Clinical Ophthalmology

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ORIGINAL RESEARCH

Microscope Integrated Optical Coherence Tomography Guided Descemet Stripping Automated Endothelial Keratoplasty in Congenital Hereditary Endothelial Dystrophy

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Purpose: To describe the outcomes of descemet stripping automated endothelial keratoplasty (DSAEK) in congenital hereditary endothelial dystrophy (CHED) and to evaluate the role of microscope integrated optical coherence tomography (Mi-OCT) during the surgery.

Design: Retrospective data analysis.

Methods: A retrospective study from the medical records of all those patients who were diagnosed with CHED and underwent DSAEK at our centre from 2015 were evaluated. All patients underwent Mi-OCT-guided standard DSAEK procedure. Intra-operative difficulties, visual outcomes and graft survival were recorded.

Results: A total of 48 eyes of 29 patients with a mean age of 9.87 ± 8.2 years and mean follow-up of 17.3 months were evaluated. Thirty-nine eyes underwent primary DSAEK and 9 eyes underwent PKP. Three eyes who underwent PKP had failed graft for which they underwent DSAEK. The mean preoperative Snellen's visual acuity was 1.71 ± 0.66 and the mean preoperative central corneal thickness was 1.10 ± 0.174 mm. Intraoperatively, all the grafts were attached which was confirmed using Mi-OCT. Graft detachment was seen in the immediate postoperative period in 10.4% (4 eyes) of primary DSAEK, out of which DM scoring was not performed in 2 eyes. Following DSAEK, cornea cleared at four-week follow-up in 89.7% eyes and in all the eyes the cornea cleared at six-week follow-up.

Conclusion: Primary DSAEK could be a preferred option over PKP for CHED with early presentation and in those eyes with failed primary PKP. Mi-OCT is a very useful tool in these eyes for various intraoperative procedures, thereby improving the outcomes of the procedure.

Keywords: DSAEK, CHED, Mi-OCT

Introduction

Congenital hereditary endothelial dystrophy (CHED) is a rare genetic disorder which is characterized by bilateral corneal clouding due to dysfunctional and degenerative corneal endothelium.[1] Though the pathology is in the corneal endothelium and Descemet membrane (DM), penetrating keratoplasty (PKP) had been the standard treatment till the time when Busin et al[2] suggested that descemet stripping automated endothelial keratoplasty (DSAEK) allowed the rapid restoration of corneal clarity with minimal intra-operative and post-operative complications.

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Received: 19 January 2021
Accepted: 8 April 2021
Published: 27 July 2021

Microscope Integrated Optical Coherence Tomography (Mi-OCT) has been recently introduced which has helped to refine various surgeries.[3,4] Mi-OCT provides real-time OCT images of the eye during the entire procedure which aids in various surgical steps during the entire procedure. There are few studies which have focused on the role of Mi-OCT in DSAEK.[5–7] In the current study, we have evaluated its role during the surgery and also evaluated the postoperative outcomes in cases where DSAEK was done for CHED.

Materials and Methods

This study was conducted at Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi. This is a retrospective study carried out at Dr Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi, India. Ethical clearance was obtained from the institutional review board (Ref No. IECPG-291/ 07.09.2017, RT-37/ 29.11.2017; Institute Ethics Committee, All India Institute of Medical Sciences). Case records of all patients who were diagnosed with CHED and underwent DSAEK at our centre since 2015 were evaluated. Corneas for all our cases were donated voluntarily with written informed consent which was conducted in accordance with the Declaration of Istanbul. A written informed consent statement was obtained from all our patients. All cases were performed by experienced surgeons using Mi-OCT (OPMI Lumera 700 and RESCAN 700, Carl Zeiss, Meditec, AG, Jena, Germany). The Mi-OCT device has a commercially available platform which is fully integrated with the operating microscope and real-time OCT images are projected in a heads-up fashion on the screen as well as in the oculars. RESCAN 700 captures 27,000 A-scans/ second with an axial resolution of 5 microns. The intraoperative details of the surgery were recorded in all cases. Surgical video recordings were evaluated.

The following parameters were noted from the case records: patient demographic details, indication for surgery, preoperative parameters (best-corrected visual acuity (BCVA), intraocular pressure (IOP), central corneal thickness (CCT), associated ocular findings), intraoperative surgical details (DM scoring, lenticule thickness, lenticule diameter, complications), postoperative complications (graft detachment/ displacement and need for re-bubbling, raised IOP), BCVA, IOP and CCT at follow-ups, need for re-surgery based on graft survival].

