (EK), is reported to achieve excellent visual outcomes with relatively low complication rates in specialized centers.[5] However, little is known about the real-world outcomes of DMEK.

In the current study, we retrospectively analyze prospectively collected NOTR data and report the real-world outcomes of DMEK in the Netherlands in terms of graft survival, longitudinal trends in visual acuity, refraction, endothelial cell density (ECD), and complications.

METHODS

GRAFT REGISTRY AND DATA COLLECTION

Data for this multicenter prospective registry study was obtained from the NOTR, a prospective national database founded by the Netherlands Transplantation Foundation (NederlandseTransplantatieStichting [NTS], https://www.transplantatiestichting.nl/over-de-nts). In the Netherlands, donor corneas are centrally allocated and registered in NOTR. Therefore, data regarding graft survival is complete and independent of center/surgeon reporting. Using NOTR, the NTS prospectively captures data related to the recipient, donor, eye bank processing, and surgical procedure of all corneal transplantations performed in the Netherlands except for one clinic. Corneal surgeons prospectively complete relevant follow-up data at predefined time points using a standardized electronic data capture system. The evaluating factors defined in the prospective study protocol include donor characteristics: age, gender, and ECD; recipient characteristics: age, gender, and indication for transplantation; surgery characteristics: date of surgery, transplant type, previous corneal transplants, baseline visual acuity and refraction, complications, and lens status; and postoperative data: date of follow-up, graft status, visual acuity, refraction, ECD, adverse events, interventions, graft failure specification and date, last known follow-up date, lost to follow up status. Data collection continues until graft failure or loss to follow-up. For this study, the NOTR steering group provided institutional review board approval for data extraction and analysis. Informed consent was obtained from all patients to participate in the registry and for the use of data for research. The study adhered to the tenants of the declaration of Helsinki and Dutch legislation.

POPULATION

DMEK tissue was provided by two eye banks. Ten corneal clinics registered DMEK in NOTR. In line with institutional review board approval, information on center and surgeons was not made available. The first DMEK surgery registered in NOTR was performed on October 5th, 2011. The study cohort included all consecutive DMEK procedures until May 31st, 2018. All patients received a tapered topical corticosteroid regimen during the first six months after surgery, followed by low dose maintenance thereafter.

OUTCOME MEASURES

The primary outcome measure was graft survival. Graft failure was reported by the corneal surgeon as defined by the coding guidelines provided by NOTR, or identified in case of a subsequent corneal transplantation in the same eye.Graft failure occurring within three months of transplantation was defined as early graft failure (EGF). Secondary outcomes were: best spectacle-corrected visual acuity (BSCVA), ECD, spherical equivalent (SE), hyperopic shift, and rebubbling.Snellen acuity was converted to the logarithm of the minimum angle of resolution (logMAR) for statistical analyses. Spherical equivalent was defined as the sum of the spherical value and half of the cylindrical value. Refractive shift was defined as the difference in postoperative SE and preoperative SE. Refractive shift was calculated for single DMEK as data on target refraction was not available in triple DMEK.

STATISTICAL ANALYSIS

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, N.Y., USA). Baseline characteristics were reported as frequencies with percentages or mean ± standard deviation (SD). The number of transplants over time was tested using the $\chi 2$ goodness of fit test.

