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Donor and recipient characteristics associated with rebubbling rate, endothelial cell loss, and graft failure in primary descemet membrane endothelial keratoplasty

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ABSTRACT

Aim: To determine whether donor and recipient characteristics are associated with rebubbling rate, endothelial cell loss (ECL), and graft failure 3 years after primary Descemet membrane endothelial keratoplasty (DMEK).

Material and Method: Records of 295 consecutive DMEK surgery and match with corresponding donor data were reviewed at a tertiary referral clinic. Recipients with intraoperative complications and coexisting ocular pathologies were excluded. Age, sex of donor and recipient, cause of donor death, death-to-preservation time (DtPT), storage time, donor endothelial cell density (ECD), and indications for surgery were analyzed for correlation with rebubbling rate, postoperative ECL, and graft failure. Further, subgroup analyses of the cause of death, donor sex, DtPT (median value, 3.5 h), and indications were performed. Multiple regression and receiver operating characteristics (ROC) analysis were used to determine the independent risk factors for graft failure.

Results: This study included 114 eyes that underwent DMEK for bullous keratopathy (BK; 64%) and for Fuchs' endothelial corneal dystrophy (FECD; 36%). The graft failure percentage was the only parameter that was higher in patients with DtPT > 3.5 h (p=0.047) than those with shorter DtPT. The probability of graft failure was seven times higher in eyes with DtPT > 3.5 h than with shorter DtPT (odds ratio 7.36, 95% confidence interval CI 1.34-40.53) and 10 times higher in eyes with BK than those with FECD (odds ratio 10.29, 95% CI 1.01-104.54).

Conclusion:. DtPT and recipients with BK diagnosis were found to be independent risk factors for graft failure. Therefore, surgeons should consider DtPT for DMEK in eyes with BK.

Keywords: descemet membrane endothelial keratoplasty, death-to-preservation time, graft failure, bullous keratopathy, Fuchs endothelial corneal dystrophy

INTRODUCTION

Over the past two decades, anterior and posterior lamellar keratoplasties, such as deep anterior lamellar keratoplasty, Descemet stripping automated endothelial keratoplasty (DSAEK), or Descemet membrane endothelial keratoplasty (DMEK), have supplanted penetrating keratoplasty (PK) in selective replacement of diseased corneal stroma or endothelium[1]. Globally, DMEK has become the standard surgery for pseudophakic bullous keratopathy (BK) and Fuchs' endothelial corneal dystrophy (FECD) due to better visual outcomes and rapid visual rehabilitation (1).

Donor and recipient characteristics can help determine the success of keratoplasty. The Cornea Donor Study (CDS) and Corneal Protection Time Study (CPTS) results highlighted the evidence-based donor selection criteria for PK or DSAEK procedures (2, 3). However, clinical trials similar to CDS and CPTS studies, have not yet been conducted in DMEK. Therefore, it is not yet clear to what extent specific donor and graft characteristics affect the success of DMEK surgery.

The purpose of this study is to investigate the effects of donor and recipient characteristics on rebubbling rates, endothelial cell loss (ECL), and graft failure 3 years after primary DMEK. Secondary to those analyses, we hoped to provide DMEK surgeons with clues that will allow them to evaluate donor tissue and recipient characteristics together for donor selection.

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MATERIAL AND METHOD

The study was carried out with the permission of University of Health Sciences Dr. Lütfi Kırdar Kartal City Hospital Noninvasive/ Clinical Researches Ethics Committee (Date: 29.04.2020, Decision No: 2020/514/176/1). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design

Data from the medical records were retrospectively reviewed for DMEK procedures performed between January 1, 2014, and March 30, 2019, at a tertiary referral center. Furthermore, the database of the local eye bank was reviewed for corresponding corneal donor tissue parameters. BK and FECD recipients were followed up at least 3 years after primary DMEK were included in the study. Recipients with intraoperative complications or coexistence of other ocular pathologies, such as retinal disorder or glaucoma, vitrectomized and aphakic eyes, or regrafts, were excluded to achieve homogeneity and avoid misleading results. Further, the first 25 cases of DMEK representing the learning curve of this technique were excluded from this study.

