



Case report

Long-term clinical outcomes after Descemet Membrane Endothelial Keratoplasty (DMEK) in Irido-Corneal Endothelial Syndrome

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ABSTRACT

Purpose: To evaluate the long-term clinical outcomes after Descemet Membrane Endothelial Keratoplasty (DMEK) in Irido-Corneal Endothelial Syndrome (ICE).

Observation: Four eyes of four patients diagnosed with ICE syndrome were treated with DMEK. Postoperatively, best corrected visual acuity (BCVA) and central endothelial cell density (ECD) were documented at 6, 12, 24 and 36 months for all the cases. All procedures were uneventful. Average follow-up time was 36 months. BCVA improved in all eyes. Mean BCVA improved significantly from 1.54 ± 0.71 log MAR preoperatively to 0.11 ± 0.14 logMAR at the final follow-up. Average donor ECD was 2895 ± 357 cells/mm² preoperatively and 1992 ± 321 cells/mm², 1816 ± 395 cells/mm², 1571 ± 299 cells/mm² and 1305 ± 246 cells/mm² at 6, 12, 24 and 36 months after DMEK surgery respectively. This represented an average endothelial cell loss (ECL) of 31.3%, 37.7%, 46.8% and 55.1% at 6, 12, 24 and 36 months respectively. Postoperative intraocular pressure (IOP) rise was seen in 3 eyes at 1 month which normalized under topical antiglaucoma medications.

Conclusion: DMEK is a relatively safe procedure providing favourable clinical outcomes in eyes with ICE syndrome. Since angle closure is progressive in these condition, regular IOP monitoring and glaucoma control is critical for long term survival of the graft.

Importance: Till date management of ICE syndrome has always been a great challenge due to its varied presentation and complex anatomical abnormalities. Replacing the endothelial cells in an irregular anterior chamber poses additional difficulty. Even well-trained DMEK surgeons find it difficult to appose the Descemet's Membrane (DM) in such a scenario and we in this article provide key surgical tips for successful long term management of these cases.

1. Introduction

The iridocorneal endothelial (ICE) syndrome is a rare ocular disorder characterized by proliferative and structural abnormalities of the corneal endothelium, progressive obstruction of the iridocorneal angle, and iris anomalies such as atrophy and hole formation.¹ It comprises a spectrum of clinical entities: Progressive Essential Iris Atrophy, Cogan-Reese Syndrome, and Chandler's syndrome.² The surgical management of ICE syndrome has always been a challenge in the past years.

Outcomes with Penetrating Keratoplasty (PK) in ICE syndrome have been relatively poor with high rates of rejection and endothelial failure.³ Endothelial keratoplasty (EK) is a surgical procedure that selectively replaces dysfunctional endothelium, sparing the corneal stroma and epithelium. This surgical technique offers several advantages for the treatment of corneal edema in ICE syndrome when compared with PK,

such as rapid visual recovery with minimal refractive changes, avoiding the use of sutures and better maintenance of corneal recipient integrity and innervation. Price et al. found that selective replacement of dysfunctional endothelium with Descemet's Stripping Endothelial Keratoplasty (DSEK) can successfully treat corneal edema and associated visual loss and pain caused by ICE syndrome.⁴ DSEK has the potential to provide good short-term visual outcomes in eyes with ICE syndrome. However, long-term graft survival beyond 2 years is poor because of late endothelial failure.⁵

Descemet membrane endothelial keratoplasty (DMEK) allows for selective replacement of damaged endothelial cells, using only donor Descemet's membrane with endothelium.⁶ There is sufficient evidence to demonstrate that DMEK is superior to DSEK in achieving a faster visual recovery, a better visual outcome and a lower immune rejection rate. Currently, DMEK is performed mostly in eyes with Fuchs'

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endothelial dystrophy and uncomplicated bullous keratopathy.⁷ Even though DMEK has been shown to be performed successfully in eyes with prior vitrectomy and trabeculectomy or glaucoma drainage device placement, anterior chamber intraocular lens, large iris defect, or absence of lens support, still DSEK remains the preferred procedure to treat eyes with complex endothelial dysfunction and abnormal anatomy. Except for Sorokin et al. who first reported the applicability of DMEK in cases of ICE syndrome and Posterior Polymorphous Corneal Dystrophy (PPCD) with excellent early outcomes, there are no studies establishing the long term outcomes of DMEK in eyes with ICE syndrome.⁸ In our series, we report the long term clinical outcomes of Descemet membrane endothelial keratoplasty (DMEK) for the treatment of corneal decompensation in patients with ICE syndrome. Four eyes of four patients diagnosed with ICE syndrome were treated with DMEK. Their case summary is as follows:

1.1. Case 1

A 38 year old female presented with complaint of gradual diminution of vision in right eye with blurring more in the waking time. Her BCVA was 20/80. Ocular examination showed a mild microcystic corneal edema with bullae and shallow anterior chamber with irregular depth due to peripheral anterior synechiae (PAS) and corectopia suggestive of ICE Syndrome (Fig. 1a). Other eye was normal. DMEK was done and postoperatively her BCVA was 20/20 at 3 months. At about the end of 2 years she developed mild anterior uveitis, which resolved after hiking the steroid levels for a month. Clinically cornea was clear (Fig. 1b) till her recent 3 year follow up with Endothelial cell density (ECD) of 1621 cells/mm² (Fig. 1c).