Surgical Technique

All surgeries were performed under general anaesthesia. The surgical steps were as follows:

Donor preparation: The donor cornea was mounted on an artificial chamber (Moria ALTK; Moria, Doylestown, PA) and the donor lenticule was prepared. Mi-OCT guided donor corneal thickness was measured, and the microkeratome head was chosen accordingly. In our study, microkeratome heads ranged from 350 to 450 microns were used. The residual lenticule thickness was measured using Mi-OCT intraoperatively. Though Mi-OCT does not have a measuring scale for direct measurement, a 9 mm cube was used for analysis and the measurements were done as described.[8] The lenticule was then cut using handheld disposable trephines depending on the host corneal diameter.

Recipient bed preparation: Epithelial trephination mark using disposable handheld trephine was made with the same trephine that was used to cut the donor lenticule. Two side port incisions were made using a 20-gauge microvitreoretinal blade. These incisions are moved towards the surgeon by 1–2 mm rather than the centre to avoid the pupillary region, thereby preventing inadvertent lens damage during subsequent manoeuvres. Pupils were constricted using pilocarpine 2% to avoid lens touch during instrumentation. The anterior chamber was formed with ophthalmic viscosurgical devices (OVD). Scoring of the DM was done using reverse Sinskey hook in few cases whereas in rest this step was avoided. A 23-gauge infusion cannula was used for anterior chamber maintenance during the procedure. The main incision was made either clear corneal incision using a 3.2 mm keratome blade or through the scleral tunnel using a crescent blade (Supplementary Video S1).

The prepared lenticule was loaded on the Busin glide (Moria USA, Doylestown, Pennsylvania, USA) and the lenticule was pulled inside the anterior chamber using 23-gauge Internal Limiting Membrane (ILM) peeling forceps (Grieshaber® DSP). This was followed by air injection with a 27-gauge blunt cannula through one of the side port incision after removing the anterior chamber maintainer. The entire process was monitored through Mi-OCT. Peripheral iridectomy was done in all cases.

Mi-OCT was used at various steps during the surgery right from the assessment of the posterior stroma, DM, iris and anterior chamber before the start of the procedure, to various intraoperative manoeuvres. Any area of peripheral

anterior synechiae could be assessed which could help in planning the incisions. Mi-OCT was useful during the scoring of DM to ensure complete scoring without any Descemet's or stromal tags. In hazy corneas, it was also useful to ensure the orientation and proper unfolding of extremely thin lenticules. The most important advantage of Mi-OCT was to ensure complete graft adhesion at the end of the procedure as most eyes of CHED have hazy corneas which could hamper visualization of the graft.

Results

Total of 48 eyes of 29 patients (55% female and 45% male) who had been diagnosed with CHED and had undergone Mi-OCT guided DSAEK at our institution in the past 5 years were evaluated. Diagnosis of CHED was made clinically and was confirmed with the histopathological report in the post-operative period wherever available. All the patients were phakic with a clear crystalline lens at the time of presentation.

The mean age at which surgery was performed for the patients was 9.87 ± 8.2 years (8 months to 42 years). The mean follow-up of our patients was 17.3 months (8–58 months). Most eyes with CHED had nystagmus as the most common ocular association (19/48 eyes; 39.5%). Other ocular associations that were observed were glaucoma (14/48 eyes; 29.1%), squint (9/48 eyes; 18.75%), microcornea (2/48 eyes; 4.16%) and myopia (2/48 eyes; 4.16%). Out of 14 eyes who had associated glaucoma, 13 eyes had undergone trabeculectomy and one eye underwent Diode Laser Cyclophotocoagulation (DLCP). Systemic associations were seen in 5 patients (three had hearing loss, one had hypothyroidism and one had juvenile diabetes).

