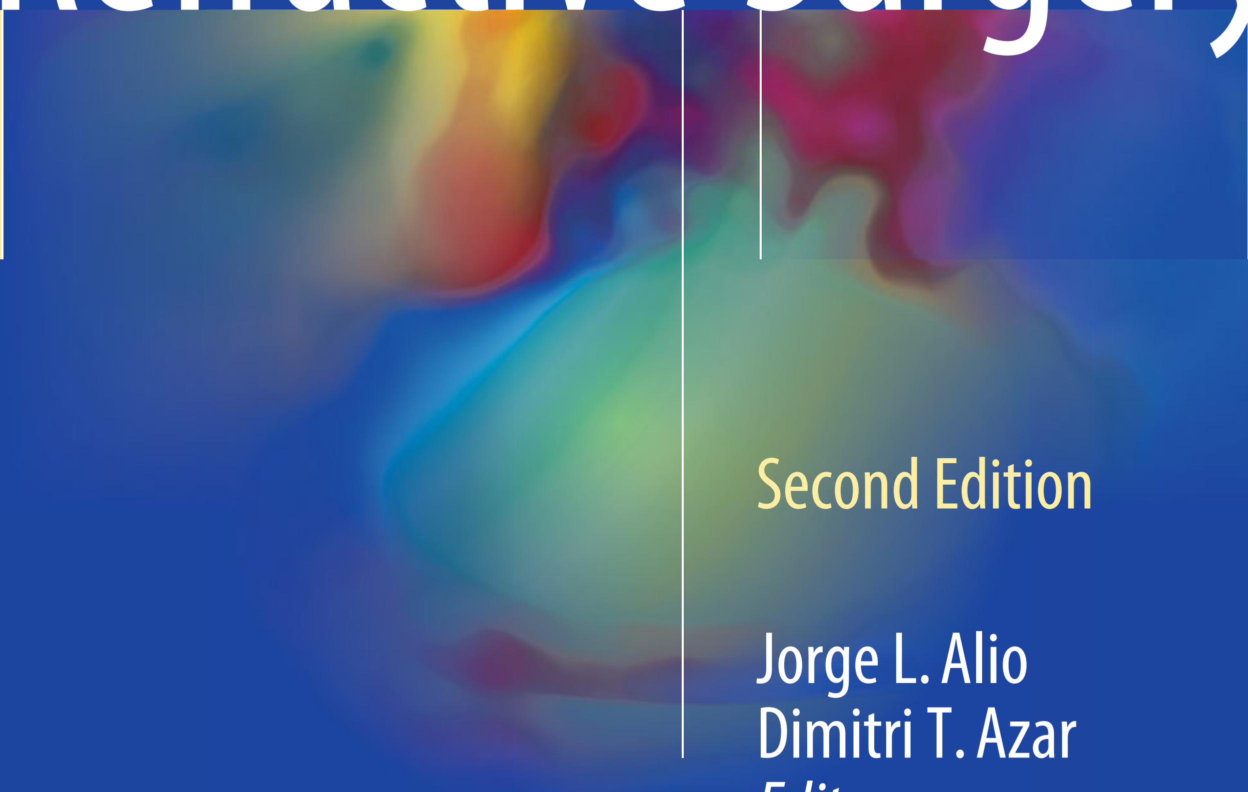
Management of Complications in Refractive Surgery



Second Edition

Jorge L. Alio
Dimitri T. Azar
Editors

Springer

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in Refractive Surgery

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Editors
Jorge L. Alio
Department of Ophthalmology
Miguel Hernandez University
Alicante, Spain

Dimitri T. Azar
Department of Ophthalmologic Research
University of Illinois at Chicago
Chicago, IL
USA

Verily Life Sciences
Alphabet, SF, CA
USA

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List of Associate Editors

Jorge L. Alio del Barrio Cornea, Refractive and Cataract Surgery Unit, Vissum/Instituto Oftalmológico de Alicante, Alicante, Spain

Department of Ophthalmology, Universidad Miguel Hernández, Alicante, Spain

Joelle Hallak Department of Ophthalmology and Visual Sciences, Ophthalmic Clinical Trials and Translational Center, University of Illinois at Chicago, Chicago, IL, USA

Contents

List of Contributors

Ahmed A. Abdelghany, M.D., Ph.D. Ophthalmology Department, Faculty of Medicine, Minia University, Minia, Egypt

Natalie A. Afshari Shiley Eye Institute, University of California, San Diego, CA, USA

Jorge L. Alio, M.D., Ph.D., F.E.B.O. Vissum Corporation-Instituto Oftalmológico de Alicante, Alicante, Spain

Department of Ophthalmology, Universidad Miguel Hernández, Alicante, Spain

Jorge L. Alio del Barrio, M.D., Ph.D. Cornea, Refractive and Cataract Surgery Unit, Vissum/Instituto Oftalmológico de Alicante, Alicante, Spain