1.2. Case 2

A 55 year old male was referred after phacoemulsification and intraocular lens implantation in right eye and the referring surgeon had noted down patches of iris atrophy and PAS preoperatively. On presentation to us, his BCVA was 20/600 in right eye with cornea showing signs of corneal decompensation with extensive PAS and iris atrophic patches suggestive of ICE syndrome (Fig. 2a). Other eye was normal. We performed DMEK for the right eye. Postoperatively, on day 1, the AC was shallow as the air had gone behind the iris. Air bubble was released back

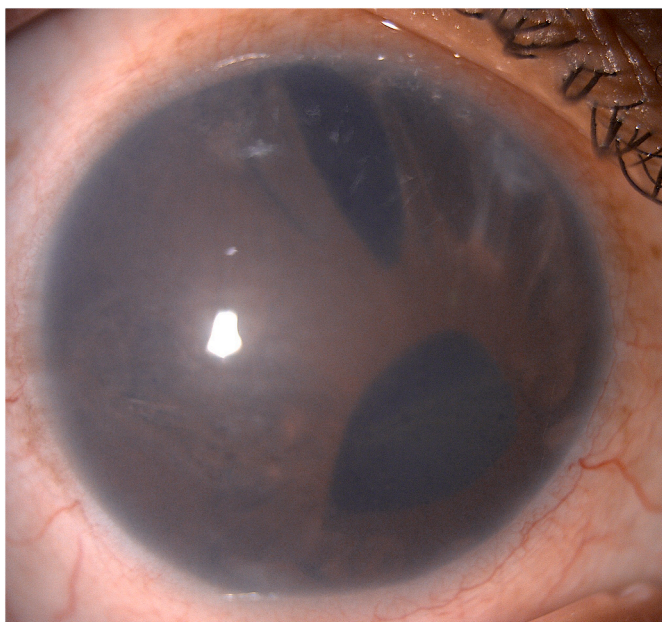


Fig. 1a. Preoperative (Case 1)

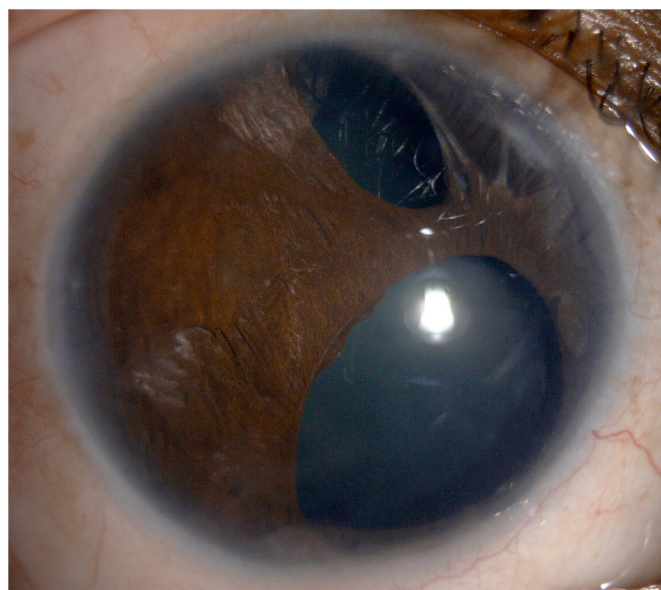


Fig. 1b. Postoperative - 3 years

into the AC and 1% pilocarpine was applied to constrict the pupil. Subsequently the cornea cleared (Fig. 2b) and at 3 years the patient retained a BCVA of 20/20 and ECD of 1302 cells/mm² (Fig. 2c).

1.3. Case 3

A 52 year old female presented with recurrent episodes of pain, redness and defective vision in right eye with BCVA of 20/600. Ocular examination showed diffuse microcystic corneal edema with peripheral anterior synechiae, peculiar aberrant iris vessels and complicated cataract suggestive of Chandler's Syndrome (Fig. 3a). We planned for DMEK with phacoemulsification and intraocular lens implantation. Iris vessels were cauterized with a pencil tip wet cautery used in retinal surgeries prior to phacoemulsification to prevent any inadvertent bleeding. Postoperatively patient had mild bleeding till 1 month, which spontaneously resolved and she was followed up for 3 years (Fig. 3b) with no further episodes of bleeding and a BCVA of 20/40 and ECD of 1020 cells/mm² (Fig. 3c).

1.4. Case 4

A 50 year old female was referred for corneal decompensation in left eye post cataract surgery. In the left eye visual acuity was Hand Movements only and the ocular examination showed severe corneal edema with scarring and iris atrophy, PAS and corectopia (Fig. 4a). Her right eye also showed similar findings confirming the rare diagnosis of bilateral ICE syndrome (Fig. 4b). DMEK was done in left eye following which her BCVA improved to 20/30 at 6 months and remained stable at 3 years follow up (Fig. 4c) with an ECD of 1278 cells/mm² (Fig. 4d).