Collection of Donor Data

Before postmortem excision, serological and microbiological tests were done and seronegative donor corneas were used. University of Health Sciences Dr. Lütfi Kırdar Kartal City Eye Bank provided all donor corneal buttons, which were stored in a short-term storage solution (Eusol-C®, Corneal Chamber, Alchimia, Ponte San Nicolo, Italy) at 4°C. Eligible donor corneas were obtained from individuals aged 10–75 years who had endothelial cell density (ECD) values of 2300–3300 cells/mm^2 in line with the standard criteria of the Eye Bank Association of America (EBAA) (4), measured using a specular microscope (Konan Eye Bank KeratoAnalyzer, EKA-04, Japan). Donor and recipient age, sex of donor (male/female), cause of death, death-to-preservation time (DtPT), and storage time (ST) until grafting were recorded. ECL was calculated as the difference between preoperative and 36-month ECD values, expressed as a percentage of preoperative ECD. Death-to-preservation time was divided into two times intervals according to median average of 3.5 hours (<3.5 h and >3.5 h) for statistical analyses.

Surgical Technique and Postoperative Treatment

The donor graft preparation and DMEK procedures were all performed by one experienced surgeon (BK) according to the techniques described in the literature (1, 5). The graft was prepared on the same day as the DMEK surgery and used without delay. Descemet membrane were detached and cut using a 8.00-mm punch. Asymmetric triangle marking was used in all DMEK graft preparations to ensure placement of the graft in the correct position, as described previously (6). In all phakic cases, standard phacoemulsification and intraocular lens implantation were performed prior to DMEK surgery.

Following the DMEK surgery, all eyes were treated with a topical antibiotic (0.5% moxifloxacin hydrochloride; Vigamox, Alcon Pharma GmbH, Freiburg, Germany) and a corticosteroid (0.1% dexamethasone; Maxidex, Alcon Pharma GmbH) five times daily. The antibiotic was discontinued after 10 days. Dexamethasone was replaced with 0.5% loteprednol etabonate (Lotemax, Bausch + Lomb, Bridgewater, NJ, USA) four times daily 3 months after the surgery. According to the patient's clinical outcomes, the local steroid treatment was then gradually decreased to a maintenance dose of once daily.

Collection of Recipient Data

The standardized eye examinations included best corrected visual acuity (BCVA) assessment by Snellen chart (means and medians BCVA were converted to logarithm of the minimum angle of resolution (logMAR) units), slit lamp examination, tonometry, funduscopy, subjective refractometry, corneal topography (Sirius Scheimpflug Placido topographer, Costruzione Strumenti Oftalmici, Florence, Italy), and corneal pachymetry (Optikon pacline, Rome, Italy) for central corneal thickness (CCT). ECD (Topcon Corporation, Tokyo, Japan) measurement was carried out both preoperatively and at 3, 6, and 12 months and then annually for up to at least 3 years postoperatively. Graft-attachment/detachment was evaluated with anterior segment optical coherence tomography (Optos PLC, Dunfermline, United Kingdom) at each follow-up visit. Rebubbling (air reinjection after partial graft detachment) rates were also recorded. If the endothelial graft was more than one-third detached, rebubbling was performed 24–36 hours after surgery. If the endothelial graft was less than one-third detached with presence of corneal edema, patients were followed up for 2–3 weeks. If edema persisted, rebubbling was performed.

Postoperative complications were also recorded. Graft failure was defined as corneal edema and haze due to endothelial decompensation (7). We classified cases as primary graft failure, which is defined as a cornea that failed to be clear in the presence of an attached graft, whereas secondary graft failure was defined as corneal decompensation after an initial period of a functional graft after DMEK (7). In cases of graft failure, DMEK was repeated or PK was performed.

Statistical Analysis

The Number Cruncher Statistical System 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Homogeneity tests were performed with the Shapiro–Wilk test and graphical analysis. An independent *t*-test was used to compare the preoperative and postoperative BCVA, ECD, and CCT values. One-way variance analysis and dependent groups *t*-test were also used where appropriate. Pearson chi-square, Fisher's exact, and Fisher–Freeman–Halton exact tests were used to compare qualitative data. Statistical significance was assigned if $p < 0.05$.

Pearson correlation analysis was used to evaluate associations between patient age, donor age, DtPT, ST, and donor ECD with graft failure 36 months after DMEK. In addition, logistic regression and receiver operating characteristics (ROC) analysis were performed to determine the independent risk factors for graft failure. Based on logistic regression analysis, sensitivity, specificity, PPV, NPV, and overall accuracy percentages were calculated for DtPT and graft failure indications of recipients.

