Effects of Systemic Diseases on Graft Preparation in Descemet Membrane Endothelial Keratoplasty

Burak Özkan, M.D., Yusuf Koçluk, M.D., and Burcu Kasim, M.D.

Objectives: To evaluate the effects of the systemic diseases and drugs of the donor on Descemet membrane (DM) graft preparation.

Methods: Seventy-eight corneas of 58 donors, of whom the DM grafts were used in Descemet membrane endothelial keratoplasty (DMEK) surgery, between January 2018 and January 2020, were enrolled in this retrospective study. The hospital records of the donors were analyzed. Age, sex, blood type, systemic diseases, and drugs; complete blood count; biochemistry panel for liver and kidney functions in the past 48 hours; and the drugs used in the hospital, if any, in the past 24 hours were recorded. The grafts with tears that occurred while preparation were included in group 1, and the successful grafts with no tears were included in group 2.

Results: There were no statistically significant differences in the characteristics of the donors between groups. However, breast cancer and the use of sevelamer were found to be significantly higher in group 1 (P=0.010, P=0.033, respectively). No statistically significant difference in the use of other drugs was found between groups.

Conclusion: Although diabetic donors have been reported to be inappropriate candidates for the preparation of DM grafts for DMEK, most of the donors with several systemic diseases including diabetes can be used in DMEK surgery, with the right technique in DM graft preparation.

Key Words: Descemet membrane endothelial keratoplasty—Donor—Graft tear—Systemic diseases.

(Shaurya Prakash, 2022;48: 527–533)

Descemet membrane endothelial keratoplasty (DMEK) is a lamellar keratoplasty, in which the posterior corneal layer is transplanted selectively with a lower rejection risk, a faster visual recovery, and a better anatomical restoration than penetrating keratoplasty.1,2 The procedure has been modified since it was first described in 2006.1–3 Surgically induced astigmatism and suture-related problems are minimal because of the minimal manipulation on the host anterior surface.4 Several techniques have been described in the preparation of Descemet membrane (DM) graft in DMEK.5–7 Successful DM graft preparation without any tears is a critical step in DMEK surgery. It has been shown that the surgeon’s skill and experience are the most important factors in dissection techniques and rescuing the central and peripheral tears in grafts with tight DM adhesions.9 These tears in the DM graft complicate the effective use of this delicate tissue of 10 μm in thickness. Apart from the surgical manipulation, the structural differences in donor tissue also have a role in the tears in DM grafts while preparing the tissue.9 Moreover, the effect of the systemic disease and the drugs of the donor in a successful DM graft remain unclear.

In diabetic patients, abnormal adhesions between DM and posterior stroma and an increased risk of tissue preparation failure have been reported.10,11 These findings made us think that systemic drugs and other systemic diseases may have an effect on graft preparation. This study aims to evaluate the effect of systemic diseases and drugs of the donor on DM graft preparation.

MATERIALS AND METHODS

Seventy-eight corneas of 58 donors, DM grafts from whom were used in DMEK surgery in an ophthalmology clinic of a training and research hospital between January 2018 and January 2020, were enrolled in this retrospective study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards (Adana City Training and Research Hospital, January 29,2020, 49, 701).

The grafts from donors were harvested by an experienced personnel of our eye bank. The hospital records of the donors and the donor information form were analyzed (Table 1). Age, sex, blood type, systemic diseases, and drugs; complete blood count; biochemistry panel for liver and kidney functions in the past 48 hours; and the drugs used in the hospital, if any, in the past 24 hours were recorded. The donors were from White race.

