Endothelial Cell Loss Curve in Descemet Stripping Automated Endothelial Keratoplasty versus Descemet Membrane Endothelial Keratoplasty

Comparação de Curvas de Perda de Células Endoteliais na Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) e na Descemet Membrane Endothelial Keratoplasty (DMEK)

Rodrigo Vilares-Morgado[1,2,3], Ana Luísa Barbosa[4], Ana Filipa Moleiro[1,2], Luís Torrão[1], Pedro Neves-Cardoso[1], Raul Moreira[1], Fernando Falcão-Reis[1,2], João Pinheiro-Costa[1,2]

[1] Department of Ophthalmology, Centro Hospitalar Universitário de São João, Porto, Portugal
[2] Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal
[3] Department of Biomedicine – Unit of Anatomy, Faculty of Medicine, University of Porto, Porto, Portugal
[4] Faculty of Medicine, University of Porto, Porto, Portugal

Recebido/Received: 2021-12-04 | **Aceite/Accepted:** 2022-01-04 | **Publicado/Published:** 2022-06-30

DOI: https://doi.org/10.48560/rspo.25960

ABSTRACT

INTRODUCTION: Our purpose was to compare best corrected visual acuity (BCVA), endothelial cell density (ECD) and postoperative complications in adult patients with corneal endothelial disorders who were submitted to descemet stripping automated endothelial keratoplasty (DSAEK) or descemet membrane endothelial keratoplasty (DMEK).

METHODS: Retrospective, single-centre, observational cohort study. Fifty one eyes from 51 patients with corneal endothelial disorders who were submitted to either a traditional DSAEK (*n*=23 patients) or a DMEK (n=28 patients) at Centro Hospitalar Universitário S. João (Porto, Portugal), and followed for at least one year after the procedure in our department were included. Patients without at least one ECD determination after transplantation and those who experienced primary graft failure were excluded. Patient demographics, BCVA with the logMAR scale before and one year after grafting, indication for transplantation, and postoperative complications were recorded. Specular microscopy with ECD determination (in cells/mm^2) was performed on all donor corneas before grafting and regularly after transplantation, as part of our patient's usual follow-up.

RESULTS: Patients' demographics, indications for transplantation and BCVA before grafting were similar in both groups. BCVA 1-year after transplantation was better in the DMEK group (0.26 ± 0.19 *vs* 0.47 ± 0.29 in the DSAEK group; *p*=0.003). ECD in donor corneas before grafting was similar in both groups (*p*=0.986). Graft ECD after transplantation was higher in the DMEK group at up to 5 months (*p*<0.001), 5 to 9 months (*p*=0.037) and 9 to 15 months follow-up (*p*=0.003), being similar in posterior determinations. 2 DMEK eyes required rebubblin. Two DSAEK eyes suffered graft rejection.

CONCLUSION: In our cohort, DMEK presented better visual outcomes than DSAEK. The DMEK group showed higher mean ECD and lower ECD loss in the first 15 months of follow-up,

but posterior measurements were similar in both groups. Therefore, both techniques had similar long-term mean ECD and ECD loss and other criteria should be used to determine which one is best suited for each case in our clinical practice.

KEYWORDS: Corneal Transplantation; Descemet Stripping Endothelial Keratoplasty.

RESUMO

INTRODUÇÃO: O nosso objetivo foi comparar melhores acuidades visuais corrigidas (MAVC) e densidade das células endoteliais corneanas (DCE) em adultos com patologias endoteliais corneanas que foram submetidos a *descemet stripping automated endothelial keratoplasty* (DSAEK) ou a *descemet membrane endothelial keratoplasty* (DMEK).

MÉTODOS: Estudo retrospetivo observacional de centro único. Foram incluídos 51 olhos de 51 doentes com patologias endoteliais corneanas que foram submetidos ou a DSAEK tradicional (n=23 olhos) ou a DMEK (n=28 olhos), no Centro Hospitalar Universitário S. João (Porto, Portugal), com seguimento de pelo menos 1 ano após o procedimento. Doentes sem pelo menos uma determinação da DCE após o procedimento e doentes com falência primária do enxerto foram excluídos. Foram colhidos os dados demográficos dos doentes, as suas MAVC antes e após transplante (escala logMAR), as indicações cirúrgicas para transplante e as complicações pós-operatórias. Foi realizada microscopia especular com determinação da DCE (em células/mm^2) em todas as córneas dadoras e nos enxertos transplantados, como parte do nosso seguimento habitual destes doentes.