2. Methods and Materials

All the four patients of ICE syndrome underwent DMEK at our institute. Diagnosis was based on clinical slit-lamp findings and since the corneas were hazy preoperative specular was not possible in all the four cases. Preoperatively all patients underwent the Best Corrected Visual Acuity (BCVA) using the Snellen chart, slit lamp examination, Goldman's Applanation Tonometry (GAT) and dilated fundus examination. Ultrasonography (USG) B-scan was done in eyes where the fundus details were not clearly visible. All DMEK grafts were harvested at Sankara Eye Bank, Coimbatore and stored in organ culture medium (Cornisol)

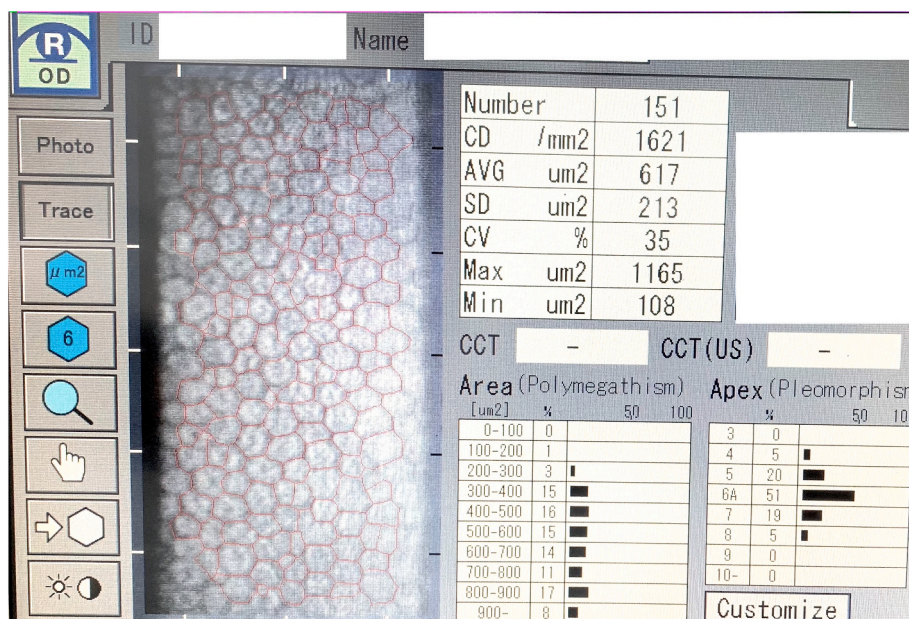


Fig. 1c. Specular - 3 years.

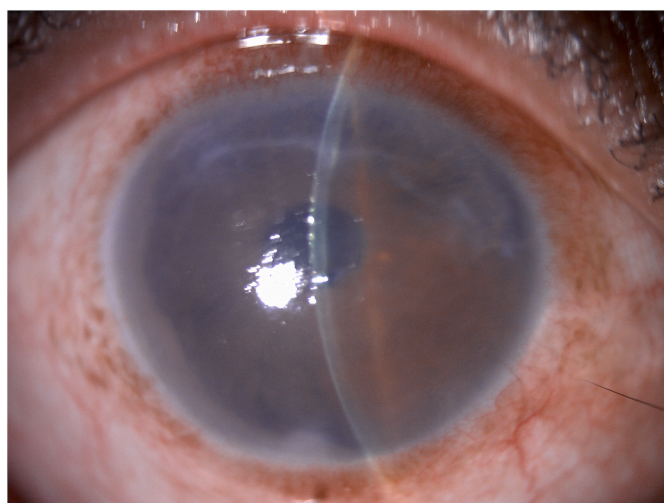


Fig. 2a. Preoperative (Case 2)

