Clinical Outcomes and Risk Factors for Graft Failure After Deep Anterior Lamellar Keratoplasty and Penetrating Keratoplasty for Macular Corneal Dystrophy

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Purpose: The aim of this study was to compare visual acuity, clinical outcomes, complications, and risk factors for graft failure after deep anterior lamellar keratoplasty (DALK) and penetrating keratoplasty (PK) for macular corneal dystrophy.

Methods: Retrospective comparative case series.

Results: The PK group consisted of 109 eyes of 84 patients and the DALK group consisted of 21 eyes of 20 patients. The mean logarithm of the minimum angle of resolution best-corrected visual acuity at 3 and 12 months was 0.5 versus 0.5 ($P = 0.285$) and 0.4 versus 0.4 ($P = 0.67$) in the DALK and PK groups, respectively. There was no significant statistical difference in astigmatism and spherical equivalent between the 2 groups at 12 months. In the PK group, graft rejection that was the most common cause of graft failure was seen in 27 eyes (25%), of which 55% occurred within 1 year. In the DALK group, Descemet membrane microperforation occurred in 5 eyes (24%) intraoperatively, and early postoperative Descemet membrane detachment with double anterior chamber occurred in 9 eyes (43%). Kaplan–Meier estimate of graft survival in PK versus DALK groups were 93% versus 80% at 1 year and 78% versus 70% at 4 years, respectively.

Conclusions: Visual and refractive outcomes are comparable between DALK and PK groups. DALK was superior to PK in its safety against postoperative complications such as endothelial rejection and secondary glaucoma. Graft failure in DALK was mostly associated with either intraoperative or early postoperative complications. DALK is a viable surgical option in cases with macular corneal dystrophy.

Key Words: macular corneal dystrophy, deep anterior lamellar keratoplasty, penetrating keratoplasty, complications, double anterior chamber

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Macular corneal dystrophy (MCD) is an autosomal recessive inherited disorder characterized by bilateral progressive stromal clouding and central corneal thinning.[1] Although MCD is identified throughout the world, it is most prevalent in India, Saudi Arabia, Iceland, and parts of the United States.[2] Clinically, irregular ill-defined areas of diffuse clouding are noted in the central cornea in the initial stages, which subsequently become confluent and eventually involve the periphery and deeper layers leading to visual impairment. Histologically, MCD is characterized by accumulation of glycosaminoglycans in stromal lamellae, within the keratocytes and endothelium, which stain positive with periodic acid–Schiff, alcian blue stain, metachromatic dyes, and possess affinity for colloidal iron.[3]

Traditionally, penetrating keratoplasty (PK) was the treatment of choice for MCD.[4–7] Because of the long-term complications such as endothelial rejection and endothelial cell loss with PK, anterior lamellar keratoplasty is considered an alternative to PK for various diseases not involving the endothelium. With the success of anterior lamellar keratoplasty in other conditions such as keratoconus, deep anterior lamellar keratoplasty (DALK) has been tried in stromal dystrophies not involving Descemet membrane (DM) or the endothelial membrane. Tsubota et al[8] have reported a case of deep lamellar keratoplasty in MCD as early as 1998 with good success. Later, small series were published for deep lamellar keratoplasty for MCD.[9–11] Recently, in a larger series of 43 eyes, Unal et al[12] have shown good success of DALK for MCD. In direct comparison of DALK and PK for MCD, Kawashima et al[9] have suggested that DALK may not be a safe option for MCD, whereas Patel et al,[13] in their case report have shown comparable results in both the groups. A more recent study by Chen et al[14] has shown a better best-corrected visual acuity (BCVA) in the PK group and recurrence of disease as one of the major risk factors for graft failure in both the groups. Sogutlu Sari et al[15] have shown comparable BCVAs and contrast sensitivity between the 2 groups, with graft rejection as the major risk factor for graft failure in the PK group and endothelial failure in the DALK group. The aim of this study was to compare the refractive outcomes, complications, and risk factors for graft failure after DALK and PK for MCD.

