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doi.org/10.58931/cect.2024.3242

Endothelial Corneal Dystrophy

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Introduction

Fuchs endothelial corneal dystrophy (FECD) was first described by Ernst Fuchs in 1910. It is a bilateral corneal endothelial dystrophy characterized by progressive loss of corneal endothelial cells and formation of excrescences at the level of Descemet's membrane called guttae. The diseased endothelium leads to corneal edema and loss of corneal clarity. FECD typically manifests in the fifth and sixth decade of life coinciding with the development of cataracts. Careful preoperative evaluation and surgical technique allows for selection of patients who can safely undergo cataract surgery alone. Some patients, however, would benefit from both cataract surgery and endothelial transplantation (EK). This can be done as a staged surgery (cataract surgery then EK or vice versa) or in combination as a single procedure. This review evaluates the management strategies for individuals with cataract and FECD to help guide surgical decision-making and planning.

Pre-operative Assessment

Patient History

Clinical history should aim to differentiate if symptoms are related to cataract, FECD, or both. Symptoms such as glare, blurry vision and decreased contrast sensitivity overlap between FECD and cataracts. FECD patients may experience blurry vision upon awakening which gradually improves throughout the day. They may also report a foreign body sensation and pain if bullae are present.[1,2] Cataracts are more likely to cause a significant myopic shift.

Slit Lamp Exam & Diagnostic Testing

Slit lamp examination should assess the presence and distribution of guttae, typically described as a beaten bronze appearance. Guttata in FECD tend to be central and slowly become more prominent peripherally. By contrast, Hassall-Henle bodies represent peripheral guttata that are not associated with corneal edema and are seen as a normal change in the cornea with advancing age. Signs of manifest corneal edema, such as epithelial or stromal edema, Descemet's folds, or posterior fibrosis, should be evaluated. Most patients seen in clinical practice have Stage I or II disease (**Table 1**). When evaluating the cataract, it is important to assess cataract density and depth of the anterior chamber. A denser lens and shallow anterior chamber indicate higher risk of increased cumulative dissipated energy (CDE) near the corneal endothelium and a higher risk of corneal decompensation with surgery.

Diagnostic Testing

Slit lamp examination does not account for the presence of subclinical edema, an important indicator for the risk of corneal decompensation following cataract surgery. Diagnostic testing plays a role in evaluating FECD patients with subclinical edema and identifying eyes at a higher risk for post-operative corneal decompensation following cataract surgery.

Historically, central corneal thickness (CCT) >640 µm measured with pachymetry was used as a marker to predict risk of corneal edema following cataract surgery. CCT is now understood to be a weak predictor of prognosis, especially without previous measurements to compare to which may indicate progressive corneal edema.

Specular microscopy provides information on endothelial cell density (ECD); variable enlargement (polymegethism), loss of hexagonal shape (pleomorphism), guttae variation, and CCT. Risk factors for persistent post-operative corneal edema include endothelial cell count below 1000 cells/mm^2, high pleomorphism (>50% of non-hexagonal cells), and high polymegethism (>0.4 coefficient of variation).[3] When significant cell dropout has occurred, specular microscopy decreases in accuracy given that the guttae cannot easily be measured, characterized, and counted. Confocal biomicroscopy has shown promise for measuring corneal transparency and assessing backscatter, an objective measurement

Stage	Vision loss	Symptoms	Clinical Findings
I	None	Rare glare Mild colour vision deficit	• Non-confluent central guttae • Pigment deposition on posterior surface • Grayish thickened Descemet membrane
II	Mild	Diurnal glare	• Confluent central guttae with peripheral spread • Transient stromal edema
III	Moderate	Painful hydrops	• Persistent stromal edema • Epithelial and subepithelial microcysts and bullae
IV	Severe	Painless	• Peripheral neovascularization • Subepithelial pannus, scarring, and opacification

Table 1. Clinical stages of Fuchs endothelial corneal dystrophy; *adapted from Adamis AP et al. Fuchs endothelial dystrophy of the cornea. Surv Ophthalmol.1993;38:149–68.*

of corneal haze. Both specular and confocal microscopy can be operator-dependant and not easily accessible by all ophthalmologists.

