Review Article

Keratoconus: imaging modalities and management

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ABSTRACT

Background: Keratoconus (KCN) is characterized by gradual thinning and steepening of the cornea, which can lead to significant vision problems owing to high astigmatism, corneal scarring, or even corneal perforation. The detection of KCN in its early stages is crucial for effective treatment. In this review, we describe current advances in the diagnosis and treatment of KCN.

Methods: This narrative review focuses on recent advancements in the diagnosis and treatment of KCN, especially evolving approaches and strategies. To ensure the inclusion of the most recent literature, relevant publications discussing advanced imaging techniques and treatment options for KCN were extensively gathered from the PubMed/MEDLINE and Google Scholar databases. The following index terms and keywords were used for the online search: keratoconus, diagnosis of keratoconus, advances in the diagnosis of keratoconus, topography or tomography, anterior segment optical coherence tomography, treatment of keratoconus, advances in the treatment of keratoconus, collagen crosslinking, intrastromal ring, keratoplasty, and new techniques in keratoconus.

Results: Various screening methods such as corneal topography, tomography, anterior segment optical coherence tomography, and assessment of corneal biomechanics have been developed to identify KCN in its early stages. After diagnosis, KCN management focuses on preventing disease progression. Corneal collagen crosslinking is a minimally invasive treatment that can slow or stop the progression of the condition. Recent research has also explored the use of copper sulfate eye drops (IVMED-80) as a noninvasive treatment to prevent the progression of KCN. Current treatment options for visual improvement include scleral lenses, intracorneal ring segments, corneal allogeneic intrastromal ring segments, and deep anterior lamellar keratoplasty. Recently, novel alternative procedures, such as isolated Bowman layer transplantation, either as a corneal stromal inlay or onlay, have demonstrated encouraging outcomes. Artificial intelligence has gained acceptance for providing best practices for the diagnosis and management of KCN, and the science of its application is contentiously debated; however, it may not have been sufficiently developed.

Conclusions: Early detection and advancements in screening methods using current imaging modalities have improved diagnosis of KCN. Improvement in the accuracy of current screening or diagnostic tests and comparison of their validities are achievable by well-designed, large-scale, prospective studies. The safety and effectiveness of emerging treatments for KCN are currently being investigated. There is an ongoing need for studies to track progress and evaluate clinicians' knowledge and practices in treating patients with KCN. Artificial intelligence capabilities in management approach considering the currently available imaging modalities and treatment options would best benefit the patient.

KEYWORDS

anterior eye segments, corneas, keratoconus, tomographies, optical coherence tomography, corneal cross linking, intracorneal ring segments, allograft, bowmans membrane, cornea transplantation, lamellar keratoplasty, keratoplasty, machine intelligence, computational intelligence

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INTRODUCTION

Keratoconus (KCN) is a multifactorial disease. Inflammatory factors play a significant role as the offending causes and are strongly related to chronic ocular microtraumas such as eye rubbing and nocturnal ocular compression [1-3]. Additionally, KCN appears to have a genetic predisposition [4]. KCN is characterized by steepening, irregular shape, and thinning of the cornea, which contribute to visual impairment [4]. The initial signs of KCN include displacement of the thinnest point of the cornea, variations in corneal epithelial thickness, irregular corneal astigmatism, and central corneal stromal thinning [5].

KCN commonly manifests during the pubescent years, with its onset typically occurring in adolescence [4]. KCN impacts both sexes, though it manifests earlier and advances more swiftly in male individuals [6, 7]. Diagnostic tests reveal irregular astigmatism, scissor reflex during retinoscopy, increased keratometry measurements coupled with distorted mires, and alterations in corneal topography and tomographic maps. Additionally, signs observed during slit-lamp examination, such as Vogt's striae, and in advanced cases, diminished central corneal thickness, Munson's sign, Rizzuti's sign, Fleischer's ring, and stromal scarring, can be found in KCN [4].

A more accurate diagnosis is possible by incorporating assessments such as retinoscopy, keratometry, refraction, and slit-lamp examinations [8]. Corneal topography is useful for measuring the anterior corneal curvature but lacks detail on the posterior curvature and corneal thickness. The rotating Scheimpflug camera enabled tomographic visualization of the anterior and posterior corneal surfaces, in addition to corneal thickness [8-10]. The actual prevalence of KCN may surpass that reported a few decades ago, primarily because of the use of more sophisticated diagnostic techniques [11].