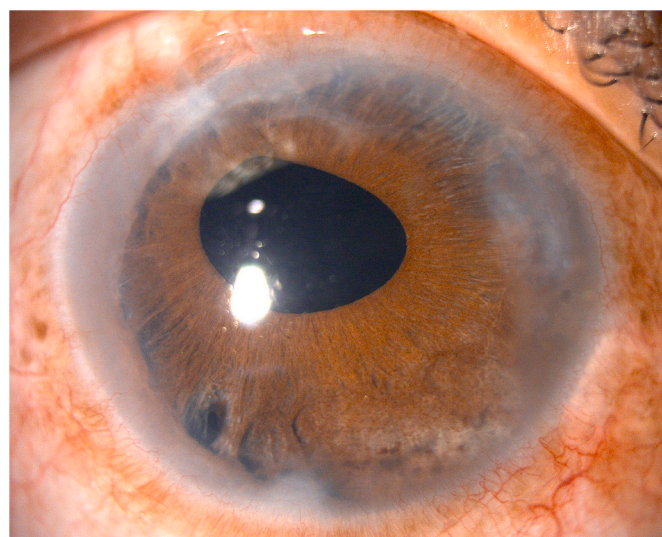


Fig. 2b. Postoperative - 3years

until transplantation. Postoperatively, BCVA and central ECD were documented at 6, 12, 24 and 36 months. Donor tissues above 50 years were selected and we strictly adhered to our regular DMEK surgical protocol to ensure a smooth transfer and correct attachment of DM in these complicated cases. Our protocol included donor DM preparation in the operating room (OR) by the surgeon using a single pull technique with a curved non toothed forceps to shorten the peel time (3–5 minutes) and reduce the endothelial cell loss. The stripped DM was marked on the stromal side with an L-shaped stamp to identify the endothelial side during unfolding in the AC. The prepared DM was injected into the recipient using a self-made injector which was assembled using a 1 cc syringe, regular C-type intraocular lens (IOL) cartridge and a sterile IV tubing. After unfolding DM in the correct orientation the AC was completely filled with air for 1 hour and was subsequently burped till the eccentric pupillary margin was reached to avoid pupillary block glaucoma.

3. Results

All four patients were diagnosed with ICE syndrome. 2 eyes (50%) were phakic and 2 eyes (50%) were pseudophakic. One of the phakic eyes had cataractous lens, for which DMEK was combined with phacemulsification with implantation of an intraocular lens. Rest 3 patients underwent only DMEK. All procedures were uneventful.

Average follow-up time was 36 months. BCVA improved in all eyes (Table 1). Mean BCVA improved significantly from 1.54 ± 0.71 LogMAR preoperatively to 0.11 ± 0.14 LogMAR at the final follow-up.

Average donor ECD was 2895 ± 358 cells/mm² preoperatively and 1992 ± 321 cells/mm², 1816 ± 395 cells/mm², 1577 ± 299 cells/mm² and 1305 ± 246 cells/mm² at 6, 12, 24 and 36 months after DMEK surgery respectively (Table 2). This represents an average endothelial cell loss rate of 31.3%, 37.7%, 46.8% and 55.1% at 6, 12, 24 and 36 months respectively. Postoperative specular microscopy examinations found normal endothelial morphology. There were no occurrences of immunologic graft rejections or graft failures. There was no evidence of

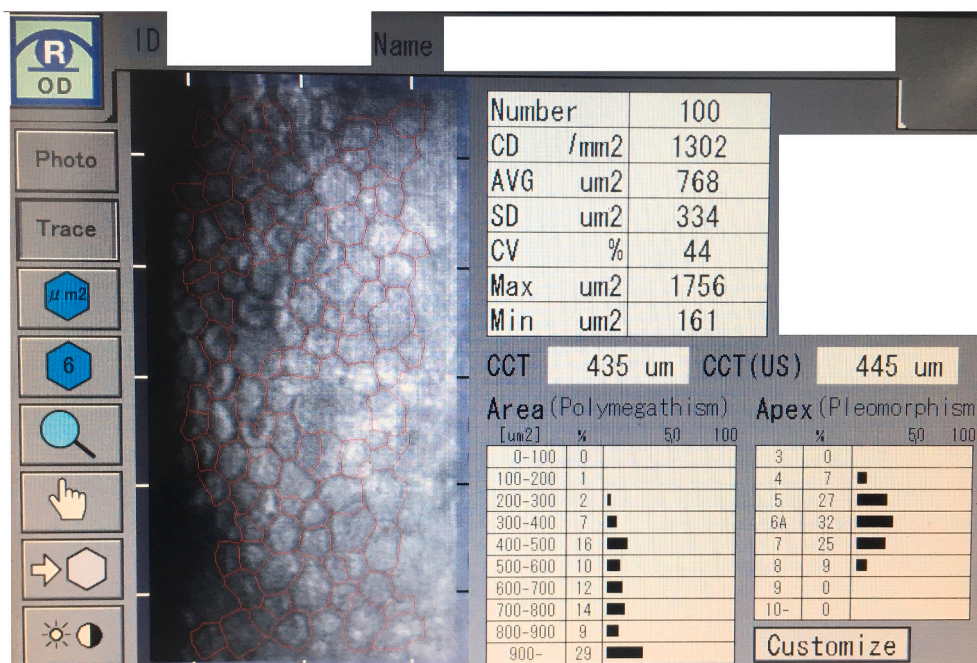


Fig. 2c. Specular - 3 years.

