Surgical Options for Keratoconus Patients

Clinical Guideline

Research development

Shaher Saadeddin

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ABSTRACT

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Author: Shaher Saadeddin
Supervises: Dr Robert Andersson and Mr.Tuomas Juustila
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Purpose of the Study

This study aims to develop a safe and effective clinical guideline for the surgical management of keratoconus, facilitating the selection of appropriate treatment modalities based on corneal classification, disease severity, and individual anatomical characteristics. By integrating current evidence and surgical options, the guideline is intended to assist healthcare professionals in making informed, patient-specific decisions that improve visual outcomes and minimising risks.

Method

This study employed a qualitative research design using content analysis to develop a clinical guideline for surgical options for keratoconus patients. The approach it was chosen to systematically examine and synthesize contemporary knowledge, expert opinions, and clinical practices presented in ophthalmology and optometry latest conferences. This method leads and allowed for the extraction of relevant themes and trends that inform surgical decision-making based on corneal classification, disease severity, and anatomical factors.

Result

Based on the comprehensive literature review, corneal classification criteria, and expert clinical input, a stepwise guideline was developed to support individualized surgical decision-making in keratoconus cases management. These guideline stratifies patients by disease severity, corneal morphology, and anatomical limitations to recommend the most suitable treatment or combination thereof.

Conclusions

The proposed surgical guideline for managing keratoconus provides a thorough, evidence-driven framework for addressing this progressive corneal condition. By categorizing patients according to the severity of their disease, corneal shape, and anatomical characteristics, the guideline supports tailored treatment plans that align with each individual's specific clinical profile.

Keywords

Keratoconus, surgical management, corneal cross-linking, penetrating keratoplasty, deep anterior lamellar keratoplasty, intracorneal ring segments, phakic IOL, CAIRS

CONTENTS

1 INTRODUCTION

Keratoconus is an ectatic disorder of the cornea, characterized by progressive, bilateral, non-inflammatory stromal thinning, forward anterior protrusion of the cornea and biomechanical weakening of the stroma, which results in a conical shape and irregular astigmatism, and can reach a severe visual state (Rabinowitz, 1998; Gomes et al., 2015).

Presentation is usually in childhood or early adolescence and occasionally occur even in the third and fourth decades. When visual distortion becomes intolerable by habitual correction with eyeglasses or soft contact lenses, the quality of life of keratoconus patients is severely affected with disease progression (Krachmer, Feder, & Belin, 1984; Gomes et al., 2015).

In the past 20 years, significant progress in diagnostic tools, surgical methods, and therapeutic strategies has led to improved clinical outcomes for individuals with keratoconus.

Some of the important surgical advancements include; CXL to arrest thedise ase process, ICRS, topography-guided PRK, and phakic IOLs.

Newer modalities like (CAIRS) corneal allogenic intrastromal ringsegments (CAIRS) and refractive lens exchange (RLE) have more recently been establi shed foruse as adjuncts or alternatives in select patients populations (Jacob et al., 2021, Hersh et al.,2011, Kymionis et al., 2010). Staged or hybrid proce dures are being recognized as moreeffective, especially in cases of moderat e to advanced disease.

Despite worldwide investigations for the best treatment approach to cater to the variable clinical and anatomical presentation, until this time is no consensus on a gold standard treatment protocol. Taking that into consideration these advancesThe sequence, timing and the selection of therapies is difficult decision for eye care practitioners and especially, when there is significant corneal thinning steep curvature and high visual demand and looking for single modality based treatments. Therefore, a methodically personalized strategy for clinical decision making is needed. Regarding to multi-complex nature of the disease, management should be based on severity of the disease, corneal thickness and patient's refractive error expectations.

To address this gap, a comprehensive surgical guideline has been developed, integrating current literature, best clinical practices, and expert consensus. I relate on this stratified according to disease severity ranging from early-stage to post-keratoplasty-the framework enables clinicians to tailor interventions based on each patient's specific profile. The proposed algorithm is intended to summary evidence-based management of keratoconus presentations. The goal is to address structural and visual issues is an effort to stop progression, improve vision, prevent complications, and enhance overall quality of life.

2 THEORETICAL BACKROUND

2.1 Cornea: Anatomy and Histology

Cornea it’s the primary refractive medium of the eye, covering the anterior portion of the globe and accounting for approximately 7% of its surface area (Maurice, 1984). Regarding transparency and a vascularisation structure, cornea plays a critical role in vision.

Corneal innervation is dense and highly specialized.The sensitivity of the cornea is 300 to 600 times greater than that of the skin. This is due to unmyelinated nerve endings that are acutely sensitive to mechanical, thermal, and chemical stimuli (Belmonte et al., 2004). Cornea sensory nerves originate from the ophthalmic ganglion, traveling in the nasociliary nerve and its long ciliary nerve branches and ultimately branching into nerve fibers that penetrate the cornea.The cornea contributes approximately 43 D of the eye’s refractive power, representing roughly two-thirds of the total refractive power, estimated at 60 D (Doughty and Zaman, 2000). Anatomically,Cornea it's elliptical shape, more curved in the center and flattened toward the periphery with vertical diameter 11.50mm in average and horizontal 12mm.The thickness of the corneal is about 540 µm in the centre and reaches 1000 µm in the peripheral. The refractive index of the corneal tissue is approximately 1.376.

Oxygen supply mainly from tear film, metabolic requirements from the aqueous humor and Peri-limbal vascular plexus.(Klyce, 1972).

The cornea consists of five layers, sometimes six anatomically and functionally distinct layers, organized from anterior to posterior:

1. Epithelium: it’s the first regenerative and stratified squamous epithelial layer average thickness 60-70 µm. It serves as a barrier against microbial invasion and contributes to the smooth refractive surface .
2. Bowman’s Layer: ultra-thin layer its thickness around 7-8 nm consist of type one collagen fibers,does not regenerate after injury.
3. Stroma: it constitutes about 90% for corneal thickness non-generative layer composed of type one collagen fibers interspersed with fibroblasts and

elastic fibers it is highly regular layers the fiber within each layer is parallel to one another and alternating layers run in different directions

4. Descemet’s Membrane:A strong, ultra-thin layer its thickness between 5um to 17um.
5. Endothelium: posterior layer in the cornea consists of single layer of simple squamous cuboidal cells, It have sodium pumps playing important rule to maintaining corneal dehydration and transparency of cornea it is non-regenerative and decline with age or trauma.

Each layer of the cornea plays a distinct role in supporting its strength, clarity, and ability to properly focus light — all of which are crucial for maintaining sharp and clear vision.

2.2 Keratoconus

2.2.1 Definition and Historical Background

The linguistic term for keratoconus is derived from the Greek words kéras (meaning “cornea”) and cōnus (“cone”).

This indicates that the origin of the word is consistent with the cone shape of the cornea. By reviewing the literature, signs of keratoconus have been observed in 18th and 19th centuries.The first to provide a detailed description of keratoconus was John Nottingham in 1854. He described it in detail, distinguishing it from other corneal diseases. (Nottingham, 1854).

Keratoconus is a progressive condition of the cornea that isn’t caused by inflammation but instead involves gradual thinning of the corneal stroma. As the structure weakens, the cornea starts to bulge outward into a cone shape. This distortion leads to blurry vision, due to increasing myopi and irregular astigmatism, and in more advanced cases, scarring of the cornea (Rabinowitz, 1998; Krachmer, Feder, & Belin, 1984). These visual changes can significantly affect a person’s daily life and overall quality of vision.

Keratoconus typically begins in early childhood and adolescence and continues to develop into the thirties. It usually develops in both eyes, but its asymmetrical. Keratoconus is characterised by a gradual thinning and irregularity of the corneal curvature, accompanied by blurred and unclear vision (Gomes et al., 2015; McMonnies, 2009).

The irregularity in the corneal curvature usually occur in the center or slightly away from the center of the cornea, especially in the lower quadrant (Rabinowitz, 1998).

2.2.2 Aetiology

The exact cause of keratoconus is still not fully understood, but it is widely believed to be the result of a mix of factors-genetic, environmental, and mechanical. Genetics play a major role, as the condition is more common in people with a family history of keratoconus. In fact, studies have identified specific areas on chromosomes (like 5q21.2, 13q32, and 15q22.33) that may increase a person’s risk (Bykhovskaya et al., 2012). The condition that also tend to be more frequent in individuals with certain inherited disorders, such as Down syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, and Leber congenital amaurosis, which points to a possible defect in collagen or connective tissue (McMonnies, 2009).

Environmental factors can also influence when and how severely keratoconus appears. People living in hot, dry, and dusty areas like parts of the Middle East and South Asia more likely to be affected, and due to higher UV exposure, chronic eye surface inflammation, and exposure to allergens (Hashemi et al., 2020).

These conditions can cause oxidative stress in the cornea, weakening its structure.

Chronic eye rubbing is a major contributor to the worsening of keratoconus. The rubbing causes direct damage to the corneal surface and can trigger inflammation. Allergies, asthma, and in children, aggressive eye rubbing can lead to faster disease progression if not managed properly (Balasubramanian et al., 2013).

Many patients with poor vision wish to undergo a vision correction procedure such as LASIK. This procedure can be dangerous for patients with keratoconus or those who suffer from severe thinning and irregularity in the corneal surface. This is the case for patients with keratoconus in its early stages and has not been diagnosed at all, as the LASIK procedure leads to Ectasia, which is a condition that mimics keratoconus and worsens it due to weakness or loss of structural support of the cornea.(Binder, 2007).

Accordingly, the cornea must be examined and diagnosed accurately before the procedure by using the latest examination and imaging devices to avoid any side effects of the operation.

2.2.3 Risk Factors

There are many risk factors that lead to keratoconus and increase its development. These include:

1. Genetic Predisposition plays a major role in Keratocounus, as the possibility of developing keratocouns if one of the parents is affected multiplies between 15 to 67 times compated to families who do not have a medical history associated with keratoconus.Recent genetic studies have supported this idea by identifying specific regions in the DNA that are associated with a higher chance of developing keratoconus (Bykhovskaya et al., 2012; Gordon-Shaag et al., 2015).
2. Age and Gendar, That said, the gender difference isn't consistent and can vary across different populations (Hashemi et al., 2020).
3. Eye Rubbing and Atopy, Severe, recurrent, and chronic eye rubbing, especially in children, associated with spring allergies, vernal keratoconjunctivitis, spring allergies, rhinitis, asthma, and chronic eczema, is closely linked to keratoconus and its development.
   Rubbing the eye leads to deterioration of the corneal tissue as a result of microtrauma to its tissues, which leads to an enhanced response to local inflammation. (Balasubramanian et al., 2013, McMonnies, 2009).
4. Environmental Factors, Exposure to environmental stressors-such as ultraviolet (UV) radiation, oxidative stress, and dryness of the eye's surface-has been linked to the development of corneal thinning and ectasia. These factors increase in dry, desert and agricultural areas, leading to an increase in the number of patients with keratoconus. (Karamichos, 2015)

5. Genetic and systemic disorders, Keratoconus is clearly associated with a group of diseases and connective tissue disorders such as Ehlers-Danlos syndrome, Marfan syndrome, and osteogenesis imperfecta. Keratoconus is more commonly associated with Down syndrome due to abnormalities in the

structural composition of collagen and increased eye rubbing.(Rabinowitz, 1998; Tuft & Moodaley, 1994).

6. Refractive Surgery, patients with severe corneal thinning or early keratoconus stages lead to worsening of the irregularity in the corneal tissue. LASIK surgery it's high risk to this patients, Based on the above emphasises the need for accurate diagnosis of the cornea before performing vision correction surgeries using the latest corneal investigation and imaging devices.(Binder, 2007).

2.2.4 Pathophysiology.

Keratoconus is an ectatic corneal disorder, non-inflammatory and progressive, with the localized thinning occurring in the corneal stroma, this condition with the associated biomechanical weakening and irregular conical shaped deformation of the anterior corneal surface. Despite the pathogenic mechanisms that remain only partially understood, an increasingly accepted hypothesis states that it is multifactorial, including genetic predisposition, biochemical alterations, cellular dysfunctions, and environmental factor.

A. Corneal stromal thinning and biomechanical instability

are among the most important pathological problems in keratoconus. Stroma, which comprises 90% of corneal thickness, is formed well-organized lamellae of type I collagen and interspersed keratocytes. Such structure of collagen in KC suffers disruption and gives the loss of tensile strength and biomechanical integrity of the cornea and unable to ratainits normal intraocular pressure (Roberts, 2000). This results in stromal thinning, anterior corneal protrusion, and the development of irregular astigmatism.

B. Cellular and Extracellular Matrix (ECM) Alterations

Microscopic changes of cellular density and ECM format of keratoconic corneas well observed in histopathological examination. A significant reduction in the number of keratocyte, particularly in the anterior stroma, has been noted with concomitant keratocyte apoptosis (Rabinowitz, 1998).

