Original Article

Repeat keratoplasty in failed Descemet stripping automated endothelial keratoplasty

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Purpose: To evaluate the clinical factors associated with repeat Descemet stripping automated endothelial keratoplasty (DSAEK) or penetrating keratoplasty (PKP) in cases of failed DSAEK. **Methods:** Retrospective observational study of cases with failed DSAEK admitted to our center for a repeat keratoplasty over 5 years (January 2013–Decemeber 2017) was undertaken. Demographic and perioperative details of all cases and type of repeat keratoplasty were recorded. Logistic regression analysis was performed to analyze the factors affecting the type of repeat keratoplasty. **Results:** A total of 94 eyes with failed DSAEK were evaluated. Repeat DSAEK was performed in 66% and PKP in 34% of cases. Significantly increased odds for requiring PKP were observed in association with stromal scarring [odds ratio (OR) = 2.9, $P = 0.018$)], trainee surgeons (OR = 4.05, $P = 0.008$), intraoperative complications (OR = 4.58, $P = 0.003$), scleral fixated intraocular lens or anterior chamber intraocular lens *in situ* (OR = 33.8, $P < 0.001$), secondary glaucoma (OR = 3.02, $P = 0.015$), peripheral anterior synechiae (OR = 8.6, $P < 0.001$), preoperative corneal thickness (OR = 1.01, $P < 0001$), time to primary surgery (OR = 1.03, $P = 0.03$), post-DSAEK host thickness (OR = 1.01, $P < 0.001$), and time interval from graft failure to regraft (OR = 1.18, $P < 0.001$). All eyes with congenital hereditary endothelial dystrophy, bee-sting-induced corneal decompensation, Axenfeld-Rieger syndrome, and multiple failed grafts underwent secondary PKP. All cases (nine eyes) that required surgical intervention for secondary glaucoma underwent secondary PKP ($P < 0.001$). **Conclusion:** Repeat DSAEK is feasible in up to two-third of cases of failed DSAEK. A PKP is required in one-third of cases, and various preoperative, intraoperative and postoperative factors are associated with unsuitability for repeat DSAEK.

Key words: Descemet stripping automated endothelial keratoplasty, failed DSAEK, failed endothelial keratoplasty, repeat keratoplasty, repeat keratoplasty after DSAEK

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1729_18

Quick Response Code:

Endothelial keratoplasty has replaced full-thickness penetrating keratoplasty (PKP) as the procedure of choice in cases with endothelial decompensation owing to a more rapid visual recovery, superior visual quality, and better patient satisfaction.[1-3]

Graft failure after Descemet stripping automated endothelial keratoplasty (DSAEK) may be observed in 1%–12% of cases.[4-7] Histopathologic studies have identified endothelial cell loss as the main causative factor leading to graft failure.[8-10] Presence of interface material, such as fibrocellular tissue, retained Descemet's membrane, and epithelial ingrowth, has also been identified as potential cause of graft dislocation and subsequent failure.[9,10]

In cases of failed DSAEK, a repeat keratoplasty may either be partial thickness (re-DSAEK) or full thickness in the form of PKP. Good visual and anatomical outcomes have been reported after repeat keratoplasty.[11,12] However, no study has evaluated the factors associated with the choice of the second procedure after an initial failed DSAEK. We herein evaluated the clinical factors associated with repeat DSAEK or PKP in cases of failed DSAEK.

Methods

A retrospective observational study of cases with failed DSAEK was undertaken at an apex tertiary care ophthalmic setup. Ethical clearance was obtained from the institutional review board. The study adhered to the tenets of the Declaration of Helsinki.