Department of Ophthalmology, Universidad Miguel Hernández, Alicante, Spain

Norma Allemann, M.D. Department of Ophthalmology, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil

Noel Alpins, AM., FRAZCO., FRC.Ophth, FACS. Department Ophthalmology, Melbourne University, Cheltenham, VIC, Australia

Renato Ambrósio Jr, M.D., Ph.D. Instituto de Olhos Renato Ambrósio, Visare Personal Laser & Refracta-RIO, Rio de Janeiro, Brazil

Department of Ophthalmology, Federal University of São Paulo—"Escola Paulista de Medicina", São Paulo, Brazil

U. Andrea Arteaga Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

Konstantinos Andreanos, M.D. Department of Ophthalmology, G. Gennimatas General Hospital, University of Athens, Athens, Greece

Fernando A. Arevalo, B.S. Retina and Vitreous Service, Clinica Oftalmologica Centro Caracas, Caracas, Venezuela

J. Fernando Arevalo, M.D., F.A.C.S. Retina Division, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Jean Louis Arne, M.D. University of Toulouse, Toulouse, France

Dimitri T. Azar Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

College of Medicine, University of Illinois, Chicago, IL, USA

Michael W. Belin Department of Ophthalmology and Vision Science, The University of Arizona, Tucson, AZ, USA

Sina Bidgoli Vissum Corporation-Instituto Oftalmológico de Alicante, Alicante, Spain

Roberto Fernández Buenaga, M.D., Ph.D. Vissum Madrid, Madrid, Spain

Claudia Castell, M.D. Bogota Laser Ocular Surgery Center, Bogota, Colombia

Wallace Chamon, M.D. Department of Ophthalmology, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil

Arturo S. Chayet Codet Vision Institute, Tijuana, Mexico

Béatrice Cochener, M.D. University of Brest, Brest, France

Jose de la Cruz, M.D. Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

Pan-American Cornea Society, University of Illinois at Chicago, Chicago, IL, USA

Konstantinos Droutsas, M.D., Ph.D. Department of Ophthalmology, G. Gennimatas General Hospital, University of Athens, Athens, Greece

Daniel Elies, M.D. Cornea and refractive Surgery Unit, Instituto de Microcirugia Ocular (IMO), Barcelona, Spain

David Fahd Cornea, Cataract, and Refractive Surgery, Kesrwan Medical Center, Metn, Lebanon

Fernando Faria-Correia, M.D. Rio de Janeiro Corneal Tomography and Biomechanics Study Group, Rio de Janeiro, Brazil

Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal

Marta S. Figueroa, M.D., Ph.D. Department of Retina and Vitreous, Vissum Madrid, Madrid, Spain

Department of Ophthalmology, Ramón y Cajal University Hospital, Madrid, Spain

University of Alcalá de Henares, Madrid, Spain

Veronica Vargas Fragoso Vissum Corporation, Alicante, Spain

Jose L. Güell, M.D., Ph.D. Cornea and Refractive Surgery Unit, Instituto de Microcirugia Ocular (IMO), Barcelona, Spain

Eric E. Gabison, M.D. Department of Ophthalmology, Fondation Ophtalmologique A. de Rothschild and Bichat Hospital, Paris, France

CNRS UMR 7149, University Paris XII, Paris, France

Reinaldo A. Garcia, M.D. Clínica Oftalmológica El Viñedo, Valencia, Venezuela

Javier Gaytan, M.D. Cornea, Cirugia Refractive y seg. Anterior, Hospital Angeles Puebla, Puebla, Mexico

Ramon C. Ghanem Sadalla Amin Ghanem Eye Hospital, Joinville, SC, Brazil

Vinicius C. Ghanem Sadalla Amin Ghanem Eye Hospital, Joinville, SC, Brazil

Almutez M. Gharaibeh, M.D. Faculty of Medicine, The University of Jordan, Amman, Jordan

Andrea Govetto, M.D. Department of Ophthalmology, Ramón y Cajal University Hospital, Madrid, Spain

Retina Division, Stein Eye Institute, University of California Los Angeles, Los Angeles, CA, USA

Enrique O. Graue-Hernández, M.D., M.Sc Cornea and Refractive Surgery, Instituto de Oftalmología Fundación Conde de Valenciana, Mexico City, Mexico

Universidad Nacional Autónoma de Mexico, Mexico City, Mexico

Oscar Gris, M.D., Ph.D. Cornea and refractive Surgery Unit, Instituto de Microcirugia Ocular (IMO), Barcelona, Spain

Joelle Hallak Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

Department of Ophthalmology and Visual Sciences, Ophthalmic Clinical Trials and Translational Center, University of Illinois at Chicago, Chicago, IL, USA

Ramon Hallal Rio de Janeiro Corneal Tomography and Biomechanics Study Group, Rio de Janeiro, Brazil

Department of Ophthalmology, Hospital Federal da Lagoa, Rio de Janeiro, Brazil

Sadeer B. Hannush Department of Ophthalmology, Wills Eye Hospital, Philadelphia, PA, USA

Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, USA

David R. Hardten, M.D. Minnesota Eye Consultants, Minnetonka, MN, USA

Department of Ophthalmology, University of Minnesota, Minneapolis, MN, USA

Adeline G. Hardten Minnesota Eye Consultants, Minnetonka, MN, USA

Department of Ophthalmology, University of Minnesota, Minneapolis, MN, USA

Sophia A. Hardten Minnesota Eye Consultants, Minnetonka, MN, USA

Department of Ophthalmology, University of Minnesota, Minneapolis, MN, USA

Teresa S. Ignacio IntraLase Corp., Irvine, CA, USA

Sandeep Jain, M.D. Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL, USA

Department of Ophthalmology, Cornea Service, Chicago, IL, USA

Translational Biology Laboratory, University of Illinois at Chicago, Chicago, IL, USA

Dry Eye Service and oGVHD Service, University of Illinois at Chicago, Chicago, IL, USA

Advaite, LLC, Chicago, IL, USA

Investigative Ophthalmology and Visual Sciences, Ocular Surface, Chicago, IL, USA

Soraya M.R. Jonker, M.D. University Eye Clinic Maastricht, Maastricht University Medical Center, Maastricht, The Netherlands

Vikentia J. Katsanevaki, M.D., Ph.D. University of Crete, Crete, Greece

Andreas Katsanos, M.D. Universidad de Alcalá Madrid, Madrid, Spain

Clínica Novovision de Madrid, Madrid, Spain

Bhairavi Kharod-Dholakia Cornea and Refractive Surgery, Emory Eye Center, Atlanta, GA, USA

George Kymionis, M.D., Ph.D. Department of Ophthalmology, G. Gennimatas General Hospital, University of Athens, Athens, Greece

Richard L. Lindstrom, M.D. Minnesota Eye Consultants, Minnetonka, MN, USA

University of Minnesota, Minneapolis, MN, USA

Javier Lopez Codet Vision Institute, Tijuana, Mexico

Carlo F. Lovisolo, M.D. Quattroelle Eye Centers, Milan, Italy

Felicidad Manero, M.D. Cornea and Refractive Surgery Unit, Instituto de Microcirugia Ocular (IMO), Barcelona, Spain

Antonio A.P. Marinho, M.D., Ph.D. Hospital Arrábida, Porto, Portugal

Merce Morral, M.D., Ph.D. Cornea and Refractive Surgery Unit, Instituto de Microcirugia Ocular (IMO), Barcelona, Spain

Andreas Mouchtouris, M.D. Department of Ophthalmology, G. Gennimatas General Hospital, University of Athens, Athens, Greece

Rudy M.M.A. Nuijts, M.D., Ph.D. University Eye Clinic Maastricht, Maastricht University Medical Center, Maastricht, The Netherlands

M. Emilia Mulet, M.D., Ph.D. Department of Ophthalmology, Miguel Hernández University, Alicante, Spain

Department of Research and Development, Vissum Instituto Oftalmologico de Alicante, Alicante, Spain

David P.S. O'Brart, M.D., F.R.C.S, F.R.C.Ophth, D.O. King's College, London, UK

Guy's and St. Thomas' NHS Foundation Trust, London, UK

Konstantinos Oikonomakis, M.D. Department of Ophthalmology, G. Gennimatas General Hospital, University of Athens, Athens, Greece

Renan F. Oliveira Sadalla Amin Ghanem Eye Hospital, Joinville, SC, Brazil

Konrad Pesudovs, Ph.D. NH&MRC Centre for Clinical Eye Research, Department of Optometry, Flinders University, Adelaide, SA, Australia

Isaac Ramos, M.D. Rio de Janeiro Corneal Tomography and Biomechanics Study Group, Rio de Janeiro, Brazil

Jerome C. Ramos-Esteban Department of Ophthalmology, General Boynton Beach, Boynton Beach, FL, USA

J. Bradley Randleman, M.D. Roski Eye Institute, University of Southern California, Los Angeles, CA, USA

Department of Ophthalmology, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA

Antonio Renna, M.D. Vissum, Instituto Oftalmológico Alicante, Alicante, Spain

Department of Medical and Biological Sciences—Ophthalmology, University of Udine, Udine, Italy

Emanuel Rosen, M.D., F.R.C.S.Ed. Private Practice, Manchester, UK

Julie M. Schallhorn, M.D., M.S. Roski Eye Institute, University of Southern California, Los Angeles, CA, USA

Department of Ophthalmology, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA

Juan Carlos Serna-Ojeda, M.D. Instituto de Oftalmología Fundación Conde de Valenciana Mexico City, Mexico City, Mexico

Pete Setabur Department of Ophthalmology and Visual Sciences, University of Illinois, Champaign, IL, USA

Bryan Sires Allure Facial Laser Center, University of Washington, Kirkland, WA, USA