MATERIALS AND METHODS

In this retrospective study, we reviewed the clinical records of 104 patients with MCD who underwent corneal

transplantation at the Cornea, Anterior Segment and Refractive Surgery Services of LV Prasad Eye Institute, Hyderabad, India, between April 2001 and June 2009 with a postoperative follow-up of at least 12 months. The study was approved by the institutional review board and was conducted in strict adherence to the tenets of the Declaration of Helsinki. Eighty-four patients underwent PK, and 20 patients underwent DALK. Patients who had a significant decrease in visual acuity or who were intolerant to symptoms because of recurrent erosions were advised surgery. Data collected included demographic details, preoperative and postoperative BCVA, manifest refraction, intraoperative and postoperative complications, and postoperative clinical course. Decision to perform DALK or PK was taken based on the level of deposits noticed on clinical examination. If the deposits were seen in the deeper layers of the cornea on slit-lamp biomicroscopy, PK was preferred (Fig. 1).

Surgical Technique

All except 1 patient underwent surgery under peribulbar anesthesia.

Deep Anterior Lamellar Keratoplasty

DALK was performed using the big-bubble technique as previously described.[10] In cases where the big bubble was not achieved, baring of DM was achieved by dissecting the stroma in layers using a crescent blade and Vannas scissors. Cases with large perforation in DM were converted to PK.

Penetrating Keratoplasty

PK was performed by the standard technique. Cases with significant cataract underwent cataract extraction with insertion of posterior chamber intraocular lens in the capsular bag (combined procedure).

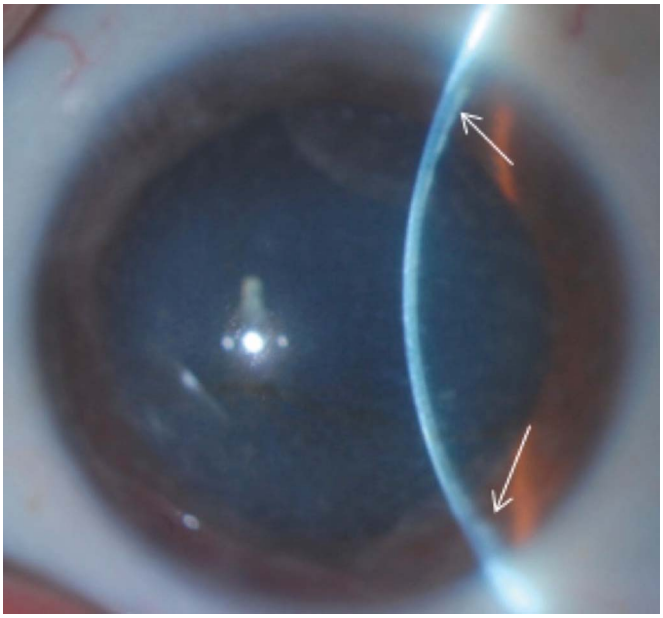

FIGURE 1. Slit cornea photograph of a patient with MCD with deposits in deep layers and on DM (arrows).

Donor Preparation

Corneas stored in McCarey-Kaufman medium were used for transplantation. The donor cornea was oversized by 0.2 mm in DALK and 0.5 mm in PK. In DALK, after staining the endothelial side with 0.06% trypan blue dye (Blue Rhexis; Contacare Ophthalmics & Diagnostics, Vadodara, Gujarat, India), DM was peeled off with fine nontoothed forceps. The donor lenticule was secured with 10-0 monofilament nylon by 16 interrupted sutures.

Postoperative Course

All patients received topical prednisolone acetate 1% in tapering doses over several months and topical antibiotic drops for 1 to 2 weeks. Follow-up visits were generally at 1 day, 1 week, 1 month, and then every 2 to 3 months. Suture removal was performed based on wound healing and factors such as vascularization or loose sutures. If stable and low astigmatism was achieved, sutures were retained in some patients.

Statistical Analysis

For comparison of mean age and donor size between groups, an independent sample *t* test was used. For related categorical data, such as improvement in preoperative-to-postoperative visual acuity, McNemar test was used. For survival analysis, we used Kaplan–Meier Survival plots to depict the difference of survival probability between DALK and PK groups. For all statistical analysis, we used SPSS Version 16.0 windows (SPSS, Chicago). A 2-tailed *P* value of <0.05 was considered statistically significant.

