Surgical Management of Fuchs Endothelial Corneal Dystrophy: A Treatment Algorithm and Individual Patient Meta-Analysis of Descemet Stripping Only

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Purpose: This study aims to determine predictive factors for success of Descemet stripping only (DSO) in Fuchs corneal endothelial dystrophy and propose a DSO treatment algorithm.

Methods: Ovid MEDLINE, Embase, and Cochrane CENTRAL databases were searched to evaluate DSO case series, including combined phacoemulsification and DSO, and the use of Rho-kinase inhibitors (ROC-i). Our primary outcome was success of corneal clearance. Secondary outcomes included the time to corneal clearance, the postoperative endothelial cell count (ECC), and the impact of ROC-i.

Results: Sixty-eight cases were evaluated with a mean follow-up of 12.4 months. DSO corneal clearance was achieved in 85% (n = 58) with a mean time of 4.9 weeks for the ROC-i group compared with 10.1 weeks in the observation group ($P < 0.0001$). The mean central ECC postoperatively was higher in the ROC-i group compared with the observation group 1151 ± 245 versus 765 ± 169 cells/mm^2, respectively ($P < 0.018$). The postoperative best-corrected visual acuity (BCVA) improved in 61 eyes (90%), with mean final BCVA of 0.17 (0.26) logMAR ($P = 0.001$), which was statistically significant compared with preoperative BCVA. Factors influencing success were 4-mm descemetorhexis size, a clear peripheral ECC with no clinical sequelae of decompensation or guttae, and a low central corneal thickness. No intraoperative complications were noted. The commonest postoperative complication was deep corneal stromal scars noted at the descemetorhexis edge (n = 9).

Conclusions: DSO has a role in the treatment of a subset of patients with Fuchs corneal endothelial dystrophy and that adjuvant treatment with ROC-i may lead to faster corneal clearance.

Key Words: Descemet stripping only, Fuchs endothelial corneal dystrophy, Rho-kinase inhibitors

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The corneal endothelium plays a critical role in maintaining a state of deturgescence and corneal clarity. The mitochondrial-rich corneal endothelial cells actively pumps ions through the Na+K+ATPase pump into the aqueous humor, thereby generating an osmotic force to keep the cornea in an optimal state of dehydration.[1–3]

Traditional perspectives contend that endothelial cells are arrested in the G1 phase of the cell cycle. Although they possess a proliferative capacity, corneal endothelial cells typically do not proliferate in vivo.[4] There is a higher density of corneal endothelial cells in the periphery and paracentral regions, which have been shown in vitro to help the migration of these peripheral endothelial cells.[5,6] Over time, however, there is a progressive decline in endothelial cells, which can be hastened by either a primary or a secondary endotheliopathy. This leads to loss of barrier function and subsequently fluid accumulates, leading to a loss of transparency, painful epithelial bullae, and, in chronic cases, stromal scarring.[7]

Fuchs endothelial corneal dystrophy (FECD) is the most common endothelial dystrophy and the leading indication for corneal transplantation.[8] This condition is characterized by the progressive decline of corneal endothelial cells, leading to polymegethism, pleomorphism, and the deposition of extracellular matrix excrescences called guttae.[9,10] Although medical treatments are available for symptom management, surgical management remains the definitive treatment. Melles introduced the concepts of posterior lamellar keratoplasties, with Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty (DMEK) being the techniques of choice for endotheliopathies.[11–13] Comparative studies have shown DMEK to outperform Descemet stripping automated endothelial keratoplasty in FECD, resulting in faster and better visual acuity, higher final endothelial cell count (ECC),

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reduced rejection risk, and less postoperative astigmatism.[14–17] However, DMEK is not without its own disadvantages including a steeper learning curve, risk of repeated rebubble, and graft rejection.[16,17] Therefore, newer techniques have been sought to eliminate both short-term and long-term sequelae of endolamellar keratoplasties.

Reports of spontaneous visual recovery and corneal clarity after deliberate or accidental removal of Descemet membrane without endothelial keratoplasty have prompted the notion of endothelial rejuvenation.[18] The proposed mechanism for this phenomenon has been the migration of existing host peripheral endothelial cells to occupy the absent area of Descemet membrane and corneal endothelium.[19,20] This technique, termed Descemet stripping only (DSO) or descemetorrhexis without endothelial keratoplasty, represents an exciting evolution in the current surgical paradigm. Today, numerous clinical studies have been published, showcasing DSO as a promising technique for treating corneal decompensation and visual symptoms in a carefully chosen subgroup of patients with FECD. These cases have the advantage of not being subjected to allograft tissue rejection, long-term steroids, potential secondary glaucoma, and intraoperative and postoperative complications arising from current endolamellar keratoplasties.[20–22] However, because of the paucity of higher-level studies, and most data restricted to case series, making meaningful conclusions to guide surgical management is challenging.

For this reason, in this individual patient meta-analysis, we analyze the entire global cohort of published cases of DSO. To the best of our knowledge, this is the largest quantifiable analysis assessing predictive factors for success of DSO in FECD and proposes a treatment algorithm to aid corneal surgeons in deciphering when to opt for DMEK or DSO.