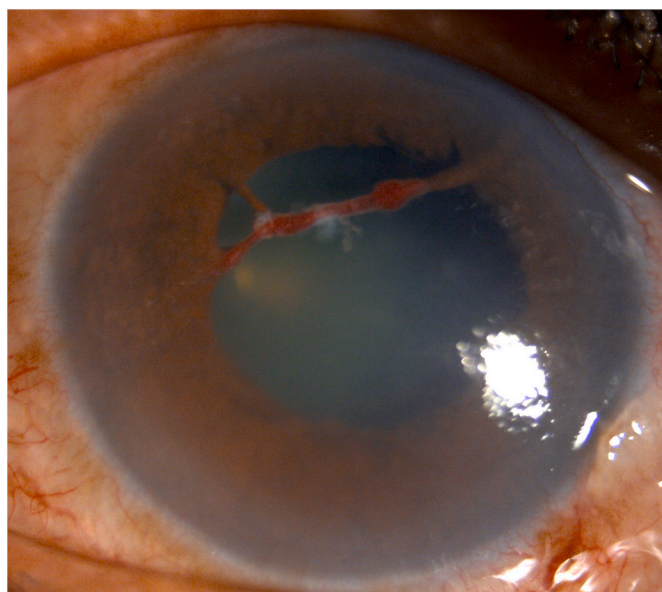


Fig. 3a. Preoperative (Case 3)

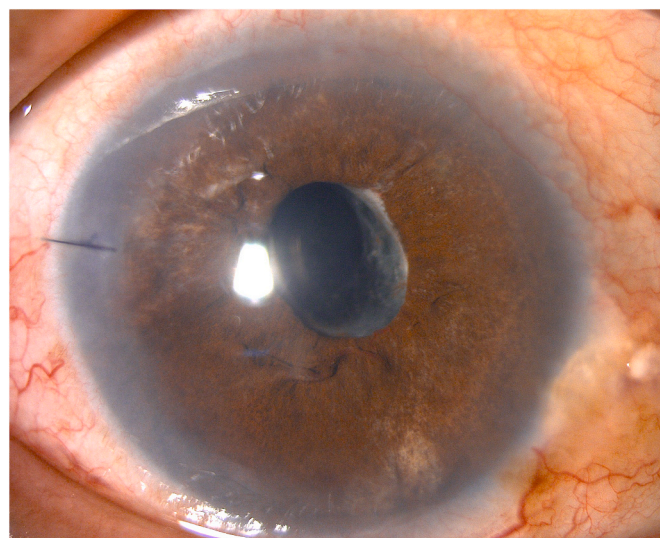


Fig. 3b. Postoperative - 3years

glaucoma progression in any of the cases.

4. Discussion

Long term outcomes of DMEK is well established in most endothelial conditions, but to the best of our knowledge, this is the first reported series with long term outcomes after DMEK in ICE syndrome.

All four patients achieved an excellent visual outcome with BCVA of 20/20- 20/40 at 6 months after DMEK. Fajgenbaum et al.⁵ showed an improvement of BCVA from 20/20–20/40 in 7 of 9 grafts at 6 months post op following DSEK in ICE patients. But subsequently they reported a significant fall in BCVA with only 12% of grafts having BCVA of 20/40 or better at 24 months follow up. Again, their ECL over 1 year was 78% and seven of the nine grafts failed because of late endothelial failure after a

mean of 18 months. They proposed that this increased perioperative and late endothelial cell loss observed in eyes with ICE to be multifactorial. They attributed that excessive perioperative endothelial cell loss which occurred during insertion and positioning of the DSEK tissue as the most significant factor which limited the graft survival in their series. Also, associated glaucoma surgeries and a fragile blood–aqueous barrier which increases the tendency to inflammatory and rejection episodes can cause disturbances in ICE syndrome and contribute to medium to long-term DSEK failure. We feel that the insertion of an additional tissue of 150–200 μm into an already irregular and cramped anterior chamber promotes iris touch, PAS formation and subsequent inflammation and glaucoma also a contributing factor for graft failure in DSEK. Price et al. described 3 cases of ICE syndrome that were managed with Descemet’s Stripping Automated Endothelial Keratoplasty (DSAEK) surgery,⁴ showing excellent visual outcomes till 14 months. All the patients achieved a BCVA of 20/20 to 20/30 within 6 months with no complications.

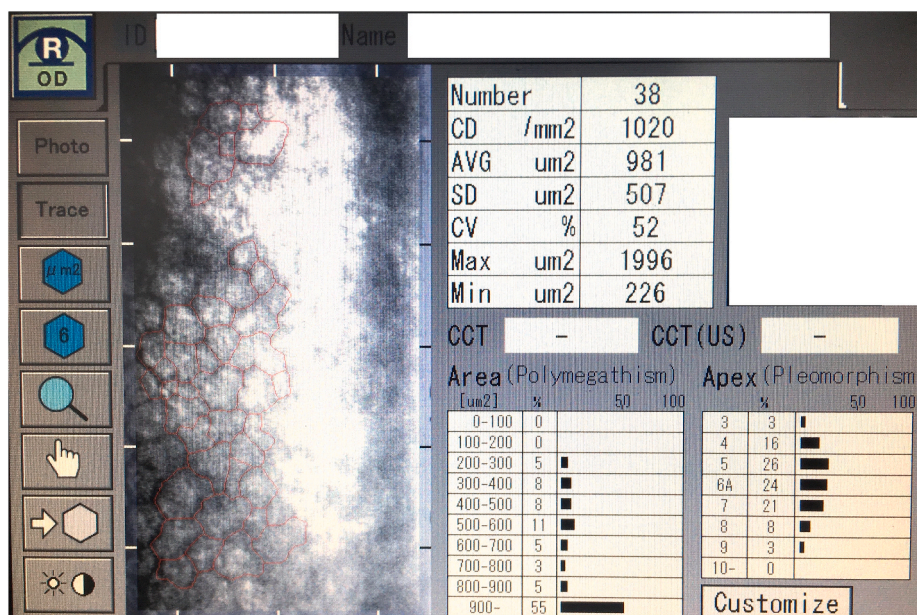


Fig. 3c. Specular - 3 years.