RESULTS

In total, 295 DMEK cases were reviewed retrospectively. Overall, 114 eyes that met the inclusion criteria with a minimum 3 years of follow-up time were included in the study, which included 73 (64.0%) eyes with BK and 41 (36%) eyes with FECD. The mean follow-up time was 41.7 (±4.5, range 36–72) months. Patients' and donors' data and visual and clinical outcomes are provided in **Table 1**.

Postoperatively, 11 eyes (9.6%) required rebubbling. There was no association between patient or donor characteristics on the rebubbling rate, 36-month ECL values, and graft failure (**Table 2, Figure 1**). Only the percentage of graft failure was greater in patients with DtPT > 3.5 h (p=0.047) (**Table 2**).

Mean DtPT was 4.8 (±4.05) hours. According to logistic regression analysis, the probability of graft failure for grafts from donors with DtPT > 3.5 h was 7.3 times higher than for those with shorter DtPTs (**Table 3**). The probability of graft failure was 10.3 times higher in eyes with BK than those with FECD (**Table 3**). Further, 9 (90%) of 10 graft failures occurred in eyes with BK (**Table 3**).

ROC analysis was performed using predicted probability values (DtPT and BK) obtained as a result of the model performed for graft failure. For the probability of graft failure, the area under the ROC curve was 0.861 (95% CI=0.748, 0.973, $p < 0.001$; **Figure 1**).

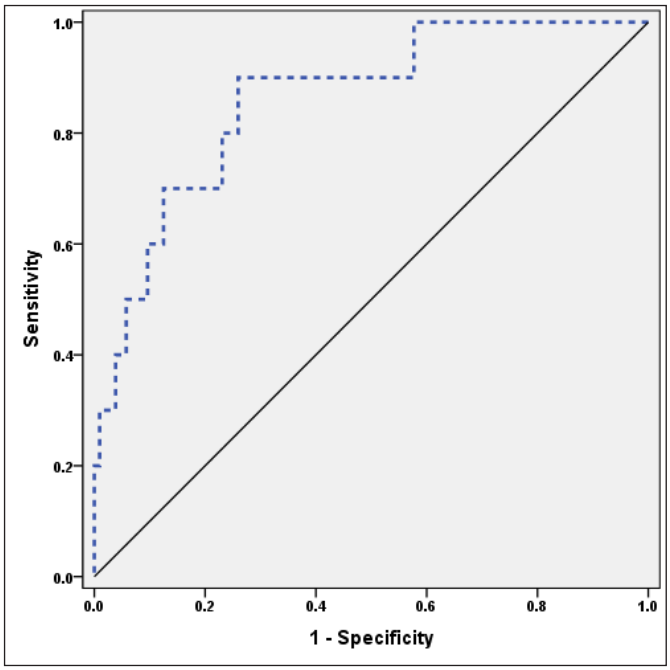

Figure 1. Receiver operating characteristics curve of predicted probabilities obtained as a result of regression analysis for graft failure

Table 1. Patients' and donors' data and visual and clinical outcomes.

	Range (Min–Max)	Mean±SD	p
Recipient age (year)	30–93	69.56±11.78	
Preoperative BCVA (LogMAR)	0.3–2	1.56±0.47	**0.001**
36-month BCVA (LogMAR)	0–1.3	0.48±0.55	
Preoperative CCT (µ)	609–898	734.01±62.65	**0.001**
36-month CCT (µ)	453–742	567.4±71.41	
Donor ECD (cells/mm²)	2087–3236	2628.54±266.98	**0.001**
36-month ECD (cells/mm²)	715–2550	1602.64±431.57	
ECL (%)	0.04–0.72	0.39±0.16	
Donor age (year)	38–70	58.56±7.69	
DtPT (hours)	0.33–18.42	4.8±4.05	
ST (day)	1–17	4.78±2.96	
	N	**%**	
Recipient diagnosis			
BK	73	64.0	
FECD	41	36.0	
Eye			
Right	60	52.6	
Left	54	47.4	
Donor sex			
Female	42	36.8	
Male	72	63.2	
Cause of death			
Cardiopulmonary arrest	75	65.8	
Multiple trauma	12	10.5	
Cancer	13	11.4	
Others	14	12.3	
Postoperative complications	18	15.8	
Graft failure	10	8.8	

[a]Pearson correlation coefficient, [b]Independent samples t-test, [c]One-way analysis of variance. Bold p values indicate statistically significant (*p < 000.1) Abbreviations: PBK: Pseudophakic bullous keratopathy; FECD: Fuchs endothelial corneal dystrophia, BCVA: best corrected visual acuity, CCT: central corneal thickness, ECD: endothelial cell density, ECL: endothelial cell loss, DtPT: Death-to-preservation time; ST: Storage time, SD: standard deviation (In order to make the groups, sub-analyses, pre-, and post-DMEK values more understandable and organized, gray shading was drawn in all tables).