The video records of DM graft preparation were analyzed. All the grafts were prepared just before the procedure in the operating room by the same experienced surgeon (Y.K.). The grafts were divided into two groups. The grafts with tears occurred during preparation were included in group 1, and the successful grafts with no tears were included in group 2. The surgical technique is shared in Videos 1 and 2, Supplemental Digital Content, http://links.lww.com/ICL/A237, http://links.lww.com/ICL/A238 (DM graft with tear and without tear, respectively).
TABLE 1. Donor Information Sheet

| Information person: | Date: | Time: |
|---------------------|-------|-------|

| Donor's hospital: | City: |
|--------------------|-------|
| Hospital phone number: | Fax number: |
| Coordinator name: | Phone number: | Signature: |

Donor:

| Kidney: | Liver: |
|---------|-------|
| R □ L □ |      |

| Heart: | Heart valve: |
|--------|-------------|

| Lung: | Pancreas: |
|-------|----------|
| R □ L □ |       |

| Bowel: | Cornea: | Other: |
|--------|--------|-------|

Donor information

| Name: | Gender: M □ F □ | Age: | Reason for hospital admission: |
|-------|----------------|------|-------------------------------|

| Cause of death: | Date and time of death: |
|-----------------|--------------------------|

| Length: .......... cm | Weight: ............ kg | Chest circumference: ....... cm | Abdominal circumference: ....... cm |
|---------------------|------------------------|-------------------------------|-------------------------------|

| Types of blood: | Rh: ( ) | Types of HLA: A ........../.......... | B ........../.......... | DR ........../.......... |
|-----------------|--------|----------------------------------|-----------------------|-----------------------|

ANAMNESIS

| Smoking: ............ box/year | Alcohol use: |
|------------------------------|-------------|

| Narcotic use: | Other: |
|---------------|-------|

TABLE 1. (Continued)

| Diseases: |
|-----------|

| Previous surgeries: |
|---------------------|

| Regularly used drugs: |
|-----------------------|

| Hypertension: How long: Treatment: |
|-----------------------------------|

| Diabetes Mellitus: Type of diabetes mellitus: |
|---------------------------------------------|

| Neurological status prior to admission |
|----------------------------------------|

| Other pathologies: |
|-------------------|

| Clinical Information: |
|----------------------|

| Intensive care admission time: Connect to ventilator time: |
|----------------------------------------------------------|

| Lung X-ray: Secretion |
|-----------------------|

| Echocardiography % EF: ECG: |
|----------------------------|

| Abdominal USG: CT: |
|-------------------|

| MR: Other diagnostic tests: |
|-----------------------------|

| Trauma: Explanation: |
|----------------------|

| Dosage and duration of administration of routinely used drugs (antibiotic, diuretic, anti-diuretic, etc) used: |
|----------------------------------------------------------------------------------------------------------|

| Blood culture: Time: Urine culture: Time: |
|------------------------------------------|

| Tracheal aspiration culture: Time: Other: Time: |
|-----------------------------------------------|

| Infection: |
|-----------|

| Blood pressure: ............../........ mmHg Pulse: ............../min CVP: Fever: .............. °C |
|---------------------------------------------------------------|

| Hypotension: Yes ☐ No ☐ Time: |
|--------------------------------|

| Hypertension: Yes ☐ No ☐ Time: |
|---------------------------------|

| Cardiac arrest: Yes ☐ No ☐ Time: |
|-----------------------------------|

| Reanimation: Yes ☐ No ☐ Time: |
|--------------------------------|

| Respiratory arrest: Yes ☐ No ☐ Time: |
|---------------------------------------|

| Reanimation: Yes ☐ No ☐ Time: |
|---------------------------------|
The grafts from donors with a history of ocular surgery, Descemet folds, and/or endothelial precipitates were not used for the DM graft.12 The donor corneas were preserved in Eusol-C (Corneal Chamber, Alchimia, Ponte San Nicolo, Italy) at +4°C. Descemet membrane graft preparation and DMEK surgery were performed within 7 days.

The first 200 cases of the surgeon, that is, the surgeries that include another procedure, such as synechiotomy, vitrectomy, and anterior-chamber lens implantation were excluded from the study.