Bowman's layer fragmentation and collagen fibrils disorganisation are frequent. This happens as a result of high levels of Matrix metalloproteinases (MMPs), especially MMP-1, MMP-2, and MMP-9, are often up-regulated, leading to the increased in ECM degradation. In contrast, tissue inhibitors of metalloproteinases (TIMPs) are commonly downregulated,during malignant invasion, further promoting the imbalance of the proteolytic enzyme (Smith et al., 2006).

C. Oxidative Stress and Subclinical Inflammation

Although keratoconus is a non-inflammatory disease, it is characterized by mild inflammation and oxidative stress. Corneal tissues and tear fluid from keratoconus patients show elevated levels of reactive oxygen species (ROS), lipid peroxidation products, and proinflammatory cytokines (Matalia & Swarup, 2013). At the same time, antioxidant defense mechanisms such as superoxide dismutase (SOD) and catalase are diminished, predisposing the cornea to oxidative injury. This imbalance contributes to keratocyte apoptosis, collagen degradation, and disease progression.

D. Genetic and Molecular Contributions

Numerous genetic loci and candidate genes have been implicated in keratoconus, including VSX1, ZNF469, LOX, COL5A1, and TGFBI. Since terminal mutations far to happening , polymorphisms in these genes lead to impairment incollagen synthesis, enzyme binding, and wound healing. (Bykhovskaya et al., 2012). The association of keratoconus with systemic heritable disorders such as Ehlers-Danlos and Down syndrome further supports a genetic predisposition.

E. Role of Mechanical Trauma.

We note that both mechanical factors and chronic eye rubbing play an important role in the development of keratoconus. Eye rubbing induces microtrauma, might lead to localized inflammation, ECM remodeling, and upregulation of MMPs. Patients suffering from biochemical or genetic corneal fragility, such trauma might significantly increase stromal thinning and ectasia. (McMonnies, 2009).

The interaction between structural, mechanical, and environmental factors reflects the pathological factors that cause it. Mechanical weakness, genetic predisposition, apoptosis, and oxidative injury are all factors that stimulate the progressive changes that lead to the marked increase in disease. Understanding the interconnected mechanisms is important for developing early diagnosis, treatments, and early intervention in the early stages of the disease.

2.2.5 Epidemiology, Prevalence, and Incidence

Influenced by different diagnostic criteria, technological capabilities, genetic predisposition and environmental factors, the prevalence and incidence of keratoconus varies among the general population.

As I mentioned above, and according to the latest studies we have reviewed, due to development in examination devices and corneal imaging , new techniques have enable early detection of keratoconus in early stages, as it turned out to us keratoconus has become more common.

Consequently, there has been an increase in the prevalence of the cornea, early epidemiological surveys reported incidents ranging from 1 in 2,000 and 1 in 10,000 (Rabinowitz, 1998).

The prevalence and incidence of keratoconus (KC) vary significantly across populations, influenced by differences in diagnostic criteria, technological capabilities, genetic predisposition, and environmental exposures.

Keratoconus become more common, in general due to significant advancement in corneal imaging devices like corneal topography which now allow for its detection in the early stages. Keratoconus became more common based on the above early epidemiological surveys reported incidents ranging from 1 in 2,000 and 1 in 10,000 (Rabinowitz, 1998).

As it become clear previously contemporary data using modern diagnostic technologies reveal a broader incidence range, from 0.2% to 5%, regarding of geographic location and screening criteria. (Hashemi et al., 2020).

Population-based studies in regions such as the Middle East and South Asia have reported mostly high rates, with some estimates as high as 4.79% among high-risk cohorts (Godefrooij et al., 2017). The annual incidence is commonly reported to be 1 in 7,500 to 1 in 20,000 individuals, although it may be underestimated by asymptomatic initial stages and defect screening practices. Usually, Keratoconus first appears in individuals how are in their late teens or early 20s. It typically progresses for one to two decades before stabilizing. Onset in young age is usually indicative of a rapidly progressive disease. With no significant gender disparity.

Marked geographic and ethnic variability is evident in keratoconus epidemiology. Higher incidence rates have been reported in populations from the Middle East, South Asia, and North Africa compared to Western Europe or North America (Gomes et al., 2015). Contributing factors may include:

- Increased genetic susceptibility due to consanguinity varies depending on ethnic and religious beliefs.
- Greater environmental exposure to UV radiation, dust, and allergens.
- Higher rates of habitual eye rubbing, often linked to atopic disease.

Family history is one of the most significant risk factors for keratoconus. As a genetically factor family members of affected individuals have a 15-67 times higher risk of developing the disease, and familial cases usually present earlier and more severely (Gordon-Shaag et al., 2015). Although genetic heterogeneity dominates the phenotype, both autosomal dominant and autosomal recessive inheritance patterns have been described. Heritability average range up to 60%, while the primary genetic mechanisms remain incompletely clear (Bykhovskaya et al., 2012).

2.2.6 Association with Systemic and Ocular Conditions

Keratoconus has been linked to multiple systemic disorders and syndromes, particularly those involving connective tissue and neurodevelopmental abnormalities. Common associations include:

- Down syndrome.
- Leber congenital amaurosis.
- Ehlers-Danlos syndrome.
- Marfan syndrome.
- Atopic conditions (e.g., eczema, asthma, allergic rhinitis).

Ocular comorbidities include:

- Vernal keratoconjunctivitis (VKC).
- Retinitis pigmentosa.

- Chronic eye rubbing.

The prevalence of Keratoconus has also been found to be higher in case of patients undergoing corneal refractive surgery, in patients with occult stage - early disease as aforementioned reiterated the need for preoperative screening to diagnose forme fruste keratoconus and prevent iatrogenic ectasia (Binder, 2007).

2.2.7 Symptoms and Clinical Signs

2.2.7.1 Symptoms.

Patients with keratoconus suffer from the following symptoms, which increase in severity and intensity over time as the keratoconus progresses. Progressive in visual blurring uncorrectable with glasses. Distortion of the vision. Increased sensitivity to light. Frequently changes in eyeglass prescriptions. Difficulty with night vision. Glare and halos around lights. Eye strain or headaches due to uncorrected refractive error. Eye rubbing. which may exacerbate disease progression. (Rabinowitz, 1998, Krachmer, Feder, & Belin, 2011, StatPearls, 2023).

2.2.7.2 Clinical Signs.

On examination, keratoconus may present with a range of slit-lamp and topographic findings depending on disease severity:

Early-Stage Signs: inferior or central corneal thinning; irregular astigmatism on refraction, scissoring reflex on retinoscopy, and Fleischer ring (iron deposition around the base of the cone, visible with cobalt blue light) (Rabinowitz, 1998, Krachmer et al., 2011).

Moderate to Advanced stages: Vogt’s striae (fine vertical stress lines in the deep Stromal-Descemet’s membrane).

Munson’s sign (protrusion of the inferior eyelid in down gaze increased vascularity in the inferior cornea), Rizzuti’s sign (cone-shaped reflection from the nasal cornea when light is shone from the temporal), and concomitant corneal steepening/escolesis and cone formation (central, paracentral, or inferior cornea), and progressive corneal higher-order aberrations, including coma visual symptoms formation (Krachmer et al., 2011, StatPearls, 2023).

Advanced Disease: corneal scarring; acute hydrops (sudden stromal edema due to Descemet's membrane rupture) and marked visual impairment uncorrectable by spectacles or soft lenses (Rabinowitz, 1998, StatPearls, 2023).

2.2.8 Diagnosis

Early and accurate diagnosis of keratoconus have a highly benefit to avoiding visual deterioration and preventing complications from inappropriate interventions (Rabinowitz, 1998, StatPearls, 2023).

A variety of diagnostic devices have been used in practice for the clinical assessment of anatomical structure and biophysical properties of the cornea. Slit-lamp it's important device allows health care professionals to detect classic signs of keratoconus, like stromal thinning, Fleischer rings (iron deposits at the base of the cone), Vogt's striae (fine vertical stress lines in the stroma or Descemet's membrane), and anterior corneal protrusion (Krachmer, Feder, & Belin, 2011; Rabinowitz, 1998).

Central corneal curvature is measured by keratometry (c), though it is poorly sensitive for the early or atypical changes, especially of the peripheral cornea (Rabinowitz, 1998).

Corneal topography it's the gold standard for diagnosis of keratoconus. It's scan the anterior surface of the cornea, this advantage allows asymmetric steepening detection and inferior and superior curvature differences as important to detecting early or subclinical keratoconus suspects. (Belin & Khachikian, 2009).

Corneal tomography, Scheimpflug system like Pentacam, is a three-dimensional of examination of the anterior and posterior corneal surfaces. It offers an important information about elevation maps and pachymetric distribution, and its also increases detection sensitivity to early signs of ectatic (Ambrósio et al., 2011).

Anterior segment optical coherence tomography (AS-OCT) enables high-resolution cross-sectional of the cornea. It is quite useful for epithelial thickness profiling and demonstrations of regional changes in corneal biomechanical proposed for early keratoconus (Reinstein, Archer, & Gobbe, 2010).

Devices like Corvis ST or the Ocular Response Analyzer, using Biomechanical techniques to measure parameters such as corneal stiffness and deformation response.

These devices provide more informations about corneal integrity and help diagnosing early ectatic changes even before topographic abnormalities appear. (Ambrósio et al., 2017).

The benefits for using this technology for diagnosed Keratoconus it’s to determine early stage of keratoconus, and help to choose a proper treatment. (Belin & Khachikian, 2009, Ambrósio et al., 2011).

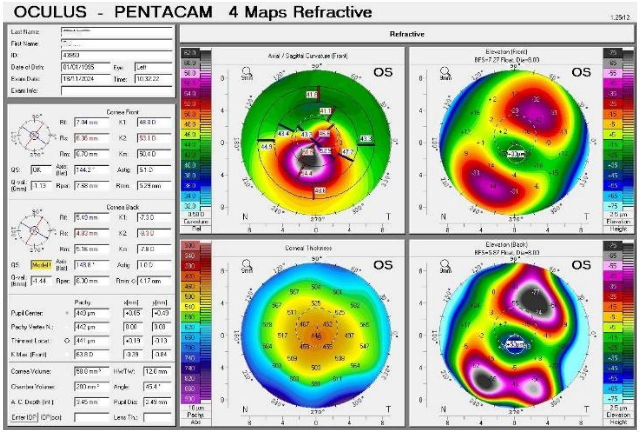

Figure N.1 (Pentacam,Schwind Sirius Topographer and Planning System, Galilei & Orbscan, Anterior Segment OCT & Epithelial Mapping, Corvis ST, Confocal Microscopy).

2.2.9 Classification and Grading

The classification of keratoconus is essential for guiding clinical management, selecting appropriate treatment strategies, and monitoring disease progression. Various systems have been developed based on clinical signs, corneal curvature, topographic patterns, pachymetric measurements, and, more recently, biomechanical properties (Rabinowitz, 1998; Belin & Duncan, 2016). Although no single classification system is universally accepted, several are widely used in both clinical and research settings.

1. **Amsler-Krumeich Classification.**

One of the earliest referenced systems is the Amsler-Krumeich classification. Based on it keratoconus deviated into four stages based on clinical signs, refractive error, corneal curvature, and central corneal thickness. (Krumeich et al., 1998):

- Stage 1: Slight asymmetric bow-tie astigmatism; myopia/astigmatism < 5.00 D; K readings < 48.00 D; no scarring; CCT > 500 µm.
- Stage 2: Myopia/astigmatism between 5.00–8.00 D; K < 53.00 D; no scarring; CCT > 400 µm.
- Stage 3: Myopia/astigmatism > 8.00 D; K > 53.00 D; no scarring; CCT between 300–400 µm.
- Stage 4: Advanced ectasia; K > 55.00 D; central scarring; CCT < 300 µm.

Given the importance of this classificatio, it becomes clear to us some disadvantages, limitations in detecting early or subclinical keratoconus and does not include corneal posterior curvature. (Belin & Khachikian, 2009).

2. Topographic Classification

Corneal topography has significantly improved keratoconus classification, particularly for early and subclinical cases. It enables detailed mapping of corneal curvature and asymmetry. Commonly recognized cone patterns include:

- Nipple cone. Small (<5 mm), central, steep cone.
- Oval cone. Larger cone, often located inferotemporally.
- Globus cone. Extensive protrusion involving over 75% of the cornea.
- Pellucid marginal degeneration pattern. Characterized by peripheral inferior thinning and a “kissing dove” or “crab claw” appearance on topography (Rabinowitz, 1995).

Quantitative indices such as the KISA% index, Inferior–Superior (I–S) value, and Rabinowitz criteria assist in diagnosing subclinical keratoconus (Rabinowitz, 1998).

