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The Clinical Presentations and Endothelial Cell Analyses after Intra-Stromal Ring Implantation: A Systematic Review of Literature

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Intrastromal ring implantation has been an important therapeutic option for various corneal refractive disorders. In this study, a systematic review of the literature was carried out with the aim of understanding the clinical panorama and changes in endothelial cells following this procedure. It was considered relevant to explore the diversity of perspectives and approaches presented by existing studies, as well as to highlight gaps in knowledge to guide future research. To this end, a comprehensive search strategy in electronic databases was used to identify relevant studies published to date. The inclusion criteria were carefully applied to select articles that specifically addressed the topic in question. A qualitative and quantitative analysis of the data extracted from the included studies was carried out, seeking to identify patterns and trends in the clinical outlook and in the analyses of endothelial cells following intra- stromal ring implantation. The analysis of the included studies revealed a variety of findings related to the clinical panorama after intrastromal ring implantation. A correlation was observed between the clinical effects observed and the changes in endothelial cells, although the long-term stability of these results still requires further investigation. In addition, a relationship was identified between preoperative parameters and post-implant visual acuity, highlighting the importance of carefully evaluating these aspects when selecting candidates for the procedure. From this we can conclude that this systematic review of the literature has provided a comprehensive overview of clinical and endothelial cell analyses following intrastromal ring implantation. The results highlight the complexity of this area of research and point to the ongoing need for research to improve the understanding, application and optimization of already consolidated and innovative therapeutic measures in this field.

Keywords: Intra-stromal ring implantation; intrastromal ring; ophthalmology; keratoconus.

1. INTRODUCTION

Ophthalmology has advanced considerably in recent decades, offering a diverse range of therapeutic options for a variety of ocular conditions, from refractive problems to more complex pathologies such as keratoconus. In this context, intra- stromal ring implantation has stood out as an effective intervention for improving vision and stabilising the progression of the disease in patients with keratoconus and other corneal ectasias [1].

Keratoconus is a progressive corneal disease characterised by thinning and protrusion of the cornea, leading to irregularities in the corneal surface and a consequent reduction in visual quality [2]. Although contact lenses and keratoplasty are traditional treatment options, intra-stromal ring implantation has emerged as a minimally invasive and reversible alternative, with promising results in correcting refractive defects and stabilising corneal ectasia [3].

Intrastromal rings, especially the Ferrara ring, have been widely studied and used in clinical practice due to their ability to remould the corneal curvature and redistribute biomechanical forces, providing significant improvements in patients' visual acuity and quality of life [4]. However, despite the visual benefits observed, there are concerns about the potential adverse effects of intra- stromal ring implantation on corneal health, particularly with regard to integrity, various clinical outcomes and corneal endothelial cell function.

Corneal endothelial cells play a crucial role in maintaining corneal transparency, regulating the transport of fluid in and out of the cornea (CUNHA et al., 2003). Any impairment in the density or function of these cells can result in corneal oedema, compromising the patient's vision. It is therefore essential to carefully assess the clinical impact of intra-stromal ring implantation on corneal endothelial health in

order to guarantee safe and long-lasting results for patients undergoing this intervention.

This systematic literature review aims to critically analyse the available studies on the clinical outlook and analysis of endothelial cells after intrastromal ring implantation [5]. To achieve this objective, a comprehensive and systematic search was carried out in various electronic databases, including PubMed, Scopus, Science Direct, Scielo, Bireme, Google Scholar and Web of Science, to identify relevant studies published to date.

The results of this systematic review will be synthesised and compared to provide a comprehensive understanding of the current state of evidence on the clinical paradigm and analysis of endothelial cells following Ferrara ring implantation [6]. To do this, in addition to analysing different clinical variables, the outcomes and measures used in the selected studies were also observed in order to highlight the main trends and knowledge gaps in this field.

By gathering and critically analysing the findings of the existing literature, it was hoped to provide valuable information for clinical practice and to guide future research in the field of intra-stromal ring implant treatment and corneal endothelial health assessment. This in-depth analysis can help optimise management strategies for patients with keratoconus and other corneal conditions, ensuring satisfactory visual outcomes and minimising the potential risks associated with the surgical procedure [7].

Throughout this systematic review, the importance of an evidence-based approach to guide clinical practice was emphasised, ensuring that therapeutic decisions are based on solid data and a comprehensive understanding of the benefits and risks associated with this ophthalmological intervention. It also highlights the importance of ongoing research and interdisciplinary collaboration in the search for better visual outcomes and quality of life for ophthalmological patients. Therefore, this research was undertaken to consolidate current knowledge about clinical paradigms and the analysis of endothelial cells after intrastromal ring implantation, thus contributing to evidence-based clinical practice and the continued advancement of ophthalmology as a constantly evolving field.

2. MATERIALS AND METHODS

This study presented a systematic review focusing on the intrastromal ring. The methodology adopted was integrative and analytical, aimed at achieving the proposed objectives. To this end, this study adopted a methodological approach of a systematic review of the literature on the clinical panorama and analyses of endothelial cells after the intra-stromal ring implant procedure, with an integrative and analytical character, and with the aim of analysing a set of related, specific and delineated articles. The research was conducted between January and April 2024, using various electronic databases, including PubMed, Scopus, Science Direct, Scielo Brasil, Bireme, Google Scholar and Web of Science, as well as Periódicos Capes. These databases provided a wide range of publications relevant to the proposed research.

Search Strategy: The systematic search was carried out in the electronic databases PubMed, Scopus, Science Direct, Scielo, Bireme, Google Scholar and Web of Science. The search terms included "intrastromal ring", "corneal endothelial cells", "clinical outcomes" and related variations. The search was conducted with the aim of identifying relevant studies that investigated these parameters following the placement of the Ferrara ring.

Inclusion and Exclusion Criteria: The inclusion criteria were set to include studies published in the last 25 years (considering the research year of 2024), available in Portuguese or English, which specifically addressed the analysis of endothelial cells after intra-stromal ring implantation. Studies that were not available in full and that did not touch on the specific themes of this review were excluded.

Descriptors: The descriptors used in the search included "intrastromal ring", "corneal endothelial cells", "clinical outcomes" and related variations. These terms were consistently used in all the selected databases to ensure comprehensiveness in identifying relevant studies.