Stephen G. Slade, M.D., F.A.C.S. Slade & Baker Vision, Houston, TX, USA

Felipe Soria, M.D. Instituto de la Vision-Hospital La Carlota, Universidad de Montemorelos, Montemorelos, Mexico

George Stamatelatos, B.Sc.Optom NewVision Clinics, Melbourne, VIC, Australia

Roger F. Steinert, M.D. Department of Ophthalmology, University of California, Irvine, CA, USA

Karl G. Stonecipher The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

R. Doyle Stulting, M.D., Ph.D. Stulting Research Center at Woolfson Eye Institute, Atlanta, GA, USA

Nayyirih G. Tahzib, M.D., Ph.D. University Eye Clinic Maastricht, Maastricht University Medical Center, Maastricht, The Netherlands

Jonathan H. Talamo Johnson & Johnson Vision Care, Inc., Jacksonville, FL, USA

Gustavo Tamayo, M.D. Bogota Laser Ocular Surgery Center, Bogota, Colombia

Miguel A. Teus Universidad de Alcalá Madrid, Madrid, Spain

Clínica Novovision de Madrid, Madrid, Spain

Mauro Tiveron Jr., M.D. Vissum, Instituto Oftalmológico Alicante, Alicante, Spain

Universidad Miguel Hernandez, Alicante, Spain

Luis F. Torres Innova Vision, Aguascalientes, Mexico

Andre A.M. Torricelli Department of Ophthalmology, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil

Pilar Vargas, M.D. Bogota Laser Ocular Surgery Center, Bogota, Colombia

Alfredo Vega-Estrada, M.D., Ph.D. Department of Cornea and Refractive Surgery, Vissum Alicante, Alicante, Spain

Keratoconus Unit, Vissum Alicante, Alicante, Spain

Division of Ophthalmology, Universidad Miguel Hernández, Alicante, Spain

O. Bennett Walton, M.D., M.B.A Slade & Baker Vision, Houston, TX, USA

Steven E. Wilson Department of Ophthalmology, Cole Eye Institute, The Cleveland Clinic, Cleveland, OH, USA

Roger Zaldivar, M.D. Instituto Zaldivar, Mendoza, Argentina

Alice Yang Zhang, M.D. Retina Division, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Part I

Overview

1 Refractive Surgery Outcomes and Frequency of Complications

Wallace Chamon, Norma Allemann, Jorge L. Alio, and Ahmed A. Abdelghany

Core Messages

- In refractive surgery, there is no risk-free surgical procedure. The evaluation of the risk/benefit ratio should be part of a continuous process of patient care.
- Refractive surgery risks and benefits should be evaluated individually in order to choose the surgical approach properly.
- Disease distribution of each possible complication should be considered.
- Decision-making in refractive procedure is an individualized process that should be based on scientific knowledge, patient's characteristics, and surgeon experience.
- The informed consent should reflect all risks/benefits clearly to the patient candidate for any refractive surgery procedure.

1.1 Introduction

Refractive surgical procedures are generally divided into additive procedures, with implantation of phakic intraocular lens (IOL), and subtractive procedures, with ablation of the corneal tissue [1].

W. Chamon, M.D. • N. Allemann, M.D.
Department of Ophthalmology, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil

J.L. Alio, M.D., Ph.D., F.E.B.O. (✉)
Vissum Corporación, Avda de Denia s/n, Edificio Vissum, Alicante 03016, Spain

Division of Ophthalmology, Universidad Miguel Hernández, Alicante, Spain
e-mail: jlalio@vissum.com

A.A. Abdelghany, M.D., Ph.D.
Ophthalmology Department, Faculty of Medicine, Minia University, Minia, Egypt

In 2004, the European Society of Cataract and Refractive Surgeons (ESCRS) took the initiative to establish a registry for refractive surgery outcomes: the Refractive Surgery Outcomes Information System (RSOIS). The purpose of this web-based system was to record outcomes of refractive surgery and improve quality of care for these procedures. Reasons behind the initiative were the growing health in truest within the field and increasing patient complaints after refractive surgery reported in the press, in some countries [2, 3]. Patient complaints were thought to be associated with inappropriate indications and surgery outside the limits of the procedure, leading to suboptimal outcomes in refractive surgery.

In refractive surgery, the goal is to achieve optimal visual acuity, optimal refraction (usually emmetropia), and no complications [4]. Complications during and after surgery are of distinct concern as the eyes undergoing refractive surgery are usually healthy eyes.

In this chapter, we are going to discuss refractive surgery outcomes and complications in each group of refractive surgical procedures.

1.2 Laser Refractive Surgery

Laser refractive surgery is one of the most commonly performed eye surgeries worldwide and has been established to be successful in correcting refractive errors [5].

Several benchmarks have been established for laser keratorefractive surgery. The Food and Drug Administration (FDA) based on data presented by several evidence-based reviews defined the correction limitation of excimer laser (Table 1.1) [6].