METHODS

Search Strategy, Selection Criteria, and Study Screening

The preferred reporting items for systematic reviews and meta-analyses 2009 checklist was followed throughout the study.[23] A systematic literature search was performed on Ovid MEDLINE (2000–January 2021), Embase (2000–January 2021), and Cochrane CENTRAL (2000–January 2021) (Table 1). Systematic reviews, meta-analyses, or other nonoriginal articles were excluded. Studies that only reported on cohort-level data were excluded. Indications for surgery were limited to FECD, and there was no restriction based on other ocular comorbidities. All clinical trials were approved by their respective studies' institutional review board with written consent obtained from all participants. This study was conducted in accordance with the guidelines of the Declaration of Helsinki.

Two independent authors (N.D. and E.C.) reviewed the search results independently across 3 databases, first by consulting titles and abstracts, followed by full-text screening. Any discrepancies were then reviewed together, and a decision for inclusion was made through consensus.

Data Collection and Primary and Secondary Outcomes

Preoperative visual acuity, ECCs centrally and peripherally, and central corneal thickness were collected from all included studies. Intraoperatively, we included the diameter of the DSO descemetorhexis and postoperative adjuvant treatment regimen, which included ripasudil 0.4% [Rho-kinase inhibitors (ROC-i)], hypertonic saline, or no additional drops. We also included whether cataract surgery was concurrently performed. Postoperatively, the time to corneal clearance, follow-up period, final visual acuity, peripheral and central ECC, central corneal thickness, and complications were recorded.

Our primary outcome was success or failure of the DSO procedure in corneal clearance and not needing a rescue DMEK. Secondary outcomes included the time to corneal clearance, the postoperative ECC, and the impact of ROC-i.

Furthermore, we evaluated the impact of phacoemulsification alongside DSO, including postoperative visual acuity, spherical equivalent, predicted spherical equivalent, and refraction.

Using the results from individual studies and the meta-analysis, a treatment algorithm was constructed.

Statistical Analysis

Continuous baseline parameters and outcomes were represented with a mean and SD, whereas categorical variables were described as the proportion of the total sample. To conduct the meta-analysis at the individual patient level, a univariable linear or logistic regression analysis was performed as appropriate. For these analyses, an odds ratio and 95% confidence interval were reported. All predictors with an associated P value of less than 0.2 were included in a multivariable linear or logistic regression model. Throughout, a P value of less than 0.05 signified statistical significance. Statistical analysis was conducted on SPSS Statistics (version 23.0, IBM Corp).

TABLE 1. Search Terms Used for Ovid MEDLINE, Embase, and Cochrane CENTRAL

Search Database	Search Terms
Ovid MEDLINE	"corneal edema" or "Fuch's endothelial dystrophy" or "descemet"
Embase	"corneal edema" or "corneal diseases" or "descemet membrane" or "endothelium" or "cornea" or "fuch's endothelial dystrophy" or "corneal pachymetry" or "corneal topography" or "cell movement" or "cell shape" or "rho-associated kinases" or "descemetorhexis" or "descemet stripping endothelial keratoplasty" or "descemet membrane endothelial keratoplasty" or "descemet stripping"
Cochrane CENTRAL	"Descemetorhexis" or "Descemet stripping" or "endothelial keratoplasty" or "cornea" or "descemet" or "Fuch's endothelial dystrophy" or "endothelium"

RESULTS

All original studies pertaining to DSO, including randomized controlled trials and case series, were included if they reported on results after DSO for individual patients (Fig. 1). In total, 3139 studies were reviewed across all databases with 13 full-text articles eligible in our criteria. However, 4 articles were excluded, leaving 9 studies for our pooled analysis. Basic sciences studies, nonoriginal studies, repeat data, studies with low numbers of eyes (<5), studies published before 2000, and non-English language studies were excluded from this study.

Baseline Characteristics and Symptoms

Overall, 38 cases met the study inclusion criteria and were evaluated in our pooled analysis—37 DSO only procedures and 30 combined DSO and phacoemulsification (phaco + DSO) procedures. The mean (SD) patient age in the selected group was 67 ± 9 years with a greater preponderance of the female sex, 75% of cases (Table 2). The mean follow-up was 12.4 ± 11 months with a minimum of at least 3 months follow-up.

Table 3 summarizes preoperative and intraoperative data from the pooled analysis. The descemetorhexis size was documented in all eyes with 92% (62 eyes) having a 4.00 mm size, with the remainder ranging between 4.50 and 6.50 mm.[19,21,24,25,27,28] Eleven eyes (16%) were treated with ROC-i immediately postoperatively[18,29,37] with 4 eyes requiring rescue treatment after failures of the corneas to clear.[21] All cases were treated with ripasudil 0.4%.

There was a mild-to-moderate reduction of the best spectacle–corrected visual acuity of 0.37. This also corresponded to a mean central corneal thickness of 632 μm. Preoperative central endothelial cell density (ECD) was undetectable in 64 eyes (94%). Preoperative peripheral ECD was recorded in 33 eyes (48%) with an average of 1532 ± 592 cells/mm^2.