Table 2. Analyses of the relationship between donor, recipient risk factors, and their subgroups and rebubbled or non-rebubbled grafts, ECL, graft failure, or without graft failure.

	Rebubbled Graft		p	ECL ar	p	Graft Failure		p
	Yes Mean±SD	No Mean±SD				Yes Mean±SD	No Mean±SD	
Recipient age (year)	65.09±13.58	70.04±11.54	[b]0.187	0.133	0.157	64.4±18.7	70.06±10.9	[b]0.370
Donor age (year)	59.36±7.34	58.48±7.75	[b]0.718	0.065	0.493	61.3±5.14	58.3±7.86	[b]0.240
DtPT (hour)	4.14±3.38	4.87±4.13	[b]0.569	0.107	0.259	5.83±3.77	4.7±4.08	[b]0.402
ST (day)	5.05±4.02	4.75±2.85	[b]0.756	0.067	0.476	4.9±1.85	4.77±3.05	[b]0.894
DonorECD (cell/mm²)	2655.18±254.2	2625.7±269.35	[b]0.729	0.092	0.332	2531.7±217.34	2637.86±270.33	[b]0.231
	n (%)	n (%)	p	Mean±SD	p	n (%)	n (%)	p
DtPT			[d]0.751		[b]0.504			**[d]0.047***
≤3.5 h	6 (10.5)	51 (89.5)		0.38±0.16		2 (3.5)	55 (96.5)	
>3.5 h	5 (8.8)	52 (91.2)		0.4±0.16		8 (14)	49 (86)	
Recipient diagnosis			[c]0.323		[b]0.065			[c]0.092
BK	9 (12.3)	64 (87.7)		0.41±0.17		9 (12.3)	64 (87.7)	
FECD	2 (4.9)	39 (95.1)		0.35±0.13		1 (2.4)	40 (97.6)	
Donor sex			[e]0.324		[b]0.436			[e]0.743
Female	6 (14.3)	36 (85.7)		0.4±0.16		3 (7.1)	39 (92.9)	
Male	5 (6.9)	67 (93.1)		0.38±0.16		7 (9.7)	65 (90.3)	
Cause of death			[f]0.744	0.39±0.15	[c]0.639			[f]0.715
Cardiopulmonary arrest	9 (12)	66 (88)		0.35±0.19		8 (10.7)	67 (89.3)	
Multiple trauma	0 (0)	12 (100)		0.4±0.18		0 (0)	12 (100)	
Cancer	1 (10)	9 (90)		0.42±0.19		0 (0)	10 (100)	
Other	1 (5.9)	16 (94.1)				2 (11.8)	15 (88.2)	

[a]Pearson correlation coefficient, [b]Independent samples t-test, [c]One-way ANOVA, [d]Pearson chi-square test, [e]Fisher's exact test, [f]Fisher–Freeman–Halton exact test. Bold p values indicate statistically significant. *p < 0.05. Abbreviations: DtPT: Death-to-preservation time; ST: Storage time ECD: Endothelial cell density; BK: Bullous Keratopathy FECD: Fuchs endothelial corneal dystrophy; SD: standard deviation; h: hour

Table 3. Association between donor, recipient risk factors on rebubbling graft, ECL, and graft failure after primary DMEK at 3 years.