The mean preoperative Snellen's visual acuity was 1.71 ± 0.66 (0.6–2.7) and the mean preoperative intraocular pressure was 15.5 ± 3.5 mm of Hg (8–28 mm of Hg). The mean preoperative central corneal thickness was 1.10 ± 0.174 mm (0.85–1.63 mm). The mean white to white corneal diameter in our patients was 11.5 ± 0.6 mm (10–13 mm) and mean anterior chamber depth was 2.84 ± 0.34 mm (2.24–3.66). The mean thickness of the donor cornea was 525.71 ± 40.21 microns (450–641 microns). Microkeratome head used to cut the donor tissue ranged from 350 to 450 microns. The mean lenticule thickness was 119.39 ± 39.90 microns (70–225 microns). The mean lenticule diameter was 8 mm in diameter. Thirty-nine eyes underwent DSAEK and 9 eyes underwent PKP. Three out of 39 eyes who underwent DSAEK had repeat DSAEK for failed graft. Three out of 9 patients who had PKP as their initial surgery, subsequently underwent DSAEK for failed graft. Graft failure was due to graft rejection in all our cases. Intraoperatively DM scoring was performed in 18 eyes whereas, scoring was not done in 21 eyes who underwent primary DSAEK and 3 eyes in whom a repeat DSAEK was done for failed PKP. In the primary DSAEK, scoring was not done in eyes with poor visualization due to thick and hazy corneas and in infants' eyes. Intraoperatively, all the grafts were attached which was confirmed using Mi-OCT. Graft detachment was seen in the immediate postoperative period in 4 eyes of primary DSAEK (4/39 eyes; 10.4%) out of which scoring was not performed in 2 eyes. In all the cases the donor tissue remained attached following re-bubbling. 89.7% eyes (35/39 eyes) had clear cornea at four-week follow-up and all the eyes had clear cornea at six-week follow-up period. (Figure 1) Pupillary block resulting in a rise in IOP was noted in one eye. Mean final Snellen's best-corrected visual acuity of our patients at the last follow-up was 0.76 ± 0.19 (0.6–2.7) and the mean intraocular pressure was 15.91 ± 2.76 mm of Hg. In our series, following DSAEK, none of the patients had newly developed glaucoma or required additional anti-glaucoma medications to their preoperative medications. The mean refraction (spherical equivalent) was 2.01 ± 2.13 (−1 to +6.25D). One patient had cataract for which lens aspiration with posterior chamber intraocular lens implantation was done. This patient had undergone DSAEK for failed PKP. Endothelial cell density could be determined for 20 eyes at the final follow-up (mean, 17.3 months; range, 8–58 months), mean endothelial loss was 36.2% (range, 14.7 to 49.3%).

Discussion

Corneal transplantation in children could be challenging due to various ocular factors such as small eyeball, shallow anterior chamber, increased positive posterior pressure, low scleral rigidity, phakic status and decreased space for intraocular manoeuvres. These factors could lead to an increased chance of complications.[9] In recent times, lamellar keratoplasties are being preferred over the full thickness grafts due to various advantages. In CHED, PKP was widely performed with favourable results.[10–12] However, the trend is shifting towards endothelial keratoplasties over PKP due to various reasons such as suture-related complications, increased risk of graft rejection and failure, unstable refractive outcomes and need for multiple examinations under anaesthesia in post PKP children.[13–15]

