Presbyopia and the aging eye: existing refractive approaches and their potential impact on dry eye signs and symptoms.

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Conflict of interest statement: The authors have no conflicts of interest to disclose.

Keywords: Presbyopia, dry eye, contact lenses, refractive surgery, cornea

Acknowledgements and Disclosure: The authors have no proprietary interest in any of the materials mentioned in this article. This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No. 642760 EDEN ITN-EJD Project Horizon 2020.

ABSTRACT

Every part of the human body is subject to aging, including the eye. An increased prevalence of dry eye disease with age is widely acknowledged. Aging threatens ocular surface homeostasis, altering the normal functioning of the lacrimal functional unit and potentially leading to signs and symptoms of dry eye. Additional age-related processes take place within the crystalline lens, leading to presbyopia and cataractogenesis. Correction strategies for presbyopia and cataracts may directly or indirectly challenge the ocular surface. Contact lenses disturb the normal structure of the tear film and can interact negatively with the ocular surface, further deteriorating an already unbalanced tear film in presbyopes, however, newer contact lens designs can overcome some of these issues. Moreover, cataract and corneal refractive surgeries sever corneal nerves and disrupt the corneal epithelium and ocular surface, which can influence surgical outcomes and aggravate dryness symptoms in older age groups. This review summarises the current understanding of how the invasive nature of contact lens wear and cataract and refractive surgery influence signs and symptoms of ocular dryness in an aging population.

1. INTRODUCTION

The ability of the ocular surface to respond adequately to environmental challenges depends on the appropriate detection of sensations; this involves the transmission of the stimulated signal to the brain and the generation of a response, that modulates secretory function[1] and local immunity[1,2]. Any disturbance to one of the three steps of this closed loop could trigger an inappropriate response and alter the compensatory mechanisms taking place at the ocular surface.

The lacrimal functional unit (LFU) is a set of anatomical structures, whose harmonious functioning maintains tear film (TF) osmolarity within narrow limits[2]. The LFU is composed of: the lacrimal glands (LG), meibomian glands (MGs), the ocular surface (cornea and conjunctiva) and the nerves that connect them[3]. Likewise, the precorneal TF behaves as a single dynamic functional unit with different compartments. Tear dysfunction, more common with ageing, results from degenerative or pathologic processes of one or more components of the LFU, potentially leading to signs and symptoms of dry eye disease (DED).[4]

Every part of the human body is subject to aging and the LFU is no exception: LG, the eyelid area, MGs and conjunctiva are affected in terms of their structure and function over the life span[5-9]. Increasing age challenges ocular surface homeostasis by inducing drastic changes to the LFU: the LG undergoes histologic changes leading to pathological processes (for example a decrease in mass, atrophy of lacrimal ducts and acini, lymphocyte infiltration) and to a diminution in lacrimal secretion[5,6]. Furthermore, eyelids also undergo age-related changes that could promote signs and symptoms of dryness among which are: increased lid laxity[7] and MGs atrophy[8]. Conjunctivochalasis, another age-related disorder, is characterized by the presence of folds on the conjunctiva[9] which are known to impact tear meniscus distribution along the eyelid and thus tear meniscus parameters[10], and could play a role in DED onset and perpetuation.

According to the Report of the Tear Film and Ocular Surface (TFOS)[11], an increased prevalence of DED with age is widely acknowledged[12,13]. Based on estimates of the number of people over 60 years of age (2 billion people by the year 2050)[14] and an approximate prevalence of 25% for the disease, 500 million people will suffer from dry eye globally just in this age group[15]. Hence the burden to society will be immense.

Over and above the age-related changes already mentioned taking place in the LFU, two additional visual impairing processes take place within the eye's crystalline lens, leading to presbyopia and cataractogenesis respectively.