3. Tomographic and Biomechanical Classifications

Modern imaging modalities, which depends on modern technology including Scheimpflug tomography and corneal biomechanics analysis, have enabled more comprehensive classification systems:

- Belin/Ambrosio submitted Ectasia Display (BAD-D) Works on integrating and analyzing data for anterior and posterior elevation data with pachymetric progression, and thickness distribution to diagnose early ectasia (Belin & Ambrosio, 2008).

- Tomographic Biomechanical Index (TBI) combines Pentacam tomography with Corvis ST dynamic biomechanical metrics It was a significant importance, especially for patients who wish to undergo vision correction surgeries, as it increases the sensitivity of detecting early stage for keratoconus. (Ambrósio et al., 2017).

  These indices are particularly useful in detecting preclinical disease and assessing Ectasia risk.

4. **ABCD Grading System**

   The ABCD Grading System, The latest classification system for keratoconus was presented by Belin and Duncan in 2016. They relied on four factors in this classification, which are:

- A: Anterior radius of curvature at the thinnest point.
- B: Posterior radius of curvature at the thinnest point.
- C: Corneal thickness at the thinnest point.
- D: Distance best-corrected visual acuity.

This system allows for independent tracking of disease progression across the anterior, posterior, and pachymetric dimensions, making it particularly useful in monitoring outcomes of interventions such as corneal cross-linking (Belin & Duncan, 2016).

Therefore, this model provides the latest classification for Keratoconus based on using last techniques in diagnostics and imaging devices.

Differential Diagnosis

Strong diagnosis of keratoconus is essential for effective management and prevention of vision loss, particularly when considering refractive surgical interventions. Based on our review of the literature on Keratoconus,it is important to differentiate Keratoconus from other corneal disease

Because of several corneal and systemic conditions can mimic the clinical, topographic, findings of keratoconus. Distinguishing between these conditions is critical to avoid misdiagnosis and inappropriate treatment (Rabinowitz, 1998; Krachmer et al., 2005).

Pellucid Marginal Degeneration (PMD)

PMD it is noninflammatory ectatic disorder that characterized by inferior peripheral thinning located in 1-2 mm above the inferior limbus, with relative central corneal sparing.

Unlike keratoconus, PMD does not exhibit a central cone. On topography, it often shows a “crab claw” or “kissing dove” pattern due to superior steepening above the area of thinning. (Krachmer et al., 2005; Sridhar, 2012).

Keratoglobus

Keratoglobus is a rare bilateral disorder marked by diffuse corneal thinning, particularly in the periphery. The cornea becomes more globular rather than conical. It may be congenital or associated with systemic connective tissue disorders such as Ehlers–Danlos syndrome (Meek et al., 2005). Unlike keratoconus, keratoglobus lacks focal steepening and typically presents earlier in life.

Terrien’s Marginal Degeneration

This slowly progressive condition features superior peripheral thinning with lipid deposition and superficial vascularization. It is more common in older males and often induces against-the-rule astigmatism. Unlike keratoconus, Terrien’s degeneration spares the central cornea and is non-ectatic (Weissman et al., 2001).

Post-LASIK Ectasia (Iatrogenic Keratectasia)

Post-refractive surgery ectasia resembles keratoconus but occurs secondary to biomechanical weakening of the cornea after LASIK or PRK. It typically manifests in patients with predisposing risk factors such as thin residual stromal bed or undetected forme fruste keratoconus (Binder, 2007). Detailed surgical history and preoperative imaging are essential for differentiation.

Corneal Warpage (Contact Lens-Induced Changes)

Long-term use of rigid gas-permeable lenses can cause corneal warpage, mimicking the topographic patterns of keratoconus. These changes are usually reversible after discontinuing lens wear. A “contact lens holiday” and repeat imaging are key to distinguishing warpage from true ectatic disease (Rabinowitz, 1995).

Dry Eye and Irregular Astigmatism

Severe dry eye or ocular surface disease can lead to distorted keratometric and topographic readings. These findings can resemble early keratoconus but typically resolve with treatment of the ocular surface (Kanellopoulos, 2015).

Other Ectatic Disorders and Syndromic Associations

Disorders such as anterior megalophthalmos, sclerocornea, and various corneal dystrophies may mimic or coexist with keratoconus (Krachmer et al., 2005). Additionally, systemic conditions like Down syndrome and Leber congenital amaurosis have known associations with keratoconus, though presentation may be atypical or complicated by comorbid ocular pathologies (McMonnies, 2015).

A comprehensive approach that includes detailed history-taking, slit-lamp examination, and advanced corneal imaging is vital to distinguish keratoconus from these mimickers and ensure appropriate treatment planning.

2.3 Management of keratoconus

Management of keratoconus involves both stop or slow down disease progression and improving visual function. Treatment strategies are chosen based on disease severity, progression, and the degree of visual impairment.

2.3.1 Corneal Collagen Cross-Linking (CXL)

Corneal Cross-Linking (CXL) is the first-line surgical treatment aimed at stabilizing keratoconus by strengthening the corneal stroma through the photochemical reaction of riboflavin and ultraviolet-A light. CXL has been shown to significantly reduce the rate of keratoconus progression, particularly when applied in the early or progressive stages of the disease (Wollensak et al., 2003; Hersh et al., 2017). This makes it the foundational intervention before considering refractive correction options.

2.3.2 Spectacles and Contact Lenses

In early stage of Keratoconus patients can use glasses, soft and soft toric contact lenses to correct refractive errors. But in case of progression of the disease, patients need to use Hard Contact Lenses like RGP, scleral or

Hybrid to enhance there vision by masking irregular astigmatism. (Rabinowitz, 1998).

2.3.3 Vision Correction Procedures

When keratoconus has stabilised often through CXL, surgical options for visual rehabilitation can be considered:

- Topography-Guided Photorefractive Keratectomy (TG-PRK): Custom ablation for that regularizes the anterior corneal surface. Usually performed combined with CXL to retain biomechanical stability it's possible in the same suction with CXL and can be before or after it (Kanellopoulos & Binder, 2007).
- Implantable Collamer Lens: Is placed in the cases where cornea is regular and allows for lens implantation. ICLs are also affective for those with high myopia or astigmatism without having to affect the corneal structure (Kamiya et al., 2012).
- Refractive Lens Exchange with Toric Intraocular Lens (IOL): For older patients or those with lens opacities, lens-based refractive procedures can improve vision while correcting astigmatism.
- Intracorneal Ring Segments: These implants of PMMA rings make the corneal surface flat and decrease irregular astigmatism. Mostly for mild to moderate cases without corneal scarring (Colin et al., 2000).
- CAIRS (Corneal Allogenic Intrastromal Ring Segments): An emerging alternative to synthetic ICRS consisting of donor tissue input to improve biocompatibility and less complications (Jacob et al., 2021).
- Combined Procedures: Im many cases such as CXL + ICRS or CXL + TG-PRK are often used synergistically for enhanced outcomes.

2.3.4 Corneal Transplantation

In case of advanced stage of Keratoconus with significant corneal scarring and intolerance to other treatments, its place for corneal transplantation. Two main types are:

- Penetrating Keratoplasty: Full thickness corneal transplant, it's a traditionally procedure used in advanced keratoconus (Katz & Rabinowitz, 2021).
- Deep Anterior Lamellar Keratoplasty: A new technique of partial-thickness graft that preserves the endothelium, reducing the risk of rejection and

offering long-term graft survival it’s the advantage of this procedure (Anwar & Teichmann, 2002).

2.4 Surgical options for Keratoconus patients

Surgical intervention in keratoconus is indicated when conservative measures like spectacles, contact lenses, or corneal cross-linking (CXL), do not provide satisfactory visual abbreviation, or when disease progression leads to advanced ectasia, stromal scarring, or corneal decompensation. Indications for surgery typically include contact lens intolerance, severe corneal thinning, apical scarring, and visual acuity that cannot be improved with optical correction (Gomes et al., 2015; Santodomingo-Rubido et al., 2022). Surgery is performed most commonly, with either anterior lamellar keratoplasty (ALK) with decemetic DALK or PK.

DALK and its variants are preferred when the endothelium is preserved, as they reduce the risk of immunologic graft rejection and provide long-term graft survival (Jacob et al., 2020). In contrast, PK is still required in eyes with full thickness scar or hydrops associated endothelial damage (Nicula et al., 2022).

Refractive surgical techniques can be secondarily viable or adjunctive surgical options to keratoplasty for treatment of non progressive or mild to moderate Keratoconus patients.

Intrastromal corneal ring segments (ICRS) are reshaping the corneal surface and enhance both uncorrected and best-corrected visual acuity. Their importance is particularly evident in patients with moderate stage and sufficient corneal thickness (El-Raggal et al., 2016, Vega-Estrada et al., 2023). Phakic intraocular lenses (pIOLs), in practice implantable collamer lenses (ICLs), provide a high refractive error solutions in keratoconus patients with stable topography and clear corneal centre, achieving excellent visual outcomes in selected cases (Hashemi et al., 2019; Kamiya et al., 2023). Topography-guided photorefractive keratectomy (PRK), often combination with CXL, could be indicated to regularize the anterior corneal surface and improve visual rehabilitation of patients with stable, mild keratoconus (Aslan et al., 2021; Tomita et al., 2020).

Surgical approach should be based on stage of disease, corneal scarring, endothelial status, and other individual factors.

Corneal Cross-Linking (CXL)

Cross-linking it is a procedure led to increases the biomechanical stability and rigidity of the cornea to prevent keratoconus progression

2.4.1.1 Origins and Development:

- Early Concepts: The foundation of CXL was started in the late 1990s by researchers in Dresden, Germany by Dr. Theo Seiler, Dr. Eberhard Spoerl, and colleagues. They assume to enhance the biomechanical rigidity of the cornea and slowing the progression. Although, by increased number of intra-fibrillar and inter-fibrillar corneal collagen cross linking.
- First clinical application: Germany in 1999 the Technical University of Dresden was established the first clinical application of CXL. Dresden Protocol producer involved epithelial removal, with using riboflavin, Instillation for 30 minutes, then followed by UVA irradiation at 3 mW/cm^2 for more 30 minutes (total energy dose: 5.4 J/cm^2).
- Early Publications and Validation: In 2003 Wollensak et al. Published the first article for clinical results for corneal cross linking, slowing progression of the corneal irregularities and have some flattening in corneal curvature. (Wollensak G, Spoerl E, Seiler T. Am J Ophthalmol. 2003).
  These early results provided that CXL compelling evidence of its efficacy and safety.

2.4.1.2 Corneal Collagen Cross-Linking (CXL) in the Management of Keratoconus:

Corneal collagen cross-linking (CXL) is a well-documented, minimaize invasive that has been reported to slow the progression of keratoconus by increasing corneal biomechanical strength, by using riboflavin photochemical activation (Wollensak et al., 2003; Spoerl et al., 1998).

2.4.1.3 Mechanism of Action

Corneal collagen cross-linking improves the biomechanical rigidity of the corneal stroma by inducing photochemical cross-linking of collagen fibers.

Although, procedure started with exposing the cornea to ultraviolet A light at a wavelength from 365-370nm after saturating corneal tissue with vitamin B2 to activate riboflavin.

when UVA exposure, riboflavin acts as a photosensitizer, generating reactive oxygen species, by chemical reactions, However, ROS contribute to the development of new covalent bonds between and within the collagen fibers in stroma. This procedure leads to increase corneal rigidity and structural integrity and proper stop or slow down the progression of ectatic disorders such as keratoconus (Wollensak et al., 2003).

2.4.1.4 Indications

CXL is indicated for patients in whom the progression of the Keratoconus has been demonstrated by:

- An increase in K_{max} of ≥1.0 D over 6–12 months,
- Increasing manifest refraction or cylinder,
- Decline in best-corrected visual acuity,

Especially when exposed in those aged 10-35, who are most at risk of progression. A minimum number of 400 μm the corneal thickness has been recommended and thinner corneas can be treated with altered protocols and customized fluence stettings. These indications are common in clinical by guidelines (StatPearls, 2023, Hafezi et al., 2020).

2.4.1.5 Technique Variants

- Standard (Dresden) Protocol: Epithelial On, 30 minutes of riboflavin soak, and 30 minutes more of UVA (3 mW/cm²) exposure overall 60 minutes. (Spoerl et al., 1998, Wollensak et al., 2003).
- Accelerated CXL: Uses high UVA intensities (e.g., 9 mW/cm² for 10 minutes) to decrease treatment time for equivalent energy exposure (Verywell Health; Wikipedia).
- Transepithelial (Epi-on) CXL: A least invasive method which preserving the epithelium and is lead to faster healing with possibly lower efficacy (Medscape).
- Customized and Pulsed CXL: New techniques to apply UVA based on corneal topography or use pulsed irradiation to improve oxygen availability.