Corneal tomography is emerging as a valuable tool for identifying subclinical edema in FECD. Three markers have been identified to indicate subclinical corneal edema and risk of decompensation following cataract surgery.[4] These include: **(1)** loss of regular isopachs; **(2)** displacement of the thinnest corneal point; and **(3)** focal posterior corneal surface depression.[4] The four-year cumulative risk of progression/intervention after uncomplicated cataract surgery was 0% when no features were present, 50% when one or two features were present, and 75% when all features were present.[5] Corneal tomography can guide ophthalmologists in deciding whether a combined procedure should be considered and assist with counselling patients regarding their risk of significant progression in subsequent years. Arnalich-Montiel *et al.* developed a pre-operative risk score with high sensitivity and specificity, predicting the risk of corneal decompensation using Pentacam indices, including anterior layer corneal backscatter and changes in CCT.[6]

Cataract Surgery Alone

Surgical planning

Once it has been determined that a patient has a visually significant cataract in the context of FECD, patients need to be informed regarding the risk of post-operative refractive error, delayed healing, corneal decompensation, and potential need for EK.

For patients exhibiting visually significant cataract without evidence of sub-clinical or manifest edema, standalone cataract surgery is recommended, preferably performed early to minimize the risk of increased ultrasound energy causing greater endothelial damage.[1] When mild subclinical edema is present, cataract surgery can also be performed when accompanied by detailed consent regarding the risk of EK post-operatively.

Intraocular Lens Selection

Intraocular lens (IOL) selection requires a detailed pre-operative discussion due to the risk of post-operative refractive error. A hydrophobic monofocal IOL is recommended due to the potential need for EK. Hydrophilic IOLs should be avoided due to the risk of calcification and opacification after EK.[1]

FECD is postulated to cause swelling of the posterior cornea leading to posterior corneal

flattening and a myopic shift. Thus, Wacker *et al.* suggested that surgeons should target myopia (-0.50 to -1.25) in eyes with FECD.[7] When both eyes require surgery, post-operative refractive shift in the first eye can be used as a reference in optimizing refractive outcomes in the second eye.[1]

In cases where the patient seeks spectacle independence, the consideration of a toric IOL is possible; however, meticulous preoperative evaluation and discussion with the patient are crucial to minimize the risk of dissatisfaction. The corneal edema associated with FECD causes flattening of the posterior cornea surface and a hyperopic shift. This resolves if the patient proceeds to receive a corneal transplant. In mild cases of FCED without significant corneal edema, toric IOLs can be considered when the astigmatism is regular, stable, and repeatable. Obtaining optical biometry and corneal tomography prior to the development of corneal edema can aid in determining the potential for astigmatism correction at the time of cataract surgery.[8] Biometry measurements become unpredictable as edema progresses, therefore caution should be used prior to selecting a toric IOL in advanced stages of disease. The use of multifocal IOLs is relatively contraindicated in patients with FECD. With time, patients with FECD experience reduced contrast sensitivity, glare, and decreased vision. This is compounded by the implantation of a multifocal IOL leading to compromised vision post-operatively, even when done following successful Descemet's membrane endothelial keratoplasty (DMEK).[9] If a patient is keen for astigmatic correction or spectacle independence but also requires a corneal transplant, a staged procedure is recommended as discussed below.