There is no cure for KCN; however, conservative management options are available to aid vision in the early stages [12]. Spectacles or contact lenses can be used to correct refractive errors and enhance visual clarity [12]. In certain instances, custom-designed contact lenses, such as scleral or rigid gas-permeable lenses, enhance visual acuity and improve comfort during the advanced stages of KCN [12]. New alternatives for medical treatment, such as topical copper or supplementary vitamin D, have been investigated [9, 13]. However, clear evidence of their efficacy and safety is lacking.

Surgical intervention may be considered for progressive KCN or inadequate visual outcomes despite wearing contact lenses [12]. Collagen crosslinking (CXL) and intracorneal ring segment (ICRS) implantation have been used for over two decades with favorable results and acceptably low complication rates [1, 14].

Transplantation of allogeneic lamellar corneal tissue, including the Bowman layer or stroma, using various techniques such as "inlay" or "onlay" lamellar, corneal allogenic intrastromal ring segments (CAIRS), or donut-shaped inclusions, has shown promising results and apparently fewer long-term risks compared to synthetic ring segment implantation [15-18]. In exceptionally severe cases, however, either deep anterior lamellar keratoplasty or penetrating keratoplasty may be necessary for visual rehabilitation [1, 11, 19].

Early diagnosis and intervention play crucial roles in achieving positive outcomes. By promptly identifying the condition, healthcare professionals can explore treatment options to effectively manage KCN, improve vision, and enhance patients' quality of life [8, 20, 21].

However, a late diagnosis can have significant implications for treatment options. Spectacles and contact lenses may no longer be viable options when manifestations of advanced disease, such as corneal scarring, lead to structural deformities that cannot be adequately corrected with these methods [8, 20].

This narrative review aims to provide valuable insights into the latest developments in the diagnosis and treatment of KCN by incorporating recent research findings.

METHODS

This narrative review focuses on recent advancements in the diagnosis and treatment of KCN, especially evolving approaches and strategies. To ensure the inclusion of the most recent literature, relevant publications discussing advanced imaging techniques and treatment options for KCN were extensively gathered from the PubMed/MEDLINE and Google Scholar databases.

The following index terms and keywords were used for the online search: keratoconus, diagnosis of keratoconus, advances in the diagnosis of keratoconus, topography or tomography, anterior segment optical coherence tomography, treatment of keratoconus, advances in the treatment of keratoconus, collagen crosslinking, intrastromal ring, keratoplasty, and new techniques in keratoconus.

RESULTS and DISCUSSION

Advanced Imaging Techniques

Advanced imaging techniques provide valuable information about corneal morphology, topography, biomechanics, and thickness [9, 11], aiding in early detection, accurate diagnosis, and effective management of KCN [22].

Corneal tomography

New corneal tomographic imaging technologies have enhanced the diagnostic capabilities of topography by providing 3-dimensional representations of the entire cornea using techniques such as slit-scanning, Scheimpflug photography, and optical coherence tomography (OCT) [23]. Unlike traditional topography, which analyzes only the front corneal surface curvatures based on optical reflections, these tomographic methods allow for assessments of both the front and back corneal surface elevations and the corneal thickness profile [24].

Scheimpflug imaging assists in detecting ectatic changes, accurate staging of KCN, and monitoring corneal changes over time [24]. It has been used to identify early-stage KCN, which allows for early intervention and management, potentially preventing further deterioration and vision loss [24].

Studies have investigated different parameters and cutoff values for the detection of subclinical KCN. These parameters encompass the disparity between the thicknesses of the central cornea and the thinnest point of the cornea, corneal densitometry, and measures of posterior corneal elevation [25]. Several devices, such as the Pentacam HR (Oculus Optikgeraete GmbH, Wetzlar, Germany) and the Sirius anterior segment analysis system (Costruzione Strumenti Oftalmici [CSO], Florence, Italy), have been used in these investigations. Similar to the Pentacam, Sirius uses a single Scheimpflug rotating camera and a Placido disc to capture images of the cornea [25]. Scheimpflug images enable the generation of profiles for the anterior and posterior surfaces of the cornea, the front surface of the lens, and the iris. The Sirius system has been used in studies assessing corneal parameters for detecting subclinical KCN [25].