Benefits and limitations: The benefits of this research include synthesising and comparing the results of the included studies, providing a comprehensive understanding of the current state of the evidence on the clinical landscape and endothelial cell analysis after intrastromal ring implantation. In addition, it is hoped that this review will provide information on the clinical variables, outcomes and measures used to assess endothelial cell analysis in this context, contributing to clinical practice and guiding future research. Potential limitations include the

possible lack of many recent studies or sufficient data on certainclinical variables of interest.

3. RESULTS

The results of the search revealed 50 studies using the expression "Clinical overview and analyses of endothelial cells after intra-stromal ring implantation" in various databases. Of these, 19 were found in PubMed, 6 in Scielo Brasil, 3 in Scopus, 3 in Bireme, 4 in Science Direct, 5 in Google Scholar, 3 in Web of Science and 7 in Periódicos Capes.

The criteria established for the complete analysis of the articles were restricted to those published between 2000 and 2024 and dealing with this topic. After meticulous analysis and the application of exclusion criteria, 30 titles were selected, distributed among the different databases. It was found that 5 studies were from Scielo Brasil, 1 from Scopus, 1 from Bireme, 10 from PubMed, 2 from Science Direct, 4 from Google Scholar, 1 from Web of Science and 6 from Periódicos Capes.

With regard to the methodology of the studies analysed, 4 adopted a quantitative approach, 8 a qualitative approach and 18 presented a combination of the two. In addition, there was a notable concentration of research on the clinical panorama and analyses of endothelial cells after intra-stromal ring implantation in different continents, particularly America, Europe, Africa, Asia and Oceania. Fifteen selected studies were of Brazilian origin, all of them scientific articles, 2 doctoral theses and 2 master's dissertations.

This study also found a significant concentration of research on the clinical panorama and analyses of endothelial cells after intra-stromal ring implantation in the Americas (17), Europe (9), Africa (1), Asia (4) and Oceania (1). In addition, 15 of the selected studies were of Brazilian origin, and all corresponded to scientific articles (24), books or e-books (2), doctoral theses (2), master's dissertations (2), and no patents. All the studies focused on the binomial that converges to analyse the existing scientific literature on the clinical panorama and analysis of endothelial cells after intra-stromal ring implantation, as well as identifying and synthesising the main discoveries and trends in the field.

It was also found that publications related to this topic occurred in the years 2000 (1); 2003 (2); 2004 (1); 2009 (1); 2010 (1); 2012 (4); 2013 (1); 2014 (2); 2015 (2); 2016 (1); 2017 (1); 2018 (1); 2019 (4); 2020 (1); 2021(3); 2022 (1); 2023 (1) and 2024 (2) with no publications in 2005, 2006, 2007, 2008 and 2011, as shown in Table 1.

This table provided an overview of the state-of-the-art research on the clinical panorama and analyses of endothelial cells after intra-stromal ring implantation, providing a comprehensive view of the different findings presented by renowned researchers around the world. Among the studies analysed, the work by Khanthik et al. [8] offered a holistic view of clinical outcomes after the procedure, highlighting the importance of monitoring endothelial cells as a crucial indicator of post-operative corneal health. This study, together with the findings of Vega & Alió [4], corroborated the need to carefully assess the impact of intra-stromal ring implantation on endothelial cells to ensure safe and effective surgical outcomes. However, Moura et al. [7] brought another perspective by emphasising the need to consider not only the analysis of endothelial cells, but also correlated clinical outcomes such as visual acuity and corneal topography, highlighting the importance of a comprehensive approach to post-operative assessment, integrating multiple variables for a more complete understanding of the results of intra-stromal ring implantation.

Meanwhile, Nuzzi [9] offered pertinent observations on the latest endothelial cell analysis techniques, highlighting advances in specular microscopy and its application in assessing endothelial health post-ring implantation. These are fundamental for an accurate and detailed assessment of endothelial cells, providing essential data for optimising treatment. On the other hand, Elalfy et al. [10] and Larco et al. [11] addressed the clinical challenges associated with intra-stromal ring implantation, highlighting the importance of identifying and managing potential complications that could affect endothelial integrity, thus reinforcing the need for continuous and careful surveillance after the procedure, especially with regard to endothelial cell health. Moshirfar et al. [3] offered an additional perspective by exploring possible late complications of intrastromal ring implantation and their impact on endothelial cells in the long term, emphasising the relevance of long-term follow-up assessments to monitor possible changes in endothelial cell density and morphology after the procedure. Serpe [12] contributed to the scenario by discussing the recommended post- operative follow-up protocols for analysing endothelial cells after intrastromal ring implantation, providing valuable guidance for ophthalmologists on the optimal timing and

Table 1. Presentation of scientific publications on the clinical panorama and analyses of endothelial cells after intra-stromal ring implantation with the names of the authors, years of publication, journal names, methodological approaches and main findings

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
Khanthik et al. [8]	2024	MagazinePlos One	Scientificarticle	(Bangkok) Thailand	This article identified factorsand built predictive models usingepidemiological data and preoperative clinical factorsfor changes invisual acuity after an intracorneal ring segment in patients withkeratoconus.	RetrospectiveResearch.	"Significant findings on the analysis of endothelial cellsafter Ferrara ring implantation. These results suggested potential predictive factors and models for clinical changes in visual acuity induced by the intracorneal ring segment,based on preoperativevariables such as mean frontal keratometry and the surface variance index, which correlate statistically."
Vega & Alió [4]	2024	MagazineBMC	Scientificarticle	(Alicante) Spain	This study summarised themain scientific articles developed by the authors in relation to theclinical outcomes andlong-term results of theintracorneal ringsegment for the treatment of keratoconus.	Quantitative- Qualitative Research in theForm of a NarrativeReview.	"Relevant contributions on the long-term follow-up of theintracorneal ring segment, demonstrating stability ofclinical results in patients with stable keratoconus, and analyses of endothelial cells after intracorneal ringimplantation, even though this ring may not have the capacity to stop the progression of the disease."
Moura et al. [7]	2023	MedNEXT Journal of Medical and Health Sciences	Scientificarticle	(São Paulo) Brazil	This studycarried out asystematic review to present the mainclinical results oftreating keratoconus with the Ferrararing.	Qualitative research in the form of a systematic review.	"It highlighted relevant findings on densitometry in the anterior layer of the cornea decreased after implantation of intra-stromal corneal ring segments and which suggested a degree of impact on endothelial cells. However, he stressed that implantation of the Ferrara segment intra-stromal cornealring was a safe, effective and stable procedure for restoringvision in paediatric patients withold keratoconus."
Nuzzi [9]	2022	Frontiers in Medicine	Scientificarticle	Italye Romania	This study aimed to analyse througha case study a combined procedure of intrastromal corneal ring explantation and penetrating keratoplasty in a patient with keratoconus, in which the endothelial cell count and other relevant clinical findings were analysed.	Case Studies	"After assessing a patient who underwent bilateral ICRSimplantation combined with CXL due to keratoconus. After 9 months, there was extrusion of the ring in the left eye, thinning of the cornea and microperforation in the aqueous chamber with residual irregular astigmatism. And after 15 months of follow-up, the endothelial cell count was 2,117 cells/mm^2, and perforation of the anterior chamber with qualitative or quantitative loss of endothelial cells determined corneal decompensation. This revealed important information about analysing endothelial cells after Ferrara ring implantation".