RESULTADOS: Dados demográficos, indicações para transplante e MAVC prévia ao transplante foram similares em ambos os grupos. A MAVC 1 ano após transplante foi superior no grupo do DMEK (0,26 ± 0,19 *vs* 0,47 ± 0,29 unidades logMAR no grupo DSAEK; p=0,003). A DCE nas córneas dadoras foi similar em ambos os grupos (p=0,986). A DCE após transplante foi superior no grupo do DMEK nos primeiros 5 meses (p<0,001), nos 5 a 9 meses (p=0,037) e nos 9 a 15 meses após transplante (p=0,003), sendo similar em medições posteriores. Dois olhos submetidos a DMEK necessitaram de *rebubbling*. Ocorreu rejeição endotelial em 2 olhos submetidos a DSAEK.

CONCLUSÃO: Na nossa coorte, olhos submetidos a DMEK apresentaram melhores resultados visuais que olhos submetidos a DSAEK. O grupo submetido a DMEK demonstrou uma DCE média superior e uma perda de DCE inferior nos primeiros 15 meses após transplante. Posteriormente, estes parâmetros foram similares entre grupos. Assim, ambas as técnicas apresentam valores similares de perda de DCE a longo prazo, pelo que a escolha da técnica de transplante endotelial deve ter por base outros critérios e ser individualizada na prática clínica diária.

PALAVRAS-CHAVE: Perda de Células Endoteliais Corneanas; Transplante Córnea.

INTRODUCTION

Endothelial keratoplasty (EK) represents a major advance in corneal transplantation and has rapidly replaced penetrating keratoplasty (PK) as the dominant procedure of choice for corneal endothelial diseases, such as Fuchs endothelial corneal dystrophy and pseudophakic bullous keratopathy.[1-3] Benefits of EK over the traditional technique of PK include faster visual recovery, better and more predictable refractive outcomes, superior biomechanical integrity and lower incidence of sight-threatening complications such as endophthalmitis and suprachoroidal haemorrhage.[4-6]

The two main EK techniques are descemet stripping automated endothelial keratoplasty (DSAEK) and descemet membrane endothelial keratoplasty (DMEK).[2] In DSAEK, the patient's diseased endothelium and descemet's membrane are replaced with a donor disc consisting of endothelium, descemet's membrane and a thin layer of posterior stroma, prepared with an automated microkeratome.[7] In contrast, DMEK is a more anatomically precise technique that uses a manually prepared graft that consists of only descemet's membrane and endothelium without adherent donor stroma.[8,9]

Compared with DSAEK, DMEK has been shown to achieve faster visual rehabilitation, better visual outcomes, more predictable refractive outcomes, lower immune rejection rates and higher patient satisfaction.[1,9-13] In addition, unlike DSAEK, DMEK does not require expensive and sophisticated equipment such as a microkeratome for donor

dissection.[7,8] However, the steep learning curve and the technical difficulty of graft preparation and handling[14,15] represent important disadvantages of DMEK, as well as its higher rates of postoperative rebubbling compared to DSAEK.[9,13,16] Although DSAEK remains the most commonly performed EK, mainly due to the greater technical challenges associated with DMEK, corneal surgeons are increasingly adopting DMEK for the treatment of corneal endothelial dysfunction because of its advantages over DSAEK.[1- 17]

As endothelial cell function is essential for corneal transparency, endothelial cell survival is one of the main outcome measures that define the success of an EK.[9] Endothelial cell density (ECD) decreases with age, at a rate of 0.6% per year, in healthy corneas,[18] but the rate of endothelial cell loss is accelerated after corneal transplantation.[1,19] There is a steep short-term decrease in ECD in the early postoperative period after both DSAEK and DMEK and a gradual decrease afterwards.[1,9,19-22] The assessment of endothelial cell loss over time after DSAEK and DMEK may be useful to compare both techniques and to predict long-term graft survival.[23]

In this context, the aim of this study was to retrospectively compare endothelial cell loss in adult patients with corneal endothelial disorders who were submitted to DSAEK or DMEK at Centro Hospitalar Universitário S. João (Porto, Portugal), a tertiary university hospital.

METHODS

We conducted a retrospective observational study of a consecutive series of 51 eyes from 51 patients that underwent EK, either DMEK or DSAEK, between April 2015 and March 2020, performed by 2 experienced corneal surgeons with significant DSAEK experience and within the DMEK learning curve during the initial part of the study. This single-centre study took place from January 2021 to March 2021 in the Ophthalmology Department of Centro Hospitalar Universitário S. João (Porto, Portugal). Research adhered to tenets of the Declaration of Helsinki and approval for this study was obtained from the Ethics Committee of the hospital. All subjects provided written informed consent for the surgical procedure.

INCLUSION CRITERIA AND MAIN OUTCOMES

Patients followed at our cornea sub-department with corneal endothelial disorders (Fuchs endothelial corneal dystrophy, pseudophakic bullous keratopathy, iridocorneal endothelial syndromes and previous endothelial primary graft failure) who underwent either DMEK or DSAEK were included. Patients without at least one ECD determination after transplantation and those who experienced primary graft failure were excluded. We collected data of patients' demographics, best-corrected visual acuity (BCVA) in the last cornea consultation before transplantation, indication for EK, donor cornea ECD and BCVA 1-year after EK. We also collected available graft ECD measurements performed during these patients' standard follow-up examinations. Since not all graft ECD measurements were performed in the same timing after transplantation, we created time intervals for enabling comparison between DMEK and DSAEK ECD measurements.