Commonly reported symptoms were glare in 4 studies,[21,24–26] photophobia worse at night in 4 studies,[21,24–26] and blurry vision among 4 studies.[21,24,25,27]

DSO—Surgical Outcome

Surgical success was defined as achieving a complete corneal clearance, without focal or localized corneal edema and without needing to proceed to a corneal transplantation. In 58 eyes (85%), surgical success was achieved. A univariable analysis for predicting factors for surgical success was performed (Table 3). Older age and descemetorhexis size of 4.00 mm were found to be statistically significant factors for surgical success ($P = 0.017$ and $P < 0.001$, respectively). The mean time for corneal clearance was 9.1 ± 5.7 weeks. Postoperatively, central corneal ECD was recorded in 47 eyes (69%) with an average of 812 ± 195 cells/mm^2, and peripheral ECD was recorded in 36 eyes (53%) with the average of 1264 ± 458. Central corneal thickness was measured in 49 eyes (72%) with a mean ± SD of 581 ± 62 μm. Postoperative BCVA improved in 61 eyes (90%), with mean final BCVA of 0.17 (0.26) logMAR ($P = 0.001$), which was statistically significant compared with preoperative BCVA.

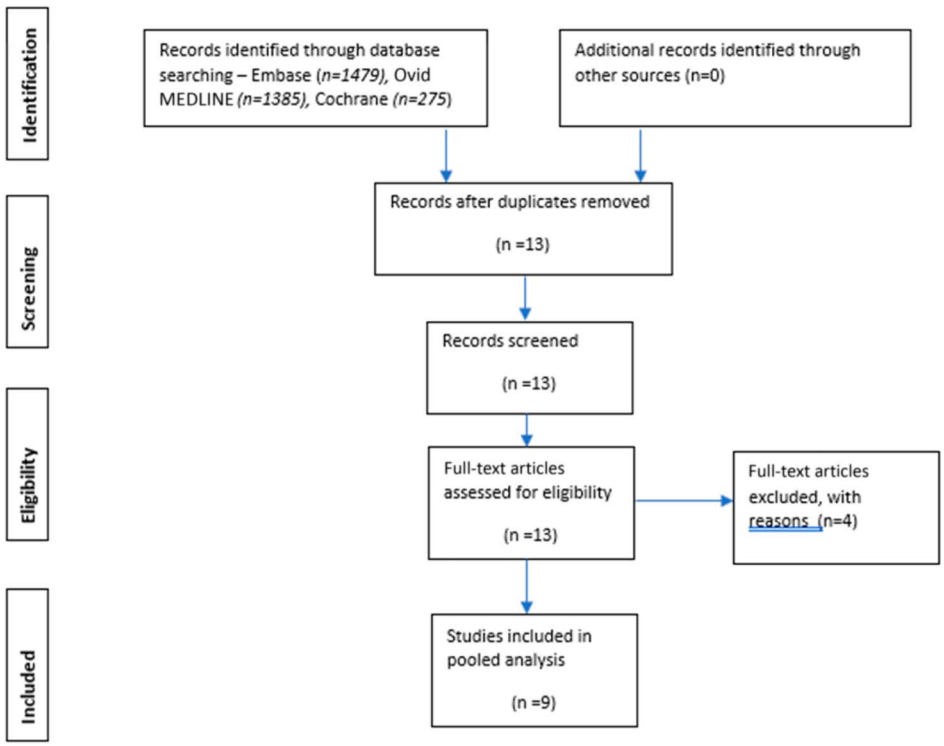

FIGURE 1. Search flow strategy for pooled analysis and final inclusion of studies. (The full color version of this figure is available at www.corneajrnl.com.)

TABLE 2. Baseline Characteristics and Patient Demographics

Article	No. Eyes	Mean Age (yr)	Sex (M/F)	Operated Eye (R/L)	Procedure	Rho-kinase-I	DSO-Size	DSO Technique
Arbelaez (2014)	3	44		2R; 1L	DSO only	no	6, 6.5	NA
Moloney (2014)	1	54	1F	1R	DSO only	no	4.5	NA
Koenig (2015)	2	68		2L	Phaco + DSO	no	6	Viscodissection/peeling
Borkar (2016)	13	65	4M; 9F	5R; 8L	Phaco + DSO	no	4	Scoring with the Sinskey hook
Iovenio (2017)	5	70	1M; 4F	4R; 1L	DSO (n = 2); Phaco + DSO (n = 3)	no	4	Scoring with the Sinskey hook
Moloney (2017)	12	—		6R; 6L	DSO	No	4	Peeled with micro forceps
Huang (2018)	12	67	3M; 9F	6M; 6F	Phaco + DSO (n = 12)	3 eyes	4	Scoring with the Sinskey hook
Macsai (2019)	18	73	2M; 16F	11R; 7L	DSO	8 eyes	4	Peeled with IA handpiece
Artieda (2020)	2	—	1M; 2F	1R; 1L	DSO	no	4	NA

ROC-i Outcomes

Table 4 describes the preoperative and postoperative patient characteristics compared between the ROC-i group and the observation group.