**Graft Preparation**

The diameter of the graft was determined according to the diameter of the cornea from limbus to limbus of the recipient’s eye. All grafts were prepared with the guidance of a technique described as submerged corneas using backgrounds away (SCUBA).13 The donor cornea was placed endothelial side up on a vacuum punch (Katena Products, Inc., New Jersey, USA). Trypan blue 0.06% solution was used to stain the edges of DM. Under the fluid, peripheral 180° of DM was stripped, from the trabecular meshwork to the central cornea by using a crescent knife, trying not to form a tear. The Descemet membrane was grasped with a Sinskey hook and 360° of stripping was performed using tying forceps. When nearly half of the DM was stripped, the graft was restained. Then, superficial partial-thickness trephination was performed from the endothelial side with a diameter that was determined before (7.50–8.50 mm). Then, the DM was grasped again with a pair of tying forceps and stripped until 360° of DM was free from the stroma. The donor graft was restained by trypan blue 0.06% and

| Dopamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Noradrenalin: | Dose: .......... Unit | Medication start date / duration of use: |
| Dobutamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Other (Specify dose, unit and duration): |

| Last hour urine: .......... ml | Last 24 hour urine: .......... ml | There is .......... ml of urine output in the last .......... hour |

| Blood transfusion performed: .......... ml | Amount of blood transfusion in the last 24 hours: .......... ml |

| Type of plasma expander given in the last 24 hours: | Amount: .......... ml |

| Hemodilution | Yes ☐ | No ☐ |

The first 200 cases of the surgeon, that is, the surgeries that include another procedure, such as synechiotomy, vitrectomy, and anterior-chamber lens implantation were excluded from the study.

**Graft Preparation**

The diameter of the graft was determined according to the diameter of the cornea from limbus to limbus of the recipient’s eye. All grafts were prepared with the guidance of a technique described as submerged corneas using backgrounds away (SCUBA).13 The donor cornea was placed endothelial side up on a vacuum punch (Katena Products, Inc., New Jersey, USA). Trypan blue 0.06% solution was used to stain the edges of DM. Under the fluid, peripheral 180° of DM was stripped, from the trabecular meshwork to the central cornea by using a crescent knife, trying not to form a tear. The Descemet membrane was grasped with a Sinskey hook and 360° of stripping was performed using tying forceps. When nearly half of the DM was stripped, the graft was restained. Then, superficial partial-thickness trephination was performed from the endothelial side with a diameter that was determined before (7.50–8.50 mm). Then, the DM was grasped again with a pair of tying forceps and stripped until 360° of DM was free from the stroma. The donor graft was restained by trypan blue 0.06% and

| Dopamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Noradrenalin: | Dose: .......... Unit | Medication start date / duration of use: |
| Dobutamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Other (Specify dose, unit and duration): |

| Last hour urine: .......... ml | Last 24 hour urine: .......... ml | There is .......... ml of urine output in the last .......... hour |

| Blood transfusion performed: .......... ml | Amount of blood transfusion in the last 24 hours: .......... ml |

| Type of plasma expander given in the last 24 hours: | Amount: .......... ml |

| Hemodilution | Yes ☐ | No ☐ |

The first 200 cases of the surgeon, that is, the surgeries that include another procedure, such as synechiotomy, vitrectomy, and anterior-chamber lens implantation were excluded from the study.

**Graft Preparation**

The diameter of the graft was determined according to the diameter of the cornea from limbus to limbus of the recipient’s eye. All grafts were prepared with the guidance of a technique described as submerged corneas using backgrounds away (SCUBA).13 The donor cornea was placed endothelial side up on a vacuum punch (Katena Products, Inc., New Jersey, USA). Trypan blue 0.06% solution was used to stain the edges of DM. Under the fluid, peripheral 180° of DM was stripped, from the trabecular meshwork to the central cornea by using a crescent knife, trying not to form a tear. The Descemet membrane was grasped with a Sinskey hook and 360° of stripping was performed using tying forceps. When nearly half of the DM was stripped, the graft was restained. Then, superficial partial-thickness trephination was performed from the endothelial side with a diameter that was determined before (7.50–8.50 mm). Then, the DM was grasped again with a pair of tying forceps and stripped until 360° of DM was free from the stroma. The donor graft was restained by trypan blue 0.06% and

| Dopamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Noradrenalin: | Dose: .......... Unit | Medication start date / duration of use: |
| Dobutamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Other (Specify dose, unit and duration): |

| Last hour urine: .......... ml | Last 24 hour urine: .......... ml | There is .......... ml of urine output in the last .......... hour |

| Blood transfusion performed: .......... ml | Amount of blood transfusion in the last 24 hours: .......... ml |

| Type of plasma expander given in the last 24 hours: | Amount: .......... ml |

| Hemodilution | Yes ☐ | No ☐ |

The first 200 cases of the surgeon, that is, the surgeries that include another procedure, such as synechiotomy, vitrectomy, and anterior-chamber lens implantation were excluded from the study.

**Graft Preparation**

The diameter of the graft was determined according to the diameter of the cornea from limbus to limbus of the recipient’s eye. All grafts were prepared with the guidance of a technique described as submerged corneas using backgrounds away (SCUBA).13 The donor cornea was placed endothelial side up on a vacuum punch (Katena Products, Inc., New Jersey, USA). Trypan blue 0.06% solution was used to stain the edges of DM. Under the fluid, peripheral 180° of DM was stripped, from the trabecular meshwork to the central cornea by using a crescent knife, trying not to form a tear. The Descemet membrane was grasped with a Sinskey hook and 360° of stripping was performed using tying forceps. When nearly half of the DM was stripped, the graft was restained. Then, superficial partial-thickness trephination was performed from the endothelial side with a diameter that was determined before (7.50–8.50 mm). Then, the DM was grasped again with a pair of tying forceps and stripped until 360° of DM was free from the stroma. The donor graft was restained by trypan blue 0.06% and

| Dopamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Noradrenalin: | Dose: .......... Unit | Medication start date / duration of use: |
| Dobutamin: | Dose: .......... Unit | Medication start date / duration of use: |
| Other (Specify dose, unit and duration): |

| Last hour urine: .......... ml | Last 24 hour urine: .......... ml | There is .......... ml of urine output in the last .......... hour |

| Blood transfusion performed: .......... ml | Amount of blood transfusion in the last 24 hours: .......... ml |

| Type of plasma expander given in the last 24 hours: | Amount: .......... ml |

| Hemodilution | Yes ☐ | No ☐ |
was aspirated into a glass injector system (DMEK Surgical Disposable Set, INNOVA Medical Ophthalmics, Toronto, Canada) in the fluid to deliver into the anterior chamber of the recipient’s eye (Fig. 1).

In case of a peripheral DM tear occurrence, while stripping from the trabecular side, the same procedure was repeated from the opposite side. If again a tear was formed, then central punching was performed by not including the tear (Fig. 2). These grafts were included in group 1, and the grafts without any tear formation were included in group 2.

**Statistical Analysis**

Data analysis was performed using the Statistical Package for Social Sciences for Windows software (SPSS version 16.0, SPSS Inc., Chicago, IL). The normality distribution of the variables was tested. The descriptive statistics of the normally distributed continuous variables were expressed as mean ± SD. The normally distributed variables were compared between the groups using a Student t-test. Categorical variables were presented as frequency (%) and compared between the groups using the chi-square test or Fisher exact test. According to the data we used in the study, the power analysis of the sample size was found to be 0.82 in the preoperative analysis. Differences with a P value of less than 0.05 were considered statistically significant.

### RESULTS

Seventy-eight corneal grafts (30 female and 48 male) from 58 White donors were enrolled in the study. The mean age of donors was 64.23 ± 7.3 years. No statistically significant differences were found in the mean age and sex between groups (P = 0.920 and P = 0.480, respectively). Twenty-four (31.2%) DM grafts were included in group 1. Tears occurred in 1 quadrant in 6 (7.8%), 2 quadrants in 7 (9.1%), and 4 quadrants in 11 (14.3%) DM grafts. Fifty-four (68.8%) DM grafts were included in group 2.