Graft survival and longitudinal trends in BSCVA, ECD, and SE were calculated for all DMEK procedures that had Fuchs endothelial dystrophy (FED) as indication excluding cases with anterior chamber intraocular lenses, and unknown lens status. Outcomes are reported over two years after surgery, due to a very low number of events (i.e. failed grafts), and limited number of cases with longer follow-up. In case both eyes of the same patient were operated or repeat transplant was performed, only the first transplant per patient was included in the primary analyses. This was done to prevent bias related to correlated measurements within the same patient or eye. Death-censored graft survival was assessed using Kaplan-Meier survival curves with log-rank test and univariable Cox regression analysis with transplant year (five categories: before 2015, 2015, 2016, 2017, 2018) as an explanatory factor. Cox regression analysis was performed over the first six months postoperatively, since the vast majority of events (i.e. graft failure) occurred during the period. Proportional hazard assumption was checked using the log(-log) survival function plot. Sensitivity analyses including all transplants were also performed. Linear mixed models (LMM) were fitted to investigate the longitudinal trend in BSCVA, ECD, SE, and hyperopic shift, where time, transplant year, ocular comorbidity, and lens status were included as fixed factors and an unstructured covariance structure was used for the repeated measures (preoperative recipient or donor, 3, 6, and 12 months). LMM assume missing at random (MAR), i.e. missingness may depend on observed variables, which should then be incorporated in the model. The differences in characteristics in patients with missing data were compared to patients without missing data (no significant differences found). Cases that developed graft failure were excluded from the analysis of BSCVA, ECD, and SE. Estimated marginal means (EMM) were reported, and changes between different time-points were tested. P-values ≤ 0.05 were considered statistically significant.

RESULTS

PRACTICE PATTERNS

In total, 752 DMEK procedures were registered in NOTR between January 1st, 2011 until May 31st, 2018. The proportion of DMEK procedures increased significantly over time (p<0.001), Figure 1. Until 2015, 104 DMEK procedures were performed. The greatest increase occurred between 2015 and 2016 (n=43 vs. n=213, respectively, P<0.001). In contrast, the proportion of Descemet stripping automated endothelial keratoplasty (DSAEK) and penetrating keratoplasty (PK) procedures decreased since 2015 (2015 vs. 2017: n=735 vs. n=527, respectively, P<0.001, DSAEK; and n=360 vs. n=248, respectively, P<0.001, PK). In 2017, the number of DMEK procedures surpassed PK for the first time. In the first half of 2018, slightly more DMEK procedures were performed compared to DSAEK (171 vs. 166, respectively).

Recipient and donor demographics, indication for surgery, and surgical procedure are given in Table 1. The leading indication was FED (90%), followed by graft failure (5%), and pseudophakic bullous keratopathy (3%). 77% of DMEK procedures were performed in pseudophakic eyes, 6% in phakic eyes, and 7% were combined with cataract extraction and intraocular lens placement (triple DMEK).

GRAFT SURVIVAL

468 DMEK procedures were available for graft survival analysis after excluding fellow eyes (n=125), indications other than FED including regrafts (n=58), anterior chamber intraocular lenses or unknown lens status (n=53), and missing data (n=48). At three, six, twelve, and 24 months 30, 98, 244, and 369 cases were censored, respectively. Overall graft survival measured 87% at three months, 85% at six months, 85% at 1 year, and 78% at two years (Figure 2). A single graft failure was registered after two years. In <2015, 2015, 2016, 2017, and 2018, 41, 34, 179, 175, and 39 cases were available for analysis, respectively. Graft survival was similar for <2015 and 2015 (P=0.85), as well as for 2016, 2017 and 2018 (all P≥0.26). When combined, transplants performed between 2016 and 2018 showed higher survival probability compared to earlier transplants (Hazard ratio [HR] = 0.4 [95% confidence interval (CI) 0.25 – 0.63], P<0.001). The database captured two graft rejection episodes. In both cases, patients did not have known risk factors for graft rejection and were treated according to standard protocol prior to graft rejection. Graft rejection was reversible in both cases.

VISUAL AND REFRACTIVE OUTCOMES

Mean BSCVA during a follow-up period of one year is shown in Figure 4. BSCVA measured 0.45 logMAR (95% CI 41 – 0.49) (n=442) preoperatively and significantly improved (overall P<0.001) to 0.17 logMAR (95% CI 0.14 – 0.21) (n=380) at three months, 0.15 logMAR (95% CI 0.11 – 0.18) (n=306) at six months, 0.12 logMAR (95% CI 0.08 – 0.16) (n=214) at one year, and 0.08 logMAR (95% CI 0.05 – 0.12) (n=45) at two years. The cumulative percentage of eyes reaching various best spectacle-corrected Snellen acuities is given in Figure 5. Twelve months after DMEK, 67% and 28% of eyes reached ≥20/25 and ≥20/20 Snellen BSCVA, respectively.