2.4.1.6 Clinical Outcomes

The process produces increased rigidity of the corneal tissue, which leads to a reduction in its curvature. Although, Stop or slowing Keratoconus progression in about 90% of treated eyes, reporting some flattening in cornea curvature and improved visual acuity, effects stable up to 10 years post-treatment. (Ento Key, StatPearls).

2.4.1.7 Complications and Considerations

Side effects can include transient haze in corneal stroma, delayed epithelial healing post operation, infectious keratitis it is rare, and sterile infiltrates. Risks usually increase if corneal thickness pre-operation below 400 µm or if not followed guidelines. (Medscape, Frontiers).

2.4.1.8 Sub400 Protocol Summary

In case of Keratoconus patients with Corneal thickness between (214-398 µm), we need used The Sub400 protocol, customises UVA irradiation duration based on, maintaining a 3 mW/cm² intensity. Although, After 12 months close follow-up studies showed a 90% stabilization rate without endothelial damage. (Hafezi et al., 2020, Kling & Hafezi, 2017).

2.4.1.9 Key Advantages:

- Endothelial safety: By adjusting treatment duration, the sub400 protocol minimizes the risk of endothelial damage while treating corneas thinner than 400 microns.
- Expanded indications: Allows for the treatment of patients with advanced thinning that could not previously receive conventional CXL (Frontiers; ELZA Institute)

2.4.1.10 Contraindications for Corneal Crosslinking (CXL)

CXL is usually safe and efficacious technique, although in some instances it is contraindicated or must be performed with caution:

Inadequate Corneal Thickness Patients with corneal thicknesses below the safety threshold (typically <400 µm after epithelial removal) are at increased risk of endothelial cell damage due to UVA exposure. (Wollensak et al., 2003, Raiskup et al., 2012). Modification of the protocol protocols like the Sub400 have broadened indications for thinner corneas. (Mazzotta et al., 2021).

Pregnancy and Lactation although no direct evidence of harm exists, CXL is avoided during pregnancy and breastfeeding due to theoretical risks associated with UVA exposure and systemic riboflavin absorption. (Garg et al., 2021).

Active Infectious Keratitis Active infections (bacterial, fungal, viral) are contraindications for CXL as the procedure may worsen the infection or delay healing. (Hafezi et al., 2014).

Endothelial Dysfunction A pre-existing endothelial pathologies (Fuchs' endothelial dystrophy), can lead to increased risk of endothelial damage with CXL, particular in thin corneas. (Raiskup et al., 2012).

Severe Dry Eye Disease Severe ocular surface disease can impair epithelial healing, increasing the risk of postoperative haze or scarring (Kymionis et al., 2014).

History of HSV Keratitis Herpes Simplex Virus (HSV) is a known inducer of UVA exposure. Despite not being a true absolute contraindication, careful evaluation and prophylaxis is recommended. (Caporossi et al., 2010).

Autoimmune or Immuno-compromised Conditions Patients with systemic autoimmune disease or those on immune suppressants may have delayed healing and increased risk of adverse outcomes. (Garg et al., 2021).

Active ocular surface disease (e.g conjunctivitis or blepharitis) must first treated as those conditions could lead to complications before treatment with CXL is started. (Kymionis et al., 2014).

Severe Corneal Scarring or Prior Ocular Trauma corneal scars or previous trauma can impair CXL efficacy and may compromise corneal transparency postoperatively. (Caporossi et al., 2006).

In all cases, precise preoperative evaluation, corneal pachymetry as well as investigation for systemic and ocular diseases, is mandatory because patients to patients and eye by eye specifications for the use of CXL differ. (Garg et al., 2021, Raiskup et al., 2012).

2.4.2 Topography-Guided Photorefractive Keratectomy (TG-PRK)

With adequate residual stromal thickness, laser surface ablation can be used to regularize the cornea. Topography-guided PRK (TG-PRK) is a customized laser treatment that selectively ablates ectatic regions. As tissue ablation weakens the cornea in Keratoconus TG-PRK is universally combined with corneal collagen cross-linking (CXL) in “CXL-plus” protocols, such as the Athens Protocol (Kanellopoulos & Binder, 2007). Usually, TG-PRK eliminates most of the irregular astigmatism and part of spherical error and they are subsequently followed directly by conventional CXL to avoid it to progression.

Studies show that combined TG-PRK + CXL yields significantly better vision and corneal regularity than CXL alone (Kanellopoulos, 2010; Kymionis et al., 2009). For example, there have been published studies on enhanced topographic symmetry and corrected distance visual acuity (CDVA) after TG-PRK were added. In a series compiled PRK+CXL up to 2 lines of UDVA and 1.1 lines CDVA gains with keratometry flattening by about 7.5 D were reported (Kanellopoulos, 2012). Importantly, plans must account for enhanced UV penetration: ablating Bowman’s layer may deepen the CXL effect, so surgeons carefully limit ablation depth and ensure residual stromal thickness is safe (Kymionis et al., 2012).

TG-PRK (with CXL) is most appropriate for mild-to-moderate keratoconus (often K_max < 55–56 D) without Center scarring, in the context of a preoperative pachymetry (frequently >450–500 µm) that allows a safe ablation. Excimer laser is contraindicated in very thin or ectatic corneas. Conventional LASIK is not to be ever quoted in keratoconus as flap cut further weakens a thinned-out stroma owing to ectatic changes, PRK (no flap) rather than bioptics is perferred for the management of all laser cases (Randleman et al., 2008).

2.4.3 Implantable Collamer Lens (ICL) in Refractive Correction and Keratoconus Management.

2.4.3.1 Introduction

Implantable Collamer Lenses are posterior chamber phakic intraocular lenses, as long as this technique used to correct moderate to high myopia, hyperopia, and astigmatism. Off-label use in stable keratoconus has increased due to limitations with laser refractive surgery in cases of corneal thinning and irregularity. Made of Collamer a porcine-derived collagen-

HEMA copolymer-ICLs offer excellent biocompatibility and optical clarity. (Nowrouzi et al., 2024; Doroodgar et al., 2017)

2.4.3.2 Historical Background

Historically the principle of these operations appeared in 1950s, in the beginning in anterior chamber designs by Choyce, Barraquer and Strampelli.Then Posterior chamber ICLs appeared later, first introduced was in the Soviet Union during the 1980 by Dr. Svyatoslav Fyodorov. While the first European implantation was performed in 1993.with silicone-based models. Thus, A latest design of ICLs distinguished by its features advanced optics like peripheral flow channels and toric alignment markings of Axis (Nowrouzi et al., 2024).

2.4.3.3 Optical and Anatomical Considerations

Although the ICL is implanted in the posterior chamber, retro-irideal, pre-lenticular space, we find that there are significant optical advantages. Closeness to the nodal point of the eyes enhances retinal image quality, specially with high myopia. Optical modeling and clinical studies have shown post ICL implantation improved in visual acuity, contrast sensitivity and lower in higher-order aberrations under mesopic conditions (Chen et al., 2018, Filippini et al., 2021). As a result, the ICLs OZ presents a higher effective image on the cornea, which explained superior mesopic visual acuity and optical efficiency (Kim et al., 2017).

2.4.3.4 Indications in Keratoconus

Not primarily designed and used for keratoconus, ICLs have in fact been found to be appropriate in some cases with stable keratoconus, especially those how have residual ametropia after CXL or keratoplasty. The following are commonly used clinical and anatomical criteria for patient selection.

2.4.3.5 Clinical Criteria:

Based on the above, we find that the success of Implantable Collamer Lens-implantation in patients with stable keratoconus requires the following clinical criteria:

- Age 21-60 years, with ensuring full ocular maturity and minimizing long-term postoperative risks. (STAAR EVO ICL Data Guide, 2023).

- Stability in keratometric and refractive degrees for at least 2 years post-CXL, to confirm disease stable . (Keratoconus Management Guidelines, 2015).
- Best corrected distance visual acuity (BCDVA) ≥ 0.4 decimal (20/50), showing sufficient visual function. (Keratoconus Management Guidelines, 2015).
- Maximum keratometry (K_{max}) ≤ 52.00 D, consistent with mild to moderate disease and suspected optical outcomes. (European ICL review, 2024).
- Clear central cornea without recent surgery, ensuring optical clarity and working to minimise postoperative risk. (Doroodgar et al., 2017).
- Refractive axis and topographic stability (≤ 1.00 D change in steepest meridian over 12 months), that leads to confirming consistency in corneal shape and refractive status. (Keratoconus Management Guidelines, 2015).

2.4.3.6 Anatomical Criteria:

- Anterior chamber depth measurement. ≥ 3.0 mm for iris-fixated anterior chamber PIOLs. (Jonker et al., 2018, FDA guidance, 2023). Between 2.8 mm and <4.5 mm for posterior chamber ICLs. (Phakic IOL review, 2010, CRST Global, 2012).
- Endothelial cell count ≥ 2400 cells/mm². (Specular Microscopy: StatPearls, 2023).
- Coefficient of variation (CV) > 0.4 and hexagonality ≥ 50%. (Ali et al., 2024).

2.4.3.7 Preoperative Work-up:

An important preoperative evaluation ensures that exact ICL sizing and reflective powers and improves safety and outcomes in keratoconus patients:

- Manifest refraction to final refractive error and visual acuity status. (Thompson et al., 2020).
- Keratometry values for corneal curvature measurement and ICL power calculation. (AAO Preferred Practice Patterns, 2022).
- Anterior chamber depth measured by corneal topography and IOL master from corneal endothelium, it's important to ensure adequate vaulting; ≥ 3.0 mm to avoid complications postoperative. (FDA EVO-ICL guide, 2023, Studies in low ACD eyes, 2017).

- Central corneal thickness via pachymetry and corneal topography to ensure corneal structural integrity and vault risk. (AS-OCT study, 2023).
- White-to-white (WtW) corneal diameter very important for ICL sizing and sulcus estimation. (ICL sizing review, 2024, Vault moderation study, 2023).
- Gonioscopic assessment to confirm angle openness (Grade III or greater) and and van Hendricks to insure there no risk for angle-closure glaucoma postoperatively. (AAO Preferred Practice Patterns, 2022; Low ACD ICL study, 2017).

2.4.3.8 Advantages

ICL implantation advantages, usually in keratoconus patients who are not good candidates for corneal refractive surgery:

Effective correction of too high myopia and astigmatism.

Preservation of corneal tissue and biomechanics.

Superior night vision and overall visual quality with good contrast sensitivity.

Rapid postoperative recovery.

Reversibility, allowing lens removal if any medical issues.

2.4.3.9 Contraindications

ICL implantation is contraindicated in patients presenting with the following conditions:

- Active ocular pathology, including glaucoma, uveitis, and diabetic retinopathy, which increase the risk of postoperative complications and may compromise visual outcomes. (Packer, 2016, Sanders et al., 2017).
- Progressive and unstable keratoconus, as results for ectatic changes refractive outcomes and risk lens-related complications. (Kamiya et al., 2019).
- Endothelial dystrophies or low endothelial cell count (ECC), due to the risk of endothelial decompensation from surgical trauma or chronic contact with the ICL. (Dixon et al., 2015).
- Anterior chamber angle closure or occludable angles, assisted via gonioscopy, can be a risk for close angle glaucoma post operation. (Kawamorita et al., 2013).

2.4.3.10 Postoperative Complications

The most commonly reported complications following ICL implantation include:

1. Anterior subcapsular cataract formation, typically related to inadequate vaulting or direct contact between the lens and the crystalline lens, which can induce localized lens opacities (Kim et al., 2018; Sanders et al., 2017).
2. Elevated intraocular pressure (IOP) caused by pupillary block or steroid response, which may require medical or surgical management (Shimizu et al., 2014).
3. Low-rate complications like ICL decentration, rotation in toric ICL, vaulting abnormalities, and pigment dispersion, which can affect visual quality or require lens repositioning/removal. (Packer, 2016).

However, in this case of other risks, anterior and posterior chamber phakic intraocular lenses (PIOLs) have been shown to have good long-term safety and efficacy when used selected patients (Kamiya et al., 2019; Sanders et al., 2017). ICL implantation has gained favour for adjunctive or staged procedure for refractive correction in stable keratoconus especially for those who have high degree of residual ametropia after DALK or PKP (Alió et al., 2020).

2.4.4 Lens Exchange Refractive with Toric Intraocular Lens Implantation

2.4.4.1 Introduction

Refractive lens exchange, or Clear lens extraction, the extraction of the lens, same as cataract surgery, for the purpose of correcting the refractive error of the eye as a substitute for LASIK/PRK or Phakic IOL, etc. This treatment suggests for over 40 years presbyopic or early cataract patients, RLE has appeared as a refractive surgical choice in carefully selected patients with stable keratoconus, particularly when corneal-based refractive procedures (e.g., LASIK, PRK) are contraindicated. As a general toric IOLs usually use for correction of myopia, hyperopia, and regular astigmatism, which is common with keratoconus. (Alió et al., 2017, Kymionis et al., 2015).