The main outcomes evaluated were mean ECD and ECD loss at each follow-up interval. BCVA 1-year after DMEK or DSAEK, rebubbling and immunologic rejection episodes were also evaluated.

The postoperative ECD was determined by an experienced ophthalmic technician with specular microscopy (Fig. 1). The endothelial cell loss was calculated as a percentage of the baseline donor cornea ECD measured with specular microscopy by our eye bank, which provided all donor corneas. We considered graft rejection as a loss of graft clarity due to edema with evidence of inflammation (such as anterior chamber cell or keratic precipitates) and primary graft failure as a lack of graft clearing or need for re-graft within the first 2 months postoperatively, as Chamberlain et al defined in their study.[24]

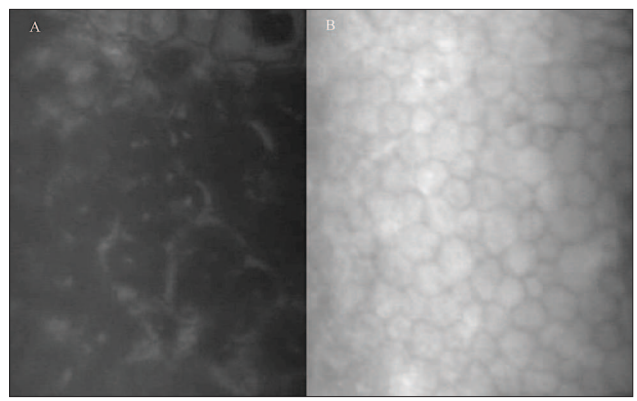

Figure 1. Specular microscopy image of the corneal endothelium. Endothelial cells of a patient with Fuchs endothelial corneal dystrophy before (A) and after DMEK (B).

SURGICALT ECHNIQUE AND POSTOPERATIVE CARE

DSAEK procedures were performed according to the technique described by Gorovoy in 2006[7] and DMEK procedures were performed according to the technique initially described by Melles *et al* in 2002[25] In summary, the recipient diseased endothelium and Descemet membrane were stripped from the planned graft area. For DSAEK, the donor lamellar dissection was performed with a microkeratome. The donor disc was inserted into the recipient eye through a 3.5 mm incision using forceps. For DMEK, donor preparation was performed by a surgeon using a submerged peeling technique and the graft was inserted into the recipient eye through a 2.4 mm incision using a glass pipette. Air was injected into the eye to keep the graft adhered to the posterior corneal surface of the recipient, leaving the eye with a 90% air fill. A surgical inferior peripheral iridotomy was performed before surgery to reduce the risk of pupillary block.

Our standard follow-up consisted of examinations at 1 day, 2 days, 1 week, 1 month, 3 months, 6 months, 9 months, 12 months, 18 months, 24 months and annually thereafter. All patients were encouraged to go to our ophthalmology emergency room (ER) immediately in the presence of symptoms that could be associated with graft rejection as eye redness, pain or irritation, change in vision and light sensitivity. For all DSAEK and DMEK cases, the prescribed topical corticosteroid regimen used to prevent graft rejection was dexamethasone phosphate 0.1% ophthalmic solution dosed 5 times daily for 1 month, tapered by 1 drop per month to once daily, continued throughout the first five months of follow-up and changed indefinitely to fluorometholone 0.1% ophthalmic solution after the first 5 months. In patients who developed steroid-associated ocular hypertension, topical glaucoma medications were started or increased.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS Statistics 26. Normally distributed data is reported as mean and standard deviation (SD) while non-normally distributed data is reported as median and interquartile range (IQR). To assess whether each variable followed a normal distribution, Kolmogorov-Smirnov and Shapiro-Wilk tests were used. Comparisons between groups (DMEK versus DSAEK) were performed using Independent-Samples T Test (for normally distributed data) or Mann-Whitney U test (for non-normally distributed data) for continuous variables, and Chi-Square Test for categorical variables. Statistical significance was considered when a p value < 0.05 was obtained.

RESULTS

One hundred and twenty-two endothelial keratoplasties (76 DSAEK procedures and 46 DMEK procedures) were performed between April 2015 and March 2020 at Centro Hospitalar Universitário S. João (Porto, Portugal), of which 71 were excluded from this study as they correspond to patients without at least one ECD determination after transplantation (61 cases) or to patients who experienced primary graft failure (10 cases).