A statistically significant hyperopic shift was observed three months after DMEK alone (0.36 D [95% CI 0.20 – 0.51], P<0.001), which stabilized thereafter. Spherical equivalents values for single DMEK are given in Table 2.

ENDOTHELIAL CELL DENSITY

Donor and postoperative ECD are given in Table 2. Donor ECD measured 2706 cells/mm^2 (95% CI 2670 – 2741), decreasing to 1799 cells/mm^2 (95% CI 1729 – 1869), P<0.001 (33% cell loss) at three months and stabilizing thereafter.

REBUBBLINGS

Rebubbling was the most common complication. In the entire cohort, 144 rebubblings were registered, corresponding to a 19% rebubbling rate. Subsequent rebubbling was performed in 3%, and a single case underwent a third rebubbling. Rebubbling rate measured 11% before 2015, 14% in 2015, 25% in 2016, 20% in 2017, and 14% in 2018. In triple DMEK, rebubbling rate did not differ significantly from single DMEK (odds ratio = 0.87 [95% CI 0.41 – 1.85], P=0.72).

Sensitivity analyses, including all transplants, did not appreciably change the outcomes. For the primary outcome measure, graft survival measured for sensitivity vs. primary analysis 87% vs. 87% at three months, 86% vs. 85% at six months, 86% vs. 85% at one year, and 77% vs. 78% two years after surgery, respectively.

DISCUSSION

This registry study analyzed the practice patterns and outcomes of DMEK in the Netherlands. To the best of our knowledge, this is the first national registry study to report the real-world outcomes of DMEK.

DMEK was introduced in the Netherlands in 2002.[6] Between 2002 and 2010, the procedure was performed in a single private clinic that does not register in NOTR. From 2011 until 2015, a total of 104 DMEK procedures were recorded in NOTR. In contrast, 213 DMEK procedures were registered in 2016 alone, marking a major turning point in the uptake of the technique. Concurrently, the number of DSAEK procedures decreased since 2016. In the first half of 2018, marginally more DMEK procedures were recorded compared to DSAEK.

In our cohort, graft survival measured 85% twelve months after DMEK. Almost all failures occurred during the first three months after surgery. This figure is lower compared to the 92% - 100% graft survival rate reported in the Ophthalmic Technology Assessment (OTA) by the American Academy of Ophthalmology.[7] While the current registry study captures data from a heterogeneous group of medical centers, including high- and low-volume as well as specialized and non-specialized centers, most of the data in the OTA arises from highly specialized centers, limiting generalizability.

DMEK survival in this NOTR cohort was also lower compared to the 94% two-year graft survival rate after DSAEK in NOTR.[3] The short-term graft survival in DMEK improved significantly over time, which suggests a learning curve on a national level for a technically challenging procedure.Indeed, the time frame in our study includes the learning curve of multiple surgeons. Another explanation for improving graft survival over time is standardization of the surgical technique during the study period. We recently reported that the survival and functional outcomes of repeat-DSAEK grafts are significantly worse compared to primary DSAEK.[4] This is important as the current study found higher DMEK graft failure rate during the early years (<2016). If repeat-DMEK is also significantly worse compared to primary DMEK, it would underscore the impact of introducing DMEK on a national level.

