Delphi-Based Global Consensus on Fuchs Endothelial Corneal Dystrophy. An Endothelial Keratoplasty Learners Group Initiative

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• PURPOSE: To identify areas of consensus among global experts for the management of Fuchs endothelial corneal dystrophy (FECD) in clinical practice, including its diagnosis, evaluation, decision-making principles with respect to intervention, and recommendations for performing cataract surgery in patients with FECD, including when to combine with keratoplasty.

• DESIGN: Modified Delphi-based global consensus.

• PARTICIPANTS: Thirty-seven ophthalmologists from around the world with significant expertise in the management and mechanisms of FECD.

• METHODS: A series of consensus statements about FECD were developed from three iterative rounds of structured questions and statements posed to the panel of experts. Two rounds were asynchronous electronic questionnaires, and the third round was a live virtual meeting. Experts responded anonymously to statements assessing consensus and to open-ended questions that invited diverse input.

• MAIN OUTCOME MEASURES: Consensus was defined as 70% agreement among experts.

• RESULTS: Consensus was reached for 90 of 91 statements after three rounds. Experts agreed that FECD is defined by the presence of central or paracentral scattered or confluent guttae with or without edema. There was strong consensus that a chronic state of subclinical edema precedes the onset of clinically detectable edema that may or may not cause symptoms. With near-unanimous consensus, disease evaluation recommendations included assessing for findings that implicate the cornea as a source of decreased vision to separate it from the effect of comorbid conditions, as this would inform whether corneal intervention is appropriate. These findings include diurnal variation in vision, clinical or subclinical (tomographic) edema, and changes or differences in central corneal thickness. Based on current evidence, experts agreed that there are no effective medical therapies for FECD, and that Descemet membrane endothelial keratoplasty is the surgical treatment of choice when indicated.

• CONCLUSIONS: The consensus statements provide current globally endorsed recommendations for the diagnosis and management of FECD. The guidelines are important and relevant for general ophthalmologists, who typically first diagnose and evaluate FECD, and for cornea special-

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ists, by allowing them to benchmark their current practice patterns against expert recommendations. This could help improve patient outcomes and establish a framework adaptable to future advances and evolving technologies in the management of FECD. (Am J Ophthalmol 2025;280: 130–143. © 2025 Elsevier Inc. All rights reserved, including those for text and data mining, AI training, and similar technologies.)

INTRODUCTION

The management of Fuchs endothelial corneal dystrophy (FECD) has rapidly evolved over the last 20 years due to advances in the understanding of the pathophysiology of the disease and improvements in surgical approaches.[1-4] Current surgical approaches result in excellent vision and graft survival over the longer-term without compromising safety.[5-7] As a result, the threshold for intervention for FECD has been safely lowered, posing new challenges for clinicians to determine when and what intervention is appropriate for individual patients with the disease.

While FECD management paradigms have changed quickly, their dissemination and adoption can be slow and perplexing, especially for practitioners with less experience with the disease. Changing practice patterns, and even the disease definition and grading of severity, can lead to controversy that might affect management.[8-10] While the American Academy of Ophthalmology provides general guidelines for the evaluation and management of corneal edema,[11] there is a need for more comprehensive and specific guidelines for managing FECD. Such guidelines, derived from broad expert consensus, will assist new clinicians and surgeons as they embark on managing cases of FECD. In addition, established clinicians and surgeons can benchmark their practice patterns against expert recommendations, recognizing that variations in practice patterns will still exist based on factors that cannot be controlled by clinicians, such as eye banking practices.

The goal of this study was to establish global consensus for the management of FECD in clinical practice, including its diagnosis, evaluation, decision-making principles with respect to intervention, and recommendations for cataract surgery and keratoplasty. The consensus statements were intended to benefit general ophthalmologists and other eye care professionals in addition to cornea specialists. A modified Delphi method was used to achieve consensus from global experts in the field of FECD by posing several iterative rounds of structured questions and statements to develop consensus about the disease.[12-15] The Delphi process for this study was facilitated by the Endothelial Keratoplasty Learners Group (EKLG), which comprises a large network of practicing cornea specialists with extensive experience in managing corneal endothelial diseases. The EKLG leadership also leveraged its prior experience with Delphi studies, including the development of consensus guidelines for endothelial keratoplasty (EK).[16]

METHODS

A modified Delphi method was used to obtain consensus from a global panel of experts about clinical management aspects of FECD. The Delphi process was facilitated and coordinated by the leadership of the EKLG. An executive committee was convened in February 2024 as a scientific advisory panel to oversee a structured process for gathering data from a larger and broader group of experts. The executive committee (Table 1) comprised the proponents of the FECD Delphi Global Consensus, who were leaders in the field of FECD, and leaders from EKLG. In addition to project oversight, the executive committee proposed the expert panel members, designed the structured questions and statements posed to the panel, reviewed the results of each round, and were responsible for drafting the final manuscript. This study was deemed exempt from review by the Mayo Clinic Institutional Review Board.