Surgical success was achieved in 11 eyes (100%) in the ROC-i group compared with 44 eyes (76%) in the observation group ($P = 0.081$). The average time for corneal clearance was found to be statistically significant between the groups ($P < 0.0001$); in the observation group, a mean (SD) clearance of 10.1 ±5.90 weeks was noted compared with 4.9 ± 1.8 weeks in the ROC-i group (Fig. 2). In addition, mean central ECD postoperatively was found to be higher in the ROC-i group compared with the observation group 765 ± 169 versus 1151 ± 245 cells/mm^2, respectively ($P < 0.018$). Table 5 summarizes the postoperative data comparing the 2 groups.

Complications

No intraoperative complications were recorded in any study. Two patients who had the combined phacoemulsification and DSO procedure developed cystoid macular edema,[25] and 4 eyes developed irregular astigmatism which was visually significant and correctable with a rigid gas permeable contact lens alone.[28,29] Nine patients had deep corneal stromal scars located at the descemetorhexis border which did not affect vision.[21,24,28] Focal Descemet detachment at the edge of the descemetorhexis was observed in 3 eyes, and an attempt to reattach by injecting an air bubble to the anterior chamber was unsuccessful in all cases.

DISCUSSION

This study is the largest evaluation of the outcomes of DSO with the aim to identify predictive factors for success in this technique and corneal clearance, as well as the impact of ROC-i. Furthermore, we evaluated the impact of phacoemulsification and intraocular lens implantation with DSO.

Faster corneal clearance with ROC-i was found to be statistically significant ($P< 0.05$), with the mean time for clearance almost twice as fast. This is in keeping with current cell biology theory. The densely packed monolayer of hexagonal endothelial cells exhibits strong contact inhibition. It has been found that the p27Kip1, a cyclin-dependent kinase prevents the transition of the endothelial cells to the S phase and hence remains in the arrested G1 phase.[35,36] Okumura et al[38] identified the Y-27632 ROC-i which is responsible for promoting adhesion, survival, and proliferation of corneal endothelial cells in vitro. These prowound healing properties of the corneal endothelium were confirmed when ROC-i were either injected intracamerally with cell suspension or applied topically.[39]

It is interesting to note that in our univariable analysis, it was found that younger patients had a higher propensity to fail. This response was noted by Soh et al and Moloney et al,[30,33] where in these early studies, the younger patients

TABLE 3. Summary of Patient Preoperative and Intraoperative Data

	All Groups (SD)
Mean patient age, yr (SD)	67 (9)
Female sex, n (%)	40 (75)
Laterality: left eyes (%)	31 (49)
Mean BCVA, logMAR (SD)	0.37 (0.20)
Mean central corneal thickness, μm (SD)	632 (64)
*Mean central ECD, cells/mm^2 (SD)	787 (273)
Mean peripheral ECD, cells/mm^2 (SD)	1532 (592)
Combined phacoemulsification and DSO surgery, n (%)	30 (44)
4.00-mm descemetorhexis size, n (%)	62 (91)

*Availability for 4 patients.

TABLE 4. Preoperative and Intraoperative Predictive Factors for DSO Success

	Success (SD)	Failure (SD)	*P*
Mean patient age, yr (SD)	68.7 (8)	58.6 (12)	**0.017**
Sex, female, n (%)	35 (87)	5 (13)	0.198
Presenting BCVA, logMAR, (SD)	0.36 (0.20)	0.43 (0.18)	0.218
Mean precentral ECD, cells/mm^2 (SD)	649 (383)	925 (2)	0.121
Mean central corneal thickness, μm (SD)	635 (86)	632 (86)	0.833
ROC-i use, n (%)	11 (100)	0	0.197
Combined procedure with phaco	24 (80)	6 (20)	0.317
Descemetorhexis size 4.00 mm, n (%)	57 (92)	5 (8)	**<0.001**

had a larger DSO size, which is a known factor for DSO failure. Despite adequate surgery, compliance with ROC-i, and good preoperative profiling, some patients still remain nonresponsive. As of yet, we are unable to explain the failure of some cases, and hence, it is important that discussions of a possible subsequent transplant surgery should form part of the surgical planning when taking informed consent in DSO.

The observed changes in the endothelial cell population after DSO surgery should be highlighted. In this study, the average peripheral ECC fell 21% from 1579 cells/mm^2 preoperatively to 1259 cells/mm^2 postoperatively. A similar 23% increase in central ECC occurred, from 657 cells/mm^2 to 808 cells/mm^2. This redistribution of existing peripheral and central endothelial cell populations has been seen in other studies.[24] In a case of a 5-year follow-up after DSO, peripheral ECC was found to decline initially, but stabilized over time.[24] These observations support a model whereby peripheral corneal endothelial cells regenerate the central corneal endothelium after DSO through cellular migration rather than through increased proliferation. Although varying figures for the preoperative peripheral ECC have been recommended, no study has demonstrated the minimum level of peripheral ECC for successful repopulation after DSO. However, a relatively high ECC, clear cornea, and no guttae are factors for success.[36]