Fig. 4a. Preoperative LE (Case 4)

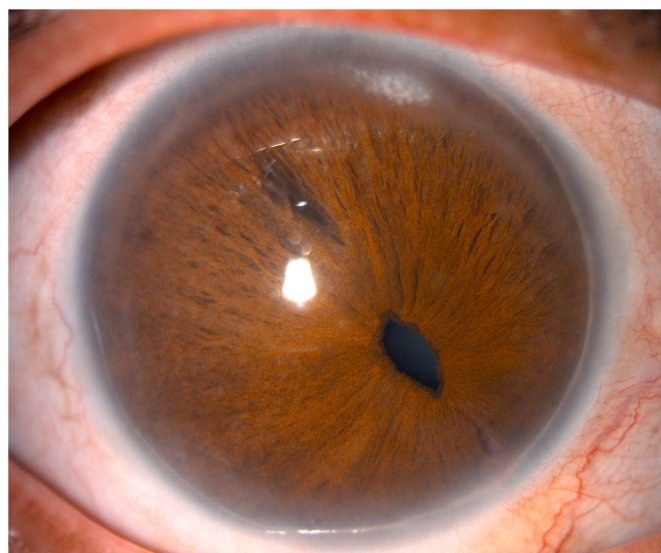


Fig. 4b. RE – Suggestive of Bilateral ICE

However, they pointed out that DSAEK can be more challenging to perform in eyes with ICE syndrome and PAS, because the shallow anterior chamber and iris abnormalities may make it more difficult for the donor tissue to be inserted through a small incision and unfolded correctly.

Buxton et al.⁹ stated that keratoplasty, rather than filtering surgery, is probably the initial surgical procedure of choice when the corneal edema is extensive and the intraocular pressure moderately increased and not associated with any objective glaucomatous changes. The largest series of PK grafts in ICE syndrome by Alvim et al. reported that overall prognosis of PK was favourable, but the patients required multiple corneal and glaucoma procedures. Also the allograft rejection episodes were found to be very frequent after PK for ICE syndrome (79%), especially after glaucoma surgery.³

However in our study, there were no primary graft failure or rejections episodes during the study period. Also we used Prednisolone acetate 1% suspension in tapering doses in the postoperative period during the first 6 months and later switched over to Loteprednol

Etabonate 0.5% gel which is equally effective in preventing immunologic graft rejection episodes after DMEK and was significantly less likely to raise IOP.¹⁰ Postoperative IOP rise was seen in 3 eyes (up to 25 mm Hg) at 1 month which normalized under topical medical treatment with Timolol Maleate 0.5% eyedrops given twice daily.

In eyes with pre-existing glaucoma or in high-risk eyes with complex anterior segment changes such as eyes with ICE syndrome there is a higher risk of uncontrolled IOP after EK which in turn also has adverse effects on the donor endothelial cells and graft survival.¹¹ Whenever DMEK is performed in such complex eyes, re-bubbling rates may be as high as 50%, and secondary graft failure occurs in up to 75% these eyes.¹² Unfortunately, data on the outcomes of DMEK in eyes with glaucoma are limited. Treder et al.¹³ found that there was no significant difference in BCVA and IOP during the early post-operative period (3 months) in patients with and without a pre-existing glaucoma who had received DMEK surgery. Aravena et al.¹⁴ published the largest series of consecutive DMEK in patients with previous glaucoma surgery. They