Future directions of IOL options may include a light adjustable lens (LAL). The LAL is made of a photosensitive silicone material and allows post-operative adjustments using targeted UV light exposure. This would be especially helpful to fine tune the refractive target following the resolution of corneal edema after cataract surgery or when done in combination with EK.[10]

Surgical Technique

In general, surgeons should utilize techniques that minimize the time of surgery and CDE. Torsional emulsification mode, lower bottle height, higher vacuum, and a phaco-chop technique where nucleus disassembly occurs within the capsular bag have been shown to minimize CDE. However, it is important to utilize the safest technique that each surgeon is most comfortable with. Ophthalmic viscosurgical devices (OVDs) are essential in cataract surgery to protect the endothelium. Generous amounts of cohesive OVDs should be used to protect the endothelium. Aliquots of cohesive OVD can be reapplied through surgery to ensure adequate coverage of the endothelium during nucleus disassembly and lens insertion. A soft-shell technique whereby a dispersive viscoelastic is used to coat the endothelium and is then followed by a cohesive OVD to deepen the anterior chamber and push the dispersive OVD upwards towards the cornea has also been shown to minimize cell loss.[11] At the conclusion of the case, excessive or forceful wound should be avoided to minimize the risk of Descemet's detachment.

Post-operative Care and Complications

Post-operative care following cataract surgery for patients with FECD is similar to that of standard procedures. Full visual recovery may be delayed if post-operative edema is present. Corneal clarity can take up to three months; hypertonic saline can be added when corneal edema persists. It has been shown that cases with intra-operative complications were 6 times more likely to develop post-operative corneal edema compared to those without intraoperative complications.[12] If a posterior capsular tear occurs during surgery, anterior chamber IOLs should be avoided; instead plan for a secondary scleral sutured or sulcus fixated IOL. If posterior capsular opacification occurs, Nd:YAG capsulotomy should also be delayed due to risk of posterior lens dislocation during EK if transplantation is required in the future.

Cataract Surgery Combined with EK in Patients with FECD

For patients with both a visually significant cataract and FECD with manifest corneal edema, both cataract surgery and EK are required. DMEK is now the most common and preferred surgery for FECD. Cataract surgery can be performed before (Phaco-DMEK), after (DMEK-Phaco) or combined as a single procedure. The decision to perform a staged or combined procedure depends on multiple variables. A meta-analysis of staged surgeries found no statistical difference between staged (Phaco-DMEK) or combined procedures regarding corrected distance visual acuity