A total of 51 eyes of 51 patients, which underwent DSAEK (n=23 patients) and DMEK (n=28 patients), were included in our study. The demographic and clinical characteristics of all eyes are summarized in Table 1. There were no statistically significant differences in patient's age, gender and indications for transplantation between the DSAEK and DMEK groups. There was also no statistically significant difference in the mean BCVA before transplantation between both groups, but the mean BCVA 1-year after transplantation was significantly better in the DMEK group than in the DSAEK group. Of the endothelial grafts analyzed, rebubbling was required in 2 DMEK eyes (7.14%) and 0 DSAEK eyes (0%) and postoperative graft rejection occurred in 2 DSAEK eyes (8.70%) and 0 DMEK eyes (0%).

ECD and ECD loss are shown in Tables 2 and 3, respectively. Donor cornea ECD before transplantation was similar in the DSAEK and DMEK groups (p=0.986). The DMEK group showed higher graft ECD after transplantation and lower ECD loss at up to 5 months (p<0.001 and p<0.001, respectively), 5 to 9 months (p=0.037 and p=0.004, respectively) and 9 to 15 months follow-up (p=0.003 and p=0.016, respectively) compared to the DSAEK group, but there were no statistically significant differences in these outcomes between both groups in posterior determinations (from 15 to 45 months follow-up). Figs 2 and 3 show a scatterplot with line of best fit of mean graft ECD over time for DSAEK and DMEK; only patients with at least 3 different measurements were included in the graph presented in Fig. 3.

Table 1. Comparison of demographic and clinical characteristics between groups.

	n	**DSAEK** *(n=23)*	*n*	**DMEK** *(n=28)*	*p*
Demographic and clinical characteristics					
Age (years)	23	71.91 ± 10.98	28	69.50 ± 12.07	*0.463*
Gender	23		28		*0.400*
Male		8 (34.8)		13 (46.4)	
Female		15 (65.2)		15 (53.6)	
Visual Acuity (LogMAR scale)	23		28		
Before transplantation		1.12 ± 0.45		0.88 ± 0.48	*0.079*
1 year after transplantation		0.47 ± 0.29		0.26 ± 0.19	***0.003***
Indication for transplantation	23		28		*0.093*
Fuchs endothelial corneal distrophy		8 (34.8)		18 (64.3)	
Pseudophakic bullous keratopathy		12 (52.2)		6 (21.4)	
Primary graft failure		3 (13.0)		3 (10.7)	
ICE syndrome		0 (0)		1 (3.6)	

Values are presented as n (%) for categorical variables, as mean ± standard deviation for continuous variables with a normal distribution and as median (IQR) for continuous variables without a normal distribution.

Table 2. Comparison of absolute corneal endothelial cell density evolution throughout follow-up between groups, as determined by specular microscopy.

	n	DSAEK (*n*=23)	*n*	DMEK (*n*=28)	*p*
Specular microscopic measurements (cells/mm²)					
Donor cornea endothelial cell density	*23*	2671.17 ± 632.83	*28*	2668.46 ± 433.86	*0.986*
Graft endothelial cell density					
Up to 5 months follow-up	*7*	812.14 ± 227.87	*19*	1657.89 ± 410.79	***0.000***
From 5 to 9 months follow-up	*8*	992.63 ± 306.87	*12*	1469.17 ± 541.21	***0.037***
From 9 to 15 months follow-up	*8*	747.50 ± 238.41	*13*	1428.54 ± 541.927	***0.003***
From 15 to 21 months follow-up	*8*	840.00 ± 439.14	*8*	1096.13 ± 400.54	*0.243*
From 21 to 27 months follow-up	*2*	926.50 ± 501.34	*11*	1067.73 ± 325.37	*0.605*
From 27 to 33 months follow-up	*2*	1020.00 ± 622.25	*5*	1386.20 ± 596.22	*0.499*
From 33 to 39 months follow-up	*5*	713.20 ± 189.40	*3*	778.67 ± 39.02	*0.587*
From 39 to 45 months follow-up	*5*	1059.40 ± 642.20	*2*	1033.50 ± 395.27	*0.961*

Values are presented as *n* (%) for categorical variables, as mean ± standard deviation for continuous variables with a normal distribution and as median (IQR) for continuous variables without a normal distribution.

Table 3. Comparison of corneal endothelial cell density loss throughout follow-up between groups, as determined by specular microscopy.

	n	DSAEK (*n*=23)	*n*	DMEK (*n*=28)	*p*
Percentage of endothelial cell density loss: ((1 – (Graft ECD/ Donor Cornea ECD)) x100) (%)					
Up to 5 months follow-up	*7*	67.86 ± 4.63	*19*	38.59 ± 15.74	***0.000***
From 5 to 9 months follow-up	*8*	64.11 ± 10.39	*12*	41.04 ± 20.73	***0.004***
From 9 to 15 months follow-up	*8*	69.19 ± 11.80	*13*	46.01 ± 22.97	***0.016***
From 15 to 21 months follow-up	*8*	67.31 ± 13.09	*8*	59.94 ± 19.11	*0.384*
From 21 to 27 months follow-up	*2*	62.96 ± 27.88	*11*	58.99 ± 13.26	*0.740*
From 27 to 33 months follow-up	*2*	60.13 ± 12.58	*5*	47.14 ± 23.49	*0.507*
From 33 to 39 months follow-up	*5*	69.59 ± 7.21	*3*	67.84 ± 4.91	*0.727*
From 39 to 45 months follow-up	*5*	57.57 ± 27.07	*2*	61.10 ± 19.62	*0.876*

Values are presented as *n* (%) for categorical variables, as mean ± standard deviation for continuous variables with a normal distribution and as median (IQR) for continuous variables without a normal distribution.