RESULTS

Patient characteristics and surgical data are summarized in Table 1. There was no significant difference between the mean age at the time of surgery in both groups ($P = 0.12$). The mean follow-up period of the PK group was 43 months, which was significantly longer than the DALK group of 17 months ($P < 0.01$). In the DALK group, a big-bubble was achieved in 12 eyes (57%). Three eyes (12.5%) required conversion to PK because of macroperforation and were

TABLE 1. Patient Characteristics and Surgical Data of the 2 Groups

Parameter	DALK	PK
Number of eyes (patients)	21 (20)	109 (84)
Mean age (SD, range) years	30 (11.9, 5–50)	34 (11.5, 18–65)
Gender, male:female (%)	14:6 (70:30)	48:36 (57:43)
Laterality, RE:LE:BE	9:10:1	34:25:25
Mean follow-up (SD, range), months	17 (8.8, 12–46)	43 (24.1, 12–104)
Mean donor size (SD)	8 (0.3) mm	8.1 (0.2) mm
Mean recipient size (SD)	7.6 (0.2) mm	7.6 (0.2) mm

BE, both eyes; LE, left eye; RE, right eye.

included in the PK group for subsequent analysis. In the PK group, 21 eyes (19%) underwent the combined procedure. The difference between the mean donor and the mean recipient size of the 2 groups was not statistically significant ($P = 0.10$, $P = 0.37$).

Visual Acuity

Visual acuity measured on a standard Snellen projector chart was converted to logarithm of the minimum angle of resolution (logMAR) equivalents for statistical analysis (Table 2). There was no statistical difference between preoperative, at 3 months, at 12 months, and at final follow-up logarithm of the minimum angle of resolution BCVA between the 2 groups. At 12 months, 14 eyes (67%) of the DALK group and 65 eyes (60%) of PK group had a BCVA of 20/40 or better. Both the groups were comparable in terms of spherical equivalent and cylindrical power at 12 months and final follow-up.

Graft Clarity

At 12 months, 17 eyes (81%) of the DALK group and 91 eyes (83%) of the PK group had clear grafts. At the final follow-up, 17 eyes (81%) of the DALK group and 84 eyes (77%) of the PK group had clear grafts. There was no statistical difference between the 2 groups both at 12 months and final follow-up ($P = 0.28$, $P = 0.88$). Four eyes (19%) in the DALK group and 25 eyes (23%) in the PK group had failed grafts at final follow-up (Table 3). In the DALK and PK groups, there was no significant association between age ($P = 0.19$, $P = 0.053$) and donor size ($P = 0.58$, $P = 0.50$) on the graft outcome. Survival rate of the DALK group was 80% at 12 months and remained 70% at 24, 36, and 48 months. Survival rate of the PK group was 93%, 88%, 83%, 78%, 65%, 65%, and 52% at 12, 24, 36, 48, 72, 84, and 96 months, respectively (Fig. 2).

TABLE 2. Comparison of Visual and Refractive Results Between the 2 Groups

Parameter	DALK	PK	*P*
Mean preoperative logMAR BCVA (SD)	1.1 (0.6)	1.3 (0.6)	0.22
Mean logMAR BCVA at 3 months (SD)	0.6 (0.4)	0.5 (0.5)	0.52
Mean logMAR BCVA at 12 months (SD)	0.4 (0.4)	0.4 (0.5)	0.89
Mean logMAR BCVA at final follow-up (SD)	0.4 (0.6)	0.6 (0.7)	0.50
Mean refractive spherical equivalent at 12 months (SD)	1.7 (3.1) D	0.3 (4) D	0.31
Mean refractive spherical equivalent at final follow-up (SD)	0.7 (2.3) D	−0.6 (3.7) D	0.29
Mean cylinder (median) at 12 mos	−3.2 (−3.5) D	−3.3 (−3) D	0.75
Mean cylinder (median) at final follow-up	−3.3 (−3) D	−2.5 (2.6) D	0.33

D, diopters; logMAR, logarithm of the minimum angle of resolution.