Surgical technique and sizing of the DSO are important factors for success. In vitro work by Davies et al and Moloney et al demonstrates that a peeling technique is superior compared with a scoring technique.[26,30] This may not have been recognized in earlier studies, with subsequent overuse of the scoring technique leading to a slower clearance rate.[18,29,30] It has been observed that a deep stromal scar postoperatively corresponds to the location of where the scoring has taken place. The theory therefore is that scoring initiates an inflammatory proscarring response leading to stromal keratocyte proliferation and fibrosis, with specular microscopic analysis showing appearance of a stromal trench at the scored site. This can impede endothelial cells migration from the periphery into the central peeled zone.[31] Our group described a "2-flap technique" that provided a consistent and trauma-free peeling of Descemet to optimize the success of DSO.[32] Ninety-three percent of the cases had a DSO size of 4 mm which also optimized success. It is not surprising that cases of Koening et al and Arbelaez et al with a diameter of 6 to 6.5 mm failed to clear because of a smaller relative surface area of endothelial cells for migration, leading to salvage DMEK surgery.[18,29] In this study, 3 cases of persistent edge separation from DSO occurred. A probably theory is that the scoring technique induces a more traumatic removal of Descemet membrane, and in an eye which is already vulnerable with a compromised Descemet, it can lead to easier separation and hence persistent edge separation. For this reason, the proposed peeling technique described above ensures a more controlled rhexis. However, despite the edge separation, there was significant residual endothelial capacity to occupy the remaining defect and resolve the corneal edema.

In our pooled analysis, 30 cases received combined phacoemulsification and DSO. However, only 1 study by Davies et al reviewed the impact on corneal astigmatism after phacoemulsification and DSO. It was found that DSO induced an increased central posterior float localized to the site of DM stripping with a tendency for the cornea to thin.[30,31,33] Irregular astigmatism can occur after DSO but is often minimal. Furthermore, it was found that DSO induces a 0.5-D hyperopic shift, which should be considered when calculating intraocular lens power.

DSO Decision Tree Algorithm for FECD Surgical Management

A decision tree algorithm (Fig. 3) was constructed to guide clinicians in case selection for FECD. One of the critical aspects to DSO success is patient selection. The top 3 symptoms reported are glare, photophobia, and reduced vision.[21,24–26] Many of the symptoms of glare and blur are attributed to corneal guttae.[21] This can cause diagnostic

TABLE 5. Preoperative and Postoperative Patient Characteristics Comparing the ROC-i and Observation Group

	Observation Group (SD)	ROC-i Group (SD)	*P*
Mean time of follow-up, mo (SD)	13.1 (12)	9.2 (4.7)	0.740
Surgical success rate, n (%)	44 (76)	11 (100)	0.081
Preoperative			
Mean peripheral ECD, cells/mm^2 (SD)	1625 (642)	1239 (91)	—
Mean central corneal thickness, μm (SD)	623 (64)	673 (50)	—
Postoperative			
Mean time for corneal clearance, wk (SD)	10.1 (5.9)	4.92 (1.8)	**<0.0001**
Mean BCVA, logMAR (SD)	0.15 (0.23)	0.15 (0.29)	0.903
Mean central ECD, cells/mm^2 (SD)	765 (169)	1086 (59)	**<0.0001**
Mean peripheral ECD, cells/mm^2 (SD)	1297 (502)	1151 (245)	0.676
Mean central corneal thickness, μm (SD)	580 (64)	583 (53)	0.871

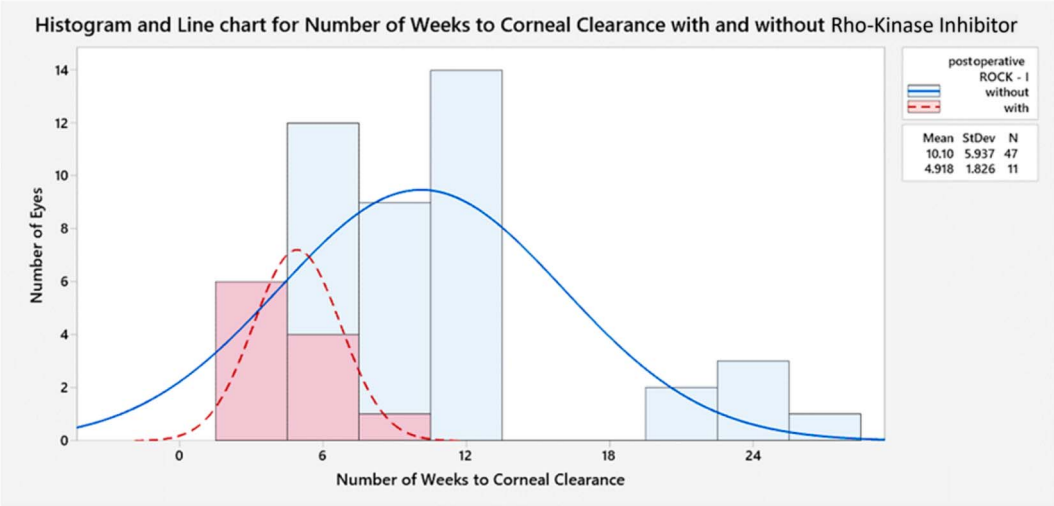

FIGURE 2. Histogram and line chart showing number of weeks to corneal clearance with or without ROC-i. (The full color version of this figure is available at www.corneajrnl.com.)