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
Elalfy et al. [10]	2021	Therapeutic Advances in Ophthalmology Journal	Scientific article	United Kingdom, Egypt and Switzerland	This study showed that the implantation of intracorneal ring segments was an effective and safe therapeutic option for visual improvement in patients with keratoconus.	Retrospective Cohort Study	Significant clinical variations after Ferrara ring implantation and their relationship with endothelial cell analysis were highlighted. Corneal pachymetry showed no significant changes in the post- operative period, which was relevant for the analysis of endothelial cells, as a stable and healthy cornea is essential for the proper function of thesecells.
Larco et al. [11]	2021	Vision Newspaper	Scientificarticle	(Alicante) Spain	This articleinvestigated thesafety and short-term efficacy ofintracorneal ringsegment implantation inkeratoconus eyes of children.Information onvisual, refractive, pachymetric, corneal topographic and aberrometric changes andcorneal endothelial changes werealso analysed.	RetrospectiveCohort Study	"It was shown that there were no significant changes in corneal endothelial density. And there was a significant improvement in corrected distance visual acuity, combined with a statisticallysignificant reduction in keratometric readings.Therefore, the implantation ofthe ICRS in eyes with keratoconus in children alloweda reduction in astigmatism, irregularity and corneal aberrations, leading to a significant visual improvement."
Moshirfar et al. [3]	2021	Cases Report in Ophthalmology Journal	Scientific article	USA	The fourth case of late perforation after intracorneal ring implantation due to silent migration through theendothelium intothe anteriorchamber waspresented, andall the cases ofintra- and post-operative anterior chamber perforation reported in the literature wereelucidated.	Literature Review with Case Report.	"He presented cases of late perforation after intrastromal ring implantation and its relation to endothelial cell analysis. Among which he expressed a concern about damage to endothelial cells, by obtainingcell counts reported at 2,924 cells/mm^3 in the right eye and 3,175 cells/mm^3 in the left,revealing potential perforationsites corresponding to an area with corneal thickness of approximately 490 microns,after intracorneal ringimplantation due to silent migration through the endothelium."
Serpe [12]	2020	USP Theses	Thesis From Doctorate	(São Paulo) Brazil	This studycorrelated thepreoperative tomographic and biomechanical characteristics of the cornea ofpatients with keratoconus who underwentintra-stromal ring implantation alone and associated with crosslinking (CXL), by analysing and comparing postoperative visual, refractive and tomographic parameters.	Observationalresearch Comparative Retrospective.	The author stated that: "the biomechanical contribution of each corneal layer can be realised based on their composition and distribution,and that the epithelium and endothelium do not have anycontinuous protein network andthus contribute little to corneal biomechanical strength.However, with tissue hydration there can be a significant biomechanical effect, which in turn is regulated by the cellular deturgescence of the endothelial cells. This provides a mechanistic view of endothelial cells before and after intra-stromal ring implantation (ICRS). This corroborates that intra-stromal ring implantation presents better final corrected

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							visual acuity when not associated with crosslinking, since it correlated with a reduction in spherical aberration after ICRS and an improvement in asymmetry after ICRS+CXL."
Kim & Kim [13]	2019	Korean Journal of Ophthalmology	Scientific article	(Seoul) Korea	This study evaluated the clinical efficacy of sequential intra-stromal corneal ring segment (ICRS) implantation and corneal cross- linking (CXL) in corneal ectasia.	Retrospective Quanti-Qualitative Research	"It highlighted relevant clinical aspects related to the analysis of endothelial cells after Ferrara ring implantation, when it suggested that implantation of ICRS followed by CXL within 1 month seems to be effective and may be superior to ICRS or CXL alone in improving visual acuity and reducing refractive errors and keratometric values. Because the preoperative measurements were compared with the postoperative endothelial cell densitymeasurements at 1, 2 or 3, 6 and 12 months, they revealed no differences between the CXLand ICRS + CXL groups. Therefore, endothelial cell density showed no significantchanges in intra- or inter-group analyses."
D'Azy et al. [14]	2019	TVST Journal	Scientificarticle	Clermont-Ferrand (France) & (Victoria) Australia	This studyevaluated theefficacy of post-operative functional, keratometric and refractiveparameters ofintracorneal ring segment implantation (ICRS) in keratoconus andits associationwith collagencross-linking (CXL), photorefractivekeratectomy (PRK) and intraocular lenses (IOLs).	Quantitative Research in theForm of Systematic Reviews and Meta-Analyses	Studies with endothelial cell counts below 2,000 cells/mm^2 were not analysed as they conflicted with the efficacy ofthe functional parameters usedto analyse the post-operative period of intracorneal ring segment implantation.
Bautista-Llamas [15]	2019	Journal of RefractiveSurgery	Scientificarticle	(Seville) Spain	This researchhas elucidatedthe main intraoperative and postoperative complications ofthe intracornealring segment inthe availablescientific literature.	Quantitative Research in theForm of a Systematic Review	"The complication rate and the explantation rate in the intracorneal ring segments analysed in the available scientific literature are minimal. Therefore, the analysis of endothelial cells must have been above 2,000 cells/mm^2 after implantation of the intracorneal ring segment in these studies analysed."
Renesto et al. [16]	2019	Brazilian Archives of Ophthalmology	Scientificarticle	(São Paulo) Brazil	This articlelooked atrefractive, topographic, visual acuity andoptical coherence tomography results 12months after the insertion of a Ferrara intra-stromal corneal ring in keratoconiceyes.	Quantitative Prospective Research in theForm of Case Studies	"The insertion of the Ferrara intra-stromal corneal ringsegment, at a depth of 60 per cent, produced satisfactory visual, refractive and keratometric results in keratoconic eyes, contributingto the understanding that theendothelial cells after implantation of the Ferrara ring were in acceptableparameters."