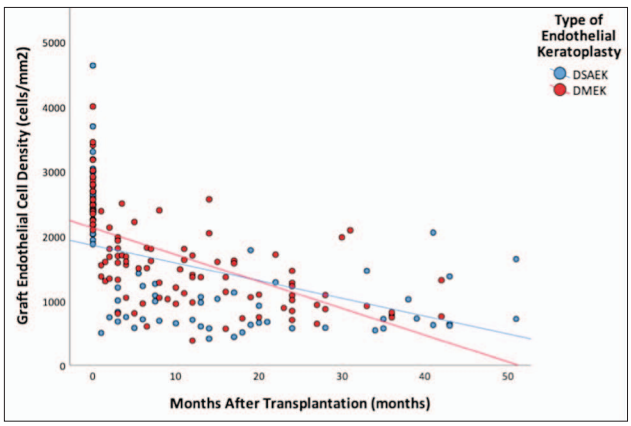

Figure 2. Scatterplot with line of best fit of mean graft endothelial cell density, measured in cells/mm2, plotted according to duration of follow-up after transplantation, measured in months.

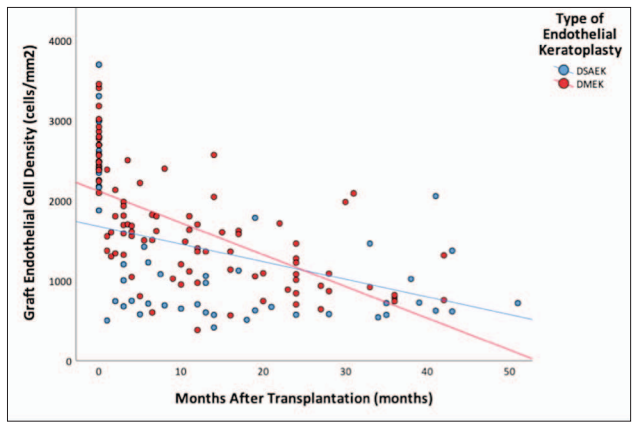

Figure 3. Scatterplot with line of best fit of mean graft endothelial cell density, measured in cells/mm2, plotted according to duration of follow-up after transplantation, measured in months. Only patients with at least 3 different measurements were included in this graph.

DISCUSSION

In our cohort, graft ECD after transplantation was higher in the DMEK group in the first 15 months of follow-up, being similar in posterior determinations (from 15 to 45 months follow-up). Percentage of ECD loss was also lower in the DMEK group in the first 15 months of follow-up. Nevertheless, patients' age, gender, indications for transplantation and donor cornea ECD before transplantation were similar in both groups. Furthermore, even though mean BCVA before grafting were similar in both groups, mean BCVA 1-year after transplantation was better in the DMEK group than in the DSAEK group. Therefore, in our cohort, DMEK presented better visual outcomes and proved to be superior to DSAEK in retaining corneal endothelial cells in the initial period after corneal grafting.

When compared with penetrating keratoplasty, both endothelial keratoplasty techniques are linked with superior visual outcomes, less surgically induced astigmatism, faster visual recovery and lower rates of transplant rejection.[4,26] Eye banks report a growing trend toward endothelial keratoplasty and, more, recently, DMEK, in patients requiring corneal transplantation due to endothelial disorders, such as Fuchs endothelial dystrophy, pseudophakic bullous keratopathy, ICE syndromes and previous endothelial graft failure.[27]

Previous studies have indicated a large ECD loss in the early postoperative period after both DMEK and DSAEK, attributing this loss to iatrogenic damage from intraoperative graft manipulation.[1,12,19,20] In our study, patients in the DSAEK group presented an ECD loss of 68±5% and patients in the DMEK group presented an ECD loss of 39±16% in the first 5 months of follow-up. Regarding the DMEK technique, these values are comparable to those reported in a recent systematic review conducted by Deng *et al*, in which mean ECD loss at 6 months was 33% (range 25%-47%). However, our mean 5-month ECD loss with the DSAEK technique was significantly higher than what Deng *et al* reported, which was a mean ECD loss of 37% at 6 months.[1]