- **THEMES:** To create practical consensus guidelines relevant to both general ophthalmologists and cornea specialists, six themes were defined to address key aspects of the management of FECD. The six themes were (1) diagnosis, including criteria for diagnosis and disease terminology; (2) pathogenesis, including current understanding of disease mechanisms as relevant to clinical practice and patient education; (3) disease severity evaluation, including clinical assessment and ancillary testing with recommendations for interpretation with respect to disease management; (4) non-surgical interventions, including current options for conservative management; (5) cataract surgery in FECD, including timing, indications, and surgical considerations; and (6) corneal surgical intervention, including timing, options, and recommendations for surgical management. With recent Delphi consensus EKLG guidelines for EK,[16] topics related to EK were omitted from the present study unless they were specifically relevant to FECD.

- **GLOBAL EXPERTS:** A panel of potential participants (experts) was proposed by members of the executive committee based on several criteria. Experts were ophthalmologists with significant experience in the management and mechanisms of FECD, as evidenced by scientific authorship in leading journals and/or recognition as a leader in the field through participation in presentations or panels at national and international meetings. All participants had to be willing to complete questionnaires in English in a timely manner and to attend a live virtual meeting for the final round

TABLE 1. Experts, Listed Alphabetically By Continent of Clinical Practice Location

North America	
Keith H. Baratz	Rochester, MN, USA
Winston Chamberlain	Portland, OR, USA
Kathryn Colby	New York, NY, USA
Mark A. Greiner	Iowa City, IA, USA
Ula V. Jurkunas[a]	Boston, MA, USA
Ellen H. Koo	Miami, FL, USA
W. Barry Lee	Atlanta, GA, USA
Gregory Moloney	Vancouver, Canada
V. Vinod Mootha	Dallas, TX, USA
Sanjay V. Patel[a]	Rochester, MN, USA
Roberto Pineda[a]	Boston, MA, USA
Francis W. Price Jr	Indianapolis, IN, USA
Divya Srikumaran	Baltimore, MD, USA
Mark A. Terry	Portland, OR, USA
Peter B. Veldman	Chicago, IL, USA
David D. Verdier	Grand Rapids, MI, USA
Central & South America	
Ticiano Giobellina	Córdoba, Argentina
Nicolas Cesário Pereira	Sorocaba, Brazil
Luis Mejia	Medellín, Colombia
Europe	
Bruce Allan	London, UK
Lamis Baydoun	Zurich, Switzerland
Maninder Bhogal[a]	London, UK
Claus Cursiefen	Cologne, Germany
Jesper Hjortdal	Aarhus, Denmark
Viridiana Kocaba	Lyon, France
Mario Matthaei	Cologne, Germany
Marc Muraine	Rouen, France
Vito Romano[a]	Brescia, Italy
Asia	
Samar K. Basak	Kolkata, India
Sunita Chaurasia	Hyderabad, India
Nidhi Gupta[a]	Delhi, India
Akira Kobayashi	Kanazawa, Japan
Eitan Livny	Tel Aviv, Israel
Jodhbir S. Mehta	Singapore, Singapore
Yoshinori Oie	Osaka, Japan
Naoki Okumura[a]	Kyoto, Japan
Australasia/Oceania	
John J Males	Sydney, Australia
Round 3 Live Meeting Moderator	
Pravin Vaddavalli	Hyderabad, India

[a]Members of the Executive Committee.

of the process. In addition, participants were selected to encompass broad geographical diversity, recognizing that practice patterns vary based on local resources, patient population, and eye banking availability and methods. Experts were invited to participate with an explanation of the goals, process, and requirements for inclusion, and their consent to participate.

• **QUESTIONNAIRE ROUNDS:** The first two rounds of the modified Delphi process were questionnaires posed to the panel of experts in March and May 2024, respectively. The third round of the process was a live virtual meeting of the global experts in September 2024. The live virtual meeting was facilitated by a cornea specialist (Table 1) who was not involved in the voting rounds. For each round, the executive committee drafted short statements and multiple-choice items relevant to the six themes. Rounds 1 and 2 questionnaires were circulated electronically with automated reminders (by using Google Forms, https://docs.google.com/forms/u/0/) sent to non-respondents until all responses were submitted; there was no group discussion so that experts were free to respond anonymously with their own opinions. Some statements assessed consensus (ie, "agree" or "disagree" statements) whereas others were open-ended to encourage diverse input. In Rounds 1 and 2, experts were invited to provide free text anonymous comments about any ambiguity of statements, alternate wording suggestions, or additional statements relevant to the project. For the live virtual meeting, consensus statements were presented electronically using a live polling system with experts stating their agreement or disagreement anonymously.

After each round, anonymous responses were collated by the EKLG administrative support team and distributed to the executive committee for review. Statements that achieved consensus were removed from subsequent rounds. Statements that did not reach consensus were revised based on wording and feedback received from the experts and presented at the next round. Anonymous responses to open-ended questions were reformulated as consensus statements for the next round. Statements not reaching consensus at the Round 3 live virtual meeting were discussed as a group at the same meeting and revised based on input. After each round, final consensus statements were shared with all experts to ensure their clarity.

For consistency and to reduce ambiguity when responding to statements, experts were asked to consider that tomography referred to Scheimpflug tomography and anterior segment optical coherence tomography, depending on which modality they used,[17] and that central corneal thickness (CCT) was determined by their preferred method in routine clinical practice. Experts were also informed that "confluent" and "scattered" guttae were as assessed by clinical slit-lamp examination instead of by specular microscopy. Finally, knowing that not all experts were performing Descemet stripping only (DSO),[18,19] experts without experience with DSO were asked to respond to statements about DSO based on their current knowledge and opinion.