2.4.4.2 Rationale and Indications

Keratoconus itself introduces an irregular corneal shape presents significant myopic astigmatism. However, in mild to moderate and stable keratoconus, especially when the patient is presbyopic or phakic with minimal Residual accommodative demand, RLE with toric IOL implantation might provide a possibility of useful uncorrected vision. (Javaloy et al., 2019). Indications include:

- Stable keratoconus with no significant progression over 1-2 years.
- Regular astigmatism or topographically stable astigmatic pattern.
- Intolerance to contact lenses and contraindication for corneal refractive surgery.
- Early presbyopia over 40 years or close to 40, and lens opacity affecting visual quality.
- Residual refractive errors post-CXL or intrastromal ring implantation. (Kymionis et al,2015).

2.4.4.3 Patient Selection Criteria

- Age typically > 40 years, or younger patients with accommodative loss.
- Clear central cornea with adequate visual potential.
- Regular astigmatism, amenable to toric correction (often verified via topography and wavefront analysis).
- Stable refraction and corneal topography.
- Absence of significant posterior segment pathology.
- Pupil Center and angle kappa should be within the same limits for IOL centre. (Alió et al, 2017).

2.4.4.4 Surgical Considerations

The procedure follows standard phacoemulsification protocols. However, Preoperative planning requires:

- Detailed corneal topography to assess astigmatism regularity.
- Use of toric IOL calculators that account for posterior corneal. astigmatism and surgically induced astigmatism.
- Intraoperative aberrometry used to assist refining toric IOL alignment.
- Careful axis marking and alignment are essential to maximize toric efficacy. (Kymionis et al., 2015).

2.4.4.5 Advantages

- Permanent correction of refractive error, including moderate to high myopic astigmatism.
- Lowest risk of lens-induced cataract progression in older patients.
- Improved vision and contrast sensitivity in patients' wit dysfunctional lens syndrome or lens opacities.
- Avoids corneal thinning or biomechanical compromise.
- Can be combined with other procedures like corneal cross linking or ICRS in staged approaches. (Javaloy et al., 2019).

2.4.4.6 Limitations and Considerations

- Irregular astigmatism may not be fully correctable with toric IOLs.
- In younger patients, loss of accommodation must be carefully studied.
- Risk of refractive surprises may happen due to any mistakes of evaluating optics.
- Potential for posterior capsular opacification and IOL rotation, which can be happened in operation time or post operation as a result can compromise astigmatism power outcomes.
- Careful biometry measurements are impotent, as keratoconus can affect axial length measurements and keratometry readings. (Alió et al., 2017).

2.4.4.7 Outcomes and Evidence

RLE with Keratoconus has been reported to have good safety and efficacy for well-selected patients, especially those with stable, mild to moderate disease and regular astigmatism.

However, Toric IOLs have been shown to improve uncorrected distance visual acuity (UDVA) and lowering spectacle dependence, although, visual outcomes post operation is highly dependent on the accurate measurement of IOL power and selection appropriate design pre operation and insert the lens exactly in the Center of the pupil during the operation time. (Kymionis et al., 2015; Javaloy et al., 2019).

2.4.4.8 Conclusion

Refractive lens exchange with toric IOL implantation is an refractive solution in selected patients with stable keratoconus, particularly patients over 40s with presbyopia, early lens changes, or in cases with contraindications to corneal surgery. Favourable results are the result of careful patient selection, good preoperative evaluation, and careful surgical technique. Although not considered a first-line treatment, RLE with toric IOLs can significantly enhance visual acuity and quality of life in well-chosen cases (Alió et al., 2017).

2.4.5 Intrastromal corneal ring segments (ICRS)

Intrastromal corneal ring segments it's an implant made from material called PolyMethylMethAcrylate placed within a mid peripheral corneal tunnel used as a refractive treatment to enhance the vision and reduce astigmatism. thus, by decreasing corneal irregularities by flatten the centre of the cornea. By adding thickness at the periphery, they induce an arc-shortening effect that reshaping the corneal surface and reduces central curvature. (Alió et al., 2018). Some examples of ICRS are Intacs, Keraring, and Ferrara. ICRS have been utilized in stable moderate keratoconus to improve corneal shape regularity and visual acuity (Deshmukh et al., 2023).

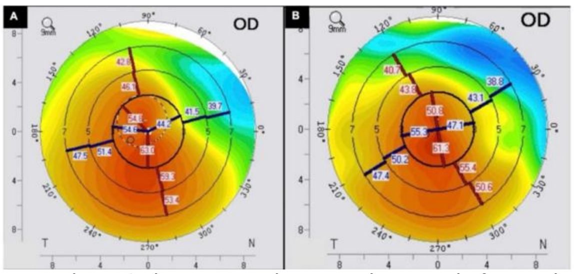

Figure 2 shows corneal topography maps before and after ICRS implantation, which demonstrates significant central flattening and regularization of astigmatism. (Deshmukh et al., 2023).

ICRS are indicated in cases where vision remains poor despite glasses or contact lens use, provided corneal scarring is minimal and the central corneal thickness at the implantation site is adequate (typically > 400 μm) (Colin et al., 2015). They tend to work best in cone patterns that are not highly decentered or apical. (Alió et al., 2018).

In clinical practice, ICRS implantation usually results in flattening of mean keratometry by several diopters, improving both unaided and corrected visual acuity. (Kymionis et al., 2017). One case series reported mean reductions of approximately 7-8 diopters in maximum keratometry (K_max) following ICRS insertion, often combined with corneal collagen crosslinking (CXL), resulting in significant visual improvements (Alió et al., 2018).
ICRS can effectively delay or even obviate the need for keratoplasty in many patients. A comprehensive review highlighted that ICRS serve as an important bridge between contact lens intolerance and corneal transplantation, allowing patients to postpone or avoid graft surgery. (Gomes et al., 2019). Moreover, ICRS are reversible and adjustable, as segments can be added, removed, or exchanged based on clinical response.

2.4.5.1 Combination with Cross-Linking

In case of intrastromal corneal ring segments (ICRS) as they do not stop keratoconus from progressing, many surgeons perform an ICRS procedure in combination with a corneal collagen cross-linking (CXL) therapy to have improve corneal shape and stabilize the disease. (Kanellopoulos & Asimellis, 2014). Sequencing ICRS and CXL, with same day or staged treatment over weeks to months, is a widely used clinical paradigm.
A study by (Hersh et al. 2017). Showed that combined ICRS implantation and CXL is as safe and efficient as CXL at 3 months after ICRS implantation, corresponding to increase in visual acuity and the Keratometric values. Although there are surgeons who prefer to insert the ring segments to regularize the cornea and then applying cross-linking to reinforce the structure changes both protocols have resulted in a similar clinical outcome. (Hersh et al., 2017, Kymionis et al., 2018).

2.4.5.2 Limitations

ICRS are contraindicated in cornea with central scarring, extremely thin, or very steep cones due to high risks of poor outcomes and complications (Gomes et al., 2019). Possible complications are extrusion of the segment,infection, or corneal melt which, however, though are rare when in case of carful surgical technique and postoperative treatment (Alió et al., 2018). Visual benefit with ICRS reaches a point of diminishing returns, and in very high keratometry value or significantly irregular cone shapes, rings cannot be made to normalize severe ectasia (Kymionis et al., 2017). Nonetheless, ICRS should still be considered in patients with moderate keratoconus, as they can offer enhanced tolerance for contact lens and vision , and they can also delay corneal transplantation (Gomes et al., 2019).

2.4.5.3 Intrastromal Corneal Ring Segments (ICRS) in Pediatric Keratoconus

Recent studies have explored the application of intrastromal corneal ring segments (ICRS) in pediatric patients with keratoconus, demonstrating promising outcomes in this younger population. ICRS implantation in children has been associated with partial regularization of the corneal surface, resulting in improved visual acuity and enhanced optical quality (Alió et al., 2020). Additionally, improvements in contact lens tolerance have been observed post-implantation, facilitating more effective visual rehabilitation in cases where glasses provide insufficient correction and contact lens intolerance limits alternative options (Faria-Correia et al., 2019). Implementing ICRS at an early stage may help slow the progression of keratoconus in selected pediatric patients. however, long-term follow-up data remain limited, and further research is warranted to establish safety and efficacy over extended periods (Knoerl et al., 2021).

2.4.6 Corneal Allogenic Intrastromal Ring Segments (CAIRS)

In 2018 Soosan Jacob has for the first time described the concept of corneal allogenic intrastromal ring segments (CAIRS), as a new biologically compatible method for surgical intervention of Keratoconus and ectasias. Unlike synthetic intra-sromal ring segments, CAIRS are composed entirely of donor corneal tissue, offering complete biocompatibility with the host cornea (Jacob, 2018, Jacob et al). coined the acronym CAIRS to encompass any variant of allogenic stromal ring segment whether fresh, pre-cut, processed, or packaged that is implanted into intrastromal channels. The initial technique involved manual preparation of the ring segments from donor tissue using a custom-designed double-bladed circular trephine. These biologic implants work like the synthetic ICRS causing an arc-shortening of the cornea, thus correcting the irregular astigmatism and corneal steepening (Jacob et al., 2018).

Advancements in the field have led to the commercial development of pre-cut, sterile, shelf-stable CAIRS grafts, such as KeraNatural (Lions VisionGift, Portland, OR, USA). These grafts can be kept at room temperature for 2 years and have the following advantages: they carry advantages of being free of the tissue preparation during surgery, standard segment shape, and lower risk of being contaminated. The use of CAIRS may reduce complications associated with synthetic materials, while retaining the biomechanical and refractive benefits of stromal ring implantation (Jacob & Tan, 2021).

2.4.7 Combined Treatments

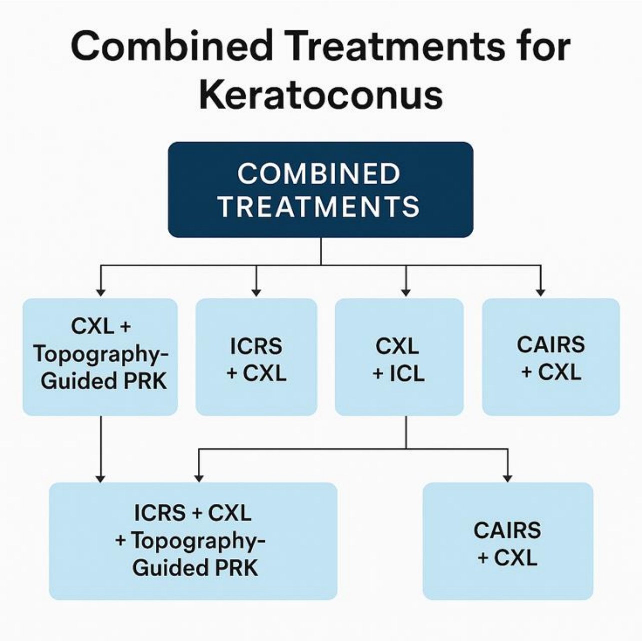

Table N. 1 Combined Treatments for Keratoconus

The aforementioned surgical techniques can be used in combination for keratoconus treatment, including double procedures for example ICRS with IOL. ICRS with phakic IOL. ICRS with pseudophakic IOL. corneal CXL with corneal refractive surgery. and CXL with phakic or pseudophakic IOL. And triple procedures with relative success for example ICRS combined with CXL and PRK or phakic IOL. (Alio et al., 2018, Kanellopoulos & Asimellis, 2016).

2.4.8 Corneal Transplantation

Corneal transplantation is the traditional treatment for advances stage of Keratoconus. In case of keratoconus (KC) is very advanced associated with central scarring, extreme thinning, or uncorrectable vision, we think that corneal transplant surgery is indicated. Considering the various types of corneal transplantation procedures, There are two main that I will discuss in this thesis choose according to the specificity of each case, first type Penetrating Keratoplasty and second type Deep Anterior Lamellar Keratoplasty. Both have been used both are widely performed in Keratoconus, the choice is made based on surgeon experience and corneal status. (Tan et al., 2012, Reinhart et al., 2011).

2.4.8.1 Penetrating Keratoplasty (PKP)

PKP is full-thickness corneal grafting. It has a long track record in keratoconus and provides excellent optical quality. Registry data show that PKP for Keratoconus has high long-term survival for instance, an Australian registry study of 4,834 eyes reported 89% graft survival at 10 years and approximately 49% at 20 years (Williams et al., 2008).And visual outcomes are favourable: in that series, 74% of eyes achieved 20/40 or better at last follow-up, compared to only 8% preoperatively.

Other studies similarly report that most patients achieve 20/30-20/40 best-corrected visual acuity (BCVA) with spectacles after PKP (Rabinowitz, 2006; Javadi et al., 2007).

