Advanced Diagnosis of Corneal Endothelial Dysfunction

Diagnóstico Avançado da Disfunção Endotelial da Córnea

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ABSTRACT

The corneal endothelium plays a vital role in maintaining corneal transparency through fluid homeostasis, which is regulated by the tight junctions and the activity of the Na^+/K^+-ATPase pump. As the endothelium is not regenerable, the loss of endothelial cells due to aging, trauma or dystrophies such as Fuchs' endothelial corneal dystrophy (FECD) can lead to corneal edema and progressive visual impairment.

Conventional methods such as slit-lamp biomicroscopy and clinical grading remain essential in advanced stages, but are limited in early detection. This review emphasizes the value of multimodal imaging in the detection of subclinical dysfunction. Specular and confocal microscopy allow quantitative assessment of endothelial cell density and morphology. Spatial thickness measurements, such as corneal thickness spatial profile (CTSP) and percent thickness increase (PTI), raise diagnostic specificity beyond traditional central corneal thickness (CCT).

Scheimpflug tomography enables early detection of subtle morphologic changes, such as isopachal irregularities, posterior surface depressions, and the "camel sign" in densitometry. Optical coherence tomography of the anterior segment (AS-OCT) refines the diagnosis by correlating the reflectance patterns with the integrity of the endothelium. Biomechanical evaluation of the cornea with Corvis ST adds dynamic parameters such as applanation times, deformation amplitude and concavity radius, which vary depending on the stage of the disease.

The genetic basis of endothelial dystrophies is also addressed, highlighting important loci and genes such as *TCF4*, *COL8A2* and *SLC4A11*, which have been implicated in autosomal dominant and complex inheritance patterns. These findings emphasize the importance of molecular diagnostics and point to future therapeutic targets.

In summary, a comprehensive diagnostic strategy that combines structural imaging, functional assessment and genetic analysis supports early detection, improves preoperative risk assessment — especially in cataract and keratoplasty planning — and could benefit from integration with artificial intelligence for predictive modelling and clinical decision making in the future.

KEYWORDS: Corneal Endothelial Cell Loss; Endothelial Cells; Endothelium, Corneal; Fuchs' Endothelial Dystrophy.

RESUMO

O endotélio corneano desempenha um papel essencial na preservação da transparência da córnea, assegurando a homeostase do fluido estromal através de complexos juncionais e da actividade da bomba Na^+/K^+-ATPase. Dada a sua natureza não regenerativa, a perda celular progressiva — decorrente do envelhecimento, de traumas ou de patologias hereditárias como a distrofia endotelial de Fuchs (FECD) — pode culminar em edema estromal e comprometimento visual progressivo.

Apesar de a biomicroscopia em lâmpada de fenda e a classificação clínica permanecerem ferramentas indispensáveis na avaliação de estádios avançados da doença, revelam-se limitadas na detecção precoce de alterações endoteliais. Neste contexto, a imagiologia multimodal tem assumido um papel central na identificação de disfunções subclínicas.

As técnicas de microscopia especular e confocal permitem a análise quantitativa da densidade e da morfologia celular, fornecendo indicadores precoces de disfunção. Paralelamente, parâmetros derivados da espessura corneana — nomeadamente o perfil topográfico da espessura (CTSP) e o aumento percentual da espessura (PTI) — demonstram maior sensibilidade diagnóstica do que a espessura central isolada (CCT).

A tomografia de Scheimpflug possibilita a identificação precoce de alterações morfológicas subtis, como irregularidades isopácicas, depressões na superfície posterior e o denominado "sinal do camelo", observado na densitometria corneana. A tomografia de coerência óptica do segmento anterior (AS-OCT) acrescenta valor diagnóstico através da análise dos padrões de reflectância da camada endotelial.

A avaliação biomecânica da córnea, realizada com o dispositivo Corvis ST, disponibiliza parâmetros dinâmicos adicionais — tempos de aplanamento, amplitude de deformação e raio de concavidade — os quais se alteram ao longo da progressão da doença.

