

Ocular surface disturbances after laser refractive surgery



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HIGHLIGHTS

In the vast majority of patients undergoing laser refractive surgery, the parameters of the tear film, ocular surface stability and corneal sensitivity normalize 2–6 months after the procedure, depending on the correction method used.

ABSTRACT

Most patients undergoing laser refractive surgery demonstrate transient and mild symptoms of dry eye disease. The article presents the main mechanisms involved in dry eye disease after the most frequently performed laser vision correction methods. Differences in the occurrence of dry eye disease between flap, surface procedures and minimally invasive lenticule extraction were highlighted.

Key words: laser in situ keratomileusis, photorefractive keratectomy, ocular surface, dry eye disease, neurotrophic keratopathy, minimally invasive lenticule extraction

INTRODUCTION

Laser refractive surgery involves a series of invasive procedures that use femtosecond and excimer lasers to modify the anterior corneal curvature and its refractive properties. According to the “2020 Refractive Surgery Market Report”, femtosecond laser is the most frequently utilized tool for refractive procedures including FemtoLASIK (femtosecond laser in situ keratomileusis) and laser lenticule extraction, such as ReLEx SMILE (refractive lenticule extraction small incision lenticule extraction) and SmartSight, which account for about 72.6% of all laser procedures. This is followed by surface procedures such as photorefractive keratectomy (PRK), LASEK (laser subepithelial keratomileusis), epi-Bowman keratectomy (EBK) or transepithelial-PRK (Trans-PRK), which account for about 23.8% of refractive procedures. Microkeratome flap LASIK procedures are currently the least common, comprising about 2.3% of laser refractive surgery [1].

LASER REFRACTIVE SURGERY

FemtoLASIK provides very efficient and stable correction of all refractive errors, with faster visual rehabilitation compared to other techniques. However, it is important to note that there are limitations, such as the risk of flap complications and a higher risk of postoperative ectasia compared to other methods. The SMILE and SmartSight methods are characterized by their short procedure duration, high efficiency, and less impact on corneal biomechanics. However, more invasive methods are needed for enhancement and none of individualized procedures based on either wavefront-guided or topo-guided algorithm are available. Surface methods offers several advantages, including a reduced risk of postoperative ectasia and the possibility to correct refractive errors in eyes with thinner corneas, epithelial basement membrane dystrophy or borderline keratometry values. These techniques; however, have some limitations, including significant postoperative discomfort lasting an average of 2 days, several weeks of visual rehabilitation, and a higher risk of anterior corneal haze and regression of refractive error.

Laser refractive surgery, due to its invasive nature, alters the ocular surface environment and induces tear film instability. The most common postoperative complication of laser corneal surgery is the disturbances of tear film physiology, which can lead to the induction of dry eye disease (DED). Nearly all patients who undergo laser refractive surgery experience symptoms of DED, although these are usually temporary. These symptoms include ocular dryness, burning, irritation, eye fatigue, a foreign body sensation, photophobia, unstable vision and ocular pain.

INFLUENCE OF LASER REFRACTIVE PROCEDURES ON THE OCULAR SURFACE

The cornea is richly innervated by various functional types of sensory nerve fibers originating from the ocular branch of the trigeminal nerve. Long posterior ciliary nerves (LPCN) contain fibers that pass limbus and enter the middle third of the corneal stroma. Then, the fibers perforate Bowman’s membrane and form a subbasal epithelial nerve plexus to terminate finally within the corneal epithelial layers. When stimulated, corneal sensory fibers evoke conscious sensations of different quality, including ocular dryness, discomfort and pain. Refractive surgery, depending on the method, involves a variable degree of damage to corneal nerves, which leads to altered expression of membrane ion channels at the injured and regenerating nerve fibers, resulting in aberrant spontaneous and stimulus-evoked nerve impulse firing. It is speculated that these abnormal sensory discharges are read by the brain as ocular surface dryness, discomfort or pain, which distinguishes ocular dryness following refractive surgery from DES associated with tear film instability. This hypothesis would explain the high incidence of dryness sensations after refractive surgery despite clinically modest disturbance of tear secretion. Interactions between genetic predisposition and environmental factors are thought to play an important role in the development of ocular pain following corneal refractive surgery [2].