• **DEFINITION OF CONSENSUS:** Consensus was defined *a priori* as ≥70% of experts agreeing with a statement, con-

TABLE 2. Diagnosis: Criteria for Diagnosis and Disease Terminology

Statement	Agreement (%)	Round	Level of Consensus
From a clinical perspective, *cornea guttata* (defined as non-progressive central guttae or central guttae in asymptomatic patients) and FECD represent different severities of the same disease rather than different diseases	73	2	M
The diagnosis of FECD is made clinically by slit-lamp examination	76	1	M
FECD can be diagnosed if guttae (whether scattered or confluent) are present in the central and/or paracentral cornea, and the findings are typically bilateral and symmetric	87	2	S
The presence of subclinical edema or clinically detectable edema is not required to diagnose FECD	89	2	S
It is not necessary to confirm the diagnosis of FECD with specular/confocal microscopy for documentation purposes	73	2	M
Compared to true guttae, pseudoguttae are typically unilateral and associated with other findings in the history or exam	89	1	S
Pseudoguttae represent endothelial stress and can be transient examination findings	95	2	U
Endothelial dysfunction, as manifest by the presence of corneal edema, in the absence of guttae should not be diagnosed as FECD	92	1	U
Corneal edema after cataract surgery in the setting of FECD should not be termed pseudophakic corneal edema	87	1	S

FECD = Fuchs endothelial corneal dystrophy; M = moderate consensus; S = strong consensus; U = near unanimous or unanimous consensus.

sistent with accepted standards and previous studies.[16,20,21] The level of consensus was further stratified as: ≥90% agreement indicating near-unanimous consensus, for which EKLG guidelines can be considered robust and widely accepted for clinical practice; 80%-90% agreement, denoting strong consensus, for which EKLG guidelines can be considered well-suited for direct clinical implementation with a high degree of confidence; and 70%-80% agreement, indicating moderate consensus and reflecting varying opinions between experts and for which EKLG guidelines may require further research, validation, or adaptation to specific regional practices. This stratified approach enables interpretation of the consensus statements with appropriate context and confidence.

RESULTS

Invitations to participate were sent to 50 experts from 18 countries (5 continents) of whom 37 experts from 16 countries (5 continents) agreed to participate (Table 1). All 37 experts responded to Rounds 1 and 2 questionnaires, and 28 experts (76%) participated in the live virtual meeting. Final consensus statements after three rounds were shared with all 37 experts after which no further revisions were deemed necessary. Of the 37 experts, 20 (54%) who did not perform DSO provided responses related to DSO based on their knowledge and opinion.

Rounds 1 and 2 comprised 67 and 66 questions, respectively, with several questions containing sub-statements; 29 statements reached consensus after Round 1 and another 50 statements reached consensus after Round 2 (Tables 2-7). Twelve statements were reformulated for Round 3, of which 10 reached consensus through anonymous polling at the live meeting. Two statements required discussion at Round 3 after which one statement reached consensus whereas the other did not (Tables 4 and 5). A total of 90 statements reached consensus after three rounds (Tables 2-7).

• **DIAGNOSIS: CRITERIA FOR DIAGNOSIS AND DISEASE TERMINOLOGY (TABLE 2):** Moderate consensus was reached that from a clinical perspective, *cornea guttata* (defined as non-progressive central guttae or central guttae in asymptomatic patients) and FECD represent different severities of the same disease rather than different diseases. There was strong consensus that the diagnosis of FECD is based on the presence of scattered or confluent central or paracentral guttae with or without edema.

• **PATHOGENESIS: CURRENT UNDERSTANDING OF DISEASE MECHANISMS AS RELEVANT TO CLINICAL PRACTICE AND PATIENT EDUCATION (TABLE 3):** All 37 experts agreed that FECD is a disease of endothelial cell dysfunction with deposition of abnormal basement membrane, and not simply a disease of endothelial cell loss. The *transcription factor-4 (TCF4)* trinucleotide repeat expansion was unanimously recognized as the major genetic risk variant associated with FECD in western populations with other known genetic risk variants contributing a small minority of cases. There was near-unanimous consensus that a chronic state of subclinical edema precedes the onset of clinically detectable edema in FECD, with strong consensus that subclinical edema may or may not be symptomatic. Similarly,

TABLE 3. Pathogenesis: Current Understanding of Disease Mechanisms as Relevant to Clinical Practice and Patient Education

Statement	Agreement (%)	Round	Level of Consensus
Prominent disease mechanisms relevant to FECD include:			
Trinucleotide repeat expansion	89	1	S
Oxidative stress	92	1	U
Transcription factor-4 (TCF4) is the major genetic risk variant associated with FECD in US/European populations	100	2	U
Known genetic associations of FECD other than *TCF4* (eg, COL8a2, LAMC1, SLC4a11, etc.) account for a minority (<5%) of cases in US/European populations	95	2	U
FECD is a disease of endothelial cell dysfunction that generates abnormal Descemet membrane and is not simply a disease of endothelial cell loss	100	2	U
With respect to patient education, FECD is a genetic/inherited disease of corneal endothelial cell dysfunction and cell loss	97	1	U
The endothelial cell mosaic typically remains intact over guttae in earlier stages of FECD but gaps between cells may appear in more advanced states of FECD as guttae enlarge	97	2	U
A chronic state of subclinical edema precedes the onset of clinically detectable edema in FECD	92	1	U
Corneal edema is unlikely, but not impossible, when guttae are scattered	84	1	S
Early vision symptoms in FECD include loss of edge clarity, loss of contrast acuity, and disability glare	100	2	U
Central scattered guttae in the absence of subclinical or clinical edema do not usually impair vision (visual acuity and/or glare)	73	2	M
Central confluent guttae in the absence of subclinical or clinical edema can impair vision (visual acuity and/or glare)	97	2	U
Patients with central confluent guttae without subclinical or clinical edema can be asymptomatic	92	2	U
Vision can be affected by subclinical edema in FECD	92	1	U
Patients with subclinical edema in FECD can be asymptomatic	84	2	S
FECD with subclinical or clinical edema can affect color perception	76	2	M
Clinically detectable edema in FECD usually affects vision	97	2	U