The blood type of donors were A Rh+ in 6 (10.5%), B Rh+ in 5 (8.8%), and 0 Rh+ in 5 (8.8%) donors in group 1 and A Rh+ in 11 (19.3%), B Rh+ in 10 (17.5%), and 0 Rh+ in 5 (8.8%) donors in group 2. There was no statistically significant difference between groups (P = 0.450).

In 72 (93.6%) donors, at least one systemic disease was found, 23 (31.9%) in group 1 and 49 (68.1%) in group 2 (P = 0.570). The systemic diseases are summarized in Table 2. Of the donors with systemic diseases, breast cancer was found only in group 1 (n = 6, 25%), and the difference was statistically significant between groups (P = 0.010) (Table 2).

The use of systemic drugs is summarized in Table 3. Sevelamer use was only found in group 1 (n = 2, 8.7%), and the difference was statistically significant between groups (P = 0.030). When we looked at the drugs included in our study, no statistically significant difference in the use of other drugs was found between groups (Table 3). There was no statistically significant difference between groups in the use of drugs in the past 48 hours for respiratory or cardiac arrest, such as dopamine, amiodarone, and adrenaline (P = 0.130).

The increased levels above the normal range in blood urea nitrogen (BUN) and creatinine were found to be higher in group 1 than group 2 (87.5% vs. 66%, P = 0.050). No statistically significant difference was found in increased levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in donors when compared between groups (P = 0.984). In addition, there was no statistically significant difference in lower hemoglobin levels between groups (P = 0.701).

| Systemic Diseases                  | Group 1 (n:24) | Group 2 (n:54) | P*  |
|-----------------------------------|---------------|---------------|-----|
| Diabetes mellitus                 | 8 (33.3%)     | 15 (28.3%)    | 0.655 |
| Hypertension                      | 9 (37.5%)     | 31 (58.5%)    | 0.08  |
| Chronic renal failure             | 7 (29.2%)     | 11 (20.8%)    | 0.419 |
| Hyperlipidemia                    | 6 (25%)       | 16 (30.2%)    | 0.641 |
| Osteoporosis                      | 1 (4.2%)      | 5 (9.4%)      | 0.424 |
| Breast cancer                     | 6 (25%)       | —             | 0.01  |
| Endometrium cancer                | —             | 4 (7.5%)      | 0.167 |
| Prostate cancer                   | 1 (4.2%)      | 1 (1.9%)      | 0.56  |
| Lung cancer                       | 2 (8.3%)      | 6 (11.3%)     | 0.691 |
| Asthma and COPD                   | 1 (4.2%)      | 9 (17%)       | 0.121 |
| CHF                               | 1 (4.2%)      | 2 (3.8%)      | 0.93  |
| Venous embolism                   | 3 (12.5%)     | 2 (3.8%)      | 0.15  |

*P value less than 0.05 were considered statistically significant.

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease.
As far as we know, no investigation between blood type and DM tears was made. In this study, the highest rate of DM tears was found in donors with a blood type of A Rh+, but no statistically significant difference was found. This finding may be due to the higher rates of A Rh+ blood type in our population.

Previous studies have shown that diabetes, hyperlipidemia, obesity, and chronic renal failure in the donors cause failure in preparation of the DM graft.20,25 It has been suggested that in diabetes, the tight adhesions between the posterior stroma and the DM may be the cause of DM tears.25 In our study, no statistically significant difference was found in the rate of diabetes between groups. All the DM grafts from diabetic donors, whether intact or with tears, were used in the surgery and no complications occurred. In addition, the use of insulin and oral antidiabetic in donors had no significant effect on DM tears, although there seems to be a trend toward a statistically significant higher tear rate with insulin use (Table 3). In a study by Tien-en Tan et al.,26 it has been shown 4.7% of failure in DM graft preparation and no effect of diabetes on DM tears. Thus, it is believed that not only metabolic diseases, such as diabetes, but also multiple structural differences may be related to the occurrence of DM tears while graft preparation.26