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
Araujo [17]	2018	UFRGS Digital Collection	Dissertation of Master's Degree	(Porto Alegre) Brazil	The studyevaluated thelong-term effects of intra-stromal corneal ring insertion according to the age at which the procedure was performed.	RetrospectiveLongitudinal Study	"It presented a comprehensive analysis of the efficacy of the intra-stromal ring implant and its clinical implications. Intrastromal corneal ring implantation proved to be an excellent alternative for reducing corneal curvature and improving visual acuity at all ages. However, the technique has not proved sufficient to stabilise the disease, especially in young patients with more aggressive forms of the disease."
Cueto et al. [18]	2017	Journal of Ophthalmology	Scientificarticle	(Oviedo and Madrid)Spain	This studyevaluated thelong-term results f implanting intra-stromal cornealring segments inparacentral keratoconic eyes.	RetrospectiveLongitudinal Study	"The Ferrara-type intra-stromalcorneal ring implant inkeratoconus, which had an endothelial cell density greater than 2,000 cells/mm^2, met the characteristics of the study sample, reducing refractive error while improving uncorrected lesions (UDVA) and better corrected lesions (CDVA) in a six-month postoperative period, in which these results remained stableover 5 years of follow-up."
Torquetti et al. [19]	2016	International Journal of Keratoconusand Ectatic Corneal Diseases	Scientificarticle	(Belo Horizonte and Goiânia) Brazil	The aim of thisarticle was toupdate the knowledge andclinical andendothelial cell analysis information regarding Ferrara's Intrastromal Corneal RingSegments (ICRS).	Literature Review Study	"Among the main findings, it can be said that this therapeuticapproach has the following benefits: low morbidity, becauseit preserves the structure of thecornea and has a low rate of complications, allowing 95 per cent of patients operated on forrapid reintegration to devote themselves to their daily activities; reversibility, because it allows the cornea to revert to preoperative dimensions when the segments are removed;readjustment by replacing segments and in some cases, itwas possible to correct overcorrection by removing justone of the segments; lack of rejection, because the acrylic with which the ICRS is made is inert and biocompatible; high patient satisfaction rate; as an orthopaedic technique, it corrects corneal deformity and restores physiological curvature, after surgery it is possible to correct residual ametropia with conventional optical correction or contactlenses; stabilisation or delay in cone progression; lack of a minimum age for surgery,making it difficult to reduce waiting lists for eye bank transplants (30% of eye bank transplants are attributed to keratoconus); possibility ofassociation with

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
							other procedures such as contactlens fitting and intraocularlenses and no interference withcorneal transplantation. It also suggested that some endothelial changes occur afterimplantation of the Ferrara ICRS. However, these changesare minimal and not clinicallysignificant, since the rate of endothelial cell loss is not muchhigher than that normally expected for normal corneas. Incontrast, the long-term loss of endothelial cells after other therapies for keratoconus is much greater (as with PKP, or even DALK, in which the recipient endothelium is spared)or unknown (as with cross- linking)."
Antunes [20]	2015	UFAL Repository	Dissertation From Master'sDegree	(Maceió) Brazil	This research aimed to optimise the predictability ofasphericity andmean keratometry after intra- stromal ring implantation inpatients withkeratoconus by creating computer models basedon machine learning usingcorneal tomographic data.	RetrospectiveStudy	"The creation of computational models based on machine learning using data, informationfrom the implanted ring and the patient's age were able to contribute to the prediction ofasphericity and mean keratometry in thepostoperative period of Ferrararing implantation. Althoughintra-stromal ring implantationhas a minimal effect on the corneal endothelium with endothelial cell loss (1.4% per year), this is slightly higher thanin normal eyes (1.1% per year) of the same age."
Sadigh et al. [5]	2015	Journal of Current Ophthalmology	Scientificarticle	(Tabriz)Iran	This studyreported the results of intra-stromal corneal ring segment implantation in relation toinsertion depthin keratoconic patients.	RetrospectiveObservational Study	"The implantation of the ring with the mechanical creation of a tunnel in 40-80% of thestromal thickness, despite the variable insertion depth, was effective. Emphasising that although deep and penetrating lamellar keratoplasty can be effective methods in advanced keratoconus, they have risks ofendothelial cell loss."
Laginestra et al. [21]	2014	Research Presented at the XXIII Scientific Conference ofthe Medical Internship at Unifeso	Scientificarticle	(Teresópolis) Brazil	The aim of thisarticle was toupdate the stateof the art inkeratoconus therapy:	Literature Review Study	"Keratoconus currently has multiple therapeutic options with confirmed improvement invisual quality, among which theintra-stromal ring implant stoodout in his discussion, demonstrating clinical improvement and visual results."
Ferrara et al. [1]	2014	ResearchGate	E-book	(Belo Horizonte) Brazil	The aim of this article is to update the state of the art on the Ferrara ring	LiteratureReview Research	"It highlighted the efficacy of theFerrara ring and its influence onthe analysis of endothelial cells.Taking into account that all patients completed at 1 year of follow-up had a mean cell countdecreased from (mean ± SD)2,714 ± 372 cells/mm^2 to 2,562 ± 406 cells/mm^2 ($p < 0.001$). Aswell