FECD = Fuchs endothelial corneal dystrophy; M = moderate consensus; S = strong consensus; U = near unanimous or unanimous consensus.

there was agreement that central confluent guttae in the absence of subclinical or clinical edema can impair vision (visual acuity and/or glare), but also that patients with central confluent guttae without subclinical or clinical edema can be asymptomatic.

• **EVALUATION: CLINICAL ASSESSMENT AND ANCILLARY TESTING, WITH RECOMMENDATIONS FOR INTERPRETATION WITH RESPECT TO DISEASE MANAGEMENT (TABLE 4):** There was complete agreement that FECD should be classified based on the distribution and extent of guttae by slit-lamp examination, and the presence or absence of edema including using tomography to detect subclinical edema. There was near unanimous consensus that corneal tomography is indicated for asymptomatic patients at baseline, and moderate consensus when considering cataract surgery in FECD. There was strong consensus that measuring central endothelial cell density in FECD is not accurate when guttae are present and is therefore of little relevance to clinical decision-making. Similarly, isolated measurements of CCT are not helpful for decision-making in clinical practice, whereas changes in CCT over time, over the course of a day, or asymmetry in CCT between fellow eyes were considered relevant in clinical practice. To determine if visual symptoms could be attributed to the cornea while a cataract was also present, there was near-unanimous agreement that diurnal variation in vision, clinical or subclinical (tomographic) edema, and changes or differences in CCT (Table 4), were factors that would suggest corneal intervention would be appropriate.

Strong consensus was reached that delaying corneal intervention is appropriate when patients are asymptomatic even if subclinical edema is present, and is usually not appropriate when clinically detectable stromal or epithelial edema are present. There was strong consensus that delaying corneal intervention until epithelial edema is present can worsen the outcome of intervention.

• **NON-SURGICAL INTERVENTION: CURRENT OPTIONS FOR CONSERVATIVE MANAGEMENT (TABLE 5):** There was strong consensus that topical corticosteroids are not an appropriate medical therapy for FECD and moderate consensus that commercially available topical rho-kinase inhibitors are not effective as an isolated medical therapy for FECD. Consensus could not be reached for hypertonic saline being effective for morning vision symptoms.

TABLE 4. Evaluation: Clinical Assessment and Ancillary Testing, With Recommendations for Interpretation With Respect to Disease Management

Statement	Agreement (%)	Round	Level of Consensus
The distribution and extent of guttae by clinical slit-lamp examination can be helpful for decision-making in clinical practice	97	1	U
Distinguishing confluent from scattered guttae is best done by using slit-lamp examination (direct illumination, retroillumination, or specular reflection) to assess for areas of coalescence	89	1	S
Endothelial cells can be present in dark areas of specular microscopy images that correspond to guttae, but they may not be visible because they are outside the focal plane of the image	86	3	S
Measuring central endothelial cell density in FECD is not accurate when guttae are present and is therefore of little relevance to clinical decision making	84	2	S
It is not necessary to routinely measure peripheral endothelial cell density in FECD when considering cataract surgery without corneal intervention	84	2	S
In clinical practice, FECD should be classified based on the distribution and extent of guttae by slit-lamp examination, and the presence/absence of edema, including using tomography to detect subclinical edema	100	2	U
Isolated values of CCT are not helpful for decision making in clinical practice	87	2	S
When corneal edema in FECD is not detectable by clinical examination, an increase in CCT could signify disease progression	97	1	U
Patients with FECD with greater CCT in the morning compared to the afternoon usually have tomographic evidence of edema	95	2	U
Assuming CCT is measured at a similar time of day, *a* $\geq$10% increase in CCT over time is usually indicative of disease progression	86	3	S
Asymmetry of $\geq$10% in CCT between fellow eyes with FECD is suggestive of edema in the thicker cornea	79	3	M
A $\geq$10% increase in CCT in morning measurements compared to afternoon measurements indicates significant edema in FECD	96	3	U
When corneal edema in FECD is not detectable by clinical examination, corneal tomography can detect subclinical edema	95	1	U
When corneal edema in FECD is not detectable by clinical examination, central endothelial cell density is not a good indicator of endothelial function	78	1	M
Corneal tomography is indicated when considering cataract surgery in FECD	76	1	M
Corneal tomography is indicated when patients with FECD have vision symptoms without clinically detectable corneal edema	87	1	S
Delaying corneal intervention:			
Is appropriate when patients are asymptomatic even if subclinical edema is present	81	1	S
Is usually not appropriate when clinically detectable stromal edema is present	84	1	S
Is usually not appropriate when epithelial edema is present	92	1	U
Until epithelial edema is present can worsen the outcome of intervention	87	1	S
When determining if vision symptoms are from FECD in addition to cataract, it is appropriate to recommend corneal intervention (ie, EK or DSO) based on:			
The presence of diurnal vision variation (ie, worse vision in the morning that improves over the course of the day)	97	2	U
The presence of subclinical edema on tomography	92	2	U
Objective data (eg, tomography patterns, a significant change in CCT, etc.) in addition to subjective clinical judgement	93	3D	U
When determining if vision symptoms are from FECD in addition to cataract, it is not appropriate to recommend corneal intervention (ie, EK or DSO) based on "cutoff values" of CCT or endothelial cell density	70	2	M
Evaluating FECD by corneal tomography is not necessary if corneal edema is clinically detectable	76	2	M
Corneal tomography is indicated for asymptomatic patients with FECD at baseline	92	2	U