The American Academy of Ophthalmologist (AAO) reports stated that the substantial level II and III evidence proved that excimer laser refractive surgery, whether laser in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK), is a safe and effective tool of correcting the full

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Table 1.1 FDA indications for LASIK and PRK [6]

	LASIK	PRK
Myopia	Less than −14.0 D with or without astigmatism between −50 and −5.00 D	Up to −12.0 D with or without astigmatism up to −4.00 D
Hyperopia	Up to +5.00 D with or without astigmatism up to +3.00 D	Up to +5.00 D with or without astigmatism up to +4.00 D
Mixed astigmatism	Astigmatism up to 6.00 D, the cylinder is greater than the sphere and of opposite sign	

spectrum of refractive errors but with some limitations in high hyperopic refractive errors [6, 7].

The latest generation of excimer laser platforms had introduced a large number of features such as faster laser, smaller spot size, a high speed tracker, pupil monitoring, and online pachymetry, all of which provided superior treatment with significant improvement of induced postoperative high-order aberrations (HOA) and control of thermal damage [8].

With the advent of keratomileusis procedures, primarily LASIK, a new anatomic region in the cornea came into existence: the potential space between anterior and posterior corneal lamellae commonly referred to as the LASIK interface. Within this region, a number of biochemical processes occur after creation of the corneal flap, including limited wound healing and intercellular reorganization [9]. The anatomy of the LASIK interface allows for a variety of potential unique complications to arise from different etiologies with often overlapping clinical presentations.

1.2.1 Common Complications Associated with Laser Refractive Surgery

1.2.1.1 Refractive Imprecision and Loss of Spectacle-Corrected Visual Acuity

The most frequent complication observed in any refractive procedure is the lack in achieving accurate refractive outcome. As a general rule, accuracy decreases with the amount of refractive error. Photoablative procedures tend to be the most accurate ones for low ametropias. PRK and LASIK deal with different variables that may affect predictability, such as corneal wound healing and stromal bed elasticity, respectively [10].

We may expect that in any photoablative procedure, approximately 60–70% of eyes will achieve 20/20 uncorrected visual acuity and will be within +/−0.50 D after surgery. If we analyze only low myopias (under 6.00 D), approximately 70–80% will achieve 20/20 uncorrected visual acuity [10–18].

1.2.1.2 Infectious Keratitis

Determining the risk of infection on photoablative procedures is a difficult task due to misdiagnoses and lack of laboratorial information. We may expect an incidence between 0.1:10.000 and 1:10.000, favoring LASIK over PRK [19–21]. Infection has been reported after LASIK with femtosecond laser [22].

Risk factors for the development of infectious keratitis include blepharitis, dry eye, intraoperative epithelial defects, intraoperative contamination, delayed postoperative reepithelialization of the cornea, use of topical corticosteroids, and patients in the health profession [23–25].

Infectious keratitis after LASIK has been divided into infections occurring within the first 2 weeks (early onset) and after 2 weeks to 3 months (late onset) [26]. The organisms responsible for early onset infections include staphylococcal and streptococcal species, whereas organisms more commonly seen in late onset infections include atypical mycobacteria and fungi [27].

In the initial phase of treatment, LASIK flaps should be lifted, cultures taken, the flap bed irrigated with fortified antibiotics, and broad-spectrum topical antibiotics started. For infections with a delayed onset, the use of amikacin may be beneficial in treating atypical mycobacteria [26]. In nonresponsive LASIK infections, flap amputation may be necessary to facilitate antibiotic penetration.

Most infections resolve with mild to moderate loss of best visual acuity [28], but rarely therapeutic penetrating keratoplasty is necessary.

1.3 LASIK

1.3.1 Interface Complications

- *Diffuse lamellar keratitis*

Diffuse lamellar keratitis (DLK) is a white blood cell infiltrate that coalesces between the flap and stromal bed that appears within a few days (1–5) after LASIK [29–31]. Confocal microscopy has confirmed the presence of inflammatory cells in the corneal stroma and interface in DLK [32]. This nonspecific interface inflammation is certainly associated with intraoperative epithelial defects [33] and has been linked to multiple rare potential inciting factors [34].

DLK has been associated with factors such as bacterial endotoxin [35], chemicals or debris [36], surgical gloves [37], and surgical marking pens [38, 39]. Patient factors shown to affect the risk for DLK include Meibomian gland secretions and peripheral immune infiltrates [40, 41] and atopy. Ultimately, DLK is likely the result of how a patient's endogenous factors respond to exogenous exposures [42].

DLK after LASIK has been reported to occur at higher frequency with femtosecond laser flap creation than with microkeratome flap creation. The incidence of DLK is estimated to range from 0.2 to 19.4% after femtosecond laser flap creation [43–47] and from 0.1 to 7.7% after microkeratome flap creation [31, 46, 48–52]. Higher energy level for flap creation with femtosecond laser and larger flap diameter were associated with an increased risk for DLK [53].