Galilei Corneal Tomography (Ziemer Ophthalmic Systems AG, Port, Switzerland) merges Placido disc-based corneal topography with Scheimpflug technology, enabling eye movement tracking, decentration detection, and motion error minimization during imaging [26]. The ability of the Galilei camera to detect KCN and subclinical KCN was also evaluated. Studies have assessed the repeatability and comparability of devices, including Pentacam, Galilei, and Sirius, for anterior segment imaging [27]. Although these devices show repeatability in certain measurements, there may be significant differences between them, and they may not be interchangeable for all imaging purposes [28].

Anterior segment optical coherence tomography

Anterior segment OCT (AS-OCT) utilizes low-coherence interferometry to generate cross-sectional images of the front portion of the eye that encompasses the cornea. AS-OCT allows the visualization and measurement of corneal thickness, epithelial thickness, corneal curvature, and anterior chamber parameters. This assists in identifying thinning, irregularities, and morphological changes associated with KCN [29, 30].

OCT has emerged as a promising non-invasive imaging modality. OCT utilizes low-coherence interferometry with near-infrared light, enabling high-resolution imaging of tissue morphology and the generation of maps displaying the thicknesses of distinct layers within the cornea [30]. There are different types of OCT systems for corneal assessment, including time-domain OCT (TD-OCT), spectral-domain (SD)-OCT, and swept-source (SS)-OCT, each with its advantages [31]. Compared with visible light-based tomography systems, OCT provides images with enhanced resolution, with shorter acquisition times and reduced motion artifact. SD-OCT (RTVue-OCT, Model RT100, Optovue Inc., Fremont, CA, USA; 3D OCT-1000, version 3.01, Mark II, Topcon Corp., Tokyo, Japan; Cirrus HD-OCT, version 3.0, Model 4000, Carl Zeiss Meditec, Inc., Dublin, CA, USA; Spectralis HD-OCT, Heidelberg Engineering GmbH, Heidelberg, Germany; Envisu, Bioptigen Inc., Research Triangle Park, NC, USA; and Copernicus HR, Optopol Technologies SA, Zawiercie, Poland) and SS-OCT (Casia SS OCT, Tomey, Nagoya, Japan and Triton SS OCT, Topcon) devices can capture anterior and posterior corneal topography and provide cross-sectional corneal imaging. These devices offer faster acquisition times while preserving detailed anatomical information [29, 30, 32].

TD-OCT (Visante-OCT™ system, Carl Zeiss Meditec and Slit-Lamp OCT, SL-OCT, Heidelberg Engineering) [29, 30] have been used for corneal pachymetry-based methods to detect corneal thinning and diagnose KCN. SD-OCT allows for higher speed and improved resolution. It generates higher readings for normal corneas than TD-OCT. SD-OCT is used to assess corneal thinning in KCN and determine diagnostic parameters based on pachymetric maps [30].

SS-OCT devices are used to analyze the anterior and posterior cornea. They have greater scanning speeds and can detect deeper layers with an improved signal detection [32]. SS-OCT has been used to detect subclinical KCN by calculating various indices derived from the data collected from the anterior and posterior corneal surfaces. Additionally, it evaluates changes in choroidal vascularity, choroidal thickness, and corneal measurements. It has a lower sensitivity for detecting subclinical KCN [30].

Fourier-domain OCT (FD-OCT) has remarkable accuracy and repeatability in measuring corneal epithelial thickness. The donut-shaped pattern observed in epithelial mapping can be used for the early detection of KCN when changes are still not evident in corneal topography [22].

Corneal biomechanical imaging

Corneal biomechanics evaluates the mechanical characteristics of the cornea, such as its stiffness, elasticity, and resistance to deformation, and provides additional information regarding its structural integrity beyond that of traditional diagnostic methods [20].

Corneal biomechanic factors play crucial roles in the development and progression of KCN. Techniques such as corneal hysteresis (CH) and corneal resistance factor measurements using devices such as the Ocular Response Analyzer (ORA) (Reichert Technologies, Depew, NY, USA) provide insights into corneal elasticity and resistance and help assess corneal biomechanical properties. These measurements aid in KCN diagnosis and monitoring of disease progression [33].