With the introduction of DMEK, anatomic restoration of the cornea became possible, avoiding interface irregularities and potentially improving vision. In our study, BSCVA improved from 0.45 logMAR before surgery to 0.12 logMAR one year after surgery. The postoperative BSCVA in DMEK is better compared to PK and DSAEK for FED in NOTR (0.39 logMAR and 0.29 logMAR at one year, respectively).[3] However, PK and DSAEK show worse BSCVA at baseline compared to DMEK (0.9 logMAR and 0.68 logMAR, respectively). The reason for this difference in baseline BSCVA may be two-fold. First, an allocation bias of eyes with better prognosis to novel techniques. Second, a lower threshold for surgical intervention at earlier stages of visual disability.[8]

Historically, the core outcome parameter for corneal transplantation shifted from graft survival in the era of PK to visual acuity with EK. However, differences in VA in modern EK procedures are small, and patients routinely undergo surgery for symptoms such as reduced contrast sensitivity or glare disability irrespectively of VA.[9-11] Patient-reported outcome measures have been developed to capture this information.[12,13] However, these are currently not part of the standard evaluation in many centers, and as such are not yet recorded in NOTR.

Randomized controlled trials offer a less biased comparison between treatment modalities under controlled circumstances. However, they are costly and under certain circumstances no longer ethical to perform. In contrast, registries provide a low-cost window into routine clinical care (real-world). The strong internal validity of RCTs goes inevitably at the expense of generalizability, while registries suffer from low internal validity. Both study designs can complement each other. Registries can provide external validity to RCTs with restrictive eligibility criteria. In the current study, BSCVA is comparable to two recent RCTs comparing DMEK and ultrathin DSAEK.[14,15] A novel study design, the randomized registry study, combines the strength of randomization with the advantages of registries and may provide a cost-effective solution for increasingly more expensive health care systems.[1]

The hyperopic shift after DSAEK is primarily thought to result from the meniscus-shaped profile of the donor lenticule.[16] In DMEK, the hyperopic shift is likely due to curvature changes in response to corneal hydration status.[17] In the current cohort, a hyperopic shift of +0.36 D after DMEK was observed three months after surgery, which is in line with the mean astigmatism change of +0.31 D reported in the OTA.[7] Consequently, DMEK can be considered a predictable and relatively refractive neutral procedure that allows safe combination with cataract surgery and intraocular lens placement.[17,18] Target refraction in triple DMEK was not captured by the registry. Cases that underwent triple DMEK were therefore excluded in the analysis of spherical equivalent and refractive shift.

In EK, most endothelial cell loss is registered early after transplantation. Three months postoperatively, mean cell loss measured 33%, stabilizing thereafter. The cell loss is in line with previous reports on DMEK,[7,14,15] and comparable to the NOTR DSAEK cohort for FED.[3]

Graft detachment necessitating rebubbling is the Achilles heel of DMEK. In the literature, the percentage of eyes requiring rebubbling ranges from 2% to 84%,[7] with most studies reporting percentages between 10% and 30%.[14,15,19]In the current cohort, 19% of eyes required underwent rebubbling. The rebubbling protocols were not standardized across medical centers. NOTR does not capture details on the degree of graft detachment. However, most surgeons in the Netherlands perform rebubbling for graft detachments that are centrally located or affect more than 1/3 of the graft surface area. There is controversy in the literature regarding complication rates with triple procedure compared with DMEK alone.[20-22] In our cohort, there was no significant or clinically relevant difference in rebubbling rate between triple and single procedures. Sulfur hexafluoride (SF_6) at various concentrations can be used instead of 100% air to decrease graft detachment rate, because SF6 has a longer tamponade time than 100% air. A recent meta-analysis reported that SF_6 20% was associated with 58% fewer rebubblings compared to 100% air.[23] However, this information was not captured prospectively by NOTR. Future registry studies could shed light on the effect of SF_6 in routine clinical practice.

Previous studies reported complication rates decrease over time as surgical experience increases.[19,23,24] While overall graft survival improved over the study period, the incidence of rebubbling procedures increased. This may be due to consecutive learning curves of multiple surgeons and/or more aggressive approach towards graft dislocation. However, in accordance with the institutional review board of NOTR, data for the current study was not stratified by surgeon or center.