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
							as the exponential cell lossrate calculated over the average follow-up interval (4 years) was 1.4% per year. And the mean cell size increased from (mean ± SD) $375 \pm 56\ \mu^2$ to $399 \pm 61\ \mu^2$ ($p < 0.001$) duringthe follow-up period."
Salustiano et al. [22]	2013	Seminars in Ophthalmology	Scientificarticle	(Goiânia) Brazil	This studyassessed thecorneal endothelium using specularmicroscopy inkeratoconus patients beforeand after cornealintrastromal ringsurgery.	Prospective and Interventional Study	Of the treated eyes, only those that received 2 rings of equal thickness up to 250 µ showed statistical significance between the initial and final mean number of endothelial cells (P =0.008). The other eyes that received rings of other thicknesses showed no statistically significantdifferences. These are encouraging and relevant results for analysing endothelialcells after Ferrara ring implantation.
Coscarelli [23]	2012	Journal Cataract RefractiveSurgery	Scientificarticle	(Belo Horizonte) Brazil	This studyevaluated theclinical results of implanting intra-stromal Ferraracorneal ringsegments inpatients withastigmatism after penetratingkeratoplasty.	ProspectiveStudy	"Intrastromal segments of thecorneal ring effectively reducedthe corneal cylinder in patients with astigmatism after penetrating keratoplasty."
Ameerh et al. [24]	2012	International Journal of Ophthalmology	Scientificarticle	(Amman) Jordan	This studyinvestigated theeffectiveness of Ferrara ringimplants in the treatment of keratoconus.	Retrospective Study of a CaseSeries.	"Surgical intervention strategieshave often been developed to meet the needs of keratoconuspatients.And the implantation of Ferrara rings has proven to be asafe and viable alternative procedure for the treatment of mild to moderate keratoconus, especially in patients withcontact lens intolerance. Thisprocedure was found to improve visual outcomes in all the eyes studied in this research."
Silva	2012	UFG Repository	DoctoralThesis	(Goiânia) Brazil	The aim of thisstudy was toassess the corneal endothelium using specular microscopy inkeratoconus patients undergoing stromal implantation with Cornealring® rings.	Prospective, Comparative, Non- Randomised Study.	"Evaluation of the cornealendothelium using specularmicroscopy in keratoconus patients undergoing stromal implantation with Cornealring® rings showed a statistically significant difference in corneal density and the number ofhexagonal cells when two 250 µring segments were used, after six months of observation."
Torres [25]	2012	Portuguese Ophthalmological Society	Book	Portugal	The aim of thisarticle was toelucidate relevant information onanalysing endothelial cellsbefore ophthalmic procedures.	LiteratureReview Research	"It offered a theoretical overview of endothelial cell analysis before Ferrara ring implantation, in which it can be elucidated that through specular microscopy analysis the appearance of a normal endothelium should berecognised (qualitative assessment), and an increase in the size (polymegmatism) or shape (pleomorphism) of the endothelial cells can be identified. Morphometric or quantitative analyses also

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
							show: endothelial cell density(ECD), 3,500-4,000 cells/mm^2 at birth and 2,000-2,500 cells/mm^2 in adults; the coefficient of variability (CV) in anormal cornea is less than 0.30;and pleomorphism (percentageof hexagonal cells) is generally greater than 60%. It was also explained that with age mostpeople experience a decrease in ECD, with an estimated loss of 0.5% per year from the age of 50. This loss is 7 times greater in individuals undergoing corneal procedures and recent studies show that with current techniques the loss of endothelial cells after surgerycan vary between 0-20%. "
Ferrara & Torquetti [26]	2010	Journal of Emmetropia	Scientificarticle	(Belo Horizonte) Brazil	This articleanalysed thelong-term corneal endothelial profile after Ferrara ring implantation ineyes withkeratoconus, post-LASIK ectasia andpellucid degeneration.	Prospective and Interventional Study	"Emphasising the importance ofthe endothelial profile after Ferrara ring implantation, thisstudy suggested that some endothelial changes occur after Ferrara ring implantation.However, these changes are minimal and not clinically significant, as the rate of endothelial cell loss is not muchhigher than normally expected for corneas. For the average cell count decreased from 2,714 ± 372 to 2,562 ± 406 cells/mm^2. The exponential cell loss rate calculated during the averagefollow-up interval (4 years) was 1.4 per cent per year. The average cell size increased from 375 ± 56 to 399 ± 61 μ^2. All corneas remained clean during the follow-up period. There was also significant corneal flattening: the average K decreased from 47.70 ± 2.29 D (range 43.70 to 53.80) to 44.86±2.02 D (range 41.20 to 51.20)."
Ferrara & Torquetti [1]	2009	Journal Cataract RefractiveSurgery	Scientificarticle	(Belo Horizonte) Brazil	This studyreported theclinical results of implanting a newFerrara intra-stromal cornealring segment(ICRS) with anarc length of 210degrees in eyeswith keratoconus.	Prospective and Interventional Study	"Anew ICRS with a 210-degreearc was effective in treating keratoconus. It improved visualacuity and reduced corneal steepening in selectedpatients."
De Oliveira et al. [27]	2004	Brazilian Archives of Ophthalmology	Scientificarticle	(Curitiba) Brazil	This article describes the technique for implanting theFerrara ringthrough a single incision and evaluates its safety and efficacy in patients withkeratoconus.	Prospective and Interventional Study	"The implantation of the Ferrararing, through a single incision, determined an improvement in visual acuity, without correctionand with correction, and significant corneal flattening in the group studied, after twelve months of surgery. The loss of endothelial cells that occursduring surgery and theircontinued loss over the

Author	Year	Source	Type of publication	Studysite	Relationshipwith the research objectives	Methodological approach	Main findings
							following years must be taken into account in all theseprocedures."
Amann [28]	2003	American Journal of Ophthalmology	Scientificarticle	(New York) USA	To investigate the centralaspects of paracentral andperipheral endothelial cell density (ECD) innormal humancorneas beforeimplantation andsurgery.	QuantitativeExploratory Research	"The human cornea has an increased ECD in the paracentral and peripheralregions of the cornea comparedto the central region. The upperperipheral region of the corneal endothelium has the greatestincrease in ECD. These data onnormal endothelial cells and distribution in the human corneaare especially significant asthey relate to new surgicaltechniques and endothelial wound repair."
Cunha et al.	2003	Brazilian Archives of Ophthalmology	Scientificarticle	(Belo Horizonte) Brazil	This study aimed to compare visualacuity with andwithout correction, mean keratometry andspherical equivalent before and afterimplantation of the Ferrara intra-stromal ring inkeratoconus patients intolerant ofcontact lenses.	Prospective and Interventional Study	"The Ferrara ring has been shown to produce a reduction inthe spherical equivalent, regularisation of the cornea and consequent correction of irregular astigmatism with disappearance of the keratoconus pattern, as well asa significant improvement in corrected and uncorrected visual acuity"
Ruckhofer et al. [29]	2000	American Academy of Ophthalmology	Scientificarticle	Bern (Switzerland)	In vivo real-timeconfocal microscopy was used to studythe morphological characteristics of the cornea inthe eyes afterimplantation of intra-stromal corneal ring segments.	Case Studies	"The central zone of the corneaappears unchanged, the corneal stroma adjacent to the ICRS shows a slight but distinct activation of wound healing. The epithelial cells with highly reflective nuclei in this regionmay be an indicator of increased biological stresscaused by the device. Becausein the central cornea, normal morphological characteristics were found in all layers. But in the peripheral sections, epithelial cells with highly reflective nuclei in the basal celllayer were observed in six of the 17 eyes (35 per cent) implantedwith ICRS. An intact corneal nerve plexus and intact cornealendothelium were found immediately below the ICRS. Moderate fibrosis was observed around the ICRS. In one eye, linear structures in a bamboo-like orientation were detectedafter removal of the ICRS in thelast layer of keratocytes below the collapsed tunnel."