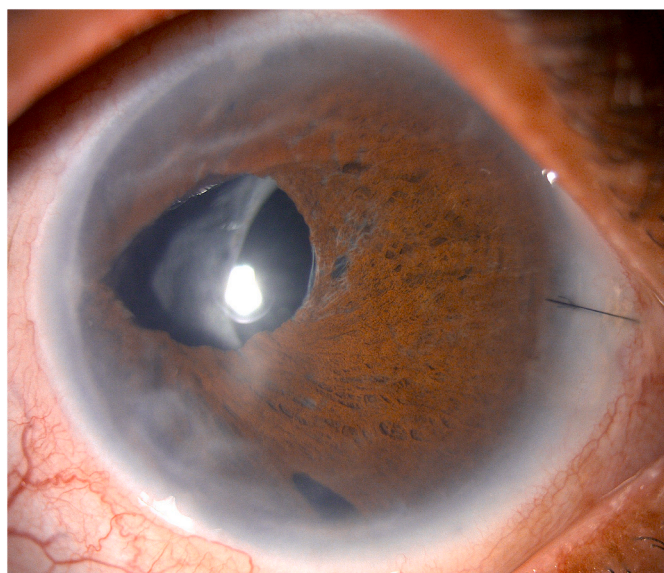


Fig. 4c. Postoperative - 3years

reported that DMEK provides excellent visual improvement without an increase in early postoperative complications in eyes who had undergone previous trabeculectomy and glaucoma drainage device implantation and there may be an advantage performing DMEK in these cases, but suggested further long term studies investigating the impact of glaucoma surgery on the endothelial cell loss and graft survival of DMEK is required. DMEK provides near perfect anatomical replacement of tissue and as there is not much change in the AC and angle dynamics, our cases remained quiet all through with IOP under control with medications.

Surgical outcomes in ICE syndrome is summarized (Table 3). Till

date published data on DMEK in ICE syndrome is limited. Weller et al.¹² in 2015 studied the feasibility and outcomes of DMEK in complex anterior segment and vitreous diseases. DMEK was performed in 3 eyes with ICE syndrome with a follow up of 6 months. Sorokin et al.⁸ recently published their clinical outcome of DMEK in cases of corneal decompensation secondary to ICE and PPCD. Both the studies found favourable short term outcomes in their series and they proposed future prospective studies to compare DMEK, DSAEK, and possibly also pre-Descemet's endothelial keratoplasty for the treatment of ICE or PPCD patients, including long-term follow-up.

DMEK is equally tough to perform in such complex anterior segment situations, but we still feel it is easier than DSAEK in ICE syndrome. DMEK offers 3 distinct advantages that render it an appealing procedure to treat patients with ICE syndrome. First, section in DMEK is small (2.8mm–3.00mm) so that the incision can be planned in an area avoiding the PAS. Second as the AC is already shallow, unfolding the DM in the AC is easier than in routine DMEK cases. Thirdly, the need for stronger dosage and the frequent usage of steroids is reduced and the chance of IOP rise in these ICE patients is less, who are otherwise pre-disposed to develop glaucoma.

However, we propose that surgery should be done only by an experienced surgeon who has previously performed DMEK successfully in

Table 1
BCVA at 6, 12, 24 & 36 months after DMEK.

S. No.	LOGMAR BCVA PREOP	LOGMAR BCVA 6 M	LOGMAR BCVA 12 M	LOGMAR BCVA 24 M	LOGMAR BCVA 36 M
Case 1	0.602	0	0	0	0
Case 2	1.477	0.602	0.176	0	0
Case 3	1.8	0.301	0.301	0.301	0.301
Case 4	2.3	0.301	0.176	0.176	0.176
Mean	1.54 ± 0.71	0.30 ± 0.24	0.16 ± 0.12	0.11 ± 0.14	0.11 ± 0.14
± SD					

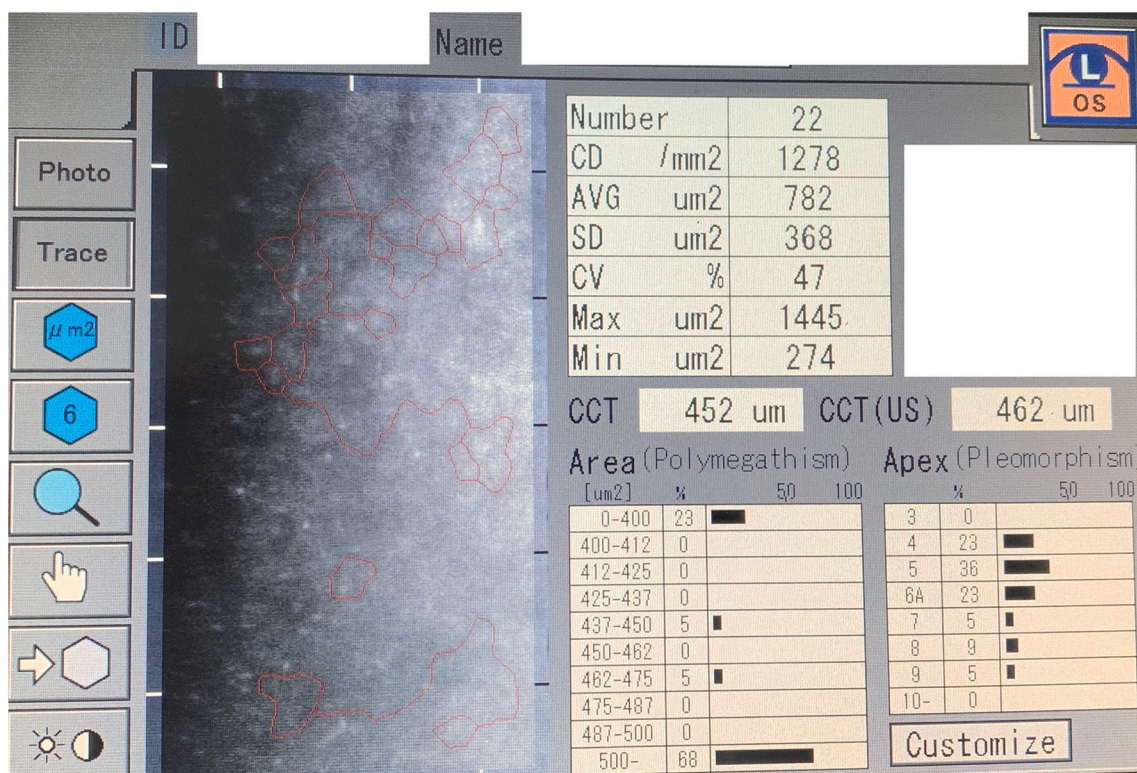


Fig. 4d. Specular - 3 years.