All cases with failed DSAEK admitted to our center for a repeat keratoplasty over 5 years (January 2013–December 2017) were enrolled. Incomplete records were excluded from the analysis. Demographic details and preoperative data of the patients were recorded, including a comprehensive history, ocular examination details, corneal thickness, duration of first surgery, and indication for primary surgery. Intraoperative details of primary DSAEK surgery and the postoperative course, including visual acuity, lenticule thickness, host

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Manuscript received: 17.10.18; Revision accepted: 26.04.19

Cite this article as: Kaur M, Titiyal JS, Gagrani M, Shaikh F, Agarwal T, Sinha R, *et al*. Repeat keratoplasty in failed Descemet stripping automated endothelial keratoplasty. Indian J Ophthalmol 2019;67:1586-92.

thickness, secondary surgical procedures, postoperative complications, and time to graft failure, were noted. The cause for failure of primary DSAEK graft and time interval between surgery and graft failure were noted. The central lenticule thickness and host thickness (in the visual axis) as recorded by anterior segment optical coherence tomography before repeat keratoplasty were noted. The type of repeat keratoplasty and the duration between graft failure and regraft were recorded. The decision for the type of repeat keratoplasty was taken by a single surgeon (JST) in all cases. DSAEK was performed in cases of corneal decompensation without central corneal scarring, stable intraocular lens (IOL), and no/minimal (less than 1 quadrant) peripheral anterior synechiae (PAS).[13] Cases with central corneal scarring, complicated aphakia with significant iris tissue defects, and extensive synechiae underwent PKP.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences 16.0 (SPSS Inc., Chicago, IL, USA). Normally distributed continuous variables were analyzed using independent *t*-test and expressed as mean ± standard deviation. Nonparametric data were expressed as median (range) and analyzed using Mann–Whitney *U*-test. Categorical data were analyzed using Chi-square/Fisher's exact test and expressed as proportions. A subgroup analysis was performed based on the type of regraft. Logistics regression analysis was used to assess the odds ratio (OR) of various factors influencing the type of regraft. A *P* value of <0.05 was considered statistically significant.

Results

A total of 627 DSAEK surgeries were performed over 5 years. A repeat keratoplasty for failed DSAEK was performed in 94 eyes of 94 patients. The mean age of the cases was 52.55 ± 17.10 years, and there were 60 males and 34 females. The preoperative characteristics before the initial DSAEK surgery are summarized in Table 1. DSAEK was performed using the graft pull-through technique in all cases.[14,15] The intraoperative details of primary DSAEK surgery are summarized in Table 2. The graft was clinically attached at the end of surgery in all cases.The postoperative course after the primary surgery is summarized in Table 3. An absence of inflammation (AC reaction and/or significant conjunctival congestion) was documented in all cases before performing primary and repeat keratoplasty.

Repeat keratoplasty in failed DSAEK

A repeat DSAEK was performed in 66% of cases (62/94) and a PKP was performed in 34% (32/94) of cases [Figs. 1-4].

A subgroup analysis was performed based on the type of regraft, either re-DSAEK or PKP. In re-DSAEK group, the primary diagnosis was pseudophakic bullous keratopathy (PBK) (37 eyes), aphakic bullous keratopathy (ABK) (2 eyes), Fuchs' endothelial corneal dystrophy (FECD) (18 eyes), and herpetic endothelitis (5 eyes). In the PKP group, the primary diagnosis was PBK (9 eyes), ABK (7 eyes), FECD (2 eyes), congenital hereditary endothelial dystrophy (CHED) (3 eyes), herpetic endothelitis (3 eyes), honeybee sting (3 eyes), failed graft (4 eyes), and Axenfeld-Rieger anomaly (1 eye) ($P < 0.001$). All eyes with CHED, honeybee sting–induced corneal decompensation, failed graft, and Axenfeld-Rieger anomaly underwent secondary PKP. The cases with CHED had preoperative corneal thickness more than 1000 μm and were in the older age group (8–15 years).

Preoperative mild paracentral stromal scarring was present in 30.6% (19/62) of cases that underwent re-DSAEK and 56.3% (18/32) of cases that underwent PKP ($P = 0.025$).