A dimensão genética destas distrofias é igualmente relevante, destacando-se os genes *TCF4*, *COL8A2* e *SLC4A11*, associados a hereditariedade autossómica dominante ou complexa. Estes avanços sublinham a utilidade do diagnóstico molecular e sugerem potenciais alvos terapêuticos.

Em suma, uma abordagem diagnóstica integrada — aliando imagiologia estrutural, avaliação funcional e análise genética — permite a detecção precoce da disfunção endotelial e apoia uma estratificação de risco mais precisa no contexto cirúrgico.

PALAVRAS-CHAVE: Células Endoteliais; Distrofia Endotelial de Fuchs; Endotélio Corneano; Perda de Células Endoteliais da Córnea.

INTRODUCTION

The corneal endothelium began to be studied in the 1950s by David Maurice in experimental studies and its behaviour has been increasingly studied over time.[1] Laing, Bourne & Kaufman were the first to obtain in vivo observations of human corneas by specular microscopy.[2]

The corneal endothelium consists of a single layer of hexagonal cells covering the posterior surface of the cornea in a well-arranged mosaic pattern. Endothelial cells secrete collagen, which forms the endothelial basal membrane (Descemet membrane, DM). At birth, DM measures 3 μm and consists in a band pattern of collagen. With age, the endothelium continues to secrete non-banded collagen, and DM thickness reaches approximately 13 μm by the age of 70.[3]

The primary function of the endothelium is to keep corneal transparency, maintaining the optimal water content of about 80%. Tight junctions between endothelial cells behave as a physical barrier, regulating the movement of aqueous humor into the stroma. The Na+K+ATPase active pump is expressed in the basolateral membrane of corneal endothelial cells and actively maintains stromal deturgescence. The cornea is avascular, and its health depends on nutrients flow from aqueous to stroma through the endothelium. The balance between passive and active pumping is known as the "pump-and-leak mechanism" and is indispensable for corneal transparency.[4]

Endothelial cells are metabolically very active. However, they are arrested in the G1 phase of the cell cycle and do not divide under normal circumstances. As such, central endothelial density decreases throughout life at an average rate of 0.6%/year. Central endothelial density is 6000/mm^2 at birth, 3000/mm^2 at age 5, and 2300/mm^2 at 85 years.[5] When corneal endothelium extensive damage occurs by trauma, infection, inflammation, or inherited disease, the cell density decreases so edema develops. Although there is no well-established cut-off where the cornea starts to swell, it is expected to be less than 500/mm^2.[6]

The corneal endothelium could be affected by primary endothelial diseases, and also by secondary conditions. Fuchs'

endothelial corneal dystrophy (FECD) is the most common disease. This is a slowly progressive and bilateral corneal dystrophy that usually becomes clinically evident in the fourth or fifth decades of life. It is characterized by gradual endothelial cell loss and dysfunction, which turn the endothelium more vulnerable. Enlarged endothelial cells secrete excess amount of abnormal bounded collagen, projecting from the posterior surface of DM and create the condition known as cornea guttata. FECD characteristically affects the central cornea and should be differentiated from peripheral corneal guttata (Hassal-Henle bodies), which is associated with normal aging.

FECD is an age-associated disease whose prevalence in the growing age population deserves attention. Moreover, cataract surgery is the most performed surgical procedure worldwide. Moreover, patients are being operated at younger ages. Thereby, endothelial function became a major concern, so that a detailed endothelial evaluation before any intraocular surgery is mandatory.

This paper aims to provide a review of a comprehensive corneal endothelium evaluation.