Dry eye disease is more likely to accompany corneal flap procedures (LASIK, FemtoLASIK) [3]. Neurotrophic keratopathy is the main factor associated with the onset of secondary DED. It occurs due to the disruption of the tear secretion reflex by the lacrimal gland, which results from cutting most of the sensory endings of the subepithelial plexus of the ocular branch of the trigeminal nerve during the preparation of the corneal flap [4, 5]. Damage to sensory fibers can cause a reduction in corneal sensation, less frequent blinking, decreased meibum secretion by meibomian glands, dryness of the ocular surface, and hyperosmolarity of tears [6]. Additional causes for ocular dryness include compressive damage to the conjunctival goblet cells (associated with the vacuum and suction ring of the microkeratome or femtosecond laser) and transient meibomian gland dysfunction (with subsequent excessive tear evaporation), postoperative inflammatory reactions, iatrogenic damage from topical medications used postoperatively, inadequate tear distribution over the modified ocular surface and altered corneal and palpebral adhesion during blinking [7, 8]. Keratorefractive procedures are associated with the induction of subclinical inflammation that involves prostaglandins and cytokines, which promote keratocyte apoptosis and the recruitment of inflammatory cells [9]. The inflammatory response is further amplified by corneal sensory nerves, which release neuropeptides, substance P, and calcitonin gene-related peptide (CGRP) proteins. These mol-

ecules, which are epithelial trophic factors, have also pro-inflammatory properties and promote limbal vasodilation, and vascular permeability [10, 11].

THE CLINICAL COURSE AND RISK FACTORS OF POSTOPERATIVE OCULAR SURFACE DISTURBANCES

It has been demonstrated that a significant number of patients experience clinical symptoms of DED following LASIK. Specifically, 94.8%, 85.4%, and 59.4% of patients reported such symptoms at 1 day, 1 week, and 1 month after surgery, respectively. Chronic ocular dryness is reported in 10–40% of patients after LASIK, in 5% of patients after PRK, and in 0.8% of patients after LASIK; in young patients (30 ± 5 years old) with no preoperative risk factors for DES [12]. The effect of LASIK surgery on the ocular surface, particularly the tear film, is multifactorial. Disruption of the ocular surface by flap dissection is directly linked to destabilization of the tear film, decreased tear film break-up time (TBUT) and increased reflex tear secretion [13]. Subsequently a decreased Schirmer test score, an increased tear osmolarity, and a decreased corneal sensitivity are observed. These symptoms typically return to the normal values within 3–6 months after the procedure [7, 14]. Regeneration of short nerve fibers and synapses can be detected 3–6 months after surgery, and the density of the stromal nerves and subbasal nerve plexus returns to preoperative values within 2–5 years after surgery [15].

It has been confirmed that the use of a narrower flap hinge is associated with a greater corneal denervation [16]. Some authors suggest that nasal hinge location, which spares some LPCN fibers, provides faster normalization of corneal innervation as well as TBUT and Schirmer's scores compared to superior flap hinge location [16, 17]. Other authors do not confirm the association of the position of the flap hinge with the severity of postoperative DED [18–20]. Female gender, postmenopausal age [21], use of a mechanical microkeratome [22], thicker flap [23], greater extent of ablation [24], and correction of hyperopia [25] are also risk factors for DED. Enhancement procedures (flap lift) do not rather pose as an additional risk factor of postoperative DED [26]. Abnormalities in the microbiota of the eyelid margins, conjunctiva and tear film associated with dry eye have been shown to further increase the risk of postoperative infectious keratitis and diffuse lamellar keratitis (DLK). Clinical observations indicate that tear film and ocular surface disturbances resolve more rapidly after surface procedures and laser lenticule extraction surgery (e.g., SMILE) [27]. DED after PRK or LASEK differs from DED after LASIK in the first 3 months following surgery. Sparing of the LPCN after PRK results in faster regeneration of the nerve plexus, particularly the subbasal plexus, than after LASIK. TBUT parameters, corneal staining, and corneal

sensitivity return to normal within 2 months after PRK and LASEK [28]. Comparative studies showed no significant differences in the normalization of the Schirmer test between PRK and thin-flap LASIK [25]. Additionally, there were no significant differences in the normalization of corneal sensitivity and subbasal plexus morphology between LASEK and thin-flap LASIK [29]. Most authors state that 6 months after surgery there are no significant differences in tear film condition and DED symptoms between PRK and LASIK procedures [11, 25, 30].