The preoperative corneal thickness was 732.8 ± 82.5 μm in the re-DSAEK group and 974.5 ± 182.5 μm in the PKP group ($P < 0.001$). The mean lenticule thickness after primary surgery was 171.5 ± 51.5 μm in the re-DSAEK group and 170.1 ± 60.7 μm in the PKP group ($P = 0.9$). The mean host thickness was 688.3 ± 110.9 μm in the re-DSAEK group and 877.6 ± 262.8 μm in the PKP group ($P < 0.001$).

The median time to primary surgery was 6 months (range 2–60 months) in the re-DSAEK group and 18 months (range 8–48 months) in the PKP group ($P < 0.001$). The median time to graft failure was 0 months (range 0–10 months) in the re-DSAEK group and 0.33 months (range 0–10 months) in the PKP group ($P = 0.59$). The median time interval between graft failure and regraft was 8 months (range 0.15–19 months) in the re-DSAEK group and 16 months (range 1–36 months) in the PKP group ($P < 0.001$). An early PKP at 1 month was performed in only one case for early visual rehabilitation.

In cases requiring re-DSAEK, 87.1% (54/62) of primary surgeries were performed by an experienced surgeon and 12.9% (8/62) of surgeries were performed by trainee surgeons. In cases requiring PKP, 62.5% (20/32) of surgeries were performed by an expert surgeon and 37.5% (12/32) of surgeries were performed by a trainee surgeon ($P = 0.008$). Intraoperative complications were present in 14.5% (9/62) of cases in the re-DSAEK group and 43.8% (14/32) of cases in the PKP group ($P = 0.004$). The intraoperative complications were significantly higher in the trainee surgeon group (13/20) when compared with the expert surgeon (10/74) ($P < 0.001$).

Secondary glaucoma was present in 38.7% (24/62) of cases in the re-DSAEK group and 65.6% (21/32) of cases in the PKP group ($P = 0.017$). In the re-DSAEK group, secondary glaucoma was managed with medical treatment alone and no case required surgical intervention. In contrast, only 57.1% (12/21) of cases with secondary glaucoma undergoing PKP could be managed on medical therapy and 42.9% (9/21) of cases required surgical intervention ($P < 0.001$). PAS was present in 14.5% (9/62) of cases in the re-DSAEK group and 59.4% (19/32) of cases in the PKP group ($P < 0.001$). In the re-DSAEK group, all cases had PAS of one quadrant or less. In the PKP group, 11 cases had PAS of one quadrant or less and 8 cases had more than one quadrant PAS ($P = 0.029$). Eccentric grafts were observed in cases with more than one quadrant PAS.

Postoperative stromal scarring was present in 30.6% (19/62) of cases in the re-DSAEK group and 71.8% (23/32) of cases in the PKP group ($P < 0.001$).

In the re-DSAEK group with pseudophakia, 95% (57/60) of cases had PCIOL *in situ* and 5% (3/60) of cases had anterior chamber intraocular lens (ACIOL) or scleral fixated intraocular lens (SFIOL) *in situ*. In the PKP group with pseudophakia, 36% (9/25) of cases had PCIOL *in situ* and 64% (16/25) of cases had ACIOL or SFIOL *in situ* ($P < 0.001$).

Table 1: Preoperative characteristics of cases with failed DSAEK undergoing re-DSAEK or penetrating keratoplasty