Our long-term ECD loss percentage in the DMEK group (61±20% at 39 to 45 months follow-up; *n*=2) was higher than those reported by Price *et al* (48±19% 5-year ECD loss; *n*=289),[28] Schlögl *et al* (44% 5-year ECD loss in DMEK eyes; *n*=42)[19] and Ham *et al* (55% 5-year ECD loss in DMEK eyes; *n*=94).[29] Our long-term ECD loss percentage in the DSAEK group (58±27% at 39 to 45 months follow-up; *n*=5) was similar to those reported by Wacker *et al* (55±15% 5-year ECD loss; n=52)[21] and Fajgenbaum *et al* (67+13% 5-year ECD loss; n=41),[22] but higher than reported by Price *et al* (47±19% 5-year ECD loss; n=442).[28] Nonetheless, we have a low number of eyes with 39 to 45-months ECD measurements, compared to the study conducted by Price *et al*.[28] We performed similar surgical techniques and postoperative management, but this study only included eyes submitted to DSAEK or DMEK due to Fuchs endothelial corneal dystrophy and had a much higher sample size. Thus, our long-term ECD loss percentages were limited by our low sample size, missing values and other indications for transplantation.

Previously, multiple studies have demonstrated that ECD loss after transplantation is similar in both EK techniques in the first 6 months after transplantation[3,9,30] or in the first 12 months of follow-up[13] even when comparing DMEK with ultrathin DSAEK (UT-DSAEK).[31] Long-term studies also demonstrated that ECD loss up to 5 years after transplantation is similar in both techniques.[22,28] In our cohort, mean ECD was significantly higher in the first 15 months of follow-up and ECD loss was significantly lower in the same period for the DMEK group. Nevertheless, after this initial follow-up, mean ECD and ECD loss were similar in both groups. Thus, even though there appears to be an initial benefit in performing DMEKs in these eyes, this benefit eventually loses its relevance, being debatable if this is an indication to perform more DMEKs in these eyes.

Regarding visual outcomes, classically, DMEK eyes present significantly better postoperative BCVA than DSAEK eyes.[3,9,27,31] In our cohort, we obtained similar results, with significantly better BCVA 1 year after transplantation in the DMEK group (0.26±0.19 logMAR units versus 0.47±0.29 logMAR units in the DSAEK group; p=0.003), despite similar BCVA before grafting (p=0.079). Patient preference has also been evaluated in some studies that compare these techniques, with more patients preferring DMEK over DSAEK,[11,32,33] which can be explained by better visual outcomes with higher contrast sensitivity and faster visual recovery after grafting.

Several initial studies comparing these techniques demonstrated that the risk of postoperative graft detachment and the proportion of eyes requiring postoperative air injection/rebubbling is higher in DMEK eyes than in DSAEK eyes.[9,16,33] Notwithstanding, a recent report by the American Academy of Ophthalmology (AAO) has concluded that the rate of air injection and repeat keratoplasty are similar in eyes submitted to DMEK or DSAEK after the learning curve for DMEK, with an average of 28.8% (range 0.2%-76%) DMEK eyes and 14% (range 0%-82%) DSAEK eyes requiring air injection.[1] In our cohort, 2 DMEK eyes (7.14%) required rebubbling while no DSAEK eyes (0%) required this procedure. Postoperative rejection rates are reportedly lower in DMEK eyes than in DSAEK eyes.[3,11,32-34] The aforementioned AAO report estimated that an average of 10% (range 0%-45%) DSAEK eyes and 1.9% (range 0%-5.9%) DMEK eyes suffered immune rejection.[1] Our study presented similar results, with 2 DSAEK eyes (8.70%) and 0 DMEK eyes (0%) undergoing postoperative graft rejection.

Our study limitations include its retrospective nature, the risk of selection and performance bias due to the lack of randomization, our low sample-size and variable follow-up period for each eye. A small proportion of eyes had ECD measurements in all follow-up intervals. Our study strengths include its heterogeneous cohort of eyes with multiple corneal endothelial disorders, validating our results for multiple indications for endothelial keratoplasty, and the analysis of DMEK operations within the learning curves of the involved corneal surgeons, admitting the possibility of even better results beyond the scope of this study.

CONCLUSION

In summary, both DMEK and DSAEK are valid therapeutic options for corneal endothelial disorders, improving visual outcomes with low associated rejection and primary graft failure rates. In our study, DMEK was associated with a better visual outcome and lower rejection rates, despite requiring graft rebubbling more often. Mean ECD was higher in DMEK eyes in the first 15 months of follow-up, but posterior measurements were similar in both techniques. ECD loss was also lower in the DMEK eyes in the first 15 months of follow-up, even though similar ECD losses were determined posteriorly. Therefore, both techniques have similar long-term mean ECD and ECD loss, as reported in previous long-term studies comparing both these techniques. Other criteria should be used to determine which technique is best suited for each case in our clinical practice.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

RVM: Collected clinical data, redacted the manuscript and contributed to its revision.