CH is widely used for assessing corneal biomechanics. CH reflects the capacity of the cornea to absorb and dissipate energy during the deformation and recovery process [33]. Lower CH values are associated with KCN, indicating a reduced corneal resistance. CH measurement [33] can differentiate between healthy corneas and those with KCN and can identify early KCN cases that may not display corneal topographic changes. Moreover, progressive biomechanical weakening has been observed during the detection of epithelial changes on the anterior surface [33, 34].

Two devices measure corneal deformation: Corvis ST (Oculus) and ORA [33, 35]. These instruments analyze the corneal response to an air puff, allowing the calculation of parameters such as corneal velocity, deformation amplitude, and time. Recent findings suggest that combining corneal biomechanical parameters with traditional diagnostic tools such as corneal topography and tomography can enhance the accuracy of KCN detection and aid in early disease identification [33].

Motion-tracking Brillouin microscopy, pioneered by Scarcelli and Yun, offers a noninvasive method for mapping the mechanical properties of the cornea with high 3-dimensional resolution, presenting an alternative to traditional biomechanical analysis [36]. The Brillouin frequency shift is directly correlated with the longitudinal viscoelastic modulus, enabling a direct estimation of this modulus through optical spectroscopy [36]. Importantly, Brillouin technology does not rely on macroscopic corneal deformation, ensuring that the extracted metrics are not influenced by other biophysical or geometrical factors of the cornea [36]. This technology has shown promise in identifying regional variations in corneas with KCN and in assessing the effects of different CXL protocols in *ex vivo* studies. However, conducting a viable *in vivo* analysis using Brillouin imaging has presented significant challenges [36].

Treatment Options for KCN

Spectacles, contact lenses, and phakic intraocular lenses

Spectacles are a suitable treatment option for early-stage KCN in patients with a visual acuity of 20/40 or better [37]. However, they cannot rectify the irregular astigmatism associated with KCN [38]. Rigid contact lenses such as Rose K, hybrid lenses, and scleral lenses are required in such cases [38]. Advances in contact lens design and imaging technologies, such as corneal topography and OCT, assist in properly adjusting and fitting contemporary lenses [38, 39].

Implantable collamer lenses (ICLs) have emerged as a reliable and versatile solution for refractive correction, particularly when corneal refractive surgeries are unsuitable. These esteemed posterior chamber phakic intraocular lenses offer faster recovery, a reduced likelihood of endothelial cell depletion, and reversibility compared to corneal refractive surgery [40]. ICLs are FDA-approved and are highly effective in managing refractive errors, including KCN with myopia or myopic astigmatism. Studies have demonstrated noticeable enhancements in visual outcomes and refractive correction following ICL implantation in patients with KCN and refractive errors [40, 41]. Newer ICL models, including a central port, have shown particularly positive results [42].

Toric ICL implantation is an additional effective and safe approach to rectify myopic astigmatism in individuals with stable KCN [43]. These findings highlight the potential of ICLs as a valuable option for managing refractive errors, particularly in patients with KCN [43].

Corneal collagen crosslinking

CXL is an innovative, FDA-approved, minimally invasive procedure for the treatment of KCN [38, 44]. The primary effect of CXL is prevention of disease progression by generating linkages between the corneal collagen fibrils [38]. Cross-links enhance corneal strength and stability by increasing resistance to enzymatic digestion and preventing further thinning and bulging. CXL strengthens the cornea and stabilizes corneal shape, ectasia, and progression of KCN and other corneal disorders [38, 45].

Standard-CXL (S-CXL) involves using a specific fluence (3 mW/cm^2) for 30 min, leading to a cumulative irradiance of 5.4 J/cm^2 [46]. Cross-linking occurs through the interaction between ultraviolet A light and riboflavin, forming cross-links between the amino acids of the collagen side chains and proteoglycans within the extracellular matrix [47]. Studies have revealed the long-term effectiveness and safety of riboflavin ultraviolet A-induced CXL in the treatment of progressive KCN among pediatric patients and younger individuals, mainly associated with the CXL-induced delay in corneal collagen turnover and the natural stabilization of KCN with age [48, 49].