DLK is typically classified clinically into four stages as described by Linebarger and colleagues [42]. Stage 1 has inflammatory cells in the far periphery only, which are first present in the corneal stroma and then coalesce in the LASIK interface. Stage 2 has a diffuse infiltrate frequently involving the paracentral and peripheral flap margins but sparing the central axis. Stage 3 has a denser infiltrate within the flap interface, which involves the visual axis and is frequently associated with decreased visual acuity. Stage 4 has a focal, coalesced dense haze with scarring, signifying flap necrosis and usually results in permanent corneal scarring.

- *Pressure-induced stromal keratopathy* (*PISK*)

In the setting of LASIK, PISK is a relatively rapid steroid response resulting in high intraocular pressure with fluid accumulation in the interface. The amount of fluid present may be relatively small, resulting in diffuse haziness in the interface and overlying stroma without an obvious fluid layer [54], or it may be pronounced, resulting in a visible fluid cleft separating the anterior flap from the posterior residual bed [55].

The degree of interface fluid accumulation masks true IOP in various ways when measured using standard approaches. In all cases, actual IOP is greater than IOP measured centrally, and peripheral measurements generate a more accurate IOP.

- *Central toxic keratopathy* (*CTK*)

CTK is a rare, acute, noninflammatory central corneal opacification that can occur within days after uneventful LASIK or PRK [56–62]. Etiology is unknown but may be related to enzymatic degradation of keratocytes [57, 60].

CTK is almost always painless, as opposed to DLK, which in almost all cases has at least a moderate foreign body sensation, and CTK is acute in onset, as opposed to the progression over time to stage 4 DLK. CTK is self-limited and treatment is not warranted [57], while some have advocated aggressive topical steroid use [61] or flap lift and irrigation [63].

- *Epithelial ingrowth*

Epithelial ingrowth at the far periphery is a normal healing response to LASIK flap creation [9], but clinically relevant epithelial ingrowth occurs when a fistula develops under the flap allowing epithelial cell growth into the interface [64]. Most cases can be observed without requiring intervention [64].

For primary LASIK, increased epithelial ingrowth incidence is associated with hyperopic LASIK treatment [65], LASIK after RK [66], epithelial defects during surgery [67], and older age [68]. For LASIK retreatment, increased epithelial ingrowth incidence is associated with the use of contact lenses after retreatment [68] and flap-lift retreatment performed three or more years after primary LASIK [69].

With femtosecond laser flap creation, the overall incidence of visually significant epithelial ingrowth has decreased [70]. The lower incidence of epithelial ingrowth after femtosecond LASIK surgery compared with mechanical microkeratome-assisted LASIK may be attributed to the anatomy of the femtosecond laser-created side cut, in contrast to that created with a mechanical microkeratome, and the creation of less peripheral trauma at the time of flap creation [71].

Treatment depends on the clinical situation. The majority of cases of mild, clinically insignificant ingrowth are managed with observation. Initial surgical treatment for epithelial ingrowth is performed with flap lift, removal of epithelial cells from the posterior surface of the flap and the stromal bed with a blade or similar instrument, and replacement of the flap without sutures or tissue glue [64, 72]. With recurrent episodes of epithelial ingrowth, additional measures are typically taken, including flap sutures [73] or YAG laser treatment [74].

1.3.2 Flap Complications

Irregular flaps related to the microkeratome cut maybe presented as incomplete flaps, free caps, buttonholed flaps, thin flaps, thick flaps, and partially cut flaps [75].

- *Bowman strip and button hole in LASIK flaps*
  The incidence of intraoperative complications related to flap creation during LASIK is between 0.19 [76] and 21.2% [77]. Several explanations have been proposed to account for Bowman strip or “buttonhole” complications, such as steep corneas, partially opened eyes, and microkeratome deficits, such as blade defect and insufficient synchronization between the movement of the blade and microkeratome translational movement. High astigmatism or conjunctival entrapment may also lead to Bowman strip or buttonhole flap [78, 79].
  Some refractive surgeons recommend waiting 3 months, relifting the flap, and bathing the bed with mitomycin C (MMC) followed by surface ablation [75, 80].

- *Early flap displacement after LASIK*

The application of femtosecond laser technology to LASIK flap creation has increased greatly since its introduction. These lasers have improved the safety and predictability of the lamellar incision step. The majority of the femtosecond laser-assisted flap complications can be well managed without significant effects on refractive outcomes [81].

The incidence of flap displacement during 12-month follow-up period after LASIK has been reported to be extremely low (0.012%). Femtosecond laser has lower incidence of flap displacement than microkeratome [82].