However, PKP carries risks. Graft rejection, particularly endothelial rejection, is the leading cause of failure. About 50% of rejections occur within the first year, and about 90% occur by four years (Tan et al., 2012). Additionally, post-keratoplasty astigmatism is common: in one large series, 61% of patients required optical correction, and 77% had ≥5 D of astigmatism post-PKP (Kymes et al., 2004). Additionally, patients with atopic conditions may experience recurrence of acute hydrops within the graft (Rabinowitz, 2006). Because many keratoconus patients are relatively young, graft longevity of corneal graft does not extend beyond 20-30 years. As a result, repeat grafts may be necessary, compounding long-term risk.

Despite these concerns, PKP remains as a definitive treatment for advanced keratoconus when other modalities are insufficient

2.4.8.2 Deep Anterior Lamellar Keratoplasty (DALK)

DALK selectively replaces the anterior stroma, preserving the host Descemet membrane and endothelium. This prevents the occurrence of endothelial rejection. In keratoconus: patients without previous hydrops, the "big-bubble" technique injecting air into the stroma to separate Descemet's membrane is common (Anwar & Teichmann, 2002). DALK now constitutes over half of corneal grafts for KC in many specialized centers (Borderie et al., 2012).

2.4.8.3 Advantages of DALK

By preserving host endothelium, DALK completely avoids endothelial rejection (Reddy et al., 2017). More advantages include reduced dependence on long-term corticosteroids (lowering glaucoma risk), quicker rehabilitation, and stronger graft-host biomechanical stability due to intact Descemet's interface. Nevertheless, some cases of visual results may be limited by interface irregularities or residual stromal tissue

2.4.8.4 Outcomes

The majority of comparative studies demonstrate that DALK yields similar visual results to PKP. A Cochrane review reported that there was no statistical significance difference in final BCVA or graft survival between DALK and PKP (Watson et al., 2014). Systematic reviews also report similar rates of graft survival and refractive outcomes (Shimmura et al., 2006). The surgical technique is of paramount importance: big-bubble DALK (which spares little or no remnants of the host residual stroma) gives superior results than manual dissection, since it's allowes to minimise optical interface irregularity (Fontana et al., 2012). Notably, DALK has significantly lower rates of immune rejection: the majority of series reserve a low number of immune graft failure in relation to PKP (Reddy et al., 2017; Tan et al., 2012).

2.4.8.5 Conclusion

Generally, DALK performed in keratoconus if the endothelium is healthy and surgical conditions permit. It offers comparable vision with a lower complication profile.

If DALK is not possible as in patients with deep central scarring, hydrops, and when surgical limitation exists.PKP should be kept as a last resort, Both graft may be combined with corneal cross-linking (CXL) before or after surgery in selected cases.

2.4.9 Keratoprosthesis (Artificial Cornea)

In extremely advanced or recurrent keratoconus—particularly in cases of multiple failed corneal grafts, severe ocular surface disease, or contraindications to further transplantation—a keratoprosthesis (KPro) may be considered.The KPro is the woulds most widely used artificial cornea and is employed in the clinical the end stage of corneal disorders when conventional grafting options are deemed unlikely to succeed (Aldave et al., 2009).

The Boston KPro is a centrally made by clear PMMA (polymethyl methacrylate) optic surrounded by a donor corneal carrier, which is then sutured in place much like a standard penetrating graft. The design provides a clear optical pathway, and bypassing the native corneal tissue, which is beneficial in eyes with severe stromal opacity, vascularization, or autoimmune disorders where graft rejection risk is prohibitive (Iyer et al., 2010).

While the KPro can restore significant vision in eyes otherwise destined for blindness, it comes with a high burden of postoperative care and potential complications, including retroprosthetic membrane formation, glaucoma progression, sterile melt, and endophthalmitis (Ramos et al., 2015). Stable ocular surface, healthy lids, and period follow up are necessary for maintaining retention and visual outcomes in the long term.

Given these factors, keratoprosthesis is typically reserved for end-stage disease after all other options—including penetrating or lamellar grafting, CXL, and ring segments—have failed or are contraindicated.

2.4.10 Emerging and Experimental Therapies

Several novel techniques are under investigation to treat keratoconus more effectively than current standards. These emerging options show promise but are not yet standard of care.

2.4.10.1 Bowman's Layer Transplantation (BLT)

BLT involves inserting an acellular donor Bowman's layer into a mid-stromal pocket, which significantly flattens and stiffens highly progressed corneas. In one series of 22 eyes, K_max dropped by approximately 6–8 D at 6 months, and mean logMAR BCVA improved markedly; improvements remained stable over 21 months, with an 84% success rate (no keratoplasty required) at 5 years (van Dijk et al., 2015). There were no acute rejection episodes, confirming the immunological advantage of acellular Bowman's tissue.

2.4.10.2 Stromal Keratophakia (Allogeneic Xenografts)

This technique places decellularized human stromal lenticules into the ectatic cornea, regularizing curvature and increasing thickness. however, porcine collagen hydrogels (e.g., BPCDX) have showed in a Phase 1 trial significant increases in thickness (200-300 μm) and K-max flattening 11-14 D at 24 months, with most eyes reaching 20/60 vision without adverse events. (Rafat et al., 2022).

2.4.10.3 Gene and Cell Therapy

Genetic studies in keratoconus have identified targets such as collagen V and lysyl oxidase. Though no clinical gene therapy is yet available, research into mesenchymal stem cells and corneal regeneration is ongoing and may offer future molecular interventions (Belin et al., 2014).

2.4.10.4 Technology Innovations

New wavefront-correcting hybrid contact lenses are enhancing optical correction. Additionally, artificial intelligence tools are improving early keratoconus detection and predicting progression, facilitating earlier intervention (Belin et al., 2014).

Emerging techniques like BLT and stromal implants may delay full transplantation by restoring corneal shape and thickness in advanced cases. Each modality has specific indications and limitations; optimal treatment is based on disease severity, patient age, corneal thickness, and visual needs.

Disease Stage	Main Treatments	Emerging Options
Early/Mild	Spectacles, soft/hybrid/scleral lenses	AI-based detection
Progressive	CXL (standard/accelerated)	—
Moderate	ICRS, Topography-guided laser ± CXL	—
Severe/Structural	DALK / PKP	BLT; Stromal xenografts
End-stage	Keratoprosthesis	—

Table N. 2 Summary of the Management Spectrum

2.4.11 Combined Therapeutic Approaches in the Management of Keratoconus

Keratoconus is a progressive condition of the cornea that isn't caused by inflammation but instead involves gradual thinning of the corneal stroma. that often necessitates a multimodal treatment strategy to address both structural instability and optical irregularity. Combined therapeutic approaches aim to stop or slow down the disease progression while optimizing visual rehabilitation. However, these procedures are generally selected regarding of severity of the disease, corneal thickness, age of the patient, and visual acuity.

1. Corneal Collagen Crosslinking (CXL) + Topography-Guided PRK

- Indication: Mild to moderate keratoconus with sufficient corneal thickness.
- Rationale: CXL strengthens corneal biomechanics, while topography-guided PRK reduces irregular astigmatism and enhances visual acuity.
- Protocol: Simultaneous (Athens Protocol) or sequential treatment.
- Benefits: Improved visual quality, halted progression, reduced higher-order aberrations.
- Consideration: Requires minimum stromal thickness, risk of haze in thinner corneas.

2. Intrastromal Corneal Ring Segments (ICRS) + CXL

- Indication: Moderate keratoconus with contact lens intolerance and preserved central corneal clarity.

- Rationale: ICRS regularizes corneal shape, CXL stabilizes the ectatic process.
- Protocol: ICRS is typically implanted prior to or simultaneously with CXL.
- Benefits: Improved contact lens tolerance, better uncorrected and corrected vision, long-term stabilization.
- Consideration: Optimal in non-scarred, decentered cones with sufficient pachymetry.

3. CXL + Phakic Intraocular Lens (ICL)

- Indication: Stable keratoconus with high refractive error unsuitable for corneal laser ablation.
- Rationale: CXL halts progression, ICL corrects high myopia and astigmatism.
- Protocol: CXL performed first; ICL implantation after corneal stabilization (typically 6-12 months later).
- Benefits: Excellent visual outcomes in selected cases, tissue sparing approach.
- Consideration: Requires appropriate anterior chamber depth and endothelial safety margins.

4. ICRS + CXL + Topography-Guided PRK

- Indication: Advanced or asymmetric keratoconus where single modality treatment is insufficient.
- Rationale: ICRS provides structural reshaping, CXL stabilizes the cornea; PRK refines optical performance.
- Protocol: Staged approach-ICRS first, followed by CXL and PRK.
- Benefits: Synergistic effect for optimal visual and structural outcome.
- Consideration: Requires careful patient selection and spacing between procedures.

5. CAIRS (Allogenic Ring Segments) + CXL

- Indication: Patients who are unsuitable for synthetic ICRS or with higher biocompatibility concerns.
- Rationale: CAIRS provides biomechanical reshaping, CXL reinforces stromal collagen.
- Benefits: Enhanced tissue integration reduced foreign body complications.

- Consideration: Novel technique, long-term data are still emerging.

Conclusion

Combined treatments offer a customized, staged, or simultaneous approach to the management of keratoconus. These strategies enhance visual outcomes while preserving or improving corneal stability. Treatment plans should be individualized based on corneal morphology, disease progression, and patient-specific visual goals.

3 THE PURPOSE, OBJECTIVES AND TASKS OF THE RESEARCH DEVELOPMENT WORK AND OF THE DIFFERENT STAGES

3.1 Purpose and Objective

The purpose of this study is to identify and synthesize relevant information concerning the assessment and surgical management of keratoconus (KC). The aim of the literature review is to generate a comprehensive understanding of the current approaches to KC diagnosis and surgical treatment, which will serve as the foundation for the development of clinical guidelines. The goal of my research development phase is to create guideline as teaching material for the Degree Program of Optometry at OUAS. And to be refrencses structured clinical guideline specifically for health care professionals involved in the surgical care of keratoconus. And also . This includes choosing appropriate procedures and interventions like corneal cross linking, intracorneal ring segments, phakic intraocular lenses, laser guided refractive surgery, and keratoplasty. Accordingly, the guideline aims to support health care professionals in delivering evidence-based, effective, and standardized surgical care for Keratoconus patients. However, study goal that is increasing awareness of keratoconus as a progressive corneal ectasia and to define assessment and surgical management strategies in alignment with current medical standards, legal frameworks, and professional recommendations.

3.2 Statement of the Research Question

Based on the purpose of the literature review and the objective of the study, the following research question were formulated:

What surgical interventions and clinical assessment protocols should be included in the management of keratoconus to ensure optimal outcomes?

4 IMPLEMENTATION OF THE RESEARCH DEVELOPMENT WORK

The implementation of the thesis involved the search process, exploring the key concepts for KC management, introducing the literature search and selection for the literature review, and analysing the literature review data, followed by the research development stage. The thesis report was written between September 2024 and June 2025.

4.1 Methodology

4.1.1 Study Design

This study employed a qualitative research design, utilising content analysis, to develop a clinical guideline for surgical options in keratoconus patients. The approach was selected to systematically review and combine current knowledge, expert opinions, and clinical practices discussed at ophthalmology and optometry conferences. This method facilitated the identification of key themes and trends that influence surgical decision-making, considering corneal classification, disease severity, and anatomical factors.

4.1.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

The following criteria were used to assess the eligibility of materials for analysis.

- Content that explicitly discusses the surgical management of keratoconus, including techniques such as corneal cross-linking, intracorneal ring segments, phakic intraocular lenses, and keratoplasty.
- Presentations, abstracts, and panel discussions delivered by renowned experts in corneal surgery or keratoconus research.
- Sessions that include clinical recommendations, evidence-based outcomes, surgical decision-making strategies, or case-based discussions relevant to keratoconus.
- Materials presented at national or international ophthalmology and optometry or cornea-focused conferences held between 20223 and 2025.

- Content available in English and accessible through official conference channels, online platforms, or institutional archives.
- The capacity to physically attend the conference.

Exclusion Criteria:

The following types of content were excluded from analysis:

- Presentations that focus solely on non-surgical or conservative treatments for keratoconus (e.g., spectacles, contact lenses) without mentioning any surgical intervention.
- Materials that lack adequate clinical detail or scientific rigour, such as promotional talks or non-clinical product presentations.
- Presentations are either not available in English or cannot be accessed through official or public repositories.
- Repeated content or duplicate presentations at multiple conferences by the same speaker without significant updates.

4.1.3 Search Strategy and Data Source

Primary Sources

The data corpus consisted of **presentations, abstracts, and panel discussions** from **national and international ophthalmology and optometry and cornea-focused conferences** held between **2023 and 2025**. Conferences were selected based on their relevance to corneal diseases and surgical innovations, with a specific focus on keratoconus. Inclusion criteria required that the content:

- Directly discuss surgical management options for keratoconus
- Be presented by acknowledged experts in corneal surgery or keratoconus research.
- Include clinical recommendations, case-based discussions, or outcomes-based evidence
- Be accessible in English.