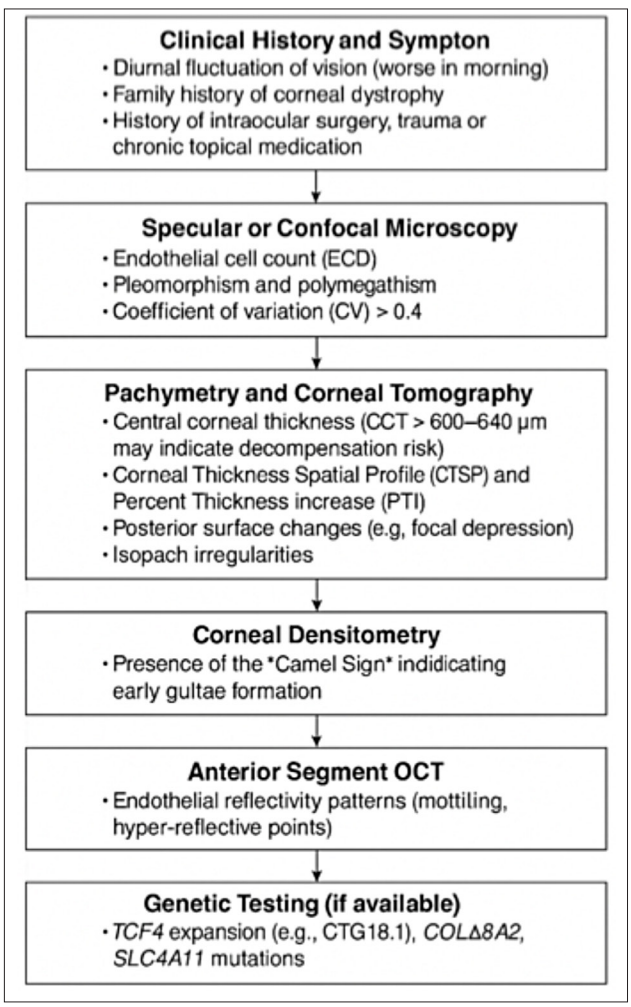

Figure 1. Suggested Diagnostic Approach to Suspected Early FECD. This flowchart outlines a step-by-step diagnostic strategy to aid in the early detection of FECD with emphasis on multimodal evaluation.

CORNEAL ENDOTHELIUM EVALUATION: STARTING FROM THE BASICS

A detailed anamnesis, including a thorough medical history, ocular surgeries, trauma, medications, and family history, plays a critical role in diagnosing corneal endothelial diseases. This comprehensive approach improves the ability to diagnose these diseases accurately, predict their progression, and develop effective, personalized treatment strategies.

For example, in the initial stages of FECD, patients frequently report experiencing blurred vision upon awakening, with gradual improvement throughout the day. This diurnal fluctuation is primarily attributable to overnight corneal edema, resulting from diminished tear film evaporation during sleep. The transient accumulation of stromal fluid compromises corneal transparency in the morning hours. Systematically inquiring about and recording this specific pattern of visual disturbance may serve as a valuable clinical indicator of early endothelial dysfunction, even in the absence of overt biomicroscopic findings.[7]

The family history is of great importance in this diagnostic context. It is an important tool for identifying genetic predispositions and hereditary patterns that influence the occurrence and progression of corneal endothelial diseases.

For many decades, slit-lamp biomicroscopy was the unique tool to evaluate corneal endothelium morphology. Stromal thickening, Descemet folds, stromal clouding, and microcystic epithelial edema are late signs of corneal dysfunction and are recognized by slit-lamp biomicroscopy. Experienced ophthalmologists also identify areas of guttae with high-resolution biomicroscopes. The Krachmer *et al* method described in 1978 and its modification are currently FECD severity grading systems.[8]

Table 1. The modified clinical grading system for Fuchs endothelial corneal dystrophy, based on the number and confluence of guttae among the presence of corneal edema.