CXL effectively inhibits KCN progression. Notably, it substantially reduces the maximal corneal refractive power. However, long-term cohort studies have revealed that KCN can progress even after cross-linking, particularly in younger patients [49]. These results underscore the significance of continuous monitoring and follow-up care to achieve the best possible results.

IVMED-80 cross –linking

A novel approach to slow the progression of KCN utilizes the natural ability of the cornea to repair itself [9]. This treatment method involves the application of eye drops containing synthetic biomolecules that trigger the physiological pathways responsible for maintaining corneal integrity and promoting healing [50]. An exciting therapy that follows this concept is IVMED-80 (iVeena Delivery Systems, Inc., Salt Lake City, UT, USA), a medication containing the active ingredient copper sulfate, which is essential for lysyl oxidase function [50]. Lysyl oxidase is a critical enzyme that regulates the extracellular matrix and facilitates the conversion of lysine into reactive aldehydes. These reactive aldehydes play a role in creating cross-links between extracellular proteins such as collagen and elastin [9, 50].

Intrastromal corneal ring segments

Polymethyl methacrylate ICRSs are inserted deep into the corneal stroma to minimize corneal distortion [51]. This is achieved by flattening the steep region and reshaping the cornea [52]. The ICRS is implanted using both mechanical and femtosecond laser-assisted techniques with similar visual and refractive results [53]. The ICRS treats various corneal conditions including KCN, post-LASIK corneal ectasia, post-radial keratotomy ectasia, astigmatism, and myopia [54].

The safety and precision of ICRS implantation are enhanced with femtosecond laser technology. Long-arc segments with an arc length of 355° were initially used for nipple-type KCN. However, reducing arc length to 340° causes fewer complications [54, 55]. A newly developed 320° ICRS was introduced to minimize potential issues, particularly with a 20° gap on each side, far from the surgical incision, rendering it safer [54]. Studies with 3–12 months of postoperative follow-up indicated significant improvements in uncorrected distance visual acuity, corrected distance visual acuity, corneal shape, and topographic astigmatism, suggesting the safety and effectiveness of 320° ICRS implantation for KCN [54, 56, 57].

Success of the surgical procedure and the improvement of vision with ICRS depend on essential factors, such as precise positioning, correct implantation depth, and suitable diameter of the optical zone. The types of ICRS used for KCN management include Keraring (Mediphacos Inc., Belo Horizonte, Brazil), Intacs (Addition Technology, Sunnyvale, CA, USA), Intacs SK (Addition Technology Inc., Lombard, IL, USA), MyoRing (Dioptex GmbH, Linz, Austria), and Ferrara (Ferrara Ophthalmics, Belo Horizonte, Brazil) [58-61].

Corneal allogenic intrastromal ring segments

The technique known as CAIRS was first performed in 2015 [16]. CAIRS involves the placement of ring segments made of allogeneic tissue into the cornea. These segments can be sourced from fresh, unprocessed, processed, preserved, or packaged tissue [16]. This procedure is becoming increasingly common because of its ability to produce refractive and topographic effects similar to, but with a wider range than, synthetic ICRS. Additionally, the allogeneic nature of the segments reduces the risk of complications such as overlying melting, necrosis, intrusion, extrusion, and migration [16].

The donut-shaped variation of the CAIRS technique represents an alternative approach for treating KCN, particularly in moderate to advanced stages in which the central cornea is clear and free of scars [15]. This represents a minimally invasive, customized technique with promising visual, refractive, and topographic effects [16].

Topography-guided custom ablation

Topography-guided custom ablation has emerged as a promising approach for managing KCN. It is a laser refractive surgical technique that utilizes corneal topography to map irregularities and guide laser ablation, aiming to improve visual acuity and corneal shape [62].

In a prospective interventional analysis, the safety and efficacy of topography-guided ablation with CXL were compared with those of standard CXL for managing advanced KCN before surgery and 1, 6, and 12 months after surgery [63]. The study concluded that customized topography-guided ablation with CXL is as safe as standard CXL, but for individuals with mild-to-moderate KCN, these treatments deliver more pronounced flattening of keratometry readings, improved corneal regularity, and enhanced visual acuity with spectacle correction [63].