	Rebubbled Grafts	p	ECL	p	Graft Failure	p
	OR (95% CI)		Beta (95% CI)		OR (95% CI)	
Donor age (year)	0.994 (0.896, 1.104)	0.915	0.001 (−0.003, 0.006)	0.554	1.020 (0.903, 1.151)	0.752
Donor ECD(cell/mm²)	1.001 (0.998, 1.003)	0.622	6.97E−5 (−4.84E−5, 1.88E−4)	0.245	0.999 (0.996, 1.002)	0.534
DtPT >3.5 hour	1.01 (0.27, 3.783)	0.988	0.02 (−0.041, 0.082)	0.519	**7.365** (1.338, 40.530)	**0.022***
ST (day)	1.066 (0.862, 1.319)	0.554	0.006 (−0.004, 0.017)	0.228	1.151 (0.866, 1.531)	0.332
Recipient diagnosis BK	3.615 (0.693,18.857)	0.127	0.069 (−0.004, −0.134)	0.039*	**10.295** (1.014, 104.536)	**0.049***
Cause of death						0.808
Cardiopulmonary arrest	2.311 (0.264,20.224)					
Multiple trauma	-	0.449	−0.027 (−0.113, 0.058)	0.531	0.620 (0.097, 3.979)	
Cancer	1.597 (0.083,30.733)	-	−0.088 (−0.213, 0.036)	0.163	-	-
Others		0.756	−0.025 (−0.152, 0.102)	0.698	-	-

Linear regression analysis for ECL, logistic regression analysis for graft failure, and rebubbling were performed. OR: Odds Ratio, CI: Confidence Interval Bold p values indicate statistically significant. *p < 0.05. Abbreviations: DtPT: Death-to-preservation time; ST: Storage time; ECD: Endothelial cell density; BK: Bullous keratopathy; FECD: Fuchs endothelial corneal dystrophy; DMEK: Descemet membrane endothelial keratoplasty; SD: standard deviation

Based on logistic regression analysis, the sensitivity, specificity, PPV, NPV, and overall accuracy are presented for DtPT and recipients' indications of graft failure. According to this, the specificity was highest (100%) among recipients with BK and with a graft DtPT > 3.5 h (**Table 4**).

Complications developed in 18 (15.8%) eyes. Primary and secondary graft failures were observed in 3 (2.6%) and 7 (6.1%) of 114 eyes, respectively. Other complications were postoperative high intraocular pressure resistant to medical treatment in four eyes (3.5%), severe keratitis in two eyes (1.7%), graft rejection in one eye (0.8%), and intraocular lens deposit in one eye (0.8%). Repeated keratoplasty was required in 10 (8.8 %) eyes (four eyes re-DMEK and six eyes PK).

Table 4. Based logistic regression analysis for DtPT and diagnosis on graft failure

Factors	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
DtPT < 3.5 h. BK-	100 (69.2, 100)	19.2 (12.2, 28.1)	10.6 (5.2, 18.7)	100 (83.2, 100)
Only DtPT > 3.5 h	90 (55.5, 99.7)	38.5 (29.1, 48.5)	12.3 (5.8, 22.1)	97.6 (87.1, 99.9)
Only BK +	70 (34.8, 93.3)	72.1 (62.5, 80.5)	19.4 (8.2, 36)	96.2 (89.2, 99.2)
DtPT > 3.5 h; BK +	0 (0, 30.8)	100 (96.5, 100)	-	91.2 (84.5, 95.7)

Abbreviations: DtPT: Death-to-preservation time, BK: Bullous keratopathy, PPV: positive predictive value, NPV: negative predictive value, h: hours

DISCUSSION

In this study, we evaluated donor age, cause of death, preoperative ECD, DtPT, ST, and recipients' diagnosis and age to determine whether these factors influenced the rate of rebubbling, ECL, and graft failure 3 years after primary DMEK while excluding cases with intraoperative complications or coexistence of other ocular pathologies. Donor age, cause of death, preoperative ECD, ST, and recipients' age were not independent risk factors for rate of rebubbling, ECL, or graft failure. However, DtPT and eyes with BK were revealed as two independent risk factors for graft failure according to multivariable regression analysis.

Several studies have been conducted to determine possible correlations between donor characteristics and the results of DMEK surgery. Donor age is one of the most debated donor characteristics in the keratoplasty literature. We found that donor age did not affect the rebubbling rate, 36-month ECL, and graft failure after DMEK. This finding is consistent with the prospective, large, multicenter, and long-term results for PK from the CDS and for DSEK/DSAEK from the CPTS (2, 3). The CPTS also pointed out that donor age will not be as important for DMEK graft success as for DSAEK graft success (3). However, donors >55 years are generally recommended for DMEK surgery because the Descemet membranes of younger donors tend to be more fragile and adherent to the stroma (8). Heinzelmann and associates performed an in-vitro study of 28 prepared DMEK grafts to investigate how donor characteristics might affect DMEK surgical outcomes (9). They found that donor age affects the duration of surgery because the Descemet membrane is more tightly scrolled in younger than in older donors, and this can complicate the process of opening the scroll in recipient eyes. Thus, they highlighted that increased unfolding times resulted in higher ECL (9). We did not find a similar effect of donor age. The reason for this result may be that there were only 17 donor grafts under the age of 55 in our study.