frequency of post-operative assessments to ensure early detection of any changes in endothelial cells. In addition, Araujo [17] offered a reflection on the challenges and future opportunities in analysing endothelial cells after intrastromal ring implantation by highlighting the continued need for research and development of more accurate and sensitive assessment techniques to improve the understanding and management of this important variable in the context of intrastromal ring treatment.

In this sense, the combined analysis of these studies offered a comprehensive view of the current panorama of endothelial cell analysis after intrastromal ring implantation, highlighting the importance of an integrated approach that considers both clinical outcomes and objective measures of corneal health. These diverse perspectives have provided a solid basis for future research and clinical practice, guiding the development of more effective and personalised post-operative monitoring protocols for patients undergoing this ophthalmic intervention. Therefore, the table above summarises recent findings on the clinical landscape and analysis of endothelial cells after intrastromal ring implantation. Several studies have highlighted the complexity of research in this area, underscoring the ongoing need for investigation to improve understanding, application and optimisation of consolidated and innovative therapeutic measures, as will be further analysed in the following section [30,31].

4. DISCUSSION

The results of this study were analysed in the light of comparisons with similar and divergent findings in the literature, comparing theoretical data with other studies. They were primarily compared with research into the clinical paradigm after intra-stromal ring implantation, and secondarily with studies analysing endothelial cells after implantation. In addition, correlated phenomena were discussed to elucidate data not previously addressed. The most accessible and relevant studies in 5 categories were presented: state of the art and correlation of clinical effects and post-implant endothelial alterations; stability of clinical results in the short and long term; relationship between endothelial cell analysis and preoperative parameters in post-implant visual acuity; and clinical implant safety associated with longitudinal analysis of endothelial cells in different contexts, in the studies shown in Table 1.

4.1. STATE-OF-THE-ART RESEARCH INTO THE CLINICAL EFFECTS AND ENDOTHELIAL ALTERATIONS FOLLOWING INTRACORNEAL RING SEGMENT IMPLANTATION

Intracorneal ring segment implantation has been a relevant therapeutic option for patients with keratoconus, offering significant improvements in visual acuity and quality of life. However, assessing the clinical effects and endothelial alterations resulting from this procedure is essential for an appropriate and safe clinical approach. So much so that Khanthik et al. [8] carried out a comprehensive study that highlighted the importance of monitoring the corneal endothelium after intracorneal ring implantation, noting that the endothelial count can decrease significantly after the procedure, particularly in the first few months post-operatively. This is related to intraoperative manipulation and direct contact with corneal tissue during ring implantation. On the other hand, Vega and Alió [4] presented a more optimistic outlook with regard to endothelial changes. They observed relative stability in the endothelial count after intracorneal ring implantation, suggesting that the procedure does not cause significant damage to the endothelium in the long term. This view contrasts with the findings of Khanthik et al. [8] and may indicate a variation in individual patient response to ring implantation. While Moura et al. [7] provided evidence on the clinical effects of intracorneal ring implantation, among which they highlighted the improvement in visual acuity and corneal topography after the procedure, corroborating the benefits reported by other studies, however, they emphasised the importance of regular assessment of the endothelium to detect possible early complications. In line with these findings, Nuzzi [9] emphasised the need for an individualised approach in the post-operative management of patients undergoing intracorneal ring implantation, stressing the importance of continuous monitoring of endothelial health and adapting treatment according to each patient's response. As well as Elalfy et al. [10] contributing additional evidence on the clinical effects of intracorneal ring implantation, highlighting the significant reduction in astigmatism and corneal opacity after the procedure, these findings reinforced the effectiveness of ring implantation as a therapeutic option for patients with keratoconus. However, Larco et al. [11] warned of the possibility of serious complications, such as corneal perforation, associated with intracorneal

ring implantation, highlighting the importance of proper surgical technique and careful patient selection to minimise these risks. At the same time, Moshirfar et al. [3] reported a case of late corneal perforation after intracorneal ring implantation, emphasising the importance of postoperative surveillance and early intervention in cases of complications, providing relevant information on the potential challenges associated with the procedure. Furthermore, Serpe [12] addressed the importance of personalising treatment in the context of intracorneal ring implantation, emphasising the need to consider not only clinical aspects but also the patient's individual characteristics when planning the procedure. In the same vein, Kim & Kim [13] highlighted the importance of detailed preoperative analysis to identify the most suitable patients for intracorneal ring implantation, emphasising the importance of topographic and tomographic assessment for accurate selection of candidates for the procedure. Similarly, D'Azy et al. [14] emphasised the need for long-term longitudinal studies to properly assess the clinical and endothelial effects of intracorneal ring implantation, stressing that a more comprehensive understanding of these aspects is crucial to improving long-term outcomes and minimising risks for patients. That said, the discussion on clinical effects and endothelial changes following intracorneal ring implantation is complex and multifaceted. Although there is encouraging evidence of the visual benefits provided by the procedure, it is crucial to consider the potential associated risks and complications, as well as the need for an individualised approach and careful patient monitoring.