Table 2

ECD and ECL at 6, 12, 24 & 36 months after DMEK.

S. No.	Donor ecd preop	6 M		12 M		24 M		36 M	
		ECD	% ECL	ECD	% ECL	ECD	% ECL	ECD	% ECL
Case 1	3400	2445	28.08	2375	30.14	1981	41.73	1621	52.12
Case 2	2717	1963	27.75	1767	34.96	1503	44.69	1302	52.08
Case 3	2584	1698	34.28	1453	43.76	1265	51.04	1020	60.68
Case 4	2880	1861	35.37	1671	41.97	1535	49.69	1278	55.62
Mean \pm SD	2895.25 \pm 357.61	1991.75 \pm 321.27	31.3 \pm 4.01	1816.50 \pm 394.83	37.7 \pm 6.31	1571.00 \pm 298.69	46.78 \pm 4.33	1305.25 \pm 246.18	55.12 \pm 4.05

Table 3

Surgical outcomes in irido corneal endothelial syndrome.

Author	Year	No. of eyes	Surgical technique	Visual acuity	Complication	Comments
Buxton et al.	1984	5	PK	20/15 to 20/30 at average follow-up of 2.7 years	–	PK is a relatively safe and effective procedure for patients with diminished vision or other complaints related to corneal abnormalities in ICE.
Alvim et al.	2000	14	PK	At average follow-up of 58 months, >20/40 in 3 (21%), 20/50–20/100 in 4 (29%), 20/200–20/400 in 5 (36%), and CF in 2 (14%) with failed grafts	6 (43%) underwent repeat PK.	Favourable outcomes can be achieved; may require multiple corneal and glaucoma procedures.
Price et al.	2007	3	DSEK	20/20 to 20/30 at follow-up ranged from 1 to 14 months	–	Visual recovery is rapid and refractive changes are minimal compared to traditional PK.
Fajgenbaum et al.	2015	4	DSEK	7 of 9 grafts achieved a visual acuity of 6/12 or better by 6 months	One eye required 1 repeat DSEK, and 2 eyes required 2 repeat DSEKs for a total of 9 DSEK operations across the 4 eyes.	Long-term graft survival was poor with 7 of 9 grafts suffering late endothelial failure.
Weller et al.	2015	24 consecutive eyes with endothelial decompensation including 3 eyes with ICE syndrome	DMEK	Overall Best-corrected visual acuity (logMAR) increased from 0.98 to 0.53, 0.53 and 0.57 after 1, 3, and 6 months respectively.	Rebubbling was necessary in 2 eyes. (ICE syndrome)	No graft failure occurred.
Sorkin et al.	2018	4 eyes with ICE syndrome & 4 eyes with PPCD	DMEK	Mean BCVA improved from 0.70 \pm 0.34 logMAR preoperatively to 0.21 \pm 0.14 logMAR at 6 months	Postoperative IOP rise (steroid response) was seen in 2 eyes.	DMEK surgery was effective in treating corneal decompensation secondary to ICE syndrome.

complex anterior segment situations. We also suggest a few adaptations in the donor selection and sizing and the surgical technique which will help the surgeons to perform DMEK without complications in these complex cases. The donor age should be above 55 years, as it will unfold easily without much manipulation in an irregular AC. The donor DM sizing is critical and should not be based on the recipient's corneal diameter and should solely depend on the extent of PAS and the non-adherent central cornea. If the donor DM diameter is more, then the peripheral DM scroll will not be able to unfold due to the PAS, leading to detachment in the immediate post-operative period. Never attempt to release any adherent iris or perform gonio-synechiolysis, as there are high chances of recurrences due to iris memory and also bleeding can be profuse such that the surgery may need to be abandoned. Intracameral Pilocarpine 0.2% can be used to constrict the pupil to prevent lens damage while manipulating the graft. Postoperatively after 1 hour, the pupil has to be dilated and air is burped to cross the eccentric pupil to prevent acute spike in IOP and prevent further PAS formation.

5. Conclusion

DMEK is a safe and successful procedure providing favourable clinical outcomes in eyes with ICE syndrome. A few surgical adaptations in the technique yields results comparable to DMEK performed in variable indications. Since angle closure is progressive in these conditions, regular IOP monitoring and glaucoma control is critical for long term survival of these grafts.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

None of the authors have any financial disclosures

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