

Clinical Knowledge of Post-LASIK Corneal Ectasia: A Review

Abdulrahman Al-Amri, MD*

Corneal ectasia is a devastating complication associated with laser in situ keratomileusis (LASIK) that occurs in an estimated 0.04–0.6% of patients. The condition occurs when the cornea begins to progressively thin and structurally weaken, resulting in an outward bulge (ectasia). Signs of post-LASIK ectasia include a progressive increase in myopia (with or without increasing astigmatism) and a decrease in uncorrected visual acuity. These signs are often accompanied by a decrease in best-corrected visual acuity, keratometric steepening, and/or asymmetric inferior corneal steepening. The condition can occur anywhere from one week to several years after surgery and results from a structural weakness in the cornea itself that was pre-existing, caused by LASIK or, in rare cases, resultant from postoperative physiochemical collagen changes (e.g., associated with pregnancy or infection). Because post-LASIK ectasia can be devastating, much effort has been given to detecting patients at a high-risk for developing the condition. Preoperative factors associated with post-LASIK ectasia include topography abnormalities, low corneal thickness, elevated posterior surface, thin post-LASIK residual corneal stromal bed, young patient age, and high myopia. This review summarizes current clinical knowledge of post-LASIK corneal ectasia and methods for detecting high-risk patients.

Key words: Incidence, Post-LASIK ectasia, Risk factors

INTRODUCTION

The cornea is a somewhat mysterious structure that is complicated, dynamic, and multi-functional. Laser in situ keratomileusis (LASIK) is safe and effective for managing many patients with refractive errors¹⁻³. Refractive surgery involves stretching the cornea with a ring segment, cutting it with a microtome or femtosecond laser, and sculpting it with an excimer laser to ultimately reshape the cornea. Because the cornea is constantly remodeling itself, any physical^{4,5} or chemical^{6,7} changes to the corneal microenvironment can affect extracellular matrix homeostasis.

These changes have decreased surgeon error, improved LASIK outcomes, and decreased postoperative complication rates^{8,9}. However, corneal ectasia, a rare and devastating complication, occurs in an estimated 0.02–0.6% of LASIK patients¹⁰⁻¹⁴. Post-LASIK ectasia was first described by Seiler et al¹⁵ in 1988 and was described as a progressive stromal thinning that results in a progressive corneal steepening and both uncorrected and corrected distance visual acuity decreases. Although rare, post-LASIK ectasia has a significant impact on patients, with 12% of LASIK-related medical claims related to corneal ectasia¹⁶. This condition mimics keratoconus, a progressive degenerative disease that involves corneal thinning, and is caused by surgically induced weakening of the inner corneal layers. Over time, the weakened cornea bulges forward, which subsequently results in distorted vision that cannot be corrected with eyeglasses. Unfortunately, if the ectasia is not successfully managed, patients may require a corneal transplant to restore vision. Post-surgical corneal ectasia occurs most often following LASIK but has also been associated with other corneal refractive procedures, including PRK, laser epithelial keratomileusis, and epi-LASIK. Signs of post-LASIK ectasia include a progressive increase in myopia (with or without increasing astigmatism) and a decrease in uncorrected visual acuity. These signs are often accompanied by a decrease in best-corrected visual acuity, keratometric steepening, corneal thinning, and/or asymmetric inferior corneal steepening^{17,18}. Post-LASIK ectasia can develop as early as one week¹⁹ or as late as several years^{20,21} after LASIK.

Pathogenic mechanisms underlying post-LASIK ectasia remain largely unknown but underlying corneal abnormalities and/or mechanical weaknesses from post-LASIK collagen tensile strength changes are thought to be involved^{22,23}. In rare cases, late-onset ectasia has been associated with specific physiochemical collagen changes induced by relaxin (a hormone that increases during pregnancy),²⁴⁻²⁶ inflammatory mediators,²⁷ and adenoviral keratitis²⁸⁻³¹.

METHODS

Search Strategy, and Quality of Studies: A systematic literature search of PubMed and Embase (Elsevier) databases was performed on August 8, 2017, and updated on August 9, 2019, using the keywords “post-LASIK ectasia, risk factors” Since the developing need of the topic, search was also performed using the same keywords on Google Scholar, web of science to include the most recently published articles.

Data Extraction: Studies related to the objective of the i.e., showing relevance with objectives of the study was included in this review.

Quality of Studies Included: All studies and news related to our objectives published /unpublished were included in the study. The articles needed to be published in English and having information matches with the objective of the study.

Data Collection and Analysis: Systematic review analysis was done, Information was gathered and mentioned in the research.

RESULT

The author reviewed 400 studies and unpublished data, after removing the duplicate information finally 345 studies and unpublished material included in this study. This review article summarizes our clinical knowledge of post-LASIK ectasia, including pre-operative risk factors and advancements in detection methods.