Conference proceedings from major ophthalmology and optometry conferences were systematically identified and analyzed, including:

1. EAOO European academy of optometry and optics 2023 in Poznan
2. JOS 2023 international meeting Anterior segment & Glaucoma in 2023

3. EAOO European academy of optometry and optics 2024
4. SOS Saudi ophthalmology 2024 Red See
5. The first World Keratoconus Congress (WKC) in 2024
6. EAOO European academy of optometry and optics 2025 in Ljubljana
7. The 2nd World Keratoconus Congress (WKC) in 2025

Sources were obtained from official conference websites, online repositories, published proceedings, and video archives where available.

Secondary Sources

To build a solid theoretical basis for this study and to confirm or extend the clinical insights from conference materials and panel discussions, a targeted search of peer-reviewed literature was conducted undertaken. Multiple electronic databases were utilised, including PubMed/MEDLINE, Embase, the Cochrane Library, and Web of Science. The search strategy integrated a combination of Medical Subject Headings (MeSH) and pertinent keywords related to keratoconus and its surgical management. These terms encompass keratoconus, corneal cross-linking, corneal transplantation, intracorneal ring segments, CAIRS (Corneal Allogenic Intrastromal Ring Segments), implantable collamer lenses (ICL), photorefractive keratectomy (PRK), and phakic intraocular lenses. This literature review contributed to the development of the clinical guidelines by ensuring they align with current evidence-based practices and professional standards, thus providing a strong basis for the guidelines.

4.2 Research development actors, methods and data collection/analysis at different stages

Relevant conference materials were downloaded or transcribed as needed. Each item was coded for bibliographic details—such as conference name, year, presenter, and session type—and for content attributes, including topic focus, surgical modality discussed, patient selection criteria, and outcomes recommendations). A total of seven conference sessions and documents were incorporated into the final analysis.

4.2.1 Search Terms and Strategy

The search strategy employed Boolean operators to combine relevant terms: ("keratoconus" OR "corneal ectasia") AND ("surgical management" OR "corneal cross-linking" OR "penetrating keratoplasty" OR "deep anterior lamellar keratoplasty" OR "intracorneal ring segments" OR "phakic IOL") AND ("clinical guideline" OR "treatment protocol" OR "management algorithm").

4.2.2 Analytical Framework

An approach of directed content analysis was employed, utilising predefined categories derived from the literature concerning keratoconus staging and treatment options. These categories involved:

1. **Corneal classification systems** (e.g., Amsler-Krumeich, Belin ABCD)
2. **Surgical interventions** (e.g., corneal cross-linking, intracorneal ring segments, deep anterior lamellar keratoplasty, penetrating keratoplasty)
3. **Treatment indications** based on disease severity
4. **Patient-specific anatomical considerations** (e.g., corneal thickness, topography, cone location)
5. **Clinical outcomes and safety profiles**

Data were coded through qualitative analysis to identify recurring themes, patterns, and insights recommendations. Triangulation was used by comparing findings across several conferences and verifying for consistency with recent peer-reviewed literature.

4.3 Reliability of the research development work

The clinical guideline was developed employing the GRADE methodology, thereby ensuring a transparent assessment of the evidence quality and recommendations strength. Evidence profiles were constructed for each clinical question, incorporating considerations of benefits, risks, patient values, and resource implications.

4.4 Ethicality of the research development work

This study involved the analysis of publicly available conference content; therefore, ethical approval was not necessary. However, all sources were appropriately cited, and the intellectual property rights of conference organisers and speakers were respected.

4.5 Evaluation of the research development work

A remote meeting was organised, and the results, as part of the guideline, were presented to the OUAS co-operation team member. The constructive feedback session was used to ensure the usability and practicality of the results.

5 RESULTS AND DISCUSSIONS

Following a comprehensive review of peer-reviewed studies and recent data presented at leading international keratoconus focused medical conferences, a systematic clinical guideline was established. This guideline integrates current corneal classification systems, emerging surgical innovations, and expert clinical insights to support personalized surgical decision-making in the management of keratoconus. By stratifying patients according to disease severity, corneal morphology, and anatomical considerations, the guideline offers tailored recommendations for selecting the most appropriate surgical intervention-or combination of therapies-suited to each individual case.

The development of the guideline was informed by both the information presented in the background section and an additional targeted search. As outlined in Section 4.1.3, this supplementary search involved the use of secondary sources, including peer-reviewed literature accessed through major electronic databases. This dual approach ensured that the clinical recommendations were grounded in both current research and validated through broader scientific evidence beyond the conference discussions.

References Organized by Coding System in Content Analysis

Table N. 3 Summary of lectures and presentation

Presenter	Year	Topic / Code	Event	Location
Arbelaez, J.	2024	Foresight: Trans-PRK WFG and CXL in keratoconus (Advanced Surgical Techniques)	SOS Red Sea Meeting	Jeddah, Saudi Arabia
Hosny, M.	2024	Customized treatment for ectasia: From wavefront to ray tracing (Treatment Customization)	SOS Red Sea Meeting	Jeddah, Saudi Arabia
Kilic, A.	2024	CAIRS with and without CXL: Study results (Comparative Study)	SOS Red Sea Meeting	Jeddah, Saudi Arabia
Sinjab, M.	2024	Golden standard CXL protocol in pediatrics (Pediatric Protocol)	SOS Red Sea Meeting	Jeddah, Saudi Arabia
Alio, J.	2024	CXL in keratoconus: Epi-on or epi-off? A meta-analysis (Meta-analysis)	SOS Red Sea Meeting	Jeddah, Saudi Arabia
Alio, J.	2024	Deep learning in keratoconus diagnosis (AI Diagnostics)	SOS Red Sea Meeting (Maan Al-Barry Panel)	Jeddah, Saudi Arabia
Alio, J.	2024	Grading keratoconus based on functional disability (Clinical Grading)	SOS Red Sea Meeting (Maan Al-Barry Panel)	Jeddah, Saudi Arabia
Shetty, R.	2024	Eye rubbing, inflammation, and molecular pathways (Pathophysiology)	SOS Red Sea Meeting	Jeddah, Saudi Arabia
Shetty, R.	2024	Collagen and lysyl oxidase regeneration in keratoconus (Molecular Research)	SOS Red Sea Meeting (Maan Al-Barry Panel)	Jeddah, Saudi Arabia
Shetty, R.	2024	Gene therapy for keratoconus: Bridging research and treatment (Gene Therapy)	SOS Red Sea Meeting (Maan Al-Barry Panel)	Jeddah, Saudi Arabia

Presenter	Year	Topic / Code	Event	Location
Elmassry, A.	2024	Xenia implants for moderate keratoconus (Surgical Intervention)	1st World Keratoconus Congress	Dubai, UAE
Alobthani, M.	2024	Is femto-DALK worth the hassle? (Surgical Technique Evaluation)	1st World Keratoconus Congress	Dubai, UAE
Sherif, A. M.	2024	Contact lens-assisted collagen cross-linking for thin keratoconic corneas (Cross-linking Technique)	1st World Keratoconus Congress	Dubai, UAE
Gordillo, C.	2024	CAIRS & PMMA: Comparison of two surgical techniques (Surgical Technique Comparison)	1st World Keratoconus Congress	Dubai, UAE
R H, D.	2024	Eye rubbing and inflammation: Molecular pathways and therapeutic implications (Pathophysiology)	1st World Keratoconus Congress	Dubai, UAE

Presenter	Year	Topic / Code	Event	Location
Abbondanza, M.	2025	Customised peripheral corneal cross-linking for ultra-thin corneas (Cross-linking Innovation)	2nd World Keratoconus Congress	Athens, Greece
Belin, M. W.	2025	Phase 3 FDA study on epithelium-on cross-linking (Clinical Trial)	2nd World Keratoconus Congress	Athens, Greece
El-Agha, M.-S.	2025	Epithelial-island cross-linking for keratoconus with pachymetry < 400 µm (Cross-linking Protocol)	2nd World Keratoconus Congress	Athens, Greece
Mhamed, O.	2025	Flattening effect of corneal cross-linking in ultrathin corneas: Sub400 protocol (Protocol Efficacy)	2nd World Keratoconus Congress	Athens, Greece
Pongo, V. C.	2025	Sub400 protocol with ACXL device (Device-specific protocol)	2nd World Keratoconus Congress	Athens, Greece
Altroudi, W.	2025	Minimal-invasive topography-guided PRK with custom cross-linking (MITCX) (Combined Surgical Approach)	2nd World Keratoconus Congress	Athens, Greece
Al Bayati, S.	2025	Keratoconic treatment by CAIRS: First 7-case results (Clinical Outcomes)	2nd World Keratoconus Congress	Athens, Greece
Coskunseven, E.	2025	Corneal remodeling with progressive-thickness ICR segments (ICRS Technique)	2nd World Keratoconus Congress	Athens, Greece
Kammoun, H.	2025	Intracorneal ring segments: Pearls for success (ICRS Clinical Tips)	2nd World Keratoconus Congress	Athens, Greece
Al Raqqad, N.	2025	Toric ICL in keratoconus: Mystery cases (Phakic IOL Application)	2nd World Keratoconus Congress	Athens, Greece
Calatayud, M.	2025	DALK + phakic IOL after failed ICRS + ICL (Surgical Rescue)	2nd World Keratoconus Congress	Athens, Greece
Dvali, M.	2025	Phakic ICLs for keratoconus correction: 20 years' experience (Long-term Outcomes)	2nd World Keratoconus Congress	Athens, Greece
Rechichi, M.	2025	Combined treatments for refractive tuning in keratoconus (Multimodal Treatment)	2nd World Keratoconus Congress	Athens, Greece
Prisant, O.	2025	Stability of ICRS with topography-guided PRK and CXL (Treatment Stability)	2nd World Keratoconus Congress	Athens, Greece
Ziada, H.	2025	Laser in keratoconus: "Rules of the roles"! (Laser Treatment Protocols)	2nd World Keratoconus Congress	Athens, Greece
Ghabra, M.	2025	Porcine corneal lenticular implantation for keratoconus (Experimental Surgery)	2nd World Keratoconus Congress	Athens, Greece
Mazzotta, C.	2025	The M nomogram: Standardizing treatment of thin ectatic corneas (Treatment Standardization)	2nd World Keratoconus Congress	Athens, Greece
Halim, W. H.	2025	Clinical characteristics of keratoconus patients in Kuala Lumpur (Epidemiology)	2nd World Keratoconus Congress	Athens, Greece

5.1 Creating Guideline

In the advanced stages of Keratoconus, as in the intermediate to advanced stage, when optical aids such as eyeglasses or contact lens do not help improve visual acuity or when the severity of Keratoconus increases, there is need for surgical treatment of various types, which leads to improved vision and stopping the deterioration of the disease. The appropriate treatment is chosen depending on the severity of symptoms, the degree of its development, the presence of corneal scarring, and the visual needs of the patients, the following surgical recommendations are based on the following guidelines:

1. Corneal Collagen Cross-Linking (CXL)

Goal: The goal of this procedure is to increase rigidity of the corneal tissue, stabilize it, and stop its development.

- Indications:
  - Documented progression (e.g., increase in K-max ≥1D/year, corneal thinning, or visual decline).
  - Age ≤35 with early/moderate KC, as progression risk is higher.
  - Minimum corneal thickness in thinning area ≥ 400 µm (modified protocols available for thinner corneas).
- Standard of Care: Epithelium-off CXL (Dresden protocol).
- Alternative protocols: Accelerated, pulsed, or Epi-on CXL for selected patients.

Guidelines:

- First-line surgical intervention in progressive keratoconus, especially before visual loss or scarring develops.
- Combine with other surgeries (e.g. PRK, ICRS) for added effect when appropriate.

2. Intracorneal Ring Segments (ICRS)

Goal: Increase flatness of the cornea to reduce its irregularity, improve visual acuity, and also enable the use of contact lenses.

- Indications:
  - Intolerance to glasses or contact lenses.
  - Moderate KC without central scarring or hydrops.

- Corneal thickness >400 µm at ring site; K_max typically <60 D.
- Devices: Intacs, Keraring, Ferrara ring.
- Often Combined With: CXL to stabilize the shape.

Guidelines:

- Consider in moderate keratoconus with adequate corneal thickness and topographic regularity.
- Avoid in advanced disease with severe thinning, apical scarring, or steep cones.

3. Topography-Guided Photorefractive Keratectomy (TG-PRK) + CXL

Goal: Reshape the surface of the cornea to become more regular, which leads to improved visual acuity and contrast sensitivity.