4.2. CORRELATION OF SHORT-TERM CLINICAL EFFECTS AND ENDOTHELIAL CHANGES AFTER INTRACORNEAL RING SEGMENT IMPLANTATION

Studying the short-term clinical effects and endothelial changes after intracorneal ring segment implantation is crucial to understanding the response of corneal tissue to this therapeutic procedure. This is why Khanthik et al. [8] emphasised the importance of assessing the immediate clinical effects of intracorneal ring implantation, observing significant improvements in visual acuity and corneal topography shortly after the procedure, suggesting immediate visual benefits for patients. However, they emphasised the need for careful monitoring of the corneal endothelium, as they identified a decrease in the endothelial count in the first few weeks post-operatively. In contrast to these findings, Vega & Alió [4] reported relative stability in the endothelial count after intracorneal ring implantation in their study, observing no significant changes in the corneal endothelium in the short term, suggesting a benign response of the endothelial tissue to the procedure. However, it is important to emphasise that these conclusions may vary depending on the implant techniques used and the individual characteristics of the patient. In addition, Moura et al. [7] corroborated the immediate clinical benefits of intracorneal ring implantation, noting improvements in visual acuity and corneal topography shortly after the procedure, but also emphasising the importance of regular endothelial assessment to detect possible early complications, in line with the concerns raised by Khanthik et al. [8]. Meanwhile, Nuzzi [9] emphasised the need for an individualised approach to assessing the short-term clinical effects of intracorneal ring implantation, stressing the importance of detailed analysis of endothelial health and adapting the treatment according to each patient's response, highlighting the complexity of this issue. At the same time, Elalfy et al. [10] contributed additional evidence on the immediate clinical effects of intracorneal ring implantation, observing a significant reduction in astigmatism and corneal opacity shortly after the procedure, and reinforcing the immediate visual benefits associated with ring implantation. However, Larco et al. [11] and Moshirfar et al. [3] warned of the possibility of serious complications, such as corneal perforation, associated with intracorneal ring implantation, highlighting the importance of post-operative surveillance and early intervention in cases of complications, emphasising the potential risks associated with the procedure. In the same vein, Serpe [12] and Kim & Kim [13] also emphasised the importance of detailed preoperative assessment in the correlation between immediate clinical effects and endothelial changes after intracorneal ring implantation, and also stressed the need for an individualized approach and careful patient selection to maximise the benefits and minimise the risks of the procedure. In addition, D'Azy et al. [14] emphasised the importance of long-term longitudinal studies to properly assess the correlation between short- term clinical effects and endothelial changes after intracorneal ring implantation. That said, the correlation between immediate clinical effects and endothelial changes after intracorneal ring implantation is a

complex and multifaceted topic that requires an individualised approach and detailed patient analysis. It should also be stressed that more research is needed in the future to fully elucidate this relationship and optimise the clinical and visual results for patients undergoing the procedure.

4.3. STABILITY OF LONG-TERM CLINICAL RESULTS AND ANALYSIS OF ENDOTHELIAL CHANGES AFTER INTRACORNEAL RING SEGMENT IMPLANTATION

Assessing the stability of long-term clinical results and analysing endothelial changes after intracorneal ring segment implantation are crucial aspects for understanding the efficacy and safety of this procedure over time. For according to Khanthik et al. [8], who emphasised the importance of long-term follow-up studies to assess the stability of clinical results following intracorneal ring implantation, by observing a significant improvement in visual acuity up to 1 year after the procedure, suggesting sustained long-term visual benefits for patients. However, they also emphasised the need for continuous monitoring to detect possible late complications, such as keratoconus progression or endothelial loss. Vega & Alió [4] corroborated these findings, reporting a sustained improvement in visual acuity and topographic stability up to 3 years after intracorneal ring implantation in their long-term follow-up study, observing no significant changes in the endothelial count over the follow-up period, suggesting a stable response of the endothelial tissue to the procedure. However, Moura et al. [7] warned of the possibility of late complications, such as displacement or extrusion of the intracorneal ring, which can negatively affect long-term clinical results, emphasising the importance of regular surveillance and early intervention in cases of complications to maximise the benefits of treatment. Furthermore, Nuzzi [9] emphasised the need for a multidisciplinary approach in assessing the stability of long-term clinical results after intracorneal ring implantation, highlighting the importance of collaboration between ophthalmologists, optometrists and other healthcare professionals for a comprehensive and individualised assessment of patients undergoing the procedure. In the same vein, Elalfy et al. [10] contributed additional evidence on the stability of long-term clinical results following intracorneal ring implantation by observing a sustained improvement in visual quality and a reduction in corneal opacity up to 2 years after the procedure, reinforcing the lasting benefits associated with ring implantation. However, Larco et al. [11] and Moshirfar et al. [3] warned of the possibility of serious late complications, such as corneal perforation, which can jeopardise the stability of long-term clinical results, highlighting the importance of continuous surveillance and early intervention to mitigate the risks associated with the procedure. Likewise, Serpe [12] and Kim & Kim [13] also stressed the importance of regular assessment and careful monitoring of patients to monitor the stability of long-term clinical results following intracorneal ring implantation, emphasising the need for an individualised approach and adapting treatment according to each patient's response to the procedure. D'Azy et al. [14] also contributed by emphasising the importance of long-term prospective studies to properly assess the stability of clinical results after intracorneal ring implantation. Therefore, assessing the stability of long-term clinical results and analysing endothelial changes after intracorneal ring segment implantation are fundamental to providing information on the efficacy and safety of this procedure over time. We also emphasise that this research was essential for a comprehensive understanding of the long-term results of the procedure and to guide future clinical practice.

4.4. THE RELATIONSHIP BETWEEN ENDOTHELIAL CELL ANALYSIS AND PREOPERATIVE PARAMETERS RELATING TO CLINICAL CHANGES IN VISUAL ACUITY AFTER INTRACORNEAL RING IMPLANTATION

The relationship between endothelial cell analysis and the preoperative parameters that influence clinical changes in visual acuity after intracorneal ring implantation is a topic of great relevance in contemporary ophthalmology. Different studies provide fundamental information about this complex relationship. This is why Khanthik et al. [8] observed a correlation between the preoperative endothelial cell count and the stability of visual outcomes after intracorneal ring implantation, as well as highlighting the importance of an adequate endothelial count as part of the preoperative assessment to predict postoperative visual outcomes and mitigate the risks of complications. On the other hand, Vega & Alió [4] emphasised the influence of other preoperative parameters, such as corneal topography and corneal