TABLE 3. Causes of Graft Failure in the 2 Groups

Cause	DALK	PK
Endothelial rejection	0	17
Secondary glaucoma	0	3
Graft infiltrate	0	3
Endophthalmitis	0	2
Intraoperative microperoration, postoperative DM detachment, C_3F_8 injection once, endothelial decompensation after cataract surgery	1	0
Poor ocular surface, sterile perforation	1	0
Postoperative DM detachment (C_3F_8 injected twice in 1 case)	2	0

Complications

In the DALK group, intraoperative microperforation was observed in 5 eyes (24%) (Table 4). In 4 eyes, microperforation occurred while excising the residual stroma in the periphery and in 1 eye during suturing. In all 5 eyes, surgery was continued by injection of air into the anterior chamber, which helped in occlusion of the site of perforation and maintaining the contour of DM. Intraoperative microperforation was seen in 3 eyes with the big-bubble and 2 eyes with the manual DALK technique. In 3 eyes (12.5%), macroperforation of DM was noticed and necessitated conversion to PK.

Postoperative DM detachment (double anterior chamber) was seen in 9 eyes (43%). Six eyes (5 C_3F_8 and 1 air) needed secondary surgical intervention, and 3 eyes were managed conservatively. Of the 5 eyes that had perfluoropropane (14% C_3F_8) injected, 4 eyes showed complete attachment of DM, whereas 1 eye required a repeat injection, which showed anatomic attachment of DM, but the graft ultimately failed. Of the 3 eyes that were managed conservatively, 1 eye had shallow superior detachment, which resolved; 1 eye that had shallow inferior DM detachment, showed very gradual anatomical attachment but the graft decompensated subsequently; and 1 eye had a split between the 2 layers of DM, which resolved by day 5 without any intervention but had persistent folds in DM. Transient rise in intraocular pressure was seen in 2 eyes, which was controlled with medications. Suture-related microbial keratitis (MK) was seen in 2 eyes, one due to *Streptococcus pneumonia* and the other due to *Pseudomonas aeruginosa*, both responded well to medical treatment.

In the PK group, spontaneous intraoperative expulsion of the lens was seen in 1 eye due to vitreous pressure. Secondary glaucoma was seen in 12 eyes (11%), which required use of topical antiglaucoma medications. Three eyes required resuturing, 2 because of wound leak in the immediate postoperative period and the other because of traumatic wound dehiscence at 3 months postoperatively. Four eyes underwent uneventful cataract surgery during the postoperative course. Corneal endothelial rejection episodes occurred in 27 eyes (24.8%), 15% of which were seen in the first year after PK. There was no significant association of age ($P = 0.40$) and donor size ($P = 0.67$) on the graft rejection rate. Suture-related MK was seen in 4 eyes (3.7%). Therapeutic PK was necessary in 2 eyes with fungal infection and 1 eye with

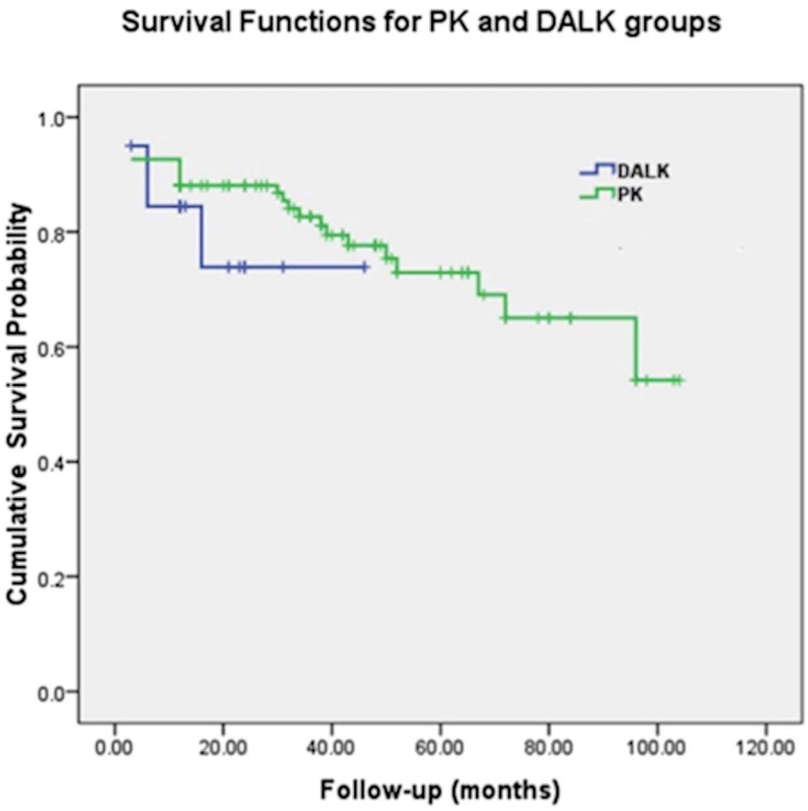

FIGURE 2. Kaplan–Meier curve showing comparison of survival rates of PK and DALK.