difficulties, especially when there are coexistent cataracts. As a result, clinical evaluation of the endothelium is an important indicator that aids with DSO decision making. Krachmer grading of an area of confluent guttae in the central 5 mm zone or less (grade 4) is a useful sign to determine the maximum potential range for DSO treatment.[30] This was one of the inclusion criteria detailed by both Moloney and Macsai.[21,27] If there is clinical evidence of symptomatic cataracts but mild Fuchs dystrophy (Krachmer grade 1 or less), then proceeding with cataract surgery is sensible with careful consenting for possible decompensation and future surgical interventions. Another consideration is that patients receiving DSO must have a normal peripheral ECC with clinically clear periphery and only central guttae. Dilated examination of the endothelium using retroillumination provides a good measure for assessing the geographical distribution and density of guttae. One of the major challenges that still remain is the objective measurement of the peripheral ECC. A number of instruments have been used to objectively measure the peripheral and central ECC, including the Nidek ConfoScan4 (Nidek, Japan), Topcon SP-2000 (Topcon, Japan), and Heidelberg Retina Tomograph 3 (HRT3, Heidelberg Engineering, Germany).[19,24,28] Using the HRT with the cornea module may help measure the far periphery; however, these machines are not as widely available and are limited by not being able to measure the same area each time. In addition, current specular technology only measures paracentrally and do not reach the periphery. In our experience, taking the average of 4 peripheral points on the ECC with the specular microscope allows us to measure the peripheral cell count.

Corneal decompensation or corneal central scarring secondary to corneal edema from FECD is indicative of an end-stage disease process not amenable to DSO surgery. Existing techniques of DMEK with possible cataract surgery is best suited for such a scenario.

In our subgroup analysis, we found a statistically significant clearance after DSO in ages above 68 years. This was contrary to our expectations because we would expect that younger patients have higher ECCs and thus would have increased peripheral endothelial cells to regenerate the central corneal endothelium. We suspect many of the early adopters of the DSO technique used a 360 degrees scoring surgical technique,[19,25,28] which may have impeded successful endothelial migration. Furthermore, younger patients were selected as DSO candidates, believing that they would have healthier endothelial cells existed in this cohort. If older than 60 years, concurrent cataract formation is likely and hence its extraction is recommended.[18,19,26,28] If younger than 60 years, then preservation of the crystalline lens will also preserve the patient's accommodation; however, this is at the discretion of the clinician.

Limitations

About limitations of the primary studies, there is a lack of a universal definition of corneal clearance. This could affect the precise time end point of resolution, thus affecting the final results. Similarly, there is lack of conformity in the surgical technique of DSO used, and in some of the studies, the technique was not well documented. This makes it difficult for comparison purposes. It would have been interesting to see the specific time point at which vision began to plateau and improve, to help identify the recovery period after DSO more accurately. Refractive outcomes after combined cataract surgery and DSO were often not reported but are worth evaluating in future studies. The search strategy was restricted to the English language literature. Furthermore, we were unable to get full access to the individual data sets from 3 studies.[25,26,37] Another important limitation and an area for future research is the detection and objective measurement of the peripheral ECC. There are still ongoing diagnostic challenges in accurately and repeatedly obtaining such cell counts. Furthermore, it is important to understand the minimum peripheral endothelial cell threshold for successful DSO.