We concluded that donor ECD is not an independent risk factor for postoperative rebubbling, ECL, or graft failure 36 months after DMEK. Our conclusions are similar to those reached by Straiko et al. (10) and are found in several other studies as well (2,3,10,11).

The role of cause of death has previously been assessed in relation to DMEK outcomes. Boydoun et al. (12) reported that noncancer donor death causes were associated with higher ECL 8 years after surgery Oellerich et al. (13) found that donors with causes of death other than cancer were associated with lower ECD values In our study, cause of donor death was not an independent risk factor for rebubbling rate, 36-month ECL, or graft failure. However, we had smaller samples per cause of death than the previous studies mentioned above.

ST did not affect post-DMEK rebubbling rates, ECL, or graft failure, which is similar with reports from Straiko et al. (10) and Patel et al. (14). However, a 5-year follow-up of 500 DMEK cases with an average graft ST of 13.5 days showed an association between graft ST and ECD decline after DMEK (8, 15). Rosenwasser et al. (16) highlighted that the effect of ST on graft success rate in DSAEK is as low as 11 days and that surgeons recommend accepting corneas stored for 12–14 days or less. Therefore, our DMEK study results agree with the results for DSAEK and do not adversely affect the DMEK results of longer protection periods (up to 13 days in our series).

We have achieved two results with DtPT in primary DMEK cases. First, we found that probability of graft failure was 7.3 times higher in donors with DtPT longer than 3.5 hours than in those with shorter DtPT. Whether DtPT affects graft success of keratoplasties has been debated (3, 10, 17-23). In the CPTS, a maximum DtPT of 11 hours was an eligibility criterion for DSAEK donors (3). In some studies, DtPT has not been found to affect graft failure (2, 10, 22). Our mean and median DtPT values were lower than the times in some previous studies. In traditional Turkish culture, the dead are buried as soon as possible (24). However, similar to our DtPT results, Gavrilov et al. (25) suggested that DtPT should be <6 hours for corneal suitability for use (25). Secondarily, when we evaluated the eyes with DtPT and eyes with BK together according to logistic regression analyses for graft failure, we found that these characteristics were two independent risk factors for graft failure at 3 years after primary DMEK. Additionally, when we examined the predicted probability values for DtPT and BK in recipients obtained from the graft failure model, our results showed that specificity was highest (100%) among recipients with BK and with a graft DtPT > 3.5 h. Therefore, the use of grafts with donor

DtPT longer than 3.5 hours in recipients with BK may increase the likelihood of endothelial decompensation. In support of this hypothesis, Armitage et al. (19) used donors with DtPT of 19–24 hours in eyes with BK and found an increased risk of endothelial failure at 5 years after surgery.

It is important to consider the distribution of indications for keratoplasty in studies evaluating graft survival. For many years, BK has been shown to be the most common indication for PK and DSAEK, and it has been reported that graft survival rates are lower in recipients with BK than in recipients with other indications (2, 3, 15, 19). Some other studies, including CDS and CPTS, have found that graft failure rates are higher in BK recipients than in FECD recipients (2, 3, 26-28). Additionally, the indications of recipients for DMEK are different between the United States (US), Europe (where FECD is the most frequent indication), and Asia (where BK is the most frequent indication) (29-32). Studies conducted in Europe and US for graft failure in DMEK found that the recipient's indication is not an independent risk factor, whereas in Asia, the recipient indication has been reported as a risk factor (13, 15, 33). In our study, 64% of graft recipients had BK and 36% had FECD, and our results highlighted that BK is an independent risk factor for graft failure in DMEK.

Mechanisms whereby eyes with BK rather than FECD reduce the rate of graft success after DMEK should also be discussed in detail. There is a large reserve of peripheral endothelial cells in FECD, and a healthy peripheral endothelium could fill damaged areas of the endothelium in the graft (34). This theory is only supported by success in FECD-diagnosed eyes treated with descemetorhexis (35). Whereas in BK, there are few healthy endothelial cells in the periphery. Additionally, in some studies, abnormal immune responses established in the anterior chamber of the eyes in recipients with BK (36, 37). These results support our finding that the probability of graft failure is 10 times higher in eyes with BK than in those with FECD.