* Department of Ophthalmology
College of Medicine, King Khalid University
Saudi Arabia
E-mail: profalamri@hotmail.com

DISCUSSION

Current Knowledge of Keratoconus: The prevalence of keratoconus has been estimated to be between 50 and 230 cases per 100,000 people in the general population³²⁻³³. The risk for developing post-LASIK ectasia, widely varies among populations and patient ethnicities³⁴⁻³⁹. Given that keratoconus can develop any time after LASIK, the incidence is expected to be higher in older groups than in younger groups. Eyes with undetected keratoconus that undergo LASIK have a high risk for developing post-LASIK ectasia^{13,29-31}. The upper estimates of keratoconus prevalence in 1966 was 230 cases per 100,000 people (0.2%)³². However, this prevalence may be increasing and has been more recently shown to be much higher among potential refractive surgery candidates (0.9%–3.7% 4–18 times the 1966 rate)⁴⁰⁻⁴³.

The primary symptom of post-LASIK ectasia is blurred, distorted vision. This results from increases in myopic and astigmatic errors that develop as the cornea non-uniformly bulges forward. Unfortunately, vision decreases are not always fully corrected by eyeglasses or soft contact lenses. Post-LASIK ectasia can develop any time after surgery, varying from a few days¹⁹ to several years^{20,21}. However, one study found that post-LASIK ectasia develops an average of 16 months after surgery⁴⁴.

Advancements in Detecting Post-Lasik Corneal Ectasia Corneal Topography and Tomography: Corneal topography and tomography systems noninvasively map corneal surface curvature and measure corneal thickness. Tomography systems create a 3-dimensional reconstruction of the cornea and surrounding anterior chamber structures⁴⁵. Topography maps, represented as false-color images (Figure 1), are particularly helpful for diagnosing corneal ectasia and locating regions of corneal thinning and/or bulging. Clinicians should remember that a variety of conditions can appear in a similar manner on topography maps and that clinical findings should also be used to make a definitive corneal ectasia diagnosis.

The false-color scale is generally standard between topography systems (Figure 1). However, different systems can use varying color step magnitude (e.g., 0.5 D vs. 1.0 D, Figure 1), which can make image

comparison between systems challenging. Smaller color steps increase sensitivity for early keratoconus detection, but also increase false keratoconus diagnosis rates.

However, with this map, small, local irregularities can be missed and peripheral curvature measurements are not always accurate.

Tangential (or instantaneous) maps are sensitive to local corneal surface variations because extreme curvature values are not smoothed out^{46,47}. Elevation maps show corneal surface height (in μm) relative to a reference surface⁴⁹. Most topography systems use a spherical reference shape that is automatically calculated for each scan. A best-fit sphere is most commonly used, but some systems use an ellipsoid, toric ellipsoid, or torus⁵⁰. Because the reference surface varies between scans, elevation measurements often have a higher within-patient variation than other map types. Some elevation-based topographers allow the same reference shape to be used in multiple scans and/or line up the x- and y-axes of serial scans to improve longitudinal comparisons. However, scan quality can vary and the “Quality Score” should be checked before elevation map interpretation. Therefore, caution should be used when comparing serial elevation maps.

Corneal Topographic Indices: Topography systems calculate various topographic indices that are helpful in understanding corneal shape and health. These include simulated keratometry (SimK, average keratometric value k-value of the steepest axis and the axis perpendicular to it)⁴⁶, central K (average keratometric power along different concentric rings)⁵¹, cylinder (Cyl, power difference between the two axes),⁴⁶ MinK (flattest k-value measured)⁴⁶, surface asymmetry index (SAI, difference in corneal power 180° apart), and surface regularity index (SRI, compares central and peripheral corneal power). The SAI is often used to quantify keratoconus progression and a high SRI suggests a high level of surface irregularity⁴⁶. Additionally, individual topography systems may calculate unique indices, including corneal uniformity index, predicted corneal acuity, and point spread function⁴⁶.