S. pneumonia infection. The other eye with *S. pneumonia* infection resolved completely with medical therapy. Two eyes developed late endophthalmitis, 1 due to *S. pneumonia*, and there was no organism isolated from vitreous or aqueous samples in the other case, both of which had a poor outcome. Of the 2 cases of late postoperative endophthalmitis, 1 was seen after intensive use of topical steroids for an episode of rejection, the other case presented to the clinic with clinical features of endophthalmitis but no infectious etiology was ascertained on microbiological evaluation. A poor ocular surface leading to persistent epithelial defect necessitating a temporary tarsorrhaphy was seen in 1 eye in the DALK group and 2 eyes in the PK group. Initial response to tarsorrhaphy was seen in the DALK eye but subsequently developed recurrent epithelial defects and sterile perforation, which was sealed by cyanoacrylate glue.

TABLE 4. Complications Noted in the 2 Groups

Complication	DALK	PK
Intraoperative		
Conversion to PK	3	—
DM microperforation	5	—
Spontaneous expulsion of lens	0	1
Postoperative		
Double anterior chamber	9	—
Wound leak: resuturing	0	2
Graft dehiscence (trauma-3 months): resuturing	0	1
PED tarsorrhaphy	1	2
Secondary glaucoma	2	12
Cataract	1	4
Graft infiltrate	2	4
Vitreous hemorrhage (PDR)	0	1
Endophthalmitis (at 12 mos)	0	2
Graft rejection episodes: endothelial	0	27

PDR, proliferative diabetic retinopathy; PED, persistent epithelial defect.

DISCUSSION

In this study, we have seen that there was no significant difference in the postoperative visual and refractive outcomes between the DALK and PK groups, the same has been shown in the literature.[9,16–20] In a closer comparison, Sogutlu Sari et al[15] have shown comparable BCVAs as seen in our series, whereas Cheng et al[14] have shown a better BCVA after PK compared with DALK. In our series, 67% eyes in the DALK group achieved 20/40 or better BCVA, which was comparable to that reported by Sogutlu Sari et al[15] (68.5%), whereas only 60% eyes in the PK group achieved a BCVA of 20/40 or better, which is less than that reported by Sogutlu Sari et al[15] (70.7%) but better than that reported by Al-Swailem et al[7] (55%). Initiation of suture removal was definitely earlier in the case of DALK; we cannot comment on astigmatism after suture removal because in some of our cases, the sutures were not removed when astigmatism was less and the BCVA was stable.

In our series, both intraoperative DM perforations and conversion to PK during DALK were higher compared with the total percentage reported in the literature, 11.7%[21]

(range, 4%–39%)[22,23] and 2%[21] (range, 1%–30%),[22,24] respectively. Postoperative DM detachment or double anterior chamber is the most important complication of DALK, which was seen in 9 eyes (43%) in our series that can be attributed to the long learning curve of DALK. The overall percentage of double anterior chamber reported in the literature is 3.5%,[21] but it can be as high as 30%.[23] Of the 9 eyes, 6 (67%) eyes required secondary surgical intervention (4 C_3F_8 once, 1 C_3F_8 twice, and 1 air once), and 3 (33%) eyes were managed conservatively. Anatomical attachment of DM was seen in all 9 eyes, which was confirmed on anterior segment optical coherence tomography. Four (44%) of the 9 eyes with postoperative DM detachment were as a consequence of intraoperative microperforation. Den et al[25] have shown that 60% (15/20) cases of postoperative pseudochamber formation were associated with intraoperative DM perforations. The percentage of eyes that had intraoperative microperforations and postoperative double anterior chamber in our study was comparable to that reported by Kawashima et al,[9] but higher than that reported by Sogutlu Sari et al[15] and Reinhart et al.[21] Conversion of DALK to PK was higher in all the studies where DALK was performed for MCD compared with other indications (Table 5).