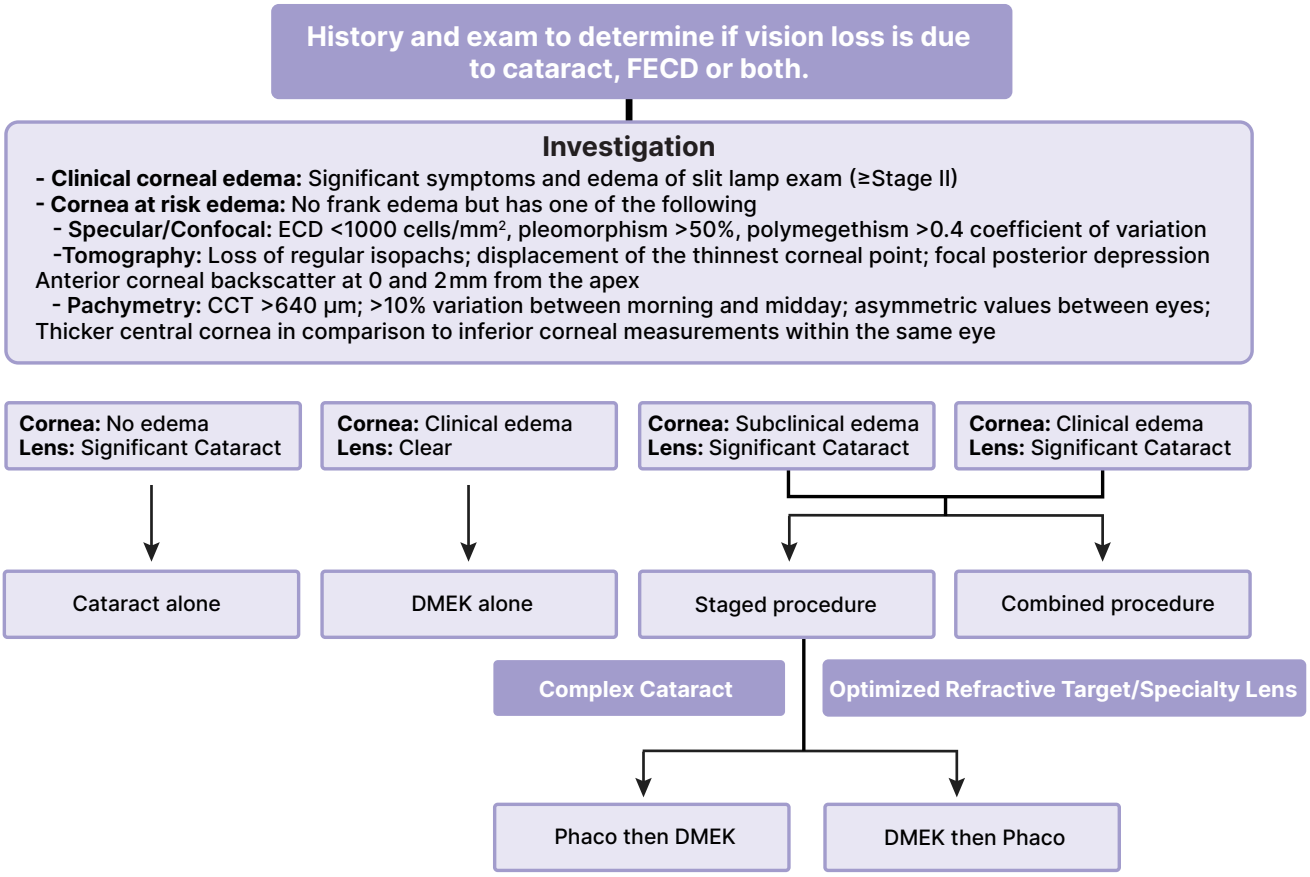

Figure 1. Algorithm describing authors approach to Fuchs endothelial corneal dystrophy (FECD) with cataract; *adapted from Ali M et al.*

improvement, post-operative ECD, re-bubbling, and primary graft failure rate.[13] Combined surgery offers the advantage of faster visual recovery and reduced risks and costs compared to undergoing two separate procedures. Cataract surgery before DMEK can be used in young patients to preserve accommodation, or in complex eyes with higher risk of complication during surgery. DMEK followed by cataract surgery is increasingly being used to optimize refractive outcomes for patients with FECD. In these cases, DMEK is performed followed by cataract surgery 3–5 months later once optical biometry has stabilized. Ultimately, the decision to opt for a staged or combined procedure should be guided by the surgeon's expertise and patient preference.[1]

Conclusion

Managing cataracts in individuals with FECD poses unique challenges for both the attending ophthalmologist and the patient. A comprehensive evaluation of the patient's medical history, slit lamp examination and diagnostic tests to detect subclinical edema are imperative. Tailoring the management approach to each patient is essential, considering the stage of the disease, cataract density, and surgeon and patient preferences (**Figure 1**). Careful surgical technique can allow for cataract surgery to be performed alone; however, some patients would benefit from both cataract surgery and EK. The choice of a combined surgery vs staged surgery is dependent on surgeon preferences and the patient's expectations regarding refractive outcome. As with any surgery, a thorough discussion with the patient is paramount to ensure satisfaction.

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Financial Disclosures

D.C.: None declared.
R.D.: None declared.