Grade	Central guttae pattern
0.5	5–12 scattered, non-confluent guttae
1	> 12 scattered, non-confluent guttae
2	1–2 mm (widest diameter) confluent guttae
3	2–5 mm (widest diameter) confluent guttae
4	> 5 mm (widest diameter) confluent guttae
5	> 5 mm (widest diameter) confluent guttae with stromal or epithelial edema

However, these classifications are highly subjective and assume disease severity to be correlated with morphologic findings rather than endothelial function.

Endothelial barrier and pump functions could be estimated from the endothelial permeability to fluorescein and by measuring the deswelling corneal rate from a 10% increase in thickness induced by 2 hours of closed-eye soft contact lens wear, respectively. However, these methods are invasive and not practical to use in daily routine.

Maurice introduced specular microscopy to observe endothelial cells in 1968. In 1976, Bourne and Kaufman used specular microscopy to detect endothelial disease, which was not seen by slit-lamp examination.[2] Endothelial cell morphology analysis includes cell area (μm²), density (cells/mm²), and shape (percentage of hexagonality). The coefficient of variation (CV) is given by the equation: standard deviation of cell area /mean area. Lower endothelial cell counts according to patient's age, presence of pleomorphism (percentage of hexagonality < 50%), and polymegathism (CV > 0.4) have diagnostic values in FECD. Confocal microscopy could also be useful when corneal edema or opacity is present and does not allow correct endothelial observation by specular biomicroscopy.

Pachymetry refers to the measurement of central corneal thickness. Typically, central corneal thickness (CCT) measurement has been used as an indicator of corneal endothelium function. CCT has a 'Gaussian' distribution with a mean CCT of 556 μm with a standard deviation of 34μm, ranging from 454 to 669 μm. The Preferred Practice Pattern of the American Association of Ophthalmology (AAO) considered a preoperative CCT of 600 μm as predictive of corneal decompensation in FECD patients, with a recommendation for triple procedure when cataract surgery had to be performed (penetrating keratoplasty, cataract extraction and intraocular lens implantation). This guideline has been revised by Seitzmann, accounting for advances in phacoemulsification techniques, and advocating a higher cut-off point of 640 μm.[9]

The cornea does not have a uniform thickness, being thinner in the center and thickening towards the periphery. FECD preferentially involves the central or paracentral area. Repp *et al* reported the central-to-peripheral (4 mm from the center) corneal thickness ratio to assess disease severity using pachymetry.[10] However, single-point measurements, such as CCT and central-to-peripheral ratio, do not well distinguish naturally thicker corneas from corneas with edema.

Corneal tomography represents the three-dimensional reconstruction of the cornea. It evaluates the anterior and posterior corneal surfaces, creating pachymetric maps that provide spatial thickness profiles. Ambrósio *et al* proposed the evaluation of the spatial variation of corneal thickness. From the thinnest point, the average thickness of twenty-two imaginary circles at 0.1 mm steps are calculated and presented in a graph (corneal thickness spatial profile – CTSP). The percentage thickness increase (PTI) is calculated for each position using the formula: (CT@ x - TP) / TP, where x represents the average of the thickness on the imaginary circles. The CTSP and PTI graphs also contain reference data with a 95% confidence interval of a normal population. The comportment of the spatial progression is a very important characteristic of normality. It can distinguish a normal thick (> mean + 1 standard deviation) cornea from a cornea with edema. A normal profile is a curved line plotted in red, following (but not necessarily within) the normative black dotted curves' standard course, and does not leave the course before the 6 mm. In FECD, the profile changes into a plateau line without the normal decrease from the center to the periphery from the early stages of the disease, while the edema is still not recognized by slit-lamp biomicroscopy.