Preoperative factor	Re-DSAEK group (*n*=62)	PKP group (*n*=32)	*P*
Indication for DSAEK[1]			
PBK	37 (59.7%)	9 (28.1%)	<0.001
ABK	2 (3.2%)	7 (21.9%)	
FECD	18 (29.0%)	2 (6.3%)	
CHED	-	3 (9.4%)	
Herpetic endothelitis	5 (8.1%)	3 (9.4%)	
Honeybee sting-induced decompensation	-	3 (9.4%)	
Failed graft	-	4 (12.5%)	
Axenfeld-Rieger	-	1 (3.1%)	
Glaucoma[1]	16 (25.8%)	5 (15.6%)	0.31
Glaucoma treatment[1]			
Medical	16 (100%)	1 (25%)	0.001
Surgical	0	4 (75%)	
Trabeculectomy		3	
Glaucoma drainage devices		1	
Lens status[1]			
Phakic	17 (27.4%)	11 (34.4%)	<0.001
Pseudophakic	44 (71.0%)	13 (40.6%)	
PCIOL	41 (66.1%)	4 (12.5%)	
SFIOL	3 (4.9%)	7 (21.9%)	
ACIOL	0	2 (6.2%)	
Aphakic	1 (1.6%)	8 (25%)	
Mild paracentral stromal scarring[1]	19 (30.6%)	18 (56.2%)	0.025
Corneal thickness (μm)[2]	732.8±82.5	974.5±182.5	<0.001
Time interval to primary surgery (months)[3]	6 (2-60)	18 (8-48)	<0.001

DSAEK=Descemet stripping automated endothelial keratoplasty; PKP=Penetrating keratoplasty; ABK=Aphakic bullous keratopathy; PBK=Pseudophakic bullous keratopathy; FECD=Fuchs' endothelial corneal dystrophy; CHED=Congenital hereditary endothelial dystrophy; PCIOL=Posterior chamber intraocular lens; SFIOL=Scleral fixated intraocular lens; ACIOL=Anterior chamber intraocular lens. [1]Results displayed as number of cases (percentage). [2]Results displayed as mean±standard deviation. [3]Results displayed as median (range)

Table 2: Intraoperative details of primary DSAEK surgery

Intraoperative factor	Re-DSAEK group (*n*=62)	PKP group (*n*=32)	*P*
Type of primary surgery[1]			
DSAEK	46 (74.2%)	20 (62.5%)	0.25
DSAEK triple	16 (25.8%)	12 37.5%)	
DSAEK + PCIOL	16 (17.0%)	5 (15.6%)	
DSAEK + SFIOL	0	5 (15.6%)	
DSAEK + ACIOL	0	2 (6.3%)	
Incision for DSAEK lenticule Insertion[1]			
Clear corneal	41 (66.1%)	20 (62.5%)	0.82
Corneoscleral	21 (33.9%)	12 (37.5%)	
Surgeon[1]			
Trainee	8 (12.9%)	12 (37.5%)	0.008
Experienced	54 (87.1%)	20 (62.5%)	
Donor size (mm)[2]	7.6±0.35	7.5±0.30	0.13
Donor endothelial cell count (cells/mm^2)[2]	2462.00±179.78	2467.50±207.50	0.89
Intraoperative complications[1] (difficult donor unfolding, floppy iris with iris prolapse, intraoperative bleeding, pigment dispersion, and vitreous in AC)	9 (14.5%)	14 (43.8%)	0.004

DSAEK=Descemet stripping automated endothelial keratoplasty; PKP=Penetrating keratoplasty; PCIOL=Posterior chamber intraocular lens; SFIOL=Scleral fixated intraocular lens; ACIOL=Anterior chamber intraocular lens. [1]Results displayed as number of cases (percentage). [2]Results displayed as mean±standard deviation

Table 3: Postoperative characteristics (after primary surgery) of cases with failed DSAEK undergoing re-DSAEK or penetrating keratoplasty