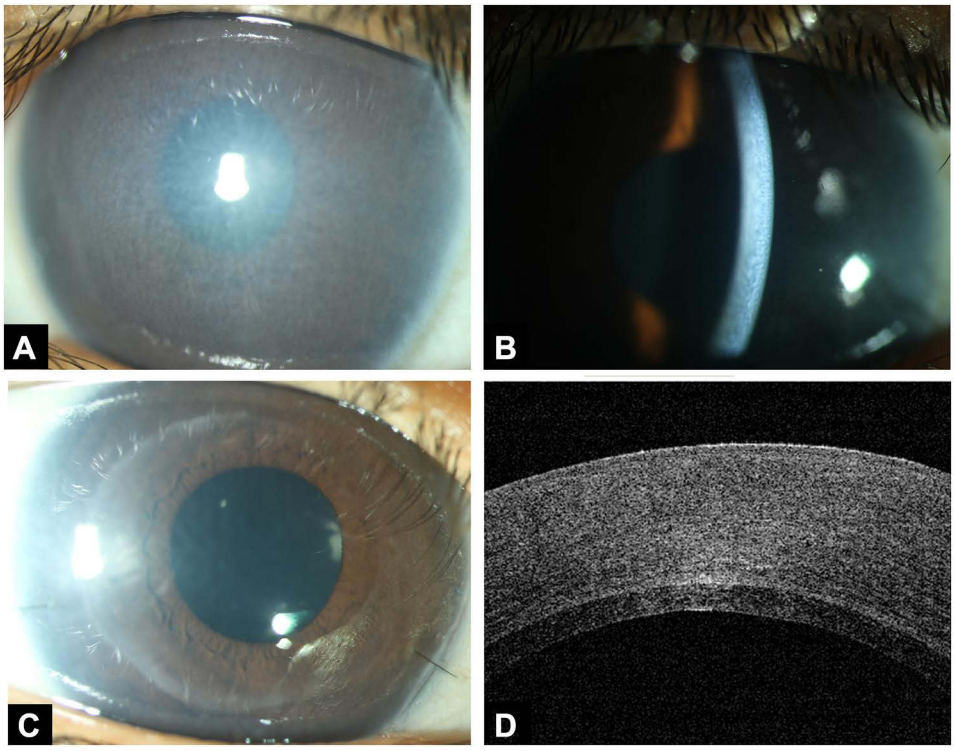

Figure 1 Pre- and Post-operative image of a CHED patient. (**A** and **B**) Diffuse and slit examination of the CHED patient using slit lamp bio-microscopy prior to surgery, (**C**) six-week post-DSAEK of the same patient with clear cornea, (**D**) ASOCT depicting a well attached graft to the host cornea.

A study by AlArrayedh et al[16] demonstrated poor outcomes from PKP in CHED due to dense amblyopia and high risk of long-term graft failure. The outcomes of PKP were better when the surgery was done at an older age when compared to the early intervention.[17] Busin et al[2] reported successful DSAEK outcomes in terms of rapid restoration of corneal clarity with less intraoperative and postoperative complications. In a series of 18 eyes of 10 CHED patients with a median follow-up of 38 months demonstrated favourable outcomes of DSAEK in CHED patients.[18] DMEK could be challenging especially in pediatric eyes, however, results are encouraging with favourable outcomes.[19] Saad et al[20] performed DMEK in 14 eyes of 8 CHED patients and reported good visual outcomes.

There are various intra-operative difficulties in performing EK in CHED patients which include poor visibility due to very severe corneal oedema in these cases[13] and strong adherence of the Descemet membrane to the underlying stroma which could result in DM retention and graft failure.[21] Stripping of DM is much easier in decompensated corneas due to other causes such as Fuch's endothelial dystrophy (FECD) in contrast to the CHED eyes.[22] This might result in residual DM remnants which would hinder the graft apposition. Mi-OCT is a very useful modality for continuous real-time visualization and complete removal of these remnants intraoperatively especially in cases of corneal clouding, which is not possible with a conventional microscope. The usefulness of this modality has been demonstrated in PIONEER study.[4] Different techniques described such as the use of chandelier illumination[22] or using crescent blade metal surface against stained DM[23] could aid in the removal of DM due to poor visibility. During the surgery, continuous visualization of the graft dynamics helped to perform various intraoperative manoeuvres that resulted in graft adherence in minimal time. Busin et al[2] performed DSAEK without Descemet stripping in infants less than one year as DM could not be identified. Donor tissue attached and the cornea cleared within a week although 4 eyes required re-bubbling which was attributed to various other factors such as poor compliance with postoperative posturing. Ashar et al[24] compared DSEK with and without Descemet stripping and concluded similar outcomes although the surgical time and intraocular manipulations were less in the latter. Various other studies have also reported that the normal DM, neither does it affect the adherence of the donor graft, nor does it influence the

Table 1 Compilation of Various Studies of Endothelial Keratoplasty in CHED Patients