CCT = central corneal thickness; D = after discussion at Round 3; DSO = Descemet stripping only; EK = endothelial keratoplasty; FECD = Fuchs endothelial corneal dystrophy; M = moderate consensus; S = strong consensus; U = near unanimous or unanimous consensus.

TABLE 5. Nonsurgical Intervention: Current Options for Conservative Management

Statement	Agreement (%)	Round	Level of Consensus
Hypertonic saline is an appropriate conservative intervention for managing some vision symptoms in FECD	87	1	S
Hypertonic saline is effective for improving morning vision symptoms in FECD	63	3D	None
If prescribing hypertonic saline to improve morning vision, it is best prescribed as an ointment at bedtime and/or as drops in the morning hours	95	2	U
Topical corticosteroids are not an appropriate medical therapy for FECD	87	2	S
Commercially available rho kinase inhibitors are not effective as a medical therapy for FECD (ie, when used unrelated to surgical procedures)	70	2	M
Carbonic anhydrase inhibitors are not contraindicated in FECD if needed to control intraocular pressure	73	2	M

D = after discussion at Round 3; FECD = Fuchs endothelial corneal dystrophy; M = moderate consensus; S = strong consensus; U = near unanimous or unanimous consensus.

TABLE 6. Cataract Surgery (Alone) in FECD: Timing, Indications, Surgical Considerations

Statement	Agreement (%)	Round	Level of Consensus
Cataract surgery in FECD should be considered whenever the cataract is deemed to be functionally significant	81	1	S
Early removal of a cataract is not recommended for attempting to prevent FECD from progressing to corneal edema	82	3	S
Cataract surgery without concomitant corneal surgery should not be delayed with the goal of preventing the onset of corneal edema	76	2	M
Extra dispersive viscoelastic should be used during cataract surgery in FECD, especially with denser lenses	76	1	M
In eyes with FECD, phacoemulsification should not be performed in the anterior chamber	100	1	U
The preferred IOL material for cataract surgery in FECD is hydrophobic acrylic	95	1	U
FLACS does not improve the outcomes of cataract surgery in FECD	87	2	S
The refractive target of cataract surgery in FECD should be slightly more myopic (0.5-1.0 D) than in non-FECD cases and adjusted towards more myopia with increasing disease severity or likelihood of needing subsequent EK	97	2	U
Toric or multifocal IOL implantation should be avoided during cataract surgery in FECD when tomography is abnormal (ie, with an abnormal posterior corneal contour indicative of subclinical edema)	95	2	U
Administering intracameral antibiotics during cataract surgery in FECD does not impair endothelial function	81	2	S
CCT should be measured before and after cataract surgery in FECD to assess resolution of postoperative edema	84	2	S

CCT = central corneal thickness; FECD = Fuchs endothelial corneal dystrophy; FLACS = femtosecond laser-assisted cataract surgery; IOL = intraocular lens; M = moderate consensus; S = strong consensus; U = near unanimous or unanimous consensus.

• **CATARACT SURGERY (ALONE) IN FECD: TIMING, INDICATIONS, SURGICAL CONSIDERATIONS (TABLE 6):** Strong consensus was reached that cataract surgery (when concomitant cornea surgery is not indicated) in FECD should be considered whenever the cataract is functionally significant, and there was moderate to strong consensus that neither early nor delayed removal of a cataract is recommended to prevent FECD from progressing to corneal edema. There was strong consensus that femtosecond laser-assisted cataract surgery does not improve the outcomes of cataract surgery in FECD, and administering intracameral antibiotics during cataract surgery in FECD does not impair endothelial function. There was near-unanimous consensus that the preferred intraocular lens (IOL) material for cataract surgery in FECD is hydrophobic acrylic, that the refractive target of cataract surgery in FECD should slightly more myopic than in non-FECD cases, and that toric and multifocal IOLs should be avoided during cataract surgery in FECD when tomography is abnormal.