Scheimpflug tomography also identifies subclinical edema in FECD, which has enormous clinical value. It provides prognostic information for educating and counseling patients, which is particularly relevant for clinical decisions. There are benefits in the early indication for endothelial keratoplasty (EK) because prolonged edema may lead to stromal changes that may limit improvement in vision after EK. Sun *et al* described three tomographic findings: loss of parallel isopachs in the pachymetric map, displacement of the thinnest point from its normal position and focal posterior corneal depression towards the posterior chamber.[11] Moreover, Ambrósio described the "camel sign" in corneal densitometry. It represents a second hump at the level of Descemet's membrane and correlates with the presence and severity of cornea gutatta.[12]

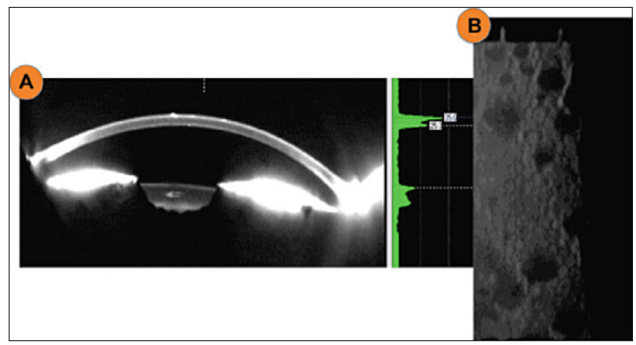

Figure 2. (A) Scheimpflug image showing "Camel Sign," which consists of a second hump on the densitometry "green" graph at the level of Descemet's Membrane. (B) The presence of the "Camel Sign" on the Scheimpflug image correlates with the presence of corneal guttata.

THICKNESS MAPS, CTSP/PTI, OCT

Corneal tomography allows the study of the posterior surface of the cornea and its asphericity. Some patients with FECD unexpectedly had hyperopic refractive outcomes after combined EK and cataract surgery (triple procedure). Fritz *et al* demonstrated that this occurs in corneas that are flatter centrally than the periphery due to edematous changes (oblate posterior profile).[13] As such, eyes with a positive Q value should be considered for additional power at the intraocular lens.

Anterior segment optical coherence tomography (AS-OCT) provides useful information regarding corneal endothelium and may represent valuable support in FECD diagnosis and staging. It was demonstrated a positive correlation between endothelial reflectivity and FECD severity. Additionally, based on OCT images, three different patterns of the corneal endothelium according to signal distribution and the level of reflectivity were defined: homogeneous hypo-reflective surface, presence of hyper-reflective orange-yellowish points, and a mottled appearance with a variable number of hyper-reflective areas. These patterns inversely correlate with corneal endothelium integrity. On

the other hand, OCT analysis is very important and may be fundamental after posterior lamellar keratoplasty to recognize early signs of Descemet membrane detachment.

The biomechanical behavior of the cornea modulates the development of several eye diseases. Ectatic corneas, which have abnormal collagen and extracellular matrix, are usually thinner and have weaker biomechanical properties than those with normal corneal tissue.

FECD results in a decrease in endothelial cells, leading to a higher water content in the corneal tissue, disrupting the complex architecture of the stroma and resulting in corneal edema. Changes in the hydration of the corneal tissue could influence the stiffness properties.

Scheimpflug technology, as implemented in the Corvis ST, records corneal dynamics following deformation by a collimated air puff. To evaluate the cornea's biomechanics, the recorded Scheimpflug images are divided into three states: Applanation 1 (A1), in which the cornea flattens as it rebounds inward; highest concavity (HC); and Applanation 2 (A2), in which the cornea flattens as it rebounds outward.

In each state, the Corvis measures ST:

- Length of the flattened cornea (A1 length and A2 length);
- Elapsed time (A1 time, HC time and A2 time);
- Velocity (A1-velocity and A2 velocity).

During the HC state, the following parameters are calculated:

- Deformation amplitude (DA): the distance of the corneal apex from the initial state to the highest concavity;
- Peak distance: the distance between the two apexes at HC;
- HC radius: the radius of curvature of the cornea at the time of maximum concavity.

These parameters are crucial for the comprehensive evaluation of the biomechanical properties of the cornea. Recent literature shows that all biomechanical parameters of the cornea, except HC time, correlate with the clinical stage of FECD, and the differences in A1 length and A1 time between the stages of FECD suggest that these parameters hold potential for monitoring disease progression and prognosis.