Study	Age	Mean Follow-Up	No. of Eyes	Pre-Operative Visual Acuity	CCT	No. of Regrafts	Graft Survival Rate	Graft Clarity	Post-Operative Visual Acuity	Post-Operative Refraction	ECD Loss	Post-Operative Complications
Our study	9.87 ±8.2y (8m-42y)	17.3m (8–58m)	48 eyes of 29 patients (39-DSAEK; 9-PKP)	1.71±0.66 (0.6–2.7)	1100 ±174 µ	3/39 in DSAEK; 3/9 in PKP	36/39 (92.3%) among primary DSAEK	36 had clear grafts 3 failed grafts	0.76±0.19		36.2% (14.7 to 49.3%)	1 eye- pupillary block 3 eyes- failed graft in primary DSAEK
Mohebbi et al[18]	8.16 ±4.2y (3–16y)	38m (19–64) m	18 (all DSAEK)	20/400 to 20/63 in 12 eyes FF in 3 eyes No FF in 3 eyes		1- re-DSAEK	16/18 eyes (88.9%)	15 clear centred graft at last f/u 1 faintly hazy graft 2 failed graft	20/100 to 20/40 FF in young	+2.5763.3 DS (at last f/u)	42.1% (at 6mo) Busin glide (35.7± 12.9%) Taco 60/40 technique (46% ±14.8%;	1 case of pupillary block on POD1 Raised IOP (61.1%) 1 graft failure at 9 months due to traumatic wound dehiscence 1 graft failure at 30 months
Yang et al[34]	4.3±4.0y (6m-13y) 6.5±3.6y (child) 0.78 ±0.18y (infant)	4±1.9y (2.5–8.5 y)	30 (19-child; 11-infant) all DSAEK	LogMAR 1.03 ±0.25 (FF to LogMAR 1.03) (child) no FF (infant)		1 (to PK)		All cleared at POW1 till 1y	LogMAR 0.54 ±0.20 (child) LogMAR 0.32 ±0.11 (infant)	NA	31.21 ±9.17% (child) Not co-operative (infant)	0 – infant 3- graft detachment (child)
Vajpayee et al[32]		6m	3 (single pass thin lenticule DSAEK)	LogMAR 1.3–3	1134µ (mean)				0.3–0.48 LogMAR	NA		2- Residual corneal haze
Bazaz et al[33]	19y	4m	nDSAEK	HMCF	>1000 µ	Nil	Not mentioned	Residual corneal opacity	FC@4m at 4mo	NA	Not possible	Nil

(*Continued*)

https://doi.org/10.2147/OPTH.S300286 DovePress

Table 1 (Continued).

Study	Age	Mean Follow-Up	No. of Eyes	Pre-Operative Visual Acuity	CCT	No. of Regrafts	Graft Survival Rate	Graft Clarity	Post-Operative Visual Acuity	Post-Operative Refraction	ECD Loss	Post-Operative Complications
Ashar et al[22]	5.6 ±1.52y (DSEK) 5.6 ±0.57y (nDSEK)	1y	6 (3-DSAEK; 3-nDSAEK)	1.3 logMAR (DSEK); 1.13 logMAR (nDSEK)		Nil		All cleared at 30 days till 1y	0.13±0 0.10 logMAR (DSEK); 0.13±0 0.10 logMAR (nDSEK)	−2 to +6DS (up to +2DC) in DSEK +0.0 to +3.5DS (up to 4DC) in nDSEK		1-graft detachment (nDSEK)
Lenhart et al[30]	8m	24m	1	central, steady, and maintained OU	600–1100 μ	Nil	NA	Mild diffuse interface haze	20/40 at 24m	+0.75DS± 0.8DC	NA	NA
Ashar et al[15]	6.6 ±2.19y (4–10y)	1y	5 eyes PK; 2 eyes DSAEK;3 eyes nDSAEK	<0.05 Snellen's decimal VA		Nil	NA	All clear grafts at 1y: PK>DSAEK (PK clear graft from POD1; DSAEK clearing started at POW1)	0.26±0.09 in PK 0.37±0.17 in DSAEK	4.5±2.19 DS (−3.12±1.37 DC) in PK-changing till 1yr 3.5±4.18 DS (−1.6±2.6 DC) in DSAEK-stabilised by 6m	Not mentioned	2 graft dislocation in DSEK Re-bubbling 1 graft dehiscence in PK Re-suturing
Madi et al[35]	6m-16y	14.5mo (3–48m)	13					All cleared at POW1 till 1y	6: Fix and follow 7: ≥20/40	0.5 to 3 DC (−4DS to +10DS)	35% (19–53%)	4- graft detachment 1-rejection
Anwar et al[24]	10y	1y	1 (nDSAEK)	FC@1m OU	921 and 821μ	Nil	NA	Moderate residual stromal haze	20/100 at 1y	+4DS−0.5DC × 180	NA	Nil
Ashar et al[20]	7.8y (5–12y)	1y	5 (all DSAEK)	FC@1/2m-20/125		Nil	NA	All cleared at POW1 till 1y	20/160- 20/50 (1y)	−7DS to +8DS (up to −2DC)	NA	Nil
Bellucci et al[23]	3m	10m	2 (nDSAEK)	No FF	620 and 640μ	Nil	NA	clear	FF, disappearance of nystagmus			Slight temporal decentration in one eye