The risk of an immunological rejection after DMEK is lower compared to previous keratoplasty techniques and often does not lead to graft failure.[25-27]Moreover, the clinical picture of graft rejection after DMEK can be very subtle.[28] For prophylaxis, local corticosteroid therapy is recommended until at least the end of the second postoperative year.[26] In our cohort, patients received a tapered topical corticosteroid regimen during the first six months, followed by low dose maintenance and two patients developed graft rejection that was reversible following local steroid injection. From six months postoperatively onwards, only six cases of graft failure occurred. The follow-up of the current cohort is insufficient to determine long-term rates of graft failure and rejection.

Every cohort study has to cope with missing data and loss to follow-up. With respect to our primary outcome, i.e. graft survival, centralized donor allocation by the Dutch Transplant Society (NTS) ensured registration of all primary- and repeated transplantations. With regard to secondary outcomes, LMM analysis uses all available data (no list-wise deletion that would only allow completers in the analyses). Almost all graft failures occurred prior to the first follow-up visit registered in NOTR, i.e. three months postoperatively, therefore, to increase the robustness of the data, graft failures were excluded from analyses of VA, ECD, and SE.

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FIGURE LEGEND

Table 1. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Baseline Patient, Donor, and Surgery Characteristics of all consecutive DMEK surgeries registered in NOTR until May 31^{st,} 2018.

Table 2. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Best spectacle-corrected visual acuity, spherical equivalent, and endothelial cell density in eyes with Fuchs endothelial dystrophy, and three, six, twelve, and 24 months after DMEK.
*Triple DMEK are excluded.

Figure 1. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: All consecutively performed DMEK procedures (blue diamonds) in the Netherlands until 2017. Descemet stripping automated endothelial keratoplasty (DSAEK, red circles) and penetrating keratoplasty (PK, green triangles), are shown for comparison. The proportion of DMEK procedures increased significantly over time (P<0.001). 2016 marks a major turning point, showing a 395% increase in the number of performed procedures compared to 2015.

Figure 2. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Overall graft survival of primary DMEK grafts for Fuchs endothelial dystrophythroughout 2 years follow-up (n=468 at time 0). Graft survival measured 85% at one year (censored cases, n=244) and 78% at 2 years (censored cases, n=369).

Figure 3. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Evolution of graft survival over time of primary DMEK for Fuchs endothelial dystrophy. Graft survival was significantly better in procedures performed since 2016 compared to earlier procedures (hazard ratio = 0.4, P<0.001). <2015 n=41, 2015 n=34, 2016 n=179, 2017 n=175, and 2018 n=39 (excluding censoring).

Figure 4. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Estimated marginal means best spectacle-corrected visual acuity (BSCVA) during a follow-up period of 2 years for primary DMEK for Fuchs endothelial dystrophy (blue diamonds). BSCVA improved significantly after DMEK and is superior to DSAEK and PK. However, baseline differences between the techniques make a direct comparison difficult.
Baseline: n=442; 3 months: n=380; 6 months: n=306; 12 months: n=214; 24 months: n=45.
DMEK = Descemet membrane endothelial keratoplasty;
DSAEK = Descemet stripping automated endothelial keratoplasty;
LogMAR = logarithm of the minimum angle of resolution;
NOTR = the Netherlands Organ Transplantation Registry; PK = Penetrating Keratoplasty.
*BSCVA in DSAEK (purple circles) and PK (green triangles) in eyes with Fuchs endothelial dystrophy of a previous NOTR study are shown for comparison.[3]

Figure 5. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Bar graph showing the best spectacle-corrected Snellen visual acuity in primary DMEK for Fuchs endothelial dystrophy before surgery (n=442), and 3 months (n=380), 6 months (n=306), 12 months (n=214), and 24 months (n=45) after surgery. Twelve months after DMEK, 67% and 28% of eyes reached ≥20/25 and ≥20/20 Snellen, respectively.

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APPENDIX

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Table 1. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Baseline Patient, Donor, and Surgery Characteristics of all consecutive DMEK surgeries registered in NOTR until May 31st, 2018.