The limitations of this study are that it was retrospective and had a small sample size. However, the strengths of our study are the exclusion of other ocular pathologies to ensure homogeneity, use of a standardized DMEK technique, and the follow-up of cases for at least 3 years.

CONCLUSION

Donor characteristics, including age of donor, cause of donor death, DtPT, preoperative ECD, graft ST, and recipient age had no significant effect on the rate of rebubbling, ECL, and graft failure at 3 years after primary DMEK. DtPT and BK in recipients were considered valuable independent factors in predicting the risk of graft failure in DMEK. In this aspect, the current study can provide clues about how donor tissue selection can maximize the success and how efficiency can be increased in using the existing corneal donor tissue pool for future studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of University of Health Sciences Dr. Lütfi Kırdar Kartal City Hospital Noninvasive/ Clinical Researches Ethics Committee (Date: 29.04.2020, Decision No: 2020/514/176/1).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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REFERENCES

1. Melles GRJ, Ong TS, Ververs B, van der Wees J. Descemet membrane endothelial keratoplasty. Cornea 2006; 25: 987-90.
2. Sugar J, Montoya M, Dontchev M, et al. Donor risk factors for graft failure in the cornea donor study. Cornea 2009; 28: 981-5.
3. Terry MA, Aldave AJ, Szczotka-Flynn LB, et al. Donor, recipient, and operative factors associated with graft success in the cornea preservation time study. Ophthalmology 2018; 125: 1700-9.
4. DeMatteo J. Eye Bank Association of America medical standards regarding Ebola policy. JAMA Ophthalmol 2015; 133: 1364.
5. 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.
6. Bhogal M, Maurino V, Allan BD. Use of a single peripheral triangular mark to ensure correct graft orientation in descemet membrane endothelial keratoplasty. J Cataract Refract Surg 2015; 41: 2022-4.
7. Lass JH, Szczotka-Flynn LB, Ayala AR, et al. Cornea preservation time study: methods and potential impact on the cornea donor pool in the United States. Cornea 2015; 34: 601-8.
8. Rodríguez-Calvo de Mora M, Groeneveld-van Beek EA, Frank LE, et al. Association between graft storage time and donor age with endothelial cell density and graft adherence after descemet membrane endothelial keratoplasty. JAMA Ophthalmol 2016; 134: 91-4.
9. Heinzelmann S, Hüther S, Böhringer D, Eberwein P, Reinhard T, Maier P. Influence of donor characteristics on descemet membrane endothelial keratoplasty. Cornea 2014; 33: 644-8.
10. Straiko MD, Bauer AJ, Straiko MMW, et al. Donor DMEK tissue characteristics: association with rebubble rate and 6-month endothelial cell loss. Cornea 2020; 39: 1267-73.