Topography-Based Corneal Ectasia Classifications: Topography-based elevation, thickness, and curvature maps can be used to classify disorder severity, type, and location^{46,51}. Eyes with post-LASIK corneal ectasia often have a bow-tie pattern on topographic curvature maps

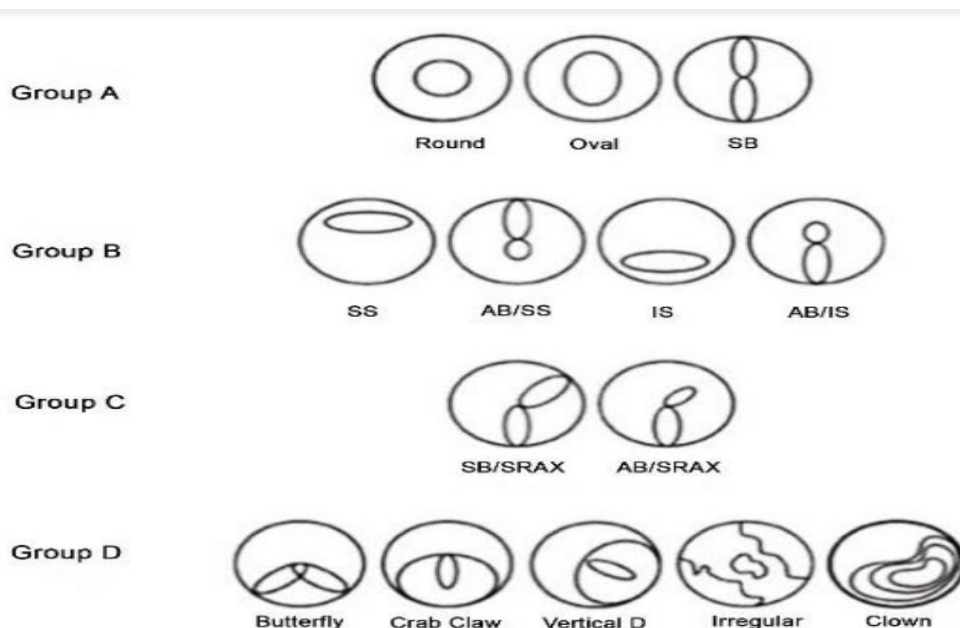


Figure 1: Example of topography false-color maps obtained with different topography systems. A. False-color topography map created using 0.5 D steps. B. False-color topography map created using 1.0 D steps.

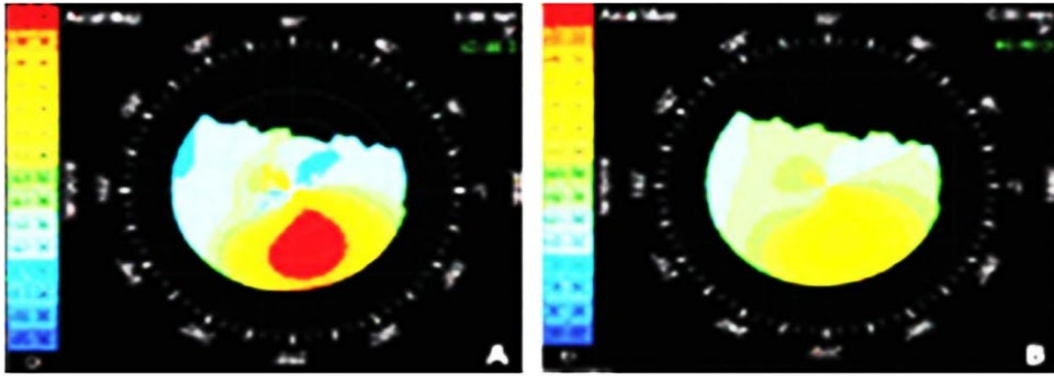


Figure 2: Corneal topography maps from eyes with various types of corneal ectasia. A. Interior steep pattern. B. Skewed (>22° between axes) inferior steep pattern. C. Symmetric bowtie pattern. D. Skewed symmetric bowtie pattern. E. Pellucid marginal degeneration (PMD) or pellucid-like keratoconus (PLK). F. Skewed PMD or PLK. G. Eccentric cone with difficult to identify steep and flat axes.

(Figure 2). Eyes with the inferior steep pattern have a steeper (larger) inferior bowtie segment than superior bowtie segment. Additionally, the central axes of the two parts are aligned and straight (Figure 2A). Eyes with a symmetrical bow-tie have equally-sized segments with axes that are aligned and straight (Figure 2C). Eyes with pellucid marginal degeneration (PMD) or pellucid-like keratoconus (PLK) may also have a bow-tie appearance, making this condition often confused with other ectatic conditions (Figure 2E). These three patterns also have a variation in which the skew between the axes is greater than 22° (Figure 2B, D, and F). The last topography pattern shows an eccentric cone with difficult to define steep and flat axes (Figure 2G). These ectasia classifications are important for making a correct diagnosis and determining treatment course and prognosis.