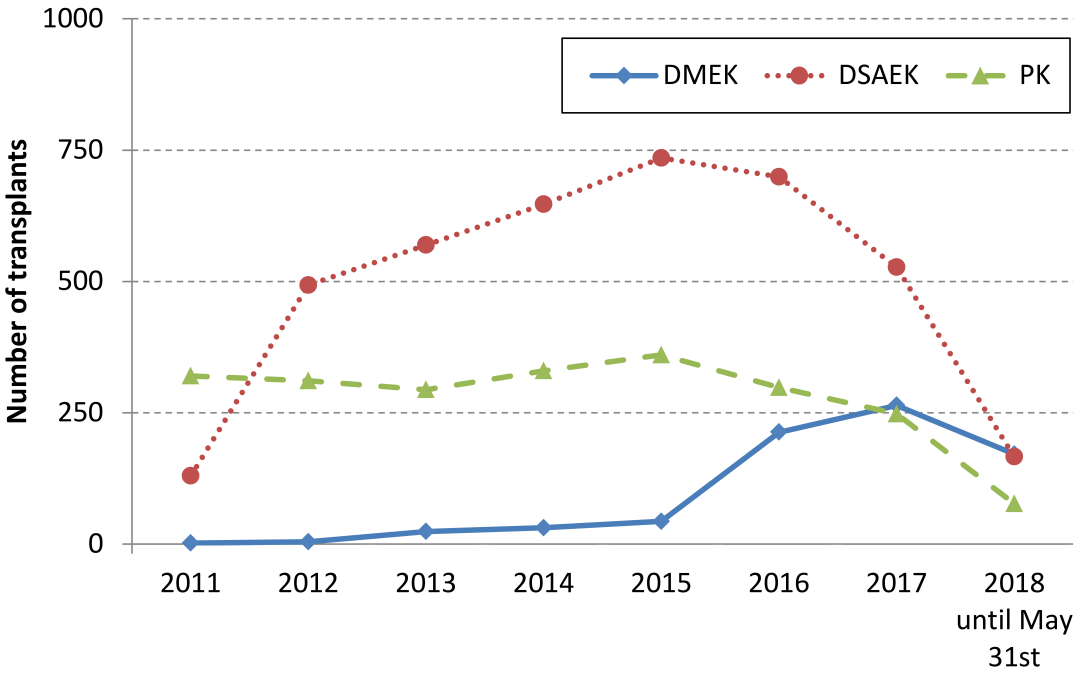
Parameter	Mean ± SD or %
Recipient	
Primary disease (% FED; PBK; graft failure)	90; 3; 5
Central Corneal Thickness (µm)	647 ± 82
Age (years)	71 ± 9
Sex (% male)	47
Eye undergoing surgery (% right)	51
Donor	
Age (years)	72 ± 8
Sex (% male)	63
Surgery	
Surgery in pseudophakic eye (%)	77
Surgery in phakic eye (%)	6
Triple procedure (%)	7
Surgery in eyes with PAC, or other (%)	10