References

1. Ali M, Cho K, Srikumaran D. Fuchs Dystrophy and Cataract: Diagnosis, Evaluation and Treatment. Ophthalmol Ther 2023;12(2):691-704. doi: 10.1007/s40123-022-00637-1 [published Online First: 2023/01/14]
2. Elhalis H, Azizi B, Jurkunas UV. Fuchs endothelial corneal dystrophy. The ocular surface 2010;8(4):173-84. doi: 10.1016/s1542-0124(12)70232-x [published Online First: 2010/10/23]
3. Weisenthal RW. Basic and Clinical Science Course. Section 08: External Disease and Cornea. 2020-2021 ed: American Academy of Ophthalmology 2018:24.
4. Sun SY, Wacker K, Baratz KH, et al. Determining Subclinical Edema in Fuchs Endothelial Corneal Dystrophy: Revised Classification using Scheimpflug Tomography for Preoperative Assessment. Ophthalmology 2019;126(2):195-204. doi: https://doi.org/10.1016/j.ophtha.2018.07.005
5. Patel SV, Hodge DO, Treichel EJ, et al. Predicting the Prognosis of Fuchs Endothelial Corneal Dystrophy by Using Scheimpflug Tomography. Ophthalmology 2020;127(3):315-23. doi: https://doi.org/10.1016/j.ophtha.2019.09.033
6. Arnalich-Montiel F, Mingo-Botín D, De Arriba-Palomero P. Preoperative Risk Assessment for Progression to Descemet Membrane Endothelial Keratoplasty Following Cataract Surgery in Fuchs Endothelial Corneal Dystrophy. American journal of ophthalmology 2019;208:76-86. doi: https://doi.org/10.1016/j.ajo.2019.07.012
7. Wacker K, Cavalcante LCB, Baratz KH, et al. Hyperopic Trend after Cataract Surgery in Eyes with Fuchs' Endothelial Corneal Dystrophy. Ophthalmology 2018;125(8):1302-04. doi: https://doi.org/10.1016/j.ophtha.2018.03.060
8. Yokogawa H, Sanchez PJ, Mayko ZM, et al. Astigmatism Correction With Toric Intraocular Lenses in Descemet Membrane Endothelial Keratoplasty Triple Procedures. Cornea 2017;36(3):269-74. doi: 10.1097/ico.0000000000001124 [published Online First: 2016/12/22]
9. Price MO, Pinkus D, Price FW, Jr. Implantation of Presbyopia-Correcting Intraocular Lenses Staged After Descemet Membrane Endothelial Keratoplasty in Patients With Fuchs Dystrophy. Cornea 2020;39(6):732-35. doi: 10.1097/ico.0000000000002227 [published Online First: 2019/12/17]
10. Eisenbeisz HC, Bleeker AR, Terveen DC, et al. Descemet Membrane Endothelial Keratoplasty and light adjustable lens triple procedure. American journal of ophthalmology case reports 2021;22:101061. doi: 10.1016/j.ajoc.2021.101061 [published Online First: 2021/03/16]
11. Hsiao CW, Cheng H, Ghafouri R, et al. Corneal Outcomes Following Cataract Surgery Using Ophthalmic Viscosurgical Devices Composed of Chondroitin Sulfate-Hyaluronic Acid: A Systematic Review and Meta-Analysis. Clin Ophthalmol 2023;17:2083-96. doi: 10.2147/opth.s419863 [published Online First: 2023/07/31]
12. Chuckpaiwong V, Muakkul S, Phimpho P, et al. Incidence and Risk Factors of Corneal Endothelial Failure after Phacoemulsification in Patients with Fuchs Endothelial Corneal Dystrophy: A 13-Year Retrospective Cohort. Clin Ophthalmol 2021;15:2367-73. doi: 10.2147/opth.s315436 [published Online First: 2021/06/12]
13. Romano V, Passaro ML, Bachmann B, et al. Combined or sequential DMEK in cases of cataract and Fuchs endothelial corneal dystrophy—A systematic review and meta-analysis. Acta Ophthalmologica 2024;102(1):e22-e30. doi: https://doi.org/10.1111/aos.15691