Corneal Pachymetry: Prior to refractive surgery, thickness maps are used to identify patients with keratoconus or insufficient corneal thickness. Pachymetry is also used to reduce corneal perforation risk during limbal relaxation incision surgery⁵² and as a glaucoma screening tool.^{53,54}

Risk Factors for Developing Post-Lasik Corneal Ectasia: In order of importance, these include abnormal topography, predicted low residual corneal bed (RSB) thickness, young patient age, thinner than normal corneas, and high myopia^{13,29-31}. Other identified risk factors include a thick corneal flap, irregular corneal thickness, varying ablation rates, and high intraocular pressure (IOP)²⁸. It should be noted that patients with no known risk factors can also develop post-operative corneal ectasia^{55,56}. In fact, post-LASIK ectasia has developed in patients with low myopia⁵⁷ and hyperopia^{58,59}.

The RSB is the corneal tissue that remains under the corneal flap after LASIK stromal ablation. Patients with a low RSB (<250 μm) are at an increased risk for developing post-LASIK corneal ectasia^{30,61} because the structural integrity of the cornea has been compromised. Both stress-strain⁶¹ and tensile strength⁶² analyses have shown that the anterior cornea is structurally stronger than the posterior cornea.

The amount of tissue ablated during LASIK is directly proportional to the needed myopic correction and deep ablation is a known risk factor for post-LASIK ectasia^{63,64}. Therefore, patients with high myopia have a higher risk for developing this complication than patients with hyperopia, astigmatism, or lower levels of myopia^{13,29}.

Indices that Detect Keratoconus and Calculate Post-LASIK Ectasia Risk: Automated algorithms calculate topography-based indices to identify patients with keratoconus and those suspected of having keratoconus. These include average simulated keratometry

readings, the modified Rabinowitz-McDonnell index (uses K and I-S values)⁵⁸, the Maeda/Klyce index (uses 8 different topography indices)⁶⁵, and the KISA% index (quantifies corneal topography patterns that are characteristic of keratoconus)⁶⁶. The KISA% index also detects subclinical keratoconus^{67,68} and is calculated using the following equation:

$$KISA\% = \text{central } K \cdot I-S \cdot AST \cdot SRAX \cdot \frac{100}{300}$$

where, central K is the keratometric value of the central cornea, I-S is the inferior-superior value, AST is the astigmatism index that quantifies regular corneal astigmatism (simK1-simK2), and SRAX is the index that quantifies irregular astigmatism associated with keratoconus⁶⁶. Fourier-domain optical coherence tomography epithelial thickness maps can also be used to reliably distinguish between normal eyes and those with FFK or corneal warpage⁶⁸. First described, and later validated⁶⁹, the Ectasia Risk Score System (ERSS) in 2008. This system assigns points to each of the following preoperative parameters in a weighted fashion (listed in order of highest to lowest weighting, risk cut-off value): topography patterns, expected RSB thickness (<300 μm), patient age (<30 years), corneal thickness (<510 μm), and refractive spherical equivalent (more severe than -8.00 D). The ERSS retrospectively identified 46 of 50 patients (92%) with post-LASIK ectasia as high-risk and only 3 of 50 (6%) patients without ectasia as high-risk⁶⁸. However, this scoring system may not identify high-risk patients with normal preoperative corneal topography^{70,71}. Mirafteb et al⁷² later modified the ERSS to improve sensitivity and specificity for identifying high-risk patients.

Risk Factors not Present Before Surgery: Post-LASIK corneal ectasia can occur in eyes with no apparent risk factors^{55,56,64}. However, pregnancy and adenoviral keratoconjunctivitis are both risk factors for late-onset post-LASIK corneal ectasia²⁸. The role of pregnancy in corneal ectasia pathogenesis remains uncertain. However, the hormone relaxin, which reaches high levels during pregnancy, has been shown to inhibit airway collagen remodeling in mice²⁴, decrease ligament and wound-healing collagen integrity²⁵ and trigger cartilage matrix degradation by matrix metalloproteinase in synovial joints²⁶. Therefore, it is reasonable to suspect that pregnancy also changes the physiochemical properties of corneal collagen.

Adenoviral adenocconjunctivitis has been associated with post-LASIK ectasia²⁸. High levels of ocular surface inflammation that occur with the infection may lead to inflammatory cytokine and metalloproteinase upregulation, result in collagen loss, and cause subsequent corneal stromal weakening^{28,68}.

CONCLUSION

Post-LASIK corneal ectasia is somewhat rare but can have devastating consequences. Multiple risk factors for developing post-LASIK ectasia have been identified, including corneal topography abnormalities, low corneal thickness, low RSB, high myopia, and young patient age. Corneal topography plays a large role in identifying high-risk patients, but early-stage keratoconus is often missed. Furthermore, corneal warping from contact lens use can mimic keratoconus and FFK. However, it is possible for any patient to develop post-LASIK corneal ectasia, even those with no known risk factors^{55,56,64}. Therefore, before undergoing LASIK, all patients should be carefully evaluated for post-LASIK ectasia risk and educated on the signs and symptoms of post-LASIK ectasia.

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