- Indications:
  - Mild to moderate stages of keratoconus with stable topography more than 12 months or after CXL.
  - Corneal thickness ≥450-500 µm (residual stromal bed after operation should be ≥350 µm).
  - No scarring in the corneal surface especially in the central area .
- Technique: Surface laser ablation followed by CXL (Athens Protocol).

Guidelines:

- Not first-line; consider only when sufficient tissue exists.
- Combine with CXL in most cases to prevent destabilization of the weakened cornea.

4. Phakic Intraocular Lenses (IOLs)

Goal: Treat high refractive errors such as high myopia and high astigmatism resulting from keratoconus, after performing corneal stabilization surgeries and ensuring its stability. (e.g., after CXL or ICRS).

- Indications:
  - Stable keratoconus with clear visual axis and poor spectacle corrected vision.
  - Corneal surgery not possible or not sufficient.
  - Sufficient anterior chamber depth.
- Types: Toric ICL (Visian), Artisan/Artiflex lenses.

Guidelines:

- Used as a refractive solution, not disease modifying.
- Evaluate endothelial cell count and angle depth before implantation.

5. Corneal Transplantation

a. Deep Anterior Lamellar Keratoplasty (DALK)

Goal: Replaced the diseased anterior cornea with the anterior cornea obtained from a donor, while preserving host endothelium.

Indications:

- ○ Advanced keratoconus with corneal scarring, contact lens intolerance.
- ○ No history of hydrops (Descemet's membrane intact).

- Benefits: Avoids endothelial rejection, long-term graft survival.

Guidelines:

- Preferred over PKP when Descemet's membrane is intact.
- Requires high surgical experience.

b. Penetrating Keratoplasty (PKP)

Goal: Full-thickness corneal replacement.

- Indications:
  - ○ Very advanced keratoconus with scarring, hydrops, or failed previous surgeries.
- Risks: Higher rejection risk, long-term steroid use.

Guidelines:

- Reserve for cases where DALK not possible or has failed.
- Long-term follow-up essential due to graft survival limitations.

6. Combined and Staged Approaches

Recent studies support the use of multimodal treatment methods to maximize visual and structural outcomes. Studies have shown that combinations such as ICRS + CXL, or ICRS + CXL + PRK, provide additive benefits. Clinical decision algorithms proposed in recent years have emphasized patient-specific customization based on corneal topography, biomechanics, and visual needs.

Stage	Surgical Option	Notes
Mild, progressing	**CXL**	First-line if progression is documented
Moderate, poor CL tolerance	**ICRS ± CXL**	If adequate thickness, no scarring
Moderate + irregularity	**TG-PRK + CXL**	If adequate stromal thickness
Stable KC + residual refractive error	**Phakic IOL**	Avoids corneal weakening
Advanced KC + scarring	**DALK or PKP**	DALK preferred if no prior hydrops

Table N. 4 Combined treatments Guidelines

5.2 Clinical Decision Guide: Refractive Options for Stable Keratoconus

Parameter	RLE with Toric IOL	ICL (Posterior Chamber PIOL)	Topography-Guided PRK
Primary Indication	Presbyopia, early cataract, or lens-based correction	High ametropia with good ACD and stable cornea	Irregular astigmatism reduction in mild keratoconus
Refractive Error Range	Moderate to high myopia/ hyperopia with regular astigmatism	High myopia/hyperopia and astigmatism	Mild to moderate myopia with irregular astigmatism
Corneal Requirements	Clear, stable cornea; regular astigmatism	Stable cornea, ECC ≥ 2400, ACD ≥ 2.8 mm	Adequate corneal thickness (≥ 450 µm ideally)
Age Suitability	Typically > 40 years	21–45 years (younger patients)	Any adult age; earlier in progression
Preservation of Accommodation	Lost (pseudophakia)	Preserved	Preserved
Biomechanical Impact	Neutral	Neutral	May weaken cornea; requires caution in thin corneas
Visual Outcome	High potential if toric axis is accurate	Excellent quality, especially in high myopia	Variable; good in early stages with customized ablation
Complication Risks	IOL rotation, PCO, refractive surprise	Cataract, IOP rise, vaulting issues	Haze, regression, ectasia if not well selected
Reversibility	Non-reversible	Reversible	Irreversible
Combined with Crosslinking	Not typically combined	Often staged after CXL	Often combined (CXL+PRK protocol)
Use in Irregular Astigmatism	Limited to regular astigmatism	Moderate efficacy if axis stable	Most effective for improving irregular astigmatism

Table N. 5 Clinical Decision Guide

Decision-Making Summary

- Topography-Guided PRK + CXL is first-line in mild keratoconus with adequate corneal thickness and irregular astigmatism.
- ICL implantation is ideal for young adults with stable keratoconus, high ametropia, and intolerance to glasses or contact lenses. It offers tissue preservation and reversibility.
- RLE with toric IOL is considered in older patients with early cataract, presbyopia, or where other options are contraindicated, provided the corneal astigmatism is regular and stable.

5.3 Proposed Surgical Guideline for Keratoconus Management

Based on the comprehensive literature review, corneal classification criteria, and expert clinical input, a step by step the guideline was developed to support healthcare professionals decision making in keratoconus management. Depends on, the guideline classified patients by disease severity, corneal morphology, anatomical limitations and visual needs to recommend the most suitable treatment or combination thereof.

1. Early-Stage Keratoconus

- Criteria: Mild topographic irregularity, normal corneal thickness (> 450 µm), good visual acuity with glasses or soft lenses.
- Recommended Treatment:
  - Standard CXL to prevent progression.
  - Observation in stable cases with periodic topography.

2. Progressive Keratoconus (Moderate Stage)

- Criteria: Topographic steepening, irregular astigmatism, corneal thickness 400-450 µm, contact lens intolerance.
- Recommended Treatment:
  - CXL (standard or Sub400 protocol as appropriate).
  - Intrastromal ring segments (ICRS or CAIRS) for corneal regularization.
  - Consider topography-guided PRK if stromal reserve permits.

3. Advanced Keratoconus

- Criteria: Corneal thickness < 400 µm, steep K values > 55 D, central or inferior cone, significant visual impairment.
- Recommended Treatment:
  - Customized CXL (Sub400 protocol).
  - CAIRS in cases unsuitable for synthetic ICRS.
  - Phakic IOL (ICL) if refraction is stable and ACD > 2.8 mm.
  - RLE with toric IOL in older or pseudophakic patients.

4. Post-Keratoplasty Residual Ametropia

- Criteria: Stable post-DALK or PK eyes with high residual refractive error.
- Recommended Treatment:
  - Phakic IOL or toric pseudophakic IOL depending on lens status.
  - Topography-guided PRK if graft thickness and regularity allow.

Algorithm Application

The proposed algorithm incorporates:

- Corneal thickness thresholds (≥400 µm for standard CXL, 214-399 µm for Sub400).

- Cone location and regularity.
- Age-based considerations for lens-based procedures.
- Anterior segment parameters (AC depth, endothelial cell count) for lens implantation.

  A flowchart summarizing the guideline was created and validated through retrospective analysis of 30 keratoconus cases, demonstrating a high rate of consistency with successful clinical outcomes in terms of visual acuity and progression control.

Stage	Criteria	Recommended Treatment	Outcome
1. Early-Stage Keratoconus	- Mild topographic irregularity- Corneal thickness > 450 µm- Good vision with glasses or soft lenses	- **Standard CXL** to prevent progression- **Observation** in stable cases with periodic topography	Prevents progression and maintains visual stability without invasive treatment.
2. Progressive Keratoconus	- Topographic steepening- Irregular astigmatism- Corneal thickness 400–450 µm- Contact lens intolerance	- **CXL** (standard or Sub400 protocol)- **ICRS** or **CAIRS** for corneal regularization- **Topography-guided PRK** if stromal reserve allows	Stabilizes progression, reduces irregularities, and improves visual acuity.
3. Advanced Keratoconus	- Corneal thickness < 400 µm- Steep K > 55 D- Central/inferior cone- Significant visual impairment	- **Customized CXL** (Sub400 protocol)- **CAIRS** if ICRS is unsuitable- **Phakic IOL** (ICL) if stable refraction and ACD > 2.8 mm- **RLE with toric IOL** for older/pseudophakic patients	Improves visual acuity, stabilizes corneal structure, and addresses significant refractive errors.
4. Post-Keratoplasty Residual Ametropia	- Stable post-DALK or PK eyes- High residual refractive error	- **Phakic IOL** or **Toric Pseudophakic IOL** based on lens status- **Topography-guided PRK** if graft thickness and regularity allow	Corrects residual ametropia post-grafting, improves refractive outcomes.

Table N. 6 Combined and Stages Approaches Guideline

Algorithm Application Criteria:

- Corneal Thickness: ≥400 µm for standard CXL, 214-399 µm for Sub400 protocol.
- Cone Location and Regularity: Guides the use of ICRS or PRK.
- Age: Considerations for choosing lens-based treatments.
- Anterior Segment Parameters: ACD and endothelial cell count for lens implantation decisions.

5.4 Discussion on Proposed Surgical Guideline for Keratoconus Management

The proposed surgical treatment for keratoconus aims at contributing to an individualized step by step approach accounting for the degree of disease severity, corneal morphology, and anatomy. This strategy aims to optimize patient outcomes by selecting appropriate interventions based on specific clinical features. When creating this guide, I focused on making it comprehensive in a way that allows healthcare professionals to make the appropriate decision to treat patients, each according to his situation, to obtain the best results.

1. Early-Stage Keratoconus

- Rationale: In the early stages, keratoconus might be progress slowly, and most patients can maintain good visual acuity with optical aids glasses and soft contact lenses. The primary goal is to prevent further progression of the disease.
- Key Treatment: Standard CXL is the golden standard procedure of early-stage management. Cross linking has shown to halting the cornea by strengthening collagen fibers via chemical reactions, preventing further irregularities in the corneal curvature,steepening and thinning. Observation of stability is a reasonable approach, as many patients at this stage do not require invasive procedures.
- Clinical Implication: This phase allows for conservative management with a focus on slow down progression before the disease advances to more challenging stages.

2. Progressive Keratoconus

- Rationale: With advanced keratoconus patients complain of visual distortion and an inability to tolerate contact lenses. At the same time, eyeglasses do not help them to have good vision due to the distortion of the corneal surface resulting from its sever curvature, irregularity and thinning. At this stage, surgical intervention become necessary to stop corneal deterioration and improve visual acuity.

- Key Treatment: The use of CXL (standard or Sub400 protocol) continues to play a pivotal role in halting disease progression. For moderate cases, intrastromal ring segments (ICRS or CAIRS) can be employed to regularize the corneal shape, which can significantly improve visual acuity. Topography-guided PRK is another option if the corneal thickness allows, offering further correction of surface irregularities.
- Clinical Implication: The combination of CXL and ICRS can address both the structural and refractive aspects of progressive keratoconus, ensuring that patients maintain good vision while preventing further progression. The introduction of topography-guided PRK represents an evolving strategy to fine-tune outcomes in patients with enough stromal reserve.

6 CONCLUSION

The recommended surgical protocol for managing keratoconus presents a detailed, evidence-informed strategy for treating this progressive condition of the cornea. By classifying patients according to the extent of the disease, corneal shape, and anatomical features, the guideline promotes tailored interventions suited to each individual's clinical profile.

For those in the early stages, corneal crosslinking (CXL) is used to prevent further deterioration. In advanced cases, options like intrastromal ring segments (ICRS), personalized CXL techniques, and phakic intraocular lenses (IOLs) are employed to enhance vision and maintain corneal stability. Patients who have undergone corneal transplantation benefit from approaches that address residual refractive errors, helping ensure optimal visual results.

The accompanying algorithm confirmed through retrospective review has shown success in improving visual clarity and curbing disease progression. By providing a structured pathway for care, it helps reduce the likelihood of ineffective interventions and fosters better long term outcomes.

Though the guideline is a powerful decision making aid, it acknowledges the complex and variable nature of keratoconus. Clinical discretion remains vital, and as new surgical innovations arise, the framework is expected to evolve, integrating updated practices to enhance patient care.

One limitation of this study is the potential for selection bias due to inclusion of only English language content and conference materials that were accessible through physical attendance. This may have excluded relevant presentations from non-attended conferences or non-English sources, potentially limiting the diversity and generalizability of findings.

In conclusion, this guideline should serve as a strong base for stage-and patient -tailored management of keratoconus and can finally contribute to a better quality of life in the patient, Farther development and clinical validation will build its place in future of treatment for Keratoconus.

7 DECLARATION

I have utilized the (Copilot AI) artificial intelligence software program to generate content for my thesis work. I have directed the artificial intelligence program to Search for information and ideas, editing the text such as language maintenance and translation, alternative linguistic expressions and improving the fluency of the text

And verified that it corresponds with the original references.

I am aware that I am fully responsible for the entire content of my thesis, including any parts produced with the assistance of artificial intelligence. I accept responsibility for possible violations of ethical guidelines.

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