ALB: Collected clinical data and contributed to the drafting of the manuscript.

AFM, LT, PNC, RM, FFR: Contributed to the redaction and revision of the manuscript.

JPC: Developed the clinical investigation hypothesis, designed the study methodology and contributed to the redaction and revision of the manuscript, being responsible for approving its final version.

RVM: Colheita dos dados clínicos, redação e revisão do manuscrito.

ALB: Colheita dos dados clínicos e contribuição na redação do manuscrito.

AFM, LT, PNC, RM, FFR: Supervisão e revisão do manuscrito.

JPC: Desenvolvimento da hipótese de investigação clínica,desenho da metodologia do estudo e contribuição para a redação e revisão do manuscrito e aprovação de sua versão final.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

Provenance and Peer Review: Not commissioned; externally peer reviewed.

Data Availability Statement: All data generated or analysed during this study are included in this article and its supplementary material files and was compiled in a database that is readily available and can be published in a repository if required. Further enquiries can be directed to the corresponding author.

REFERENCES

1. Deng SX, Lee WB, Hammersmith KM, Kuo AN, Li JY, Shen JF, et al. Descemet Membrane Endothelial Keratoplasty: Safety and Outcomes: A Report by the American Academy of Ophthalmology. Ophthalmology. 2018;125:295-310.
2. Price MO, Gupta P, Lass J, Price FW, Jr. EK (DLEK, DSEK, DMEK): New Frontier in Cornea Surgery. Annu Rev Vis Sci. 2017;3:69-90.
3. Hamzaoglu EC, Straiko MD, Mayko ZM, Sáles CS, Terry MA. The First 100 Eyes of Standardized Descemet Stripping Automated Endothelial Keratoplasty versus Standardized Descemet Membrane Endothelial Keratoplasty. Ophthalmology. 2015;122:2193-9.
4. Turnbull AM, Tsatsos M, Hossain PN, Anderson DF. Determinants of visual quality after endothelial keratoplasty. Survey of ophthalmology. 2016;61:257-71.
5. Woo JH, Ang M, Htoon HM, Tan D. Descemet Membrane Endothelial Keratoplasty Versus Descemet Stripping Automated Endothelial Keratoplasty and Penetrating Keratoplasty. Am J Ophthalmol. 2019;207:288-303.
6. Ang M, Wilkins MR, Mehta JS, Tan D. Descemet membrane endothelial keratoplasty. Br J Ophthalmol. 2016;100:15-21.
7. Gorovoy MS. Descemet-stripping automated endothelial keratoplasty. Cornea. 2006;25:886-9.
8. Dapena I, Moutsouris K, Droutsas K, Ham L, van Dijk K, Melles GR. Standardized "no-touch" technique for descemet membrane endothelial keratoplasty. Arch Ophthalmol.