A multimodal approach enhances early detection of FECD by combining specular microscopy, corneal tomography, Scheimpflug imaging, and AS-OCT. Specular microscopy identifies endothelial cell changes before clinical signs appear, while tomography and pachymetry detect subclinical edema patterns. This integrated evaluation improves diagnosis, prognosis, and surgical planning.[14,15]

Recent advances in the genetics of corneal endothelial dystrophies have elucidated the pathways and mechanisms underlying these diseases and revealed correlations between genotype and phenotype.

The genes associated with corneal endothelial dystrophies encode transcription factors, structural components of the stroma and Descemet's membrane, cell transport proteins, and other proteins. The major forms of these dystrophies, including congenital hereditary endothelial dystrophy (CHED), posterior polymorphous corneal dystrophy (PPCD), and FECD exhibit genetic diversity in terms of associated genes and mode of inheritance.

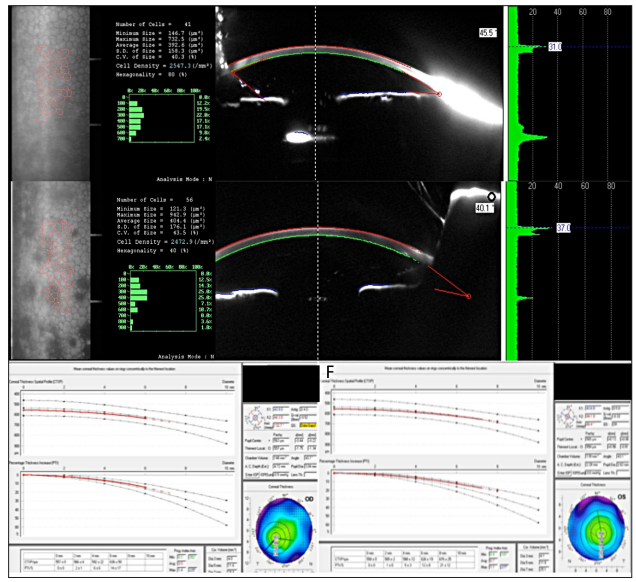

Figure 3. Multimodal imaging of a case of early FECD with subclinical edema. Specular microscopy of the right (a) and left (c) eyes shows endothelial pleomorphism and polymegathism. Scheimpflug tomography corneal densitometry (b, d) highlights the "camel sign", indicating early guttae formation and subclinical edema in both eyes. Pachymetric progression maps of the right (e) and left (f) eyes show an abnormal thickening pattern, with a more pronounced loss of parallel isopachs in the right eye, suggesting early corneal decompensation.

Table 2. Details of Genes and Loci for Corneal Endothelial Dystrophies.

Endothelial Dystrophy	Locus/gene	Inheritance	Gene function
CHED	*CHED2/SLC4A11*	AR	Not known; ion transporter–related
PPCD	*PPCD1/OVOL2*	AD	Transcription factor
	PPCD2/COL8A2	AD	Component of escemet membrane
	PPCD3/ZEB1	AD	Transcription factor promoting EMT
	PPCD4/GRHL1	AD	Transcription factor promoting MET
FECD	*FECD1/COL8A2*	AD	Component of Descemet membrane
	FECD3/TCF4	AD	Transcription factor
	FECD4/SLC4A11		Not known; ion transporter–related.
	FECD6/ZEB1	Complex	Transcription factor
	FECD8/AGBL1	AD	Glutamate decarboxylase
	FECD/DMPK	AD	Protein kinase

The application of genome sequencing is expected to facilitate the identification of new loci or novel pathogenic

changes in existing genes in the near future, thereby improving our understanding of the underlying genetics of these diseases. An important implication of these advances is the potential development of new therapies for these diseases based on known genetic and molecular mechanisms.