1.3.2.1 Keratectasia

One of the most troublesome complications after LASIK is progressive iatrogenic keratectasia, which can occur up to several months after surgery [83]. Although the actual incidence of ectasia is unknown, it has been estimated to be 0.04–0.6% [84–86]. Several risk factors have been suggested in an attempt to avoid ectasia [87, 88]. However, controversy exists as to the predictability of these factors, and some cases continue to occur without a clear etiological explanation [84, 89]. Ideally, patients at risk of ectasia would be identified prior to laser surgery and be classified as unsuitable candidates for LASIK; however, at present, there is no absolute test, system, or marker that can identify patients at risk of developing ectasia.

Randleman et al. designed the Ectasia Risk Score System, which is a method of preoperative screening based upon the use of risk scales and identification of a number of preoperative parameters that may be associated with increased risk of ectasia [90]. The most common risk factors, in order of significance, include abnormal preoperative corneal topography, low residual stromal bed thickness, young age, thin preoperative corneal thickness, and higher attempted refractive correction. These factors are then amalgamated into a risk scale. However, this risk factor scale may miss a significant proportion of patients at risk of ectasia because other factors also play a role in the risk of ectasia [91–93].

Post-LASIK ectasia can potentially be avoided by careful patient screening preoperatively to identify risk factors which might lead to this complication.

Management of iatrogenic keratectasia consists of penetrating keratoplasty and, more recently, lamellar keratoplasty [94] and collagen cross-linking (CXL) [95]. In fact, with the success observed for CXL in the treatment of progressive keratoconus, some studies have reported on the use of CXL for postoperative keratectasia in very thin corneas [96].

1.3.2.2 High-Order Aberrations After LASIK

LASIK like other corneal refractive surgeries (such as radial keratotomy, photorefractive keratectomy), is designed to modify the central corneal curvature, making it flatter to correct myopia and steeper to correct hyperopia [97]. This surgical modification might influence the optical quality of the cornea, creating aberrations that will lead to distorted images [98].

LASIK eliminates conventional refractive errors (lower-order aberration like myopia, hyperopia, and astigmatism) leaving higher-order aberrations uncorrected or inducing some higher-order aberrations (HOAs) particularly spherical aberrations [99–102] which are thought to be responsible for the patients' complaints of poor quality of vision, even with visual acuity of 20/25 or 20/20, postoperatively.

Wavefront-guided ablations for intraLase treatment have been shown to be effective and predictable in reducing the astigmatism and higher-order aberrations [103–107].

1.3.2.3 Post-LASIK Tear Dysfunction and Dysesthesia

Symptoms of tear dysfunction after LASIK occur in nearly all patients and resolve in the vast majority. Although dry eye complaints are a leading cause of patient discomfort and dissatisfaction after LASIK, the symptoms are not uniform, and the disease is not a single entity. Post-LASIK tear dysfunction syndrome or dry eye is a term used to describe a spectrum of disease encompassing transient or persistent postoperative neurotrophic disease, tear instability, true aqueous tear deficiency, and neuropathic pain states. Neural changes in the cornea and neuropathic causes of ocular surface discomfort may play a separate or synergistic role in the development of symptoms in some patients. Most cases of early postoperative dry eye symptoms resolve with appropriate management, which includes optimizing ocular surface health before and after surgery. Severe symptoms or symptoms persisting after 9 months rarely respond satisfactorily to traditional treatment modalities and require aggressive management [108].

1.3.2.4 Ocular Surface Syndrome

This complex multifactorial entity distresses patients and physicians and is characterized by the following symptoms: dry eye, micropunctate keratitis, decreased and unstable tear film, and decreased best spectacle-corrected visual acuity (BSCVA) and visual quality. Ocular surface syndrome has a neurotrophic etiology, is long lasting, and is difficult to treat [109].

1.3.2.5 Retinal Complications

There are several reports in the literature about retinal complications after LASIK for the correction of myopia. These include macular holes [110–113], retinal tears and detachments [114], retinal hemorrhages [115], and choroidal neovascular membranes [116].

1.4 PRK

1.4.1 Haze

Corneal haze reduces corneal transparency at variable degrees [117, 118]. Subepithelial haze occurs in all patients

1 month after PRK, reaching the greatest intensity at 3–6 months, and then gradually decreasing [119].

Besides the ablation depth, the severity of corneal haze is correlated with excessive ocular UV-B radiation, duration of the epithelial defect, postoperative steroid treatment, and male sex, and with certain population with brown iris [120–122].

Recently, the densitometry program of Pentacam Scheimpflug imaging system (Oculus Optikgeräte GmbH) has been proven to be a useful method for measuring corneal haze [123].

1.4.2 Mitomycin C

The use of intraoperative mitomycin C has raised the expectation for treating higher ametropias with PRK [118, 124–128].