Steroid-induced transient rise in intraocular pressure was seen in 2 eyes in the DALK group, which was managed by decreasing the frequency of topical steroids and use of topical antiglaucoma medications. The higher incidence (11%) of secondary glaucoma in the PK group was probably due to use of steroids for longer periods.[16] Topical antiglaucoma medications were used in all the cases. Three patients with intractable glaucoma subsequently developed graft failure, which is the second most common cause of graft failure seen in our series and in the literature.[26] Suture-related MK was seen in both groups (9.5%: DALK and 3.7%: PK), but in the PK group, 3 of 4 eyes required a repeat graft. The literature shows the incidence of MK after PK to be as high as 11.9%.[27] In a closer comparison, Al-Swailem et al[7] have reported an incidence of MK as 6.1% after PK for MCD. Eighty percent of infectious keratitis is seen within 1 year after PK, which was seen even in our series.[28]

Graft rejection episodes seen in our series (24%) were comparable to those reported by Al-Swailem et al[7] (20%) and Cheng et al[14] (23%) but higher than those reported by Sogutlu Sari et al[15] (12%). However, irreversible endothelial failure after endothelial rejection was definitely higher (15.5%) in our series after PK for MCD. This is probably because of late presentation and poor response to medical management. We did not see any form of rejection (epithelial or stromal) in the DALK group, which has been reported previously.[15]

At final follow-up, 81% of DALK grafts were clear, which was comparable to 80% reported by Kawashima et al[9] but less than that reported by Cheng et al[14] (85.7%). In the PK group, only 77% of grafts were clear in our series compared with 90% reported by Al-Swailem et al[7] and 87.7% reported by Cheng et al.[14] Secondary glaucoma and MK are the second most common cause of graft failure accounting for 12% each followed by endophthalmitis (8%) in the PK group. Seventy-five percent of graft failures in the DALK group were seen in patients who had either intraoperative (microperforation) or early postoperative (DM detachment) complications as shown in Table 3. Shimazaki et al[16] have reported successful cataract surgery after DALK in 2 cases, but we have seen decompensation of 1 graft after cataract surgery, which was previously associated with intraoperative microperforation and postoperative DM detachment thus compromising the endothelial cell counts. Den et al[25] have shown that intraoperative perforation during DALK is associated with decreased endothelial counts.

Histopathologically, it is shown that in MCD, deposits are seen even in the endothelium,[3] but Patel et al[13] have reported comparable endothelial counts between DALK and PK eyes, Sogutlu Sari et al[15] and Cheng et al[14] have shown higher endothelial cell loss after PK than after DALK, whereas Kawashima et al[9] have shown a decreasing trend in the endothelial counts after DALK. It is noteworthy to mention that 40% (4/10) of the cases reported by Kawashima et al[9] were associated with postoperative double anterior chamber.

The main limitation of this retrospective study is that the cases were unmatched, with more cases of PK than DALK. Also, the endothelial cell counts were not available, and the duration of follow-up was shorter in the DALK group. Although histopathologically it is shown that there is deposition of glycosaminoglycans in the endothelial cells in MCD, functional efficiency of these cells is not known.[3] Seventy-five percent of our DALK failures were associated with surgical risk factors. Based on our series, it is evident that surgical risk factors contribute significantly to endothelial decompensation after DALK rather than only to the disease process in MCD. There is potential for further research on the function of endothelial cells in MCD by monitoring endothelial cell counts in cases of mild MCD for better understanding of the fate of endothelial cells in MCD.

In summary, this study demonstrated that visual and refractive outcomes are comparable between DALK and PK with varying complication profiles. Graft survival was better in the DALK group with time compared with the PK group. Although DALK is a technically challenging procedure with a long learning curve and is associated with more intraoperative

TABLE 5. Literature Comparing Intraoperative and Perioperative complication Profile After DALK for MCD and Other Indications

Study	Indication	Eyes	Microperforation, %	Conversion to PK, %	Double AC, %
Sogutlu Sari et al[15]	MCD	35	10.7	14.6	2.8
Kawashima et al[9]	MCD	10	20	14.6	40
Present study	MCD	21	24	12.5	43
Reinhart et al[21]	All	1843 (MCD-17)	11.7	2.1	3.5

AC, anterior chamber.

complications, it has the advantage of reducing the risk of endothelial rejection compared with PK as seen in our series. DALK may be considered as an option in cases of MCD where there is no direct clinical evidence of deposits on DM.

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