thickness, on visual acuity after intracorneal ring implantation, suggesting that a comprehensive assessment of corneal parameters is crucial for proper patient selection and achieving satisfactory visual results. Furthermore, Moura et al. [7] addressed the importance of preoperative corneal curvature in predicting clinical changes in visual acuity after intracorneal ring implantation, highlighting the need for careful analysis of topographic and refractive data to identify patients most likely to benefit from the procedure. Thus, Nuzzi [9] highlighted the importance of the state of the cornea before intracorneal ring implantation, such as the presence of corneal scars or opacities, in determining post-operative visual results, while also emphasising the importance of a thorough pre-operative corneal assessment in order to properly manage patient expectations and prevent complications. Elalfy et al. [10] investigated the relationship between corneal thickness and endothelial density in predicting changes in visual acuity after intracorneal ring implantation, suggesting that a thinner cornea and greater preoperative endothelial density are associated with better postoperative visual results. However, Larco et al. [11] and Moshirfar et al. [3] warned of the need to also consider factors such as the patient's age and general state of health in the preoperative assessment, pointing out that older patients or those with comorbidities may show a different response to intracorneal ring implantation, which may influence changes in postoperative visual acuity. At the same time, Serpe [12] and Kim & Kim [13] complemented this information, highlighting the importance of an individualised approach when selecting patients for intracorneal ring implantation, and emphasising the need to consider all relevant preoperative parameters in order to optimise visual results and minimise the risk of complications. Corroborating these findings, D'Azy et al. [14] highlighted the importance of long-term prospective studies to adequately investigate the relationship between endothelial cell analysis and preoperative parameters on visual acuity after intracorneal ring implantation, as well as emphasising the need for a holistic and evidence-based approach to guide clinical practice. Therefore, investigating the relationship between endothelial cell analysis and preoperative parameters that touch on clinical changes in visual acuity after intracorneal ring implantation is an evolving field in ophthalmology. That's why these studies were necessary to ignite discussion of this state of the art and fully elucidate this relationship, as well as to develop evidence-based clinical guidelines to optimise results for patients.

4.5. CLINICAL SAFETY OF SEQUENTIAL INTRA-STROMAL CORNEAL RING IMPLANTATION AND LONGITUDINAL ANALYSIS OF ENDOTHELIAL CELLS IN DIFFERENT CONTEXTS

The clinical safety of sequential intra-stromal corneal ring implantation and the longitudinal analysis of endothelial cells in different contexts are topics of great interest in contemporary ophthalmology. Several studies contribute to a more comprehensive understanding of this complex issue, such as Khanthik et al. [8] who conducted an investigation into the safety of sequential corneal ring implantation, observing low rates of intra- and post-operative complications in their cohort of patients, also emphasising the importance of standardised surgical protocols and longitudinal follow-up to guarantee favourable and safe results. On the other hand, Vega & Alió [4] highlighted the need to carefully consider patient selection criteria for sequential corneal ring implantation, taking into account factors such as residual corneal thickness and refractive stability, while emphasising the importance of a personalised approach to minimise the risks and maximise the benefits of the procedure. In addition, Moura et al. [7] looked at the longitudinal analysis of endothelial cells after sequential corneal ring implantation, observing a satisfactory preservation of endothelial density over time in their series, suggesting that sequential corneal ring implantation may be a safe option in terms of long-term endothelial health. At the same time, Nuzzi [9] complemented this information by emphasising the importance of regular monitoring of endothelial density after sequential corneal ring implantation in order to detect early any changes that could indicate complications or deterioration in endothelial status. Elalfy et al. [10] and Larco et al. [11] investigated the effects of sequential corneal ring implantation in patients with different corneal characteristics, such as ectasia and keratoconus. And both studies observed a significant improvement in visual acuity and reasonable endothelial cell stability in their respective patient populations. On the other hand, Moshirfar et al. [3] warned of the possibility of late complications, such as corneal perforation, in selected cases of sequential corneal ring implantation, emphasising the importance of a careful assessment of the risks

and benefits of the procedure in each individual patient. Thus, Araujo [17] and Cueto et al. [18] discussed the need for long-term prospective studies to adequately assess the safety and efficacy of sequential corneal ring implantation in different patient populations, emphasising the importance of an evidence-based approach to guide clinical practice. That said, research into the clinical safety of sequential intra-stromal corneal ring implantation and the longitudinal analysis of endothelial cells in different contexts is also a constantly evolving field in ophthalmology, requiring further future research to fully elucidate the benefits and risks of this procedure and develop evidence-based clinical guidelines for its clinical use.

5. CONCLUSION

An in-depth analysis of the literature on the clinical landscape and endothelial cell analyses following intrastromal ring implantation revealed a range of divergent findings and perspectives among the various studies reviewed. Each author offered valuable contributions, outlining important nuances that shape the current understanding of this crucial ophthalmological procedure. And in this final synthesis, the perspectives presented by the different authors were amalgamated, contextualising them within the objectives of this research. With regard to investigating the clinical safety of sequential intra-stromal corneal ring implantation and the longitudinal analysis of endothelial cells in different contexts, the importance of preoperative analysis of clinical and epidemiological variables in predicting changes in post-implant visual acuity was highlighted, A mechanistic view of the role of endothelial cells in long-term clinical stability was also provided, highlighting the safety and efficacy of the Ferrara ring implant and corroborating its stability as a sight-restoring procedure. With regard to the relationship between the analysis of endothelial cells and preoperative parameters that influence clinical changes in post-implant visual acuity, the stability of clinical results in patients with stable keratoconus was highlighted, suggesting a correlation between corneal endothelial density and improved visual acuity, as was the perception of the unique biomechanical role of a stable cornea in endothelial cell function. In the context of evaluating the stability of long-term clinical results and analysing endothelial changes following the implantation of an intracorneal ring segment, the effectiveness of the Ferrara ring implant in reducing refractive error and improving visual acuity over several years of follow-up was highlighted, as were the potential complications, and the importance of post-operative monitoring and careful analysis of endothelial cells. Regarding the correlation between short- term clinical effects and endothelial changes after intracorneal ring segment implantation, the effectiveness of sequential implantation of an intrastromal corneal ring segment and corneal cross-linking in improving visual acuity was highlighted, as were the significant changes in endothelial density in patients treated with two rings of equal thickness. As such, this systematic review of the literature has revealed a complex and multifaceted picture of the clinical panorama and the analysis of endothelial cells after intra-stromal ring implantation. And although there are differences of opinion on certain aspects, such as the influence of Ferrara ring implantation on long-term endothelial stability, there is a general consensus on the efficacy and safety of this procedure as a therapeutic option for patients with keratoconus. It is suggested that future research should further elucidate the mechanisms underlying post-implant endothelial changes and develop strategies to optimise long-term clinical results.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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