It has been reported that systemic diseases, cause of death, and age of the donor may have a role in the failure of DM graft preparation.20,27 In our study, among systemic diseases of donors, only the rate of breast cancer was found to be significantly higher in group 1. Increased inflammatory response, vascular endothelial dysfunction, increased vascular endothelial growth factor response, and increased oxidative stress are parts of the pathophysiological process of breast cancer.28 Thus, the increased oxidative stress may be the cause of the dysfunction of the DM–endothelium complex of the graft and leads to the failure of DM graft preparation. Prospective studies might be required to further approve this finding.

When systemic drugs that were used more than 1 year were analyzed, only sevelamer use was found to be more common in group 1. Sevelamer is a phosphate binding agent indicated for the control of hyperphosphatemia, it effects the chloride ions by exchanging and not absorbed from gastrointestinal tract.29 Therefore, the effects on the donor may not have made a significant difference. However, it is a limiting situation that there are only 2 donors in group 1 who use sevelamer and there are no donors in group 2 who use sevelamer. With the prospective studies, these findings might be investigated.

Although no statistically significant differences were found in anemia or liver function tests between groups, renal function tests (BUN or creatinine) were found to be more common in group 1. The level of urea in the aqueous humor has been shown to increase with increased urea levels in the serum.30 The design of this study is not suitable to understand the effects of increased blood urea and creatinine levels on the DM–endothelium complex, so further studies are needed to reveal the pathophysiology.

The limitations of our study are its retrospective nature and the lack of a control group that includes naive donors without any systemic disease or use of any drug. However, it is almost impossible to find enough healthy donors in relatively old age within the criteria of donor bank to form a control group. There may be other drugs off our list that can affect the DM tear rate, so additional studies are needed (Table 3).

In conclusion, most of the death in elderly occurs with individuals with systemic diseases. On the other hand, the need

### DISCUSSION

The first step of DMEK surgery is DM graft preparation.9 One of the most concerning reasons in graft preparation is graft loss, whereas recent studies have reported successful outcomes with partially implanted grafts.13–15 The most common cause of graft loss is the tears within the graft due to the tight adhesions or increased fragility of the graft.16 Although the procedure seems to be standardized, the peripheral tears in the DM graft remain a potential risk. Although small tears may be salvageable, an extra graft must be reserved in case of a large tear.10

The differences in histochemical properties of the DM graft and the thickness of the graft may cause a change in the resistance at the peeling stage of the preparation step. The systemic diseases and drugs of the donor may also affect the elasticity and resistance of the tissue. The structural stress of the tissue increases due to the differences in adhesions between tissues. There is a narrow transition zone that includes an amorphous extracellular matrix, called interfacial matrix, between the DM and the stroma. Extracellular matrix and adhesive proteins, such as fibronectin, vitronectin, amyloid P, osteonectin/SPARC, fibrillin-1, fibrillin-1 ve fibrulin-3, keratoepithelin, and collagen type VI and VIII, are found immunohistochemically in this zone.17,18 Descemet membrane graft tears during peeling may be a result of these adhesive properties of the interfacial matrix. During DM graft preparation, adhesions between the posterior stroma and the DM may resolve spontaneously or result in DM tears if the trascional forces exceed the tensile adhesive strength.19 The structural and biochemical differences between donors may cause the different adhesive forces between the posterior stroma and the DM.18

Failure in DM graft preparation has been reported between 4.2% and 6.7%.8,20–22 The most commonly used technique in graft preparation is the SCUBA technique, in which the success rate has been reported over 95%.21,23 In this study, only the SCUBA technique is used to prepare the DM grafts. As we know that with younger donors, the adhesive forces and the possibility of tears are higher, donors younger than 40 years were also not included.24 No age-related or sex-related factor was found to affect the failure rate of graft preparation in this study.