Postoperative factor	Re-DSAEK group (*n*=62)	PKP group (*n*=32)	*P*
Lenticule thickness (μm)[1]	171.5±51.5	170.1±60.7	0.9
Host thickness (μm)[1]	688.3±110.9	877.6±262.8	<0.001
Rebubbling[2]	23 (37.1%)	10 (31.2%)	0.65
Secondary glaucoma[2]	24 (38.7%)	21 (65.6%)	0.017
Peripheral anterior synechiae[2]			
</= 1 quadrant	9 (14.5%)	19 (59.4%)	
>1 quadrant	9 (14.5%)	11 (34.4%)	0.029
	0	8 (25%)	
Glaucoma treatment[2]			
Medical	24 (100%)	12 (57.1%)	<0.001
Surgical	0	9 (42.9%)	
Trabeculectomy		5 (23.8%)	
Glaucoma drainage devices		4 (19.1%)	
Lens status[2]			
Phakic	1 (1.6%)	6 (18.8%)	
Pseudophakic	60 (96.8%)	25 (78.1%)	
PCIOL	57 (91.9%)	9 (28.1%)	<0.001
SFIOL	3 (4.8%)	12 (37.5%)	
ACIOL	0	4 (12.5%)	
Aphakic	1 91.6%)	1 (3.1%)	
Stromal scarring[2]	19 (30.6%)	23 (71.8%)	<0.001
Cause of graft failure[2]			
Primary	34 (54.8%)	12 (37.5%)	0.13
Secondary	28 (45.2%)	20 (62.5%)	
Graft infection	0	3 (9.4%)	
Graft rejection	10 (16.1%)	0	
Uncontrolled glaucoma	6 (9.7%)	(18.8%)	
Endothelial cell loss	12 (19.3%)	11 (34.3%)	
Time interval between primary DSAEK and graft failure (months)[3]	0 (0-10)	0.33 (0-10)	0.59
Time interval between graft failure and repeat keratoplasty (months)[3]	8 (0.15-19)	16 (1-36)	<0.001

DSAEK=Descemet stripping automated endothelial keratoplasty; PKP=Penetrating keratoplasty; PCIOL=Posterior chamber intraocular lens; SFIOL=Scleral fixated intraocular lens; ACIOL=Anterior chamber intraocular lens. [1]Results displayed as mean±standard deviation. [2]Results displayed as number of cases (percentage). [3]Results displayed as median (range)

There was no significant difference between the two groups regarding the type of primary surgery (DSAEK vs DSAEK triple) (P = 0.25), surgical technique (clear corneal incision or corneoscleral incision) (P = 0.82), preoperative glaucoma (P = 0.31), rebubbling (P = 0.65), or type of graft failure (primary vs secondary) (P = 0.13).

Logistics regression analysis – Factors associated with PKP

A logistics regression analysis was performed to assess the odds of requiring PKP in the presence of various factors [Fig. 4]. The presence of preoperative paracentral stromal scarring was associated with 2.9 times the risk of requiring PKP [OR = 2.9, P = 0.018, 95% confidence interval (CI) =1.2–7.0]. Cases performed by trainee surgeons were four times more likely to require PKP (OR = 4.05, P = 0.008, 95% CI = 1.44–11.36) and intraoperative complications were associated with odds of 4.58 (P = 0.003, 95% CI = 1.7–12.4). Cases with SFIOL or ACIOL *in situ* were 33.8 times more likely to require secondary PKP (OR = 33.8, P < 0.001, 95% CI = 8.2–139.7). The presence of secondary glaucoma was associated with three times increased risk (OR = 3.02, P = 0.015, 95% CI = 1.2–7.4) and PAS was associated with 8.6 times risk (OR = 8.6, P < 0.001, 95% CI = 3.2–23.4). Cases with postoperative scarring were 5.8 times more likely to undergo PKP (OR = 5.78, P < 0.001, 95% CI = 2.2–14.8). Significant odds for PKP were associated with the preoperative corneal thickness (P < 0.001, OR = 1.01, 95% CI = 1.008–1.018), time to primary surgery (P = 0.03, OR = 1.03, 95% CI = 1.003–1.06), post-DSAEK host thickness (P < 0.001, OR = 1.01, 95% CI = 1.003–1.008), and time interval from graft failure to regraft (P < 0.001, OR = 1.18, 95% CI = 1.09–1.28). The OR was not significant for rebubbling (P = 0.57, OR = 0.77, 95% CI = 0.31–1.91), post-DSAEK lenticule thickness (P = 0.9, OR = 1.0, 95% CI = 0.99–1.01), and time to graft failure (P = 0.6, OR = 1.05, 95% CI = 0.89–1.23).