TABLE 7. Corneal intervention: Timing, Options, and Recommendations for Surgical Management, (Including When Corneal Intervention Might Not Be Required)

Statement	Agreement (%)	Round	Level of Consensus
Corneal intervention after cataract surgery is recommended when patients have vision symptoms attributable to objective corneal findings (eg, clinical edema, subclinical edema) that are not improving	97	2	U
When EK is not planned as a staged procedure after cataract surgery in FECD, EK should be deferred for at least 2 mo, and longer if the cornea is improving	92	2	U
DMEK is the preferred corneal surgical treatment for most cases of FECD	92	1	U
Dispersive viscoelastic should be avoided during EK	89	2	S
Descemetorhexis diameter between 7 and 9 mm is acceptable for DMEK in FECD	97	1	U
Using larger diameter DMEK grafts (ie, close to 9 mm) for the transfer of more donor endothelial cells is not necessary in FECD because peripheral host endothelial cells are usually healthy	89	3	S
Phakic DMEK for FECD without a significant cataract is appropriate for most patients aged ≤45 y, and for some patients over 45 y depending on the degree of lenticular opacity or dysfunction	89	3	S
During combined cataract surgery with DMEK, if capsular rupture/vitreous loss are encountered, it is acceptable to attempt completion of DMEK if the IOL is stable	92	2	U
When cataract surgery (without a toric or multifocal IOL) and cornea surgery are both indicated in the setting of FECD, surgery should be combined rather than staged (ie, cataract before cornea)	76	2	M
When cataract and cornea surgery are both indicated in the setting of FECD, toric or multifocal IOL implantation should be avoided during combined surgery	89	2	S
Toric or multifocal IOLs have more predictable outcomes if cataract surgery is staged after cornea surgery for FECD	81	2	S
For cases that meet criteria for DSO, DSO is not currently considered standard of care	78	2	M
DSO is not indicated for asymptomatic patients with central guttae	97	2	U
DSO is usually not indicated if guttae are scattered	87	2	S
Peripheral endothelial cell density should be routinely measured in FECD when considering DSO	95	2	U
DSO can be combined with cataract surgery or staged before or after cataract surgery	87	2	S
For eligible cases, DMEK outcomes are better than DSO outcomes	70	2	M
DSO, when indicated, is most successful when the widest diameter of guttae is ≤4.0 mm, though it can be successful for some cases with slightly larger widest diameters	89	3	S
There is currently insufficient evidence to recommend:			
A minimum peripheral endothelial cell density for successful DSO	96	3	U
The ideal rho kinase inhibitor treatment regimen after DSO	93	3	U
Rho kinase inhibitors stimulate migration of corneal endothelial cells *in vivo*	89	1	S
Rho kinase inhibitors, when used after DSO, might stimulate proliferation of migrating cells *in vivo*	87	2	S

CCT = central corneal thickness; DMEK = Descemet membrane endothelial keratoplasty; DSO = Descemet stripping only; EK = endothelial keratoplasty; FECD = Fuchs endothelial corneal dystrophy; IOL = intraocular lens; M = moderate consensus; S = strong consensus; U = near unanimous or unanimous consensus.

• **CORNEAL INTERVENTION: TIMING, OPTIONS, AND RECOMMENDATIONS FOR SURGICAL MANAGEMENT (TABLE 7):** There was near-unanimous consensus that Descemet membrane endothelial keratoplasty (DMEK) is the preferred corneal surgical treatment of choice for most cases of FECD. Phakic DMEK for FECD without a significant cataract was considered appropriate for most patients aged ≤45 years and for some patients >45 years depending on the degree of lenticular opacity or dysfunction. There was moderate consensus that when cataract surgery (without a toric or multifocal IOL) and cornea surgery are both indicated in the setting of FECD, surgery should be combined rather than staged (ie, cataract before cornea), and strong consensus that toric or multifocal IOLs have more predictable outcomes if cataract surgery is staged after cornea surgery for FECD.

There was strong consensus that DSO, when indicated, is most successful when the widest diameter of guttae is ≤4.0 mm, though it can be successful for some cases with slightly larger widest diameters. There was near-unanimous consensus that there is currently insufficient evidence for other aspects related to DSO surgery (Table 7). There was near-unanimous consensus that DSO is not indicated for asymptomatic patients with central guttae, and strong consensus that DSO is not usually indicated if guttae are scattered.

DISCUSSION

Using a modified Delphi approach, 37 experts around the world reached consensus for many aspects of the understanding and management of FECD as relevant to clinical practice. The 90 consensus statements address critical gaps in the diagnosis and management of FECD and can help standardize clinical decision-making across diverse practice settings. The EKLG guidelines provide actionable recommendations for general ophthalmologists and other eye care professionals, who often lack access to advanced diagnostics, ensuring earlier and more precise referrals for specialized care. In addition, by emphasizing objective clinical findings, this framework could minimize subjectivity and variability in patient management, potentially improving outcomes worldwide.

There have been conflicting definitions of FECD in the past, with some considering asymptomatic scattered guttae as being an early stage of FECD,[22] and others suggesting that FECD was defined by the development of corneal edema originating from central corneal guttae.[23] With the latter, central corneal guttae without corneal edema were considered to be an age-related and asymptomatic condition,[23] sometimes referred to as *cornea guttata*. A recent editorial recommended upholding the distinction between FECD and asymptomatic corneal guttae because not all eyes with guttae will need intervention.[8] However, the majority of subjects (in western populations) with FECD grade 2 (defined as >12 central or paracentral scattered guttae[24,25]) harbor the *TCF4* trinucleotide repeat expansion genetic risk variant for FECD.[9] In addition, a chronic state of subclinical corneal edema, which can be symptomatic, exists in FECD before the development of biomicroscopically detectable edema.[26,27] Given this new understanding of the disease, consensus was reached among this global group of experts that any amount of central or paracentral guttae with or without edema could be classified as FECD, and that FECD and asymptomatic *cornea guttata* were different severities of the same disease. Because the mildest distributions of central or paracentral guttae can be non-progressive and may never require intervention, consensus guidelines were also developed for determining when FECD is functionally significant and needs cornea intervention (see below).