2011;129:88-94.
9. Tourtas T, Laaser K, Bachmann BO, Cursiefen C, Kruse FE. Descemet membrane endothelial keratoplasty versus descemet stripping automated endothelial keratoplasty. Am J Ophthalmol. 2012;153:1082-90.e2.
10. Price MO, Giebel AW, Fairchild KM, Price FW, Jr. Descemet's membrane endothelial keratoplasty: prospective multicenter study of visual and refractive outcomes and endothelial survival. Ophthalmology. 2009;116:2361-8.
11. Goldich Y, Showail M, Avni-Zauberman N, Perez M, Ulate R, Elbaz U, et al. Contralateral eye comparison of descemet membrane endothelial keratoplasty and descemet stripping automated endothelial keratoplasty. Am J Ophthalmo. 2015;159:155-9.e1.
12. Gorovoy IR, Gorovoy MS. Descemet membrane endothelial keratoplasty postoperative year 1 endothelial cell counts. Am J Ophthalmo. 2015;159:597-600.e2.
13. Li S, Liu L, Wang W, Huang T, Zhong X, Yuan J, et al. Efficacy and safety of Descemet's membrane endothelial keratoplasty versus Descemet's stripping endothelial keratoplasty: A systematic review and meta-analysis. PloS One. 2017;12:e0182275.
14. Parekh M, Salvalaio G, Ruzza A, Camposampiero D, Griffoni C, Zampini A, et al. Posterior lamellar graft preparation: a prospective review from an eye bank on current and future aspects. J Ophthalmo. 2013;2013:769860.
15. Marques RE, Guerra PS, Sousa DC, Gonçalves AI, Quintas AM, Rodrigues W. DMEK versus DSAEK for Fuchs' endothelial dystrophy: A meta-analysis. Eur J Ophthalmol. 2019;29:15-22.
16. Green M, Wilkins MR. Comparison of Early Surgical Experience and Visual Outcomes of DSAEK and DMEK. Cornea. 2015;34:1341-4.
17. Eye Bank Association of America.2019 Eye Banking Statistical Report. Chicago: EBAA; 2020.
18. Bourne WM, Nelson LR, Hodge DO. Central corneal endothelial cell changes over a ten-year period. Invest Ophthalmol Vis Sci. 1997;38:779-82.
19. Schlögl A, Tourtas T, Kruse FE, Weller JM. Long-term Clinical Outcome After Descemet Membrane Endothelial Keratoplasty. Am J Ophthalmol. 2016;169:218-26.
20. Schrittenlocher S, Bachmann B, Cursiefen C. Impact of donor tissue diameter on postoperative central endothelial cell density in Descemet Membrane Endothelial Keratoplasty. Acta Ophthalmol. 2019;97:e618-e22.
21. Wacker K, Baratz KH, Maguire LJ, McLaren JW, Patel SV. Descemet Stripping Endothelial Keratoplasty for Fuchs' Endothelial Corneal Dystrophy: Five-Year Results of a Prospective Study. Ophthalmology. 2016;123:154-60.
22. Fajgenbaum MA, Hollick EJ. Modeling Endothelial Cell Loss After Descemet Stripping Endothelial Keratoplasty: Data From 5 Years of Follow-up. Cornea. 2017;36:553-60.
23. Patel SV, Lass JH, Benetz BA, Szczotka-Flynn LB, Cohen NJ, Ayala AR, et al. Postoperative Endothelial Cell Density Is Associated with Late Endothelial Graft Failure after Descemet Stripping Automated Endothelial Keratoplasty. Ophthalmology. 2019;126:1076-83.
24. Chamberlain W, Lin CC, Austin A, Schubach N, Clover J, McLeod SD, et al. Descemet Endothelial Thickness Comparison Trial: A Randomized Trial Comparing Ultrathin Descemet Stripping Automated Endothelial Keratoplasty with Descemet Membrane Endothelial Keratoplasty. Ophthalmology. 2019;126:19-26.
25. Melles GR, Lander F, Rietveld FJ. Transplantation of Descemet's membrane carrying viable endothelium through a small scleral incision. Cornea. 2002;21(4):415-8.
26. Nanavaty MA, Wang X, Shortt AJ. Endothelial keratoplasty versus penetrating keratoplasty for Fuchs endothelial dystrophy. Cochrane Database Syst Rev. 2018;6:CD012097.
27. Singh A, Zarei-Ghanavati M, Avadhanam V, Liu C. Systematic Review and Meta-Analysis of Clinical Outcomes of Descemet Membrane Endothelial Keratoplasty Versus Descemet Stripping Endothelial Keratoplasty/Descemet Stripping Automated Endothelial Keratoplasty. Cornea. 2017;36:1437-43.
28. Price DA, Kelley M, Price FW, Jr., Price MO. Five-Year Graft Survival of Descemet Membrane Endothelial Keratoplasty (EK) versus Descemet Stripping EK and the Effect of Donor Sex Matching. Ophthalmology. 2018;125:1508-14.
29. Ham L, Dapena I, Liarakos VS, Baydoun L, van Dijk K, Ilyas A, et al. Midterm Results of Descemet Membrane Endothelial Keratoplasty: 4 to 7 Years Clinical Outcome. Am J Opthalmology. 2016;171:113-21.
30. Guerra FP, Anshu A, Price MO, Giebel AW, Price FW. Descemet's membrane endothelial keratoplasty: prospective study of 1-year visual outcomes, graft survival, and endothelial cell loss. Ophthalmology. 2011;118:2368-73.
31. Dunker SL, Dickman MM, Wisse RPL, Nobacht S, Wijdh RHJ, Bartels MC, et al. Descemet Membrane Endothelial Keratoplasty versus Ultrathin Descemet Stripping Automated Endothelial Keratoplasty: A Multicenter Randomized Controlled Clinical Trial. Ophthalmology. 2020;127:1152-9.
32. Guerra FP, Anshu A, Price MO, Price FW. Endothelial keratoplasty: fellow eyes comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. Cornea. 2011;30:1382-6.
33. Maier AKB, Gundlach E, Gonnermann J, Klamann MKJ, Bertelmann E, Rieck PW, et al. Retrospective contralateral study comparing Descemet membrane endothelial keratoplasty with Descemet stripping automated endothelial keratoplasty. Eye. 2015;29:327-32.
34. Bhandari V, Reddy JK, Relekar K, Prabhu V. Descemet's Stripping Automated Endothelial Keratoplasty versus Descemet's Membrane Endothelial Keratoplasty in the Fellow Eye for Fuchs Endothelial Dystrophy: A Retrospective Study. Biomed Res Int. 2015;2015:750567.

Corresponding Author/
Autor Correspondente:

Rodrigo Vilares-Morgado
Department of Ophthalmology of
São João Hospital,
Avenida Prof. Hernâni Monteiro,
4202 – 451 Porto, Portugal
vilaresmorgador@gmail.com

ORCID: 0000-0003-3325-2194