At postoperative 1 year after repeat keratoplasty, the graft was clear in 87.1% (54/62) of cases in the re-DSAEK group and 78.1% (25/32) of cases in the PKP group (P = 0.37). The mean corrected visual acuity in clear grafts was 0.44 ± 0.25 logMAR units in the re-DSAEK group and 0.47 ± 0.33 logMAR units in the PKP group (P = 0.62).

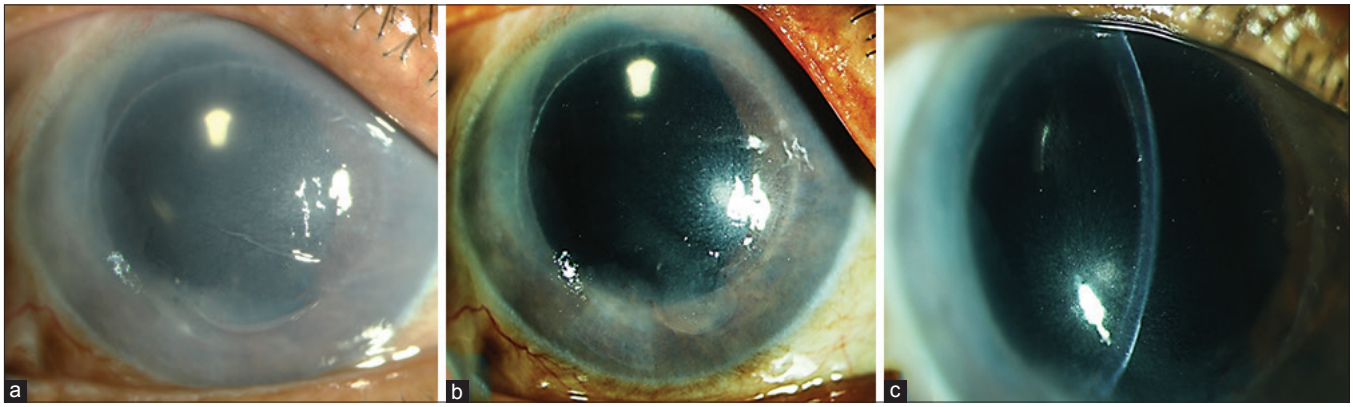

Figure 1: Repeat DSAEK after failed DSAEK. (a) Failed DSAEK with mild paracentral stromal scarring. (b) Repeat DSAEK with clear graft 6 months after surgery. (c) Slit illumination showing thin donor lenticule after repeat DSAEK