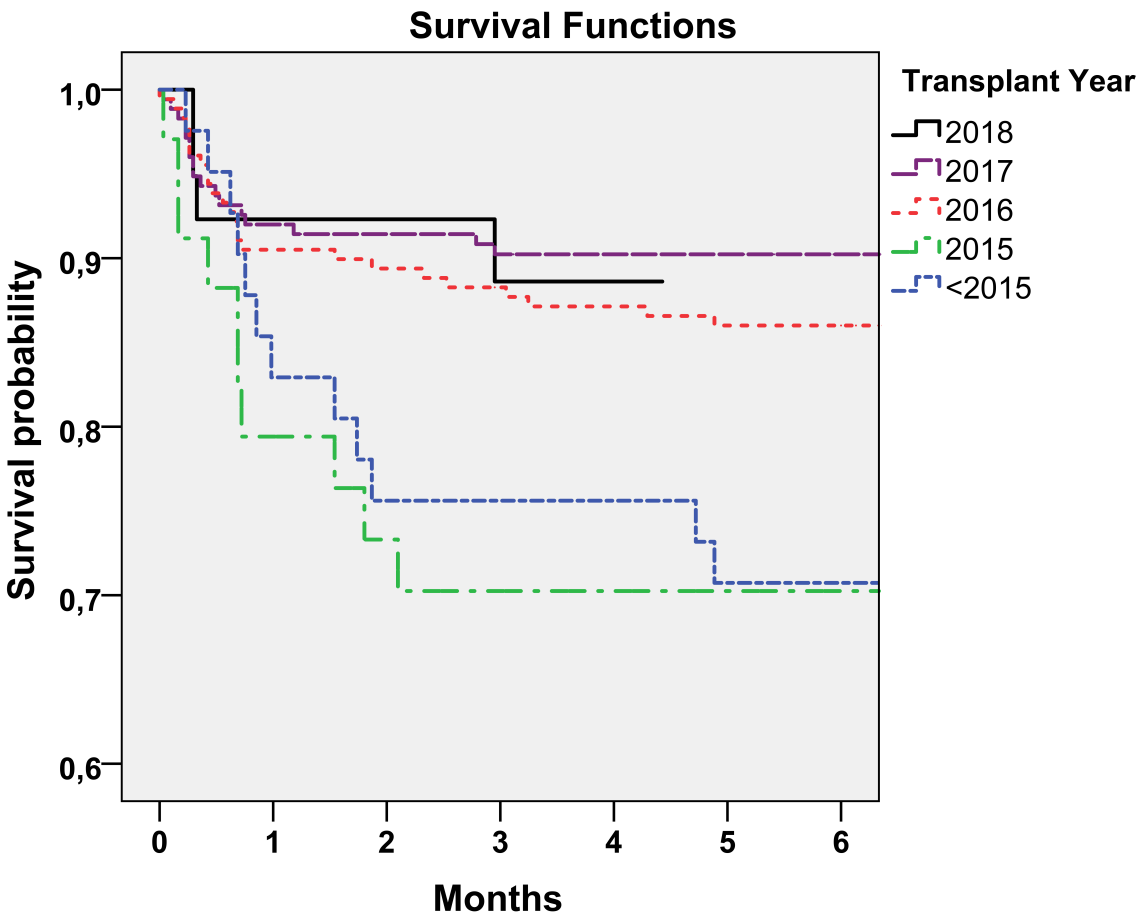
DMEK = Descemet membrane endothelial keratoplasty; FED = Fuchs endothelial dystrophy; PAC = pseudophakic, anterior chamber; PBK = Pseudophakic bullous keratopathy; SD = standard deviation.