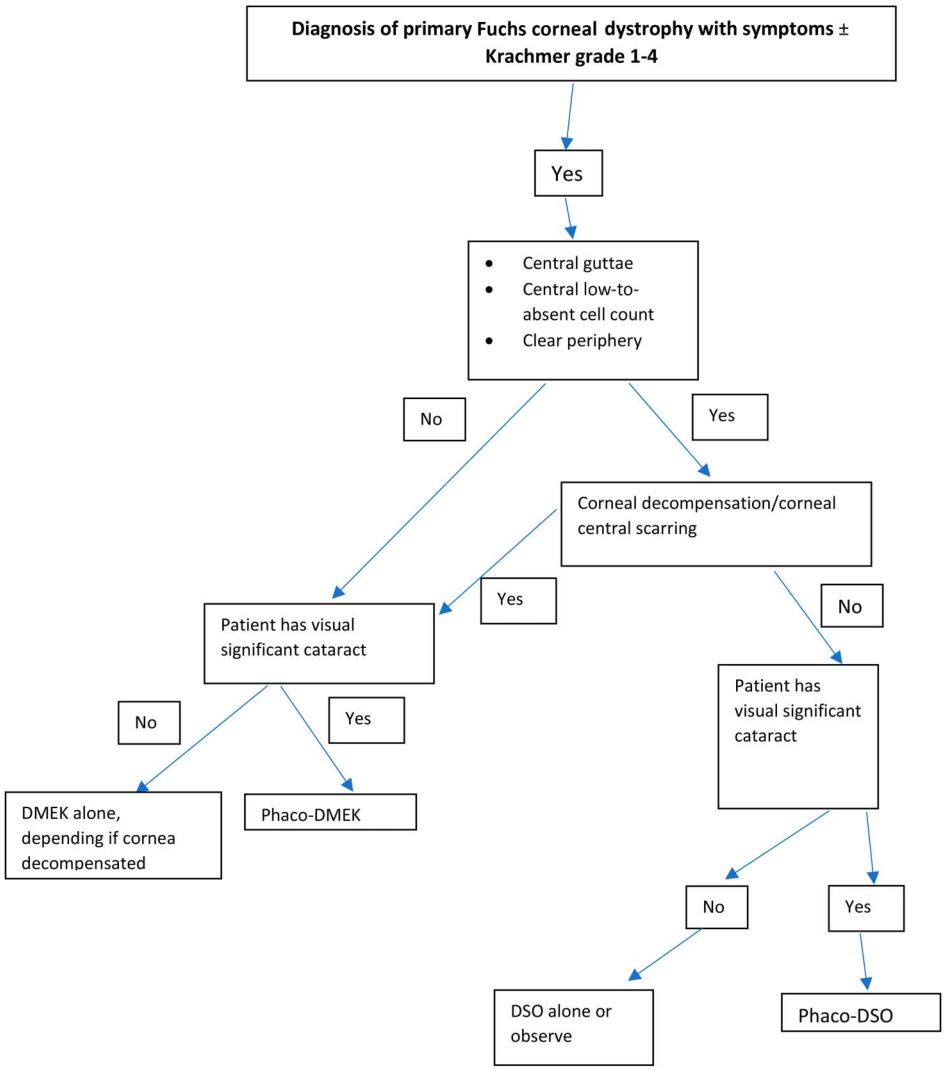

FIGURE 3. DSO decision tree algorithm for FECD. (The full color version of this figure is available at www.corneajrnl.com.)

CONCLUSION

This study demonstrates that DSO has a role in the treatment algorithm for FECD. No serious complications were encountered in this pooled study with no severe adverse effects noted with topical ROC-i. DSO remains a promising technique with obvious advantages. With global shortages of donor tissue in both short and long term, alongside an inability of developing countries to access eye banks, DSO provides a strategy to treat FECD with a less invasive surgical procedure that minimizes complications and costs of lamellar keratoplasty.[34] Furthermore, the absence of graft rejection and long-term sequelae associated with graft surgery management, renders DSO a promising technique for the corneal surgeon. Future well-designed prospective studies are necessary to further define the success of both DSO and ROC-i in this setting.

REFERENCES

1. Harris JE, Nordquist LT. The hydration of the cornea. I. The transport of water from the cornea. *Am J Ophthalmol*. 2000;40:100–110.
2. Maurice DM. Cellular membrane activity in the corneal endothelium of the intact eye. *Experientia*. 1968;24:1094–1095.
3. Maurice DM. The location of the fluid pump in the cornea. *J Physiol*. 1972;221:43–54.
4. Joyce NC, Meklir B, Joyce SJ, et al. Cell cycle protein expression and proliferative status in human corneal cells. *Invest Ophthalmol Vis Sci*. 1996;37:645–655.
5. Amann J, Holley GP, Lee SB, et al. Increased endothelial cell density in the paracentral and peripheral regions of the human cornea. *Am J Ophthalmol*. 2003;135:584–590.
6. Schimmelpfennig BH. Direct and indirect determination of nonuniform cell density distribution in human corneal endothelium. *Invest Ophthalmol Vis Sci*. 1984;25:223–229.
7. Bourne WM. Biology of the corneal endothelium in health and disease. *Eye (Lond)*. 2003;17:912–918.
8. Gain P, Jullienne R, He Z, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol*. 2016;134:167–173.
9. Krachmer JH, Purcell JJ Jr, Young CW, et al. Corneal endothelial dystrophy. A study of 64 families. *Arch Ophthalmol*. 1978;96:2036–2039.
10. Vogt A. Weitere ergebnisse der spaltlampenmikroskopie des vordern bulbusabschnittes. *Graefes Arch Clin Exp Ophthalmol*. 1921;106:63–103.
11. Melles GR, Eggink FA, Lander F, et al. A surgical technique for posterior lamellar keratoplasty. *Cornea*. 1998;17:618–626.