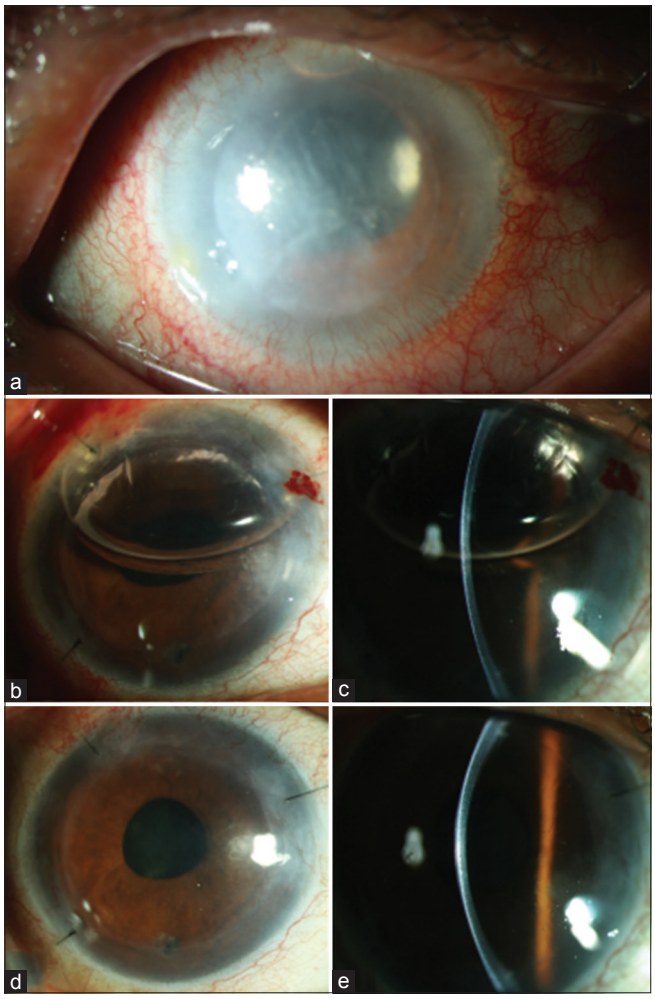

Figure 2: Repeat DSAEK after failed DSAEK. (a) Failed DSAEK due to progressive endothelial cell loss. (b and c) Postoperative day 1 after re-DSAEK showing attached donor lenticule. (d and e) Postoperative 1 year after re-DSAEK with clear graft and thin donor lenticule

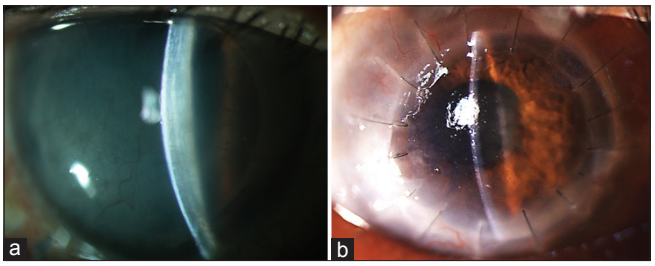

Figure 3: Repeat PKP after failed DSAEK. (a) Failed DSAEK with central fibrovascular stromal scarring. (b) Penetrating keratoplasty performed

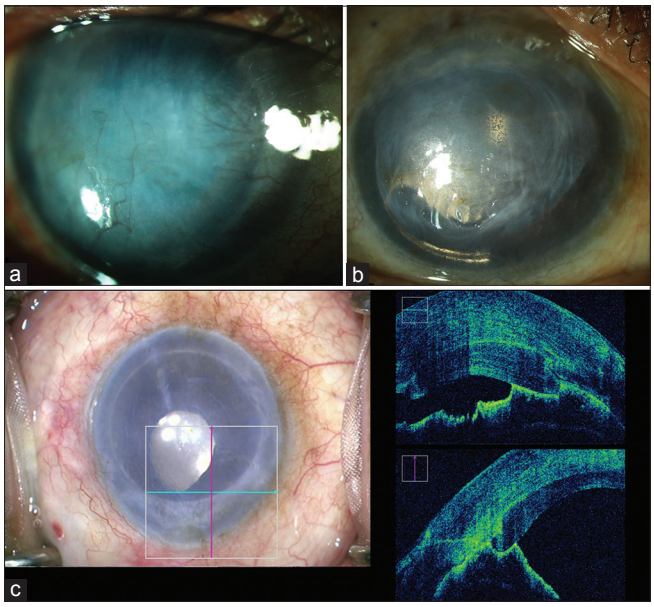

Figure 4: Factors associated with unsuitability for repeat DSAEK. (a) Failed DSAEK with fibrovascular stromal scarring involving the visual axis. (b) Failed DSAEK with central stromal scarring and ACIOL *in situ*. (c) Failed DSAEK with extensive peripheral anterior synechiae of 5 clock hours