Mitomycin C is an alkylating agent with cytotoxic and antiproliferative effects that reduces the myofibroblast repopulation after laser surface ablation and, therefore, reducing the risk of postoperative corneal haze. It is used prophylactically to avoid haze after primary surface ablation and therapeutically to treat preexisting haze. There is no definite evidence that establishes an exact diopter limit or ablation depth at which to apply prophylactic mitomycin C. It is usually applied at a concentration of 0.2 mg/ml (0.02%) for 12–120 s over the ablated stroma, although some studies suggest that lower concentrations (0.01, 0.002%) could also be effective in preventing haze when treating low to moderate myopia. This dose of mitomycin C has not been associated with any clinically relevant epithelial corneal toxicity. Its effect on the endothelium is more controversial [129].

1.4.3 Keratectasia

Although there are reports of keratectasia that occurred in normal eyes after PRK [130], most of the few cases reported so far are of forme fruste keratoconus that progressed after PRK [131–133] or phototherapeutic keratectomy (PTK) [134, 135].

1.5 Phakic Intraocular Lenses

The option of phakic IOLs (PIOLs) has gained popularity, having usually the widest range of correction (myopia up to 23D, hyperopia up to 21D, and astigmatism up to 7.00D) and being affordable and easily implantable [136–138]. It has potential advantages, including fast visual recovery, preservation of accommodation, and reversibility [139–141]. Compared to LASIK, PIOLs offer a higher range of refractive error correction and better quality of vision for high ametropes [142].

There are two available phakic IOLs now: the iris-fixated Artisan and the posterior chamber implantable Collamer lens (ICL). The Artiflex myopia phakic IOL was developed based on the Artisan platform, with a flexible, convex-concave, 6 mm silicone optic, PMMA haptics [143, 144]. It can achieve precise centration over the pupil and high rotational stability, but requires some surgical skills for enclavation [142]. It also requires some safety limitations like flat iris, endothelial cell count (ECC) of ≥2100 cell/mm^2, scotopic pupil diameter < 6.0 mm, and AC depths of ≥2.8 mm [145, 146]. The Visian ICL is made from Collamer (biocompatible material). Another type of phakic IOLs was angle supported, but is not in use now.

The toric Artisan corrects astigmatism from 1D to 7D, and toric ICL is capable of correcting astigmatism up to 6D. It is a good option especially for high errors with low baseline corneal thickness, shallow AC, and wide scotopic pupils [147, 148].

1.5.1 Common Complications Associated with Phakic IOLs

1.5.1.1 Pupil Ovalization

Eyes with anterior chamber angle-supported phakic IOLs have a tendency to present sectorial iris atrophy and consequent pupil ovalization [149].

1.5.1.2 Endothelial Cell Loss

The long-term impact of anterior chamber PIOL implantation on corneal endothelial cell loss has been a matter of significant research and debate. As a result of numerous randomized clinical trials, the safety of Artisan and Artiflex IOLs is now well established, with reported endothelial cell losses of 4.8% at 6 months, 8.3% at 5 years, and 12.6% at 7 years and long-term maintenance of the hexagonality and the cell coefficient of variation [150–152]. The minimum E-IOL distance from the center of the IOL to minimize the risk of endothelial cell loss was 1.7 mm [153].

Although posterior chamber IOLs have a lower risk of endothelial cell loss, a decrease in 5–10% after 2 years of the surgery may be expected [154].

1.5.1.3 Infection

Risk of infection in intraocular surgeries should follow the incidence of infection in cataract surgery that is approximately 1:1,000 [155–157].

1.5.1.4 Glaucoma

Pupillary block glaucoma has been reported in anterior chamber iris-supported [158], in angle-supported [159, 160], and in posterior chamber phakic IOLs [161–163]. Preoperative iridectomy is mandatory, but pupillary block has been reported even in the presence of effective iridectomy [163].

1.5.1.5 Cataract

There are two basic cataract types: anterior subcapsular opacification (in cases of ICL) and nuclear cataract (in cases of Artisan). The mean time to nuclear cataract appearance after Artisan IOL implantation was 54.83 ± 22.12, and ICL implantation was 20 ± 1 month [164].

Cataract is the main cause of PIOL explantation, especially in posterior chamber PIOLs [165].

1.5.1.6 Uveitis

Postoperative sterile uveitis has been reported in previous studies [166]. The pathogenesis of uveitis after PIOL implantation is still obscure but may be related to an inflammatory reaction caused by perioperative and postoperative mechanical irritation of the iris. It is possible to detect chronic subclinical inflammation with a laser flare-cell matter after PIOL implantation [166].

Age-related changes in the anatomy of the anterior segment may create a long-term hazard for the implanted eye [167].

1.5.1.7 IOL Dislocation

Traumatic and spontaneous IOL dislocations have been described in anterior chamber iris-supported phakic IOLs [168, 169].

1.5.1.8 Retinal Complications

Implantation of ICL or Artisan phakic IOL demonstrated comparable rates of retinal complications. Anterior chamber PIOL does not increase the risk of retinal detachment or CNVM in patients with myopia [170].

Take-Home Pearls

- Refractive surgery provides a variety of elective procedures to be performed in otherwise healthy eyes. Selecting the best surgical treatment is dependent on knowing all the associated complications.

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