### TABLE 3. Systemic Drugs of the Donors

| Systemic Drugs | Group 1 (n:24) | Group 2 (n:54) | p* |
|----------------|---------------|---------------|----|
| Insulin        | 7 (30.4%)     | 7 (13.7%)     | 0.089 |
| Metformin      | 5 (21.7%)     | 9 (17.6%)     | 0.677 |
| Amlodipine     | 2 (8.7%)      | 12 (23.5%)    | 0.132 |
| Furosemide     | 6 (26.1%)     | 8 (15.7%)     | 0.290 |
| Ramipril       | 4 (17.4%)     | 11 (21.6%)    | 0.679 |
| Carvedilol     | 4 (17.4%)     | 12 (23.5%)    | 0.553 |
| Labetalol      | 2 (8.7%)      | 4 (7.8%)      | 0.901 |
| Alpha-1 blockers | 2 (8.7%)   | 3 (5.9%)      | 0.655 |
| Metoprolol     | 5 (21.7%)     | 12 (23.5%)    | 0.865 |
| Canfacitramide | 4 (17.4%)     | 10 (18.5%)    | 0.553 |
| Ramipril       | 4 (17.4%)     | 11 (21.6%)    | 0.679 |
| Furosemide     | 6 (26.1%)     | 8 (15.7%)     | 0.290 |
| Amiodipine     | 2 (8.7%)      | 12 (23.5%)    | 0.132 |
| Valsartan      | 4 (17.4%)     | 8 (15.7%)     | 0.854 |
| Sevelamer      | 2 (8.7%)      | —             | 0.033 |

*p value less than 0.05 were considered statistically significant.
for donor corneas for the patients in transplant lists is exponentially increasing. Therefore, to provide this shortage it would be effective to use all the available donors for transplant. Although diabetic donors have been reported to be inappropriate candidates for the preparation of DM grafts for DMEK, most of the corneas of the donors with several systemic diseases including diabetes can be used in DMEK surgery with the right technique in DM graft preparation.