In another study, topography-guided customized excimer laser subepithelial ablation combined with accelerated CXL yielded notable enhancements in best spectacle-corrected distance visual acuity and a significant decrease in the maximal keratometry of the anterior surface, corneal irregularity indices, root-mean-square of higher-order aberrations, and coma [64]. Combined topography-guided photorefractive keratectomy and accelerated CXL (30 mW/cm^2) without refractive correction provided stable refraction and corneal curvature in eyes with progressive mild-to-moderate KCN [64]. This safe, convenient, and efficient treatment approach offers promising results [64]. Nonetheless, extensive, comparative, and long-term studies are necessary to establish the optimal parameters and assess the prolonged safety and effectiveness of this combined surgical procedure.

Corneal transplantation

Corneal transplantation, commonly referred to as corneal grafting, is the surgical substitution of a damaged or diseased cornea with a healthy cornea obtained from a donor [65]. It is commonly used to treat various corneal conditions including KCN. Corneal transplantation may be considered in advanced cases of KCN in which other treatment options are not feasible [66].

Penetrating keratoplasty (PK) is a traditional full-thickness corneal transplant surgery typically reserved for advanced KCN [65]. A retrospective study suggested that wedge resection is secure and effective for correcting astigmatism resulting from ectasia in the graft-host junction after PK for KCN [67]. It reduces refractive astigmatism, improves visual acuity, and has moderate efficacy [67]. Therefore, it can be an initial choice for managing high astigmatism [67, 68].

With advancements in surgical techniques, deep anterior lamellar keratoplasty (DALK) is popular because of its improved visual outcomes [69]. DALK replaces the distorted front layers of the cornea while preserving the healthy endothelium, reducing the risk of rejection and graft failure, stabilizing vision, and minimizing complications [68, 70].

Bowman layer transplantation

Bowman layer transplantation (BLT) has gained interest as a treatment for KCN, particularly when other techniques such as CXL or ICRS may not be achievable owing to corneal thickness restraints or considerable steepening [71, 72]. The principle behind BLT is replacement of the damaged or fragmented Bowman membrane, which plays a critical role in preserving corneal shape, providing biomechanical support, preventing corneal deterioration, and maintaining vision [11].

According to previous studies, BLT causes corneal flattening and halts the progression of KCN [73]. The rate of progression/complication-free survival has been reported as approximately 84% at 5 years [73]. One advantage of BLT is that there have been no reported cases of immune rejection, most likely because of the acellular nature of the Bowman membrane [73]. To improve precision and reduce the potential for microperforation during manual dissection, some surgeons use femtosecond lasers to form the stromal pocket [73]. Intraoperative AS-OCT can also enhance visualization of the dissection plane [74].

In the conventional method, the graft is positioned within the mid-stromal layer [18]. However, modifying the procedure involves inserting the graft only into the subepithelial area, thus eliminating the need for pocket creation. This modified technique has shown promising preliminary results [18].

Novel Applications of Artificial Intelligence (AI) in Keratoconus Management

Finally, we should address the role of artificial intelligence (AI) in detecting KCN, which has been the subject of a comprehensive review [75]. The management of KCN could be revolutionized by further application of artificial intelligence in the diagnosis, grading, and early detection of KCN. Artificial intelligence capabilities in management approach considering the currently available imaging modalities [76, 77] and treatment options [78] would best benefit the patient. Table 1 summarizes novel applications of AI in KCN management [79-94].

Table 1. Novel applications of artificial intelligence (AI) in keratoconus management