The surgical method of minimally invasive lenticule extraction, due to its “endoscopic technique” is associated with greater preservation of the subepithelial nerve plexus and keratocytes, less severe dry eye, and faster restoration of corneal innervation. Minimal disruption of the LPCN results in regeneration of the nerve plexus and normalization of corneal sensation within the first three months after surgery. After SMILE, TBUT, corneal staining, and the ocular surface disease index (OSDI) are less affected in the first 3–6 months compared to FemtoLASIK [31].

However, as the meta-analyses by Shen et al. [32] showed, the parameters of the Schirmer test and tear osmolarity did not differ in the first 6 months between SMILE and FemtoLASIK. Meta-analyses by He et al. [27] and Jiang et al. [33] showed no differences in the tear film condition, nerve plexus density, corneal sensation and subjective symptoms of DED after 6 months between SMILE and FemtoLASIK. In the majority of patients, dry eye symptoms following refractive surgery are mild and resolve within a few weeks. However, in 20–40% of patients who undergo LASIK, these symptoms may persist up to 6 months after the procedure [21, 34], and in rare cases (approximately 1% of patients), they may persist even for several months [12].

The main risk factors for chronic DED in young individuals without preoperative symptoms of DED are: reduced parameters of the Schirmer test (regardless of the surgical technique) of TBUT (after PRK), and higher corneal staining score (after LASIK). Stratification of local and systemic risk factors for postoperative DED is crucial to achieving optimal refractive outcomes and patient satisfaction. The occurrence of DED after laser refractive surgery is most significantly influenced by the presence of DED prior to the procedure. It was found that the occurrence of DED in candidates for laser vision correction surgery is common and affects approximately 40% of individuals. Decreased TBUT (< 5 s) and Schirmer's test score (< 5 mm) are noted in every fourth person (23.5%) who comes for a qualifying examination for the refractive procedure. Almost every second candidate for laser vision correction surgery has a history of wearing contact lenses, which is also associated with a higher occurrence of DED (OR = 2.17).

It has been demonstrated that long-term use of contact lenses is associated with elevated levels of inflammato-

ry cytokines in tears, decreased corneal sensitivity, and a longer period of time required for tear secretion to return to normal after treatment [35]. In recent years, the number of laser refractive procedures performed in people aged 40 and above, who are at risk for dry eye, to correct presbyopia has been increasing.

The presence of clinical signs of DED before refractive surgery may additionally be associated with the risk of unreliable preoperative keratometric and/or corneal tomographic measurements and postoperative refractive errors. The occurrence of DED following laser vision correction procedures significantly affects patient satisfaction. About 21.1% of dissatisfied patients report clinical signs of DED, and approximately 30% of patients in this group experience subjective symptoms of DED. One of the reasons for dissatisfaction is reduced functional visual acuity (FVA). FVA is measured after a minimum of 10 seconds of eye opening, simulating the blink rate while reading, working at a screen monitor, or driving.

Tear film instability, resulting in reduced TBUT and accompanying chronic DED may lead to the induction of irregular astigmatism and higher-order aberrations, and subsequent deterioration of vision [36]. Furthermore, it has been

demonstrated that chronic DED following LASIK is associated with a 4-fold higher risk of regression (27% vs. 7%) due to epithelial hyperplasia and corneal stroma remodeling [37]. Prior to refractive surgery, it is crucial to thoroughly evaluate the condition of the ocular surface and identify any risk factors for dry eye. Optimizing the ocular surface condition before surgery, personalization of the correction method, and appropriate perioperative and postoperative management are the key to obtaining the optimal refractive outcomes and patient satisfaction after the procedure.

CONCLUSIONS

Neurosensory abnormalities within the cornea are the main cause of tear film physiology disruption and the development of postoperative dry eye disease following laser refractive procedures. In the majority of patients undergoing laser refractive surgery, the parameters of tear film, ocular surface stability, and corneal sensitivity normalize within a specific timeframe: within 2 months after PRK or LASEK procedures, after 3 months for minimally invasive lenticule removal procedures (SMILE, SmartSight), and after 3–6 months for FemtoLASIK or LASIK procedures.

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