ARTIFICIAL INTELLIGENCE IN THE ASSESSMENT OF ENDOTHELIAL DYSFUNCTION

Artificial intelligence (AI) and machine learning are progressively being integrated into ophthalmic diagnostics, offering promising applications in the evaluation of corneal endothelial disorders. In the context of FECD, recent studies have demonstrated the potential of AI-based algorithms to automatically detect and quantify guttae on specular microscopy images, assess endothelial cell morphology, and estimate cell density with high reproducibility.[16–18]

Deep learning models trained on multimodal imaging datasets — including Scheimpflug tomography, AS-OCT, and pachymetric maps — have achieved encouraging results in classifying disease stage, predicting progression, and identifying patients at risk for corneal decompensation. Moreover, the incorporation of corneal biomechanical data into predictive models may further enhance diagnostic sensitivity in early or subclinical disease.[19]

While these technologies remain in early clinical translation, their integration into routine practice could enable automated screening, objective risk stratification, and individualized management strategies in endothelial dystrophies.

CONCLUSION

The recent scientific advances have changed the paradigm of corneal endothelium evaluation. Nowadays, more than studying the morphology and density of endothelium cells, imaging diagnostic methods look for early signs of endothelial dysfunction in corneas, which are likely to decompensate after an intraocular procedure.

The genetic characterization of endothelial dystrophies, particularly involving loci such as *TCF4*, *COL8A2*, and *SLC4A11*, contributes to diagnostic precision and may facilitate the development of targeted therapies. Moreover, recent applications of artificial intelligence have demonstrated high accuracy in detecting guttae, segmenting endothelial cells, and predicting FECD severity from multimodal imaging datasets, supporting its future integration into automated diagnostic workflows.

In this evolving context, a standardized, algorithm-driven diagnostic strategy that incorporates advanced imaging technologies, biomechanical metrics, genetic testing, and artificial intelligence is poised to become central to the contemporary management of corneal endothelial diseases.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

MV, TL, IM, FM: Responsible for gathering data, presenting results, and writing the manuscript.

TL, NSJ, RAJ: Responsible for performing complementary exams and helping in laboratory tasks.

TL, NC, FG, RAJ: Supervised the project and contributed with their expertise to its conclusion.

All authors read and approved the final manuscript.

MV, TL, IM, FM: Responsáveis pela recolha de dados, apresentação dos resultados e redação do manuscrito.

TL, NSJ, RAJ: Responsáveis pela realização de exames complementares e apoio em tarefas laboratoriais.

TL, NC, FG, RAJ: Supervisionaram o projeto e contribuíram com a sua experiência para a sua conclusão.

Todos os autores leram e aprovaram a versão final do manuscrito.

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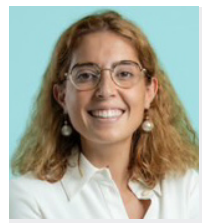
REFERENCES

1. Maurice DM. Cellular membrane activity in the corneal endothelium of the intact eye. Experientia. 1968;24:1094-5. doi:10.1007/BF02147776
2. Bourne WM, Kaufman HE. Specular Microscopy of Human Corneal Endothelium in VIVO. Am J Ophthalmol. 1976;81:319-23. doi:10.1016/0002-9394(76)90247-6
3. de Oliveira RC, Wilson SE. Descemet's membrane development, structure, function and regeneration. Exp Eye Res. 2020;197:108090. doi:10.1016/j.exer.2020.108090
4. Qazi Y, Wong G, Monson B, Stringham J, Ambati BK. Corneal transparency: genesis, maintenance and dysfunction. Brain Res Bull. 2010;81:198-210. doi:10.1016/j.brainresbull.2009.05.019
5. Valdez-García JE, Ortiz-Morales G, Morales-Mancillas N, Luis Domene-Hickman J, Hernández-Camarena J, Loya-García D et al. Age-related Changes of the Corneal Endothelium in the