12. Terry M, Ousley P. Deep lamellar endothelial keratoplasty in the first United States patients. *Cornea*. 2001;20:239–243.
13. Melles GR, Ong TS, Ververs B, et al. Descemet membrane endothelial keratoplasty (DMEK). *Cornea*. 2006;25:987–990.
14. Nanavaty MA, Wang X, Shortt AJ. Endothelial keratoplasty versus penetrating keratoplasty for Fuchs' endothelial dystrophy. *Cochrane Database Syst Rev*. 2014;2:CD008420.
15. Marques RE, Guerra PS, Sousa DC, et al. DMEK versus DSAEK for Fuchs' endothelial dystrophy: a meta-analysis. *Eur J Ophthalmol*. 2019; 29:15–22.
16. Stuart AJ, Romano V, Virgili G, et al. Descemet's membrane endothelial keratoplasty (DMEK) versus Descemet's stripping automated endothelial keratoplasty (DSAEK) for corneal endothelial failure. *Cochrane Database Syst Rev*. 2018;6:CD012097.
17. Dapena I, Ham L, Melles GR. Endothelial keratoplasty: DSEK/DSAEK or DMEK: the thinner the better? *Curr Opin Ophthalmol*. 2009;20: 299–307.
18. Koenig SB. Long-term corneal clarity after spontaneous repair of an iatrogenic descemetorhexis in a patient with Fuchs' dystrophy. *Cornea*. 2013;32:886–888.
19. Dirisamer M, Ham L, Dapena I, et al. Descemet membrane endothelial transfer: "free-floating" donor Descemet implantation as a potential alternative to "keratoplasty." *Cornea*. 2012;31:194–197.
20. Dirisamer M, Yeh RY, van Dijk K, et al. Recipient endothelium may relate to corneal clearance in Descemet membrane endothelial transfer. *Am J Ophthalmol*. 2012;154:290–296.e1.
21. Moloney G, Petsoglou C, Ball M, et al. Descemetorhexis without grafting for Fuchs' endothelial dystrophy-supplementation with topical ripasudil. *Cornea*. 2017;36:642–648.
22. Paufique L. Lamellar keratoplasty. In: Rycroft BW, ed. *Corneal Grafts*. London, United Kingdom: Butterworth and Co, Ltd; 1955:132–133.
23. PRISMA. PRISMA checklist; 2021. Available at: http://www.prisma-statement.org/PRISMAStatement/Checklist. Accessed November 22, 2021.
24. Artaechevarria Artieda J, Wells M, Devasahayam RN, et al. 5-year outcomes of Descemet stripping only in Fuchs dystrophy. *Cornea*. 2020; 39:1048–1051.
25. Huang MJ, Kane S, Dhaliwal DK. Descemetorhexis without endothelial keratoplasty versus DMEK for treatment of Fuchs endothelial corneal dystrophy. *Cornea*. 2018;37:1479–1483.
26. Davies E, Jurkunas U, Pineda R II. Predictive factors for corneal clearance after descemetorhexis without endothelial keratoplasty. *Cornea*. 2018;37:137–140.
27. Macsai MS, Shiloach M. Use of topical rho kinase inhibitors in the treatment of Fuchs dystrophy after Descemet stripping only. *Cornea*. 2019;38:529–534.
28. Iovieno A, Neri A, Soldani AM, et al. Descemetorhexis without graft placement for the treatment of Fuchs endothelial dystrophy: preliminary results and review of the literature. *Cornea*. 2017;36:637–641.
29. Arbelaez JG, Price MO, Price FW Jr. Long-term follow-up and complications of stripping Descemet membrane without placement of graft in eyes with Fuchs endothelial dystrophy. *Cornea*. 2014;33: 1295–1299.
30. Moloney G, Garcerant Congote D, Hirnschall N, et al. Descemet stripping only supplemented with topical Ripasudil for Fuchs endothelial dystrophy 12-month outcomes of the Sydney Eye Hospital Study. *Cornea*. 2021;40:320–326.
31. Garcerant D, Hirnschall N, Toalster N, et al. Descemet's stripping without endothelial keratoplasty. *Curr Opin Ophthalmol*. 2019;30: 275–285.
32. Cohen E, Din N, Mimouni M, et al. Surgical technique for Descemet stripping only–the "two flaps" technique. *Cornea*. 2021;40:1211–1214.
33. Soh YQ, Peh G, George BL, et al. Predicative factors for corneal endothelial cell migration. *Invest Ophthalmol Vis Sci*. 2016;57:338–348.
34. Ang M, Moriyama A, Colby K, et al. Corneal transplantation in the aftermath of the COVID-19 pandemic: an international perspective. *Br J Ophthalmol*. 2020;104:1477–1481.
35. Krachmer JH. Corneal endothelial dystrophy. *Arch Ophthalmol*. 1978; 96:2036.
36. Ong Tone S, Kocaba V, Böhm M, et al. Fuchs endothelial corneal dystrophy: the vicious cycle of Fuchs pathogenesis. *Prog Retin Eye Res*. 2021;80:100863.
37. Moloney G, Chan UT, Hamilton A, et al. Descemetorhexis for Fuchs' dystrophy. *Can J Ophthalmol*. 2015;50:68–72.
38. Okumura N, Ueno M, Koizumi N, et al. Enhancement on primate corneal endothelial cell survival in vitro by a ROCK inhibitor. *Invest Ophthalmol Vis Sci*. 2009;50:3680–3687.
39. Okumura N, Okazaki Y, Inoue R, et al. Effect of the rho-associated kinase inhibitor eye drop (Ripasudil) on corneal endothelial wound healing. *Invest Ophthalmol Vis Sci*. 2016;57:1284–1292.