11. Dunker S, Winkens B, van den Biggelaar F, et al. Rebubbling and graft failure in Descemet membrane endothelial keratoplasty: a prospective Dutch registry study. Br J Ophthalmol 2021; bjophthalmol-2020-317041.
12. Baydoun L, Ham L, Borderie V, et al. Endothelial survival after descemet membrane endothelial keratoplasty: effect of surgical indication and graft adherence status. JAMA Ophthalmol 2015; 133: 1277-85.
13. Oellerich S, Ham L, Frank LE, et al. Parameters associated with endothelial cell density variability after descemet membrane endothelial keratoplasty. Am J Ophthalmol 2020; 211: 22-30.
14. Patel SV, Diehl NN, Hodge DO, Bourne WM. Donor risk factors for graft failure in a 20-year study of penetrating keratoplasty. Arch Ophthalmol 2010; 128: 418-25.
15. Birbal RS, Ni Dhubhghaill S, Bourgonje VJA, et al. Five-year graft survival and clinical outcomes of 500 consecutive cases after descemet membrane endothelial keratoplasty. Cornea 2020; 39: 290-7.
16. Rosenwasser GO, Szczotka-Flynn LB, Ayala AR, et al. Effect of cornea preservation time on success of descemet stripping automated endothelial keratoplasty: a randomized clinical trial. JAMA Ophthalmol 2017; 135: 1401-9.
17. Andersen J, Ehlers N. The influence of donor age and post mortem time on corneal graft survival and thickness when employing banked donor material (A five-year follow-up). Acta Ophthalmol 1988; 66: 313-7.
18. Mohamed-Noriega K, Mehta JS. Influence of donor age and post-mortem time on the metabolic profile of donor corneas and graft survival. Expert Rev Ophthalmol 2012; 7: 121-5.
19. Armitage WJ, Jones MNA, Zambrano I, Carley F, Tole DM, NHSBT Ocular Tissue Advisory Group and Contributing Ophthalmologists OTAG Audit Study 12. The suitability of corneas stored by organ culture for penetrating keratoplasty and influence of donor and recipient factors on 5-year graft survival. Invest Ophthalmol Vis Sci 2014; 55: 784-91.
20. Patel D, Tandon R, Ganger A, Vij A, Lalwani S, Kumar A. Study of death to preservation time and its impact on utilisation of donor corneas. Trop Doct 2017; 47: 365-70.
21. Böhringer D, Reinhard T, Spelsberg H, Sundmacher R. Influencing factors on chronic endothelial cell loss characterised in a homogeneous group of patients. Br J Ophthalmol 2002; 86: 35-8.
22. Langenbucher A, Nguyen NX, Seitz B. Predictive donor factors for chronic endothelial cell loss after nonmechanical penetrating keratoplasty in a regression model. Graefes Arch Clin Exp Ophthalmol 2003; 241: 975-81.
23. Writing Committee for the Cornea Donor Study Research Group, Sugar A, Gal RL, Kollman C, et al. Factors associated with corneal graft survival in the cornea donor study. JAMA Ophthalmol 2015; 133: 246-54.
24. Bahar Z, Beşer A, Ersin F, Kıssal A, Aydoğdu NG. Traditional and religious death practices in Western Turkey. Asian Nurs Res (Korean Soc Nurs Sci) 2012; 6: 107-14.
25. Gavrilov JC, Borderie VM, Laroche L, Delbosc B. Influencing factors on the suitability of organ-cultured corneas. Eye (Lond) 2010; 24: 1227-33.
26. Ang M, Soh Y, Htoon HM, Mehta JS, Tan D. Five-year graft survival comparing descemet stripping automated endothelial keratoplasty and penetrating keratoplasty. Ophthalmology 2016; 123: 1646-52.
27. Price MO, Fairchild KM, Price DA, Price FW. Descemet's stripping endothelial keratoplasty five-year graft survival and endothelial cell loss. Ophthalmology 2011; 118: 725-9.
28. Terry MA, Shamie N, Straiko MD, Friend DJ, Davis-Boozer D. Endothelial keratoplasty: the relationship between donor tissue storage time and donor endothelial survival. Ophthalmology 2011; 118: 36-40.
29. Edelstein SL, DeMatteo J, Stoeger CG, Macsai MS, Wang CH. Report of the Eye Bank Association of America medical review subcommittee on adverse reactions reported from 2007 to 2014. Cornea 2016; 35: 917-26.
30. Birbal RS, Baydoun L, Ham L, et al. Effect of surgical indication and preoperative lens status on descemet membrane endothelial keratoplasty outcomes. Am J Ophthalmol 2020; 212: 79-87.
31. Shimizu T, Hayashi T, Yuda K, et al. Short axial length and iris damage are associated with iris posterior synechiae after descemet membrane endothelial keratoplasty in Asian eyes. Cornea 2018; 37: 1355-9.
32. Beşek NK, Yalçınkaya G, Kırgız A, et al. Graft survival and clinical outcomes of Descemet membrane endothelial keratoplasty: long-term results. Int Ophthalmol 2022; 42: 269-79.
33. Shimizu T, Yamagami S, Mizuki N, Hayashi T. Descemet membrane endothelial keratoplasty in Asian eyes. Curr Ophthalmol Rep 2020; 8: 208-15.
34. He Z, Campolmi N, Gain P, et al. Revisited microanatomy of the corneal endothelial periphery: new evidence for continuous centripetal migration of endothelial cells in humans. Stem Cells 2012; 30: 2523-34.
35. Garcerant D, Hirnschall N, Toalster N, Zhu M, Wen L, Moloney G. Descemet's stripping without endothelial keratoplasty. Curr Opin Ophthalmol 2019; 30: 275-85.
36. 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: e618-22.
37. Ibrahim O, Yagi-Yaguchi Y, Kakisu K, Shimazaki J, Yamaguchi T. Association of iris damage with reduction in corneal endothelial cell density after penetrating keratoplasty. Cornea 2019; 38: 268-74.