The concept that FECD is not simply a disease of endothelial cell loss but also of endothelial cell dysfunction with abnormal deposition of extracellular matrix onto the Descemet membrane is not new,[22,23] and a growing body of evidence supports various mechanisms of cellular dysfunction.[1,2,4] Therefore, future medical therapies will likely target restoring or preventing impairment of cellular function. In addition, using central endothelial cell density (which cannot be measured accurately in FECD) in clinical practice or as a primary outcome in clinical trials is not valid.[28] In FECD, vision is usually affected by clinically detectable edema and is often affected by the preceding chronic state of subclinical edema.[27,29] Experts agreed that scattered guttae were unlikely to affect vision, and central confluent guttae without edema may or may not affect vision. Features of when confluent guttae without edema are symptomatic could not be defined. While morphologic differences in guttae (ie, exophytic vs buried guttae) are associated with chronic edema,[30,31] it is not known if similar or other morphologic differences exist for guttae without edema, let alone if this might affect vision.[32] In fact, small studies of otherwise healthy pseudophakic eyes with FECD suggest that vision is only affected when subclinical (tomographic) edema is present.[29,33] Clinicians should therefore be cautious about assuming that guttae without edema are always visually significant.

By defining FECD to include scattered guttae without edema, it becomes critical to assess the impact of the disease state on vision because this will strongly influence whether corneal intervention would be indicated. This requires isolating (ideally objective) findings to the cornea to separate it from the effect of comorbid conditions, especially cataract, on vision. There was consensus that objective findings include edema detectable by slit lamp examination, tomography patterns of edema, and changes or differences in CCT (Table 4). In addition, diurnal variation in vision (ie, morning blur or cloudy vision that improves as the day progresses) was considered specific enough to implicate the cornea (Table 4). Although the consensus statements about CCT indicated that ≥10% changes or differences were significant (Table 4), smaller differences can sometimes be significant, especially if accompanied by other objective findings, for example, a diurnal fluctuation in CCT is usually accompanied by subclinical edema on tomography. Tomography is important not only for classifying the state of FECD,[27,34] but because normal tomography is associated with a low risk of disease progression and normal vision, and vice versa.[29,35,36] When edema cannot be detected on clinical examination, the presence of the findings described above, which indicate impaired corneal endothelial function, justifies corneal intervention for symptomatic patients. When epithelial or stromal edema are clinically detectable, prompt intervention should be considered to optimize recovery of vision that might otherwise become compromised by subepithelial fibrosis,[37-39] infected bullae,[40] or structural changes associated with posterior stromal ripples.[41] Of note, central endothelial cell density and isolated values of CCT were not deemed to be helpful for clinical decision-making, and these should not be considered as objective findings that can indicate when cornea intervention is appropriate.[28,42,43]

Currently, there is a lack of medical therapies for FECD with insufficient evidence for experts to recommend using topical corticosteroids or standalone topical rho-kinase inhibitors. However, rho kinase inhibitors are currently under active investigation for FECD and might emerge as a