Discussion

The applications of endothelial keratoplasty are continually expanding and it is increasingly being performed in complex cases.[16-20] A repeat graft is one of the most frequent indications for keratoplasty, and a re-DSAEK after failed PKP or DSAEK is safe and may be associated with superior visual outcomes.[11,12,21] However, graft survival progressively diminishes with the increase in the number of regrafts, and good decision-making

regarding the type of keratoplasty procedure is essential to ensure long-term graft survival and good functional outcomes.[22]

We evaluated the factors associated with the type of regraft in 94 cases with failed DSAEK. A repeat DSAEK was performed in 66% of cases and PKP was performed in 34% of cases. A significant association was observed between the type of regraft and the time interval till primary DSAEK as well as the duration between graft failure and regraft, with repeat PKP performed in cases with prolonged time intervals. Reducing the waiting times for surgery may lead to an increased suitability for DSAEK and an early repeat DSAEK should be attempted in cases with failed grafts. An absence of inflammation should be documented before performing regraft to minimize risk of graft rejection. Increased corneal thickness, both preoperative and after graft failure, was associated with an increased likelihood of requiring secondary PKP. The paucity of optical grade donor tissue in developing nations is associated with a longer average waiting time for surgery and this may result in cases becoming unsuitable for DSAEK in the interim period.[13]

All cases with CHED, honeybee sting–induced corneal decompensation, failed graft, and Axenfeld-Rieger anomaly had to undergo repeat PKP. The presence of an SFIOL or ACIOL was strongly associated with a repeat PKP. Successful visual and anatomical outcomes with DSAEK have been reported in CHED, bee sting–induced decompensation, and SFIOL.[16-18] However, these cases may be more suitable for a primary PKP instead of DSAEK, and a more conservative approach may be advisable during the initial decision-making to ensure optimal outcomes and minimize the incidence of graft failure. Long-term endothelial cell loss and graft failures have been reported to be significantly higher after DSAEK with ACIOL, further highlighting the necessity for careful decision-making.[19] Endothelial keratoplasty is increasingly being performed for failed grafts with successful outcomes; however, a PKP may be required in cases with multiple failed grafts.

Surgeries performed by trainee surgeons were more likely to require a PKP after graft failure. The incidence of intraoperative complications was also significantly more in cases performed by trainee surgeons. The increased complications and surgical manipulations by inexperienced surgeons may result in unsuitability of the case for a repeat DSAEK procedure.

Preoperative mild paracentral stromal scarring was associated with an increased likelihood of secondary PKP. The presence of paracentral mild scarring is not a contraindication for DSAEK because of the advantages associated with the DSAEK. However, these cases may initially have a borderline suitability for DSAEK, and the progression of endothelial decompensation after graft failure may render them unsuitable for a re-DSAEK.

Secondary glaucoma was associated with an increased risk of secondary PKP, and all cases that underwent glaucoma surgery for control of IOL required PKP after failed DSAEK. Glaucoma adversely impacts graft survival and the likelihood of re-DSAEK, and cases requiring surgical intervention for glaucoma may be more suitable for PKP than DSAEK. Graft dislocation is a common complication after endothelial keratoplasty, and repeated surgical interventions in the form of rebubbling increase the risk of graft failure.[23] However, rebubbling did not affect the suitability of the case for a repeat endothelial keratoplasty procedure. The visual and anatomical outcomes were comparable in the repeat DSAEK group and PKP group at 1 year of follow up.

Conclusion

To conclude, the present-day scenario of endothelial keratoplasty is witnessing a shift from DSAEK to Descemet membrane endothelial keratoplasty, with DSAEK increasingly being performed in more challenging cases. These cases are more prone to develop graft failure and undergo repeat keratoplasty. A successful repeat DSAEK is feasible in up to two-third of cases with failed DSAEK; however, one-third of cases require a full-thickness PKP due to various associated factors. Future prospective studies can help assess the long-term outcomes of regraft after failed DSAEK and their correlation with various perioperative factors.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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