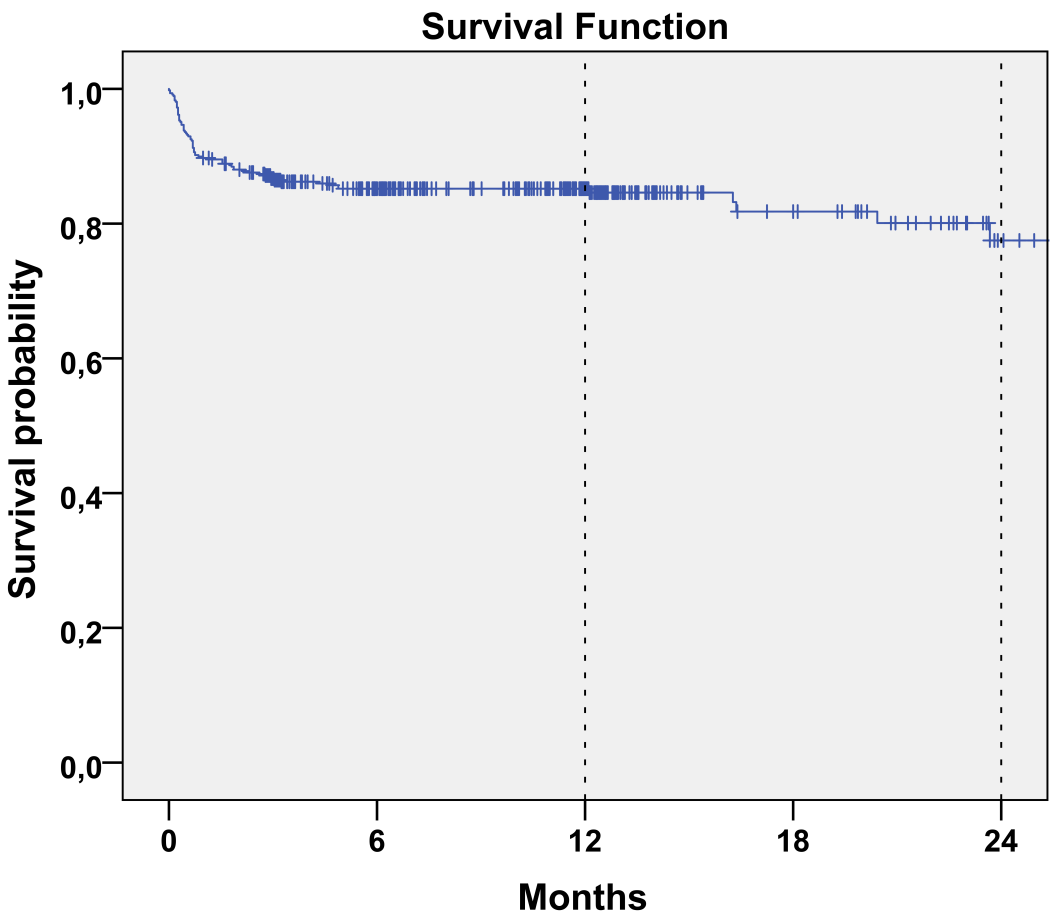
Table 2. Real-World Outcomes of Descemet membrane endothelial keratoplasty (DMEK): A Prospective Dutch Registry Study: Best spectacle-corrected visual acuity, spherical equivalent, and endothelial cell density in eyes with Fuchs endothelial dystrophy, and three, six, twelve, and 24 months after DMEK.

Follow-up	BSCVA EMM LogMAR [95% CI] (n)	SE EMM Diopter [95% CI] (n)*	ECD EMM cells/mm^2 [95% CI] (n)
Baseline or donor	0.45 [0.41 – 0.49] (442)	-0.49 [-0.75 to -0.23] (355)	2706 [2670 - 2741] (441)
3 months	0.17 [0.14 – 0.21] (380)	-0.13 [-0.39 to 0.12] (309)	1799 [1729 - 1869] (182)
6 months	0.15 [0.11 – 0.18] (306)	-0.20 [-0.46 to 0.06] (212)	1762 [1689 - 1836] (168)
1 year	0.12 [0.08 – 0.16] (214)	-0.20 [-0.46 to 0.07] (149)	1744 [1668 - 1820] (138)
2 years	0.08 [0.05 – 0.12] (45)	-0.07 [-0.44 to 0.30] (34)	1670 [1495 – 1844] (23)

BSCVA = Best spectacle-corrected visual acuity; CI = Confidence Interval;
ECD = Endothelial cell density; EMM = Linear mixed-model estimated marginal mean;
LogMAR = logarithm of the minimum angle of resolution; SE = Spherical equivalent.
*DMEK combined with cataract extraction and intraocular lens implantation are excluded.


1000
750
500
250
0
Number of transplants
DMEK
DSAEK
PK
2011
2012
2013
2014
2015
2016
2017
2018
until May
31st


Survival Functions
Survival probability
1,0
0,9
0,8
0,7
0,6
0
1
2
3
4
5
6
Months
Transplant Year
2018
2017
2016
2015
<2015


Survival Function
Survival probability
1,0
0,8
0,6
0,4
0,2
0,0
0
6
12
18
24
Months