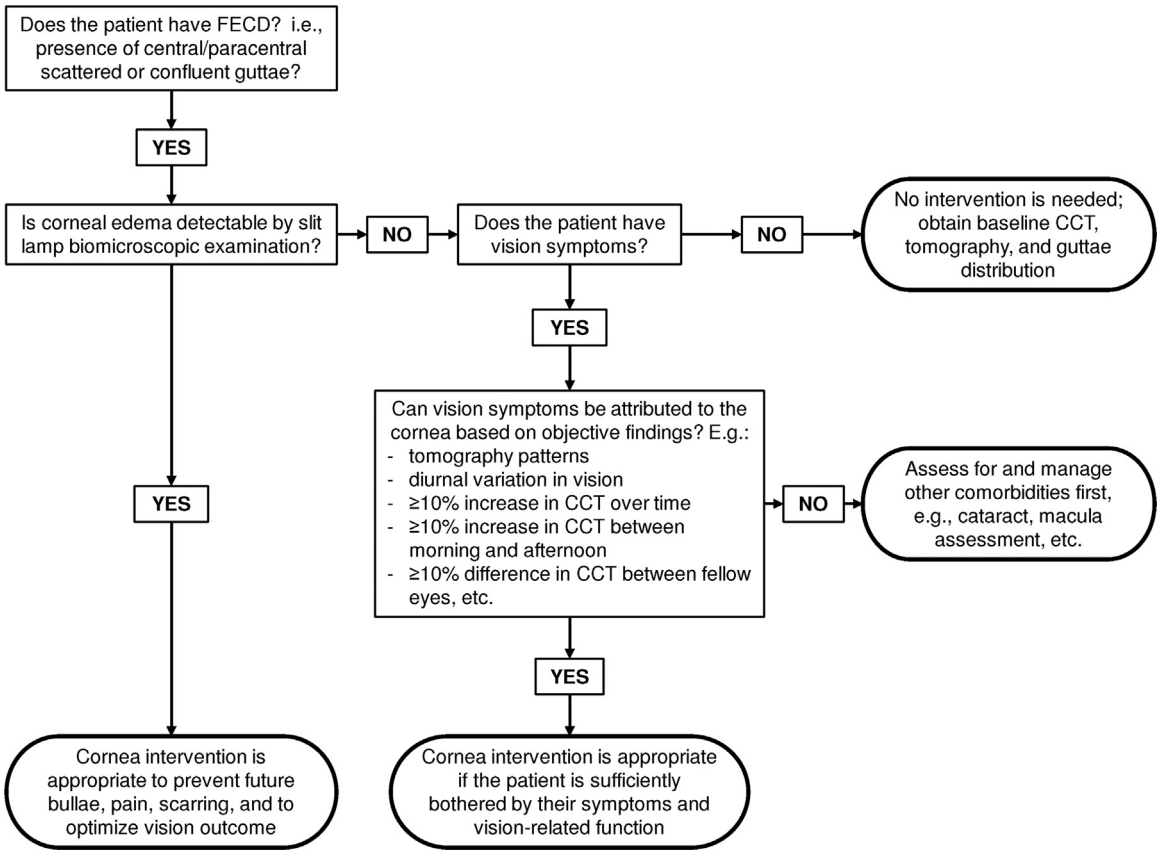

FIGURE 1. Recommended evaluation of Fuchs endothelial corneal dystrophy patients to assist with clinical decision-making based on the modified Delphi consensus of global experts.

future medical therapy.[44,45] While experts acknowledged often using hypertonic saline for vision symptoms, they were not confident of its efficacy for improving morning vision.[46]

Anecdotally, many experts on the panel have encountered patients with FECD who have been advised to undergo early cataract surgery (ie, before a cataract is functionally significant with the goal of minimizing phacoemulsification power and its potential effect on the corneal endothelium) or to delay cataract surgery (ie, despite the cataract being visually significant out of concern that surgery would induce progression to corneal edema). The EKLG panel of experts recommended that when concomitant cornea surgery is not indicated for FECD, cataract surgery should be performed whenever a cataract is deemed to be functionally significant instead of recommending early or delayed surgery. In fact, limited data suggest that the natural history of FECD progression is not affected by uncomplicated cataract surgery,[35] and with improved safety and outcomes of EK over PK,[5-7] the need for subsequent keratoplasty is not usually detrimental. For ideal refractive outcomes of cataract surgery in FECD, slight myopia should be targeted based on the known hyperopic shift induced by endothelial keratoplasty.[47] Toric and multifocal IOLs should generally be avoided in the setting of FECD, especially when tomography is abnormal because this would indicate an aberrated posterior corneal surface caused by subclinical edema[29,42] (and for which the management would be cornea intervention instead as discussed below).

When cornea intervention is required for FECD, there was near-unanimous consensus that DMEK is the surgical procedure of choice, knowing that most eyes with FECD have favorable anatomy for the procedure. When cataract surgery and DMEK are both indicated, surgery should be combined unless planning toric or multifocal IOL implantation, in which case DMEK should precede cataract surgery.[48] The latter is important because the shape of the edematous cornea will change after endothelial replacement resulting in alterations of corneal power and toricity.[49] With insufficient evidence about selection criteria and longer-term outcomes, DSO is not currently standard of care treatment for FECD, and importantly, the threshold for intervention by DSO is the same as for DMEK, that is, DSO is only indicated if vision is affected by corneal endothelial dysfunction based on the objective findings described earlier. DSO is not indicated for asymptomatic patients and is not usually indicated when guttae are scattered.

Strengths of this study include the large number of experts developing guidelines specific to FECD instead of

grouping multiple etiologies of corneal edema,[11] and that consensus was achieved using a modified Delphi method. The Delphi method enables relatively rapid consensus by allowing anonymous and asynchronous input thereby reducing individual influence on the opinions of other contributors and encouraging diverse input. However, while the EKLG guidelines reflect a global consensus, local practice variations, especially in regions with limited access to advanced tomography, surgical expertise, or donor tissue, might limit their applicability. Although only 28 of the 37 experts were present for the live virtual meeting, this was still a sufficient number for reliability of group judgment,[50] and it was unlikely that a different meeting format would have resulted in more participants. Furthermore, the final statements after the live virtual meeting were shared with all experts resulting in no requests for revision, and the final version of this article was reviewed and approved by all experts prior to publication.

These consensus statements provide current global expert opinions and recommendations specific to FECD. While there are several important statements and recommendations about various aspects of the disease, the most important recommendation is to assess for objective findings that implicate the corneal disease state as a source of decreased vision, as this will help inform whether corneal intervention is indicated based on the patient's symptoms and function (Figure 1). Many of the EKLG guidelines are important and relevant to general ophthalmologists who play a pivotal role in making the diagnosis and initially determining whether the disease is causing symptoms. The recommendations for disease evaluation empower general ophthalmologists and other eye care professionals to make informed decisions and facilitate timely intervention. The EKLG guidelines can also aid cornea specialists by allowing them to benchmark their current practice patterns against expert recommendations, potentially reducing variability in practice. FECD remains an area of active investigation with clinical trials in progress, and technology and treatments will continue to evolve resulting in changing management recommendations in the future. The consensus EKLG guidelines from the current study will therefore need to be revisited and revised in future years to enable practitioners to remain current with the management of FECD.

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