REFERENCES

1. Melles GR, Ong TS, Ververs B, et al. Descemet membrane endothelial keratoplasty. Cornea 2006;25:987–990.
2. Guerra FP, Anshu A, Price MO, et al. Endothelial keratoplasty: Fellow eyes comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. Cornea 2011;30:1382–1386.
3. Godinho IV, Mian SI. Update on Descemet membrane endothelial keratoplasty. Curr Opin Ophthalmol 2019;30:271–274.
4. Ham L, Dapena I, van Luijk C, et al. Descemet membrane endothelial keratoplasty for Fuchs endothelial dystrophy: Review of the first 50 consecutive cases. Eye 2009;23:1990–1998.
5. Lie JT, Birbal R, Ham L, et al. Donor tissue preparation for Descemet membrane endothelial keratoplasty. J Cataract Refract Surg 2008;34:1578–1583.
6. Busin M, Scorcia V, Patel AK, et al. Pneumatic dissection and storage of donor endothelial tissue for Descemet’s membrane endothelial keratoplasty. Ophthalmology 2010;117:1517–1520.
7. Parekh M, Ruzza A, Salvalaio G, et al. Descemet membrane endothelial keratoplasty tissue preparation from donor corneas using a standardized submerged hydro-separation method. Am J Ophthalmol 2014;158:277–285.
8. Parekh M, Baruzzo M, Favaro E, et al. Standardizing Descemet membrane endothelial keratoplasty graft preparation method in the eye bank experience of 527 Descemet membrane endothelial keratoplasty tissues. Cornea 2017;36:1458–1466.
9. Koçlük Y, Kasım B, Sukgen EA, et al. Descemet membrane endothelial keratoplasty: Intraoperative and postoperative complications and clinical results. Arq Bras Oftalmol 2018;81:212–218.
10. Kruse FE, Laaser K, Cursiefen C, et al. A stepwise approach to donor preparation and insertion increases safety and outcome of Descemet membrane endothelial keratoplasty. Cornea 2011;30:580–587.
11. Greiner MA, Rixen JJ, Wagoner MD, et al. Diabetes mellitus increases risk of unsuccessful graft preparation in Descemet membrane endothelial keratoplasty: A multicenter study. Cornea 2014;33:1129–1133.
12. Eye Bank Association of America Medical Advisory Board. Medical Standards. Washington, DC: Eye Bank Association of America, 2008.
13. Lam FC, Baydoun L, Dirisamer M, et al. Hemidesmembrane endothelial keratoplasty transplantation: A potential method for increasing the pool of endothelial graft tissue. JAMA Ophthalmol 2014;132:1469–1473.
14. Yoenuek E, Bartz Schindler CU. Current approaches to combat the shortage of corneal tissues: Split-DMEK and double split keratoplasty. Cornea 2015;34:6–9.
15. Koçlük Y, Kasım B. Descemet membrane endothelial keratoplasty and intraocular lens implantation in cases of aphakic bullous keratopathy. Semin Ophthalmol 2020;35:86–93.
16. Price MO, Giebel AW, Fairchild KM, et al. Descemet’s membrane endothelial keratoplasty: prospective multi-center study of visual and refractive outcomes and endothelial survival. Ophthalmology 2009;116:2361–2368.
17. Kabosova A, Azar DT, Bannikov GA, et al. Compositional differences between infant and adult human corneal basement membranes. Invest Ophthalmol Vis Sci 2007;48:4899–4909.
18. Schlötzer-Schrehardt U, Bachmann BO, Laaser K, et al. Characterization of the cleavage plane in Descemet’s membrane endothelial keratoplasty. Ophthalmology 2011;118:1950–1957.
19. Levy SG, McCarty AC, Moss J. The distribution of fibronectin and P component in Descemet’s membrane: An immunoelectron microscopic study. Curr Eye Res 1995;14:865–870.
20. Vianna LM, Stoeger CG, Galloway JD, et al. Risk factors for eye bank preparation failure of Descemet membrane endothelial keratoplasty tissue. Am J Ophthalmol 2015;159:829–834.
21. Guerra FP, Anshu A, Price MO, et al. Descemet’s membrane endothelial keratoplasty: Prospective study of 1-year visual outcomes, graft survival, and endothelial loss. Ophthalmology 2011;118:2368–2373.
22. Livny E, Groeneveld-van Beek EA, Lie JT, et al. Minimizing graft preparation failure in Descemet membrane endothelial keratoplasty. Cornea 2017;36:1452–1457.
23. Droutsas K, Giallourou E, Melles GR, et al. Descemet membrane endothelial keratoplasty: Learning curve of a single surgeon. Cornea 2013;32:1075–1079.
24. Schaub F, Enders P, Zachewicz J, et al. Impact of donor age on Descemet membrane endothelial keratoplasty outcome: Evaluation of donors aged 17–55 years. Am J Ophthalmol 2016;170:119–127.
25. Greiner MA, Rixen JJ, Wagoner MD, et al. Diabetes mellitus increases risk of unsuccessful graft preparation in Descemet membrane endothelial keratoplasty: A multicenter study. Cornea 2014;33:1129–1133.
26. Tan T-E, Devarajan K, Seah X-Y, et al. Lamellar dissection technique for Descemet membrane endothelial keratoplasty graft preparation. Cornea 2020;39:23–29.
27. Gorovoy IR, Cui QN, Gorovoy MS. Donor tissue characteristics in preparation of DMEK grafts. Cornea 2014;33:683–685.
28. Norata T, Scoccianti C, Boutron-Ruault M-C, et al. European code against cancer 4th edition: Diet and cancer. Cancer Epidemiol 2015;39(Suppl 1):S56–S66.
29. Carfagna F, Del Vecchio L, Pontoriero G, et al. Current and potential treatment options for hyperphosphatemia. Expert Opin Drug Saf 2018;17:597–607.
30. Galin MA, Nano HD, Davidson RA. Aqueous and blood urea nitrogen levels after intravenous urea administration. Arch Ophthalmol 1961;65:805–807.