Hispanic Elderly Population. Open Ophthalmol J. 2022;16. doi:10.2174/18743641-v16-e2204140
6. Price MO, Mehta JS, Jurkunas UV, Price FW. Corneal endothelial dysfunction: Evolving understanding and treatment options. Prog Retin Eye Res. 2021;82:100904. doi:10.1016/j.preteyeres.2020.100904
7. Ong Tone S, Kocaba V, Böhm M, Wylegala A, White TL, Jurkunas U V. Fuchs endothelial corneal dystrophy: The vicious cycle of Fuchs pathogenesis. Prog Retin Eye Res. 2021;80:100863. doi:10.1016/j.preteyeres.2020.100863
8. Krachmer JH. Corneal Endothelial Dystrophy. Arch Ophthalmol. 1978;96:2036. doi:10.1001/archopht.1978.03910060424004
9. Seitzman GD, Gottsch JD, Stark WJ. Cataract surgery in patients with Fuchs' corneal dystrophy. Ophthalmology. 2005;112:441-6. doi:10.1016/j.ophtha.2004.10.044
10. Repp DJ, Hodge DO, Baratz KH, McLaren JW, Patel SV. Fuchs' Endothelial Corneal Dystrophy. Ophthalmology. 2013;120:687-94. doi:10.1016/j.ophtha.2012.09.022
11. Sun SY, Wacker K, Baratz KH, Patel SV. Determining Subclinical Edema in Fuchs Endothelial Corneal Dystrophy: Revised Classification using Scheimpflug Tomography for Preoperative Assessment. Ophthalmology. 2019;126:195-204. doi:10.1016/j.ophtha.2018.07.005
12. Ambrósio R, Faria Correia F, Belin MW. Analyzing Tomographic Thickness for Detecting Corneal Ectatic Diseases. In: Alió, editor. Keratoconus, Essentials in Ophthalmology, Berlin: Springer; 2017. p.77-85.
13. Fritz M, Grewing V, Böhringer D, Lapp T, Maier P, Reinhard T, et al. Avoiding Hyperopic Surprises After Descemet Membrane Endothelial Keratoplasty in Fuchs Dystrophy Eyes by Assessing Corneal Shape. Am J Ophthalmol. 2019;197:1-6. doi:10.1016/j.ajo.2018.08.052
14. Ambrósio Jr R. Multimodal imaging for refractive surgery: Quo vadis? Indian J Ophthalmol. 2020;68:2647. doi:10.4103/0301-4738.301283
15. Ambrósio R, Guerra FP. Advanced Corneal Imaging for Fuchs Endothelial Corneal Dystrophy. Ophthalmology. 2019;126:205-6. doi:10.1016/j.ophtha.2018.09.020
16. Benetz BAM, Shivade VS, Joseph NM, Romig NJ, McCormick JC, Chen J, et al. Automatic Determination of Endothelial Cell Density From Donor Cornea Endothelial Cell Images. Transl Vis Sci Technol. 2024;13:40. doi:10.1167/tvst.13.8.40
17. Qu JH, Qin XR, Peng RM, Xiao GG, Cheng J, Gu SF, et al. A Fully Automated Segmentation and Morphometric Parameter Estimation System for Assessing Corneal Endothelial Cell Images. Am J Ophthalmol. 2022;239:142-53. doi:10.1016/j.ajo.2022.02.026
18. Liu S, Kandakji L, Stupnicki A, Sumodhee D, Leucci MT, Hau S, et al. Current Applications of Artificial Intelligence for Fuchs Endothelial Corneal Dystrophy: A Systematic Review. Transl Vis Sci Technol. 2025;14:12. doi: 10.1167/tvst.14.6.12.
19. Eleiwa T, Elsawy A, Özcan E, Abou Shousha M. Automated diagnosis and staging of Fuchs' endothelial cell corneal dystrophy using deep learning. Eye Vision. 2020;7:44. doi:10.1186/s40662-020-00209-z



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