Busin et al[2]	9y (6m-30y)	15.9m (3–48m)	15 (6-nDSAEK; 9-DSAEK)	FCCF	996µ	Nil	NA	All cleared at POWI	6: Fix and follow 8: ≥20/40 1: 20/70	+2.44D	30%	4- graft detachment
Mittal et al[14]	19y	6m	1(DSEK)	20/100 OU	>1000µ	Nil		Slight corneal haze	20/100, N18	+2DC@ 65	NA	Nil
Goshe et al[31]	8y	13m	2 eyes of same patient					Clear till last f/u	20/50 OU at 13 and 9m	−1.25 to +0.50 DS (+0.75 to 2.5 DC)	25.8–29% at 6m to 1y	Nil

Abbreviations: CCT, Central Corneal Thickness; CHED, congenital hereditary endothelial dystrophy; DSAEK, descemet stripping automated endothelial keratoplasty; DSEK, Descemet Stripping Endothelial Keratoplasty; ECD, Endothelial Cell Density; IOP, Intraocular Pressure; NA, Not Available; PK, Penetrating Keratoplasty; POD, Post, operative day; VA, Visual Acuity.

visual outcomes.[25–29] In our cases, DM stripping was done 18 eyes whereas it was not stripped in 21 eyes among primary DSAEK eyes. DM stripping was also not done in the 3 eyes which underwent DSAEK for failed graft. Re-detachment was seen in 4 eyes (2/18 eyes; 11.1% among eyes in which DM was stripped and 2/24 eyes; 8.3% among eyes in which DM was not stripped) in the immediate post-operative period for which re-bubbling was done. There was no significant difference in terms of DM detachment whether it was stripped or not in CHED eyes.

Conventionally, in DSAEK for FECD eyes, the corneal clarity improves on the table, whereas in cases of CHED, deturgescence of cornea takes much longer time affecting the visualization of the graft. Besides, the double ring sign[30] that is useful in confirmation of the graft orientation, is not always possible in CHED eyes due to thick and hazy corneas. Mi-OCT is especially useful in these cases to visualize the real-time orientation of the graft. Acute-angled bevel sign could also be useful in confirmation of the graft orientation in these cases.[31]

The mean final visual acuity in our study group is poorer than the final acuity of other studies.[2] This could be attributed to late presentation leading to thicker and hazier corneas and poorer presenting visual acuity compared to other studies.[2,25,32] Amblyopia could be one other factor for poorer visual outcomes in our patients due to thick and hazy corneas at the time of presentation. Few studies had thicker corneas at presentation similar to our study with comparable visual outcomes.[33–35] The comparative data with other studies published in literature has been compiled in Table 1. The endothelial loss at the final follow-up compared to the baseline was 36.2% (range, 14.7 to 49.3%), which was comparable to other studies in the literature.[2,18,36,37] Thirty-five eyes (35/39; 89.7%) developed clear cornea at the four-week follow-up and all the eyes had clear cornea at six week follow-up period in our study which was X relatively long compared to other studies.[2] This could again be attributed to the relatively thicker baseline corneas in our eyes compared to the other studies. Graft rejection, the leading cause for graft failure in children[38] was observed in 33% (3/9 eyes) following PKP whereas in 7.7% (3/39 eyes) following DSAEK in our series. The rejection rate observed in our case series among PKP patients was similar to other studies in the literature.[38–40] To conclude, primary DSAEK could be a preferred option over PKP for CHED with early presentation and in those eyes with failed primary PKP. Mi-OCT is a very useful tool in these eyes for various

intraoperative procedures, thereby improving the outcomes of the procedure.

The major limitation in our study is its retrospective nature without a control arm. A prospective randomized study with a control arm would add more value to the results. Intraoperative use of metallic instruments could result in shadowing beneath the instrument in the Mi-OCT which affected the visualization.

Funding

The authors have no funding to disclose.

Disclosure

No financial disclosures. None of the authors has any conflicts of interest for this work to disclose.

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