Potential application
1- Screening:
✓ Machine learning techniques could differentiate normal and keratoconic eyes, as well normal and form-fruste keratoconus [79].
✓ An AI-based model with simultaneous use of Scheimpflug and Placido corneal imaging data revealed a high diagnostic accuracy for early detection of keratoconus and discriminated keratoconic eyes from normal corneas [80].
✓ AI-based classifiers were helpful in detecting early keratoconus, but cannot replace clinical experts' opinions, notably in decision-making before refractive surgery. However, experts' opinions are not error-free [81].
✓ An AI-based algorithm discriminated accurately between normal, suspect irregular, and keratoconic corneas, similar to a corneal expert. The authors recommended applying machine learning to corneal tomography to ficilitate screening of keratoconus in large populations and refractive surgery candidates [82].
2- Diagnosis
✓ A machine learning-based algorithm could improve diagnosis of subclinical keratoconus or early keratoconus in routine ophthalmic practice. However, no consensus has been reached concerning the corneal parameters that should be included for assessment, or the optimal design [83].
✓ Combining segmental tomography with Zernike polynomials and AI achieved an excellent classification of healthy and keratoconic eyes. The AI model efficiently classified the eyes with very asymmetric ectasia as subclinical and forme-fruste keratoconus [84].
✓ The keratoconus classification performance of a random forest classifier combined with sequential forward selection method achieved a high accuracy with a reduced execution time [85].
✓ An AI-based diagnostic model using purely biomechanical parameters without corneal topographic examination, demonstrated a rapid and accurate diagnostic performance for keratoconus [86].
3- Treatment
✓ AI-based diagnostic software that included a model for the automated determination of keratoconus stage achieved an accuracy from 0.95 to 1.00 relative to the adapted Amsler–Krumeich algorithm. The software contained a standardized algorithm for determining surgical intervention indications, drived from data available in the literature and recommendations from the expert community [87].
✓ Compared with the manufacturer's nomograms an artificial neural network revealed better performance regarding better corrected vision and lowering of the coma-like aberrations in guiding intracorneal ring segments implantation in eyes with keratoconus [88].
✓ Corneal crosslinking in a 28-year-old patient with bilateral keratoconus combined with photorefractive surface ablation customized by a novel AI-based platform for calculating lower- and higher-order aberrations based on wavefront data, Scheimpflug tomography, and interferometry-based axial length measurements from a single diagnostic device achieved an accurate normalization of distorted eye optics [89].
4- Patient Follow-up
✓ The orthopedic field developed an AI-assisted follow-up system for post-operative monitoring. Its effectiveness was not inferior to that of manual follow-up and led to saving human resource costs. [90]. Similar verified AI-assisted follow-up systems, modified for compatibility with the field of ophthalmology, could be developed to monitor patients with keratoconus post-operatively.
5- Patient Rehabilitation
✓ Goodman and Zhu considered successful examples in the ophthalmology literature and proposed potential use of AI-based algorithms for personalized surgical planning to improve postoperative outcomes and visual rehabilitation in patients with keratoconus [91].
✓ Studies on AI-based algorithms for delivery of home-based virtual rehabilitation programs to adult patients revealed that incorporating AI with home-based virtual rehabilitation improved rehabilitation outcomes. The authors recommended further assessment of the effectiveness of various forms of AI-driven home-based virtual rehabilitation with consideration of its unique challenges and applying standardized metrics [92]. Similar verified AI-driven home-based virtual rehabilitation system, modified for compatibility with the field of ophthalmology, could be developed for adult patients with keratoconus.
6- Patient Education
✓ AI-based systems for online patient education in other fields have revealed promising results [93, 94]. Similar verified AI-based dialogue platforms, modified for compatibility with the field of ophthalmology could be developed for adult patients with keratoconus.

In this narrative review, we have provided an overview of the current advances in imaging modalities and treatment approaches for managing KCN. An important limitation is the heterogeneity among studies, as studies have varied in outcomes, management methods, the frequencies of application of certain methods, and the timing of treatments throughout the advancement of KCN. While this diversity can complicate comparisons between studies, each study offers valuable insights into the outcomes. To address the variations in clinical practices outlined in the literature, we suggest enhancing education, promoting interdisciplinary patient care, and conducting ongoing research to monitor advancements and assess clinicians' approaches to treating KCN.

CONCLUSIONS

KCN is a challenging ocular entity that can lead to significant visual impairment and reduced quality of life. Early detection and advancements in screening methods using current imaging modalities have improved diagnosis. Although CXL is a standard treatment, alternative options, such as copper sulfate eye drops, have emerged. ICRSs and CAIRS, which are new alternatives to synthetic ICRSs, have also demonstrated effectiveness in improving vision and corneal curvature in mild-to-moderate KCN. In advanced cases, DALK is the surgical option for visual enhancement. Continued research is essential to enhance our understanding of KCN and improve treatment outcomes.

ETHICAL DECLARATIONS

Ethical approval: This was a narrative review and no ethical approval was required.

Conflict of interest: None.

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