With age, the crystalline lens progressively loses its ability to change shape, and the eye's focusing range reaches a point were near vision is insufficient to satisfy an individual's requirements[16]. Symptoms of presbyopia appear around 45 years of age[17], although other elements may influence its onset and progression (such as pupil size, disease, medications and trauma)[18]. Specifically, presbyopia affected 1.3 billion people worldwide in 2011[19], and up to 2 billion people in 2012[20]. In this regard, with increasing life expectancies, this trend is expected to keep on rising[21].

Additionally, according to the World Health Organization (WHO), cataract is the leading cause of blindness[22] and the consequent loss of useful vision is expected to affect 16 million people worldwide[23]. Cataractogenesis encompasses a broad spectrum of changes regarding biochemical processes taking place in the crystalline lens leading to an alteration in water balance, proteins, vitamins and enzymes, being responsible for a progressive loss of lens transparency[24]. In this respect, aging is by far the major risk factor for its onset[22,23].

Nowadays, various refractive means exist to correct presbyopia. In this context, contact lenses (CLs) with different optical profiles (monovision, alternating images, simultaneous images) can be used for the purpose. However, once inserted onto the ocular surface, CLs disturb the normal structure of the TF. Refractive surgery is another option available, but due to its potential to sever corneal nerves and disrupt the corneal epithelium, tends to disrupt the ocular surface and worsen or induce signs and symptoms of dryness.

CLs and corneal refractive strategies along with cataract surgery directly or indirectly interact with the ocular surface, threatening its homeostasis. These interactions are particularly relevant for the aging eye, when degenerative processes occurring in the LFU may potentially lead to tear dysfunction. In this regard, it is relevant for the clinician to understand the potential ocular surface and dryness-related outcomes of each refractive correction or procedure in older adults.

Accordingly, this review summarises the current understanding of how the invasive nature of contact lens wear and cataract and refractive surgery influence signs and symptoms of ocular dryness in an aging population.

2. CORNEAL INNERVATION AND PHYSIOLOGICAL ROLE

Nerve fibers enter the cornea in the middle third of the stroma and then course through the superior layers forming a plexus in the sub-Bowman's layer that densely innervates central cornea[25]. Corneal nerves terminate in the wing cell layer of the epithelium after penetrating Bowman's layer and losing their myelin sheath. These nerves are key to ocular surface homeostasis, constantly adapting the ocular surface response to environmental challenges. Free nerve endings, more precisely the intra epithelial sensory terminals, are excited in response to different stimuli (mechanical forces, cooling and increased osmolarity)[26] giving rise to afferent impulses that travel along the ophthalmic branch of the trigeminal nerve to the central nervous system[27]. These allow for the detection of potentially damaging stimuli and the induction of defensive reflexes[11] provided by the efferent pathways such as lacrimation, blinking and regulation of different LG secretions[11].

Furthermore, nerve bundles play an important trophic role for the corneal epithelium (involved in nutrition processes) and modulate immune responses and wound healing processes[28]. The different surgical procedures described later on, all impact upon corneal tissue (as an entry porthole or as part of the refractive correction). As such, corneal integrity may be jeopardized, leading to alterations of the closed loop described above and to DED.

3. EYE SURGERY AND DRY EYE

3.1 CATARACT SURGERY

Cataract surgery is the most commonly performed elective surgery with an estimated 19 million procedures performed worldwide in 2013 - 2014[29,30]. The WHO has forecast a significant increase of this surgery by the year 2020 (estimated 32 million procedures a year) as the number of people over 65 is expected to increase significantly[31].

Firstly, before any surgical treatment, biometric measurements are required in order to calculate the power of the intraocular lens (IOL) to be implanted. The accuracy of these measurements, and hence the post-surgical refractive outcomes, are influenced by TF quality and stability[32,33].

Risk factors for dry eye following cataract surgery regardless of the technique used are well known, but the mechanisms through which they induce dry eye are yet to be established. The following risk factors could be related to the disruption of corneal nerves and harm to the epithelium through the surgical procedure: eyedrops containing active agents/preservatives affecting the epithelium pre-, peri- and post-surgery[34,35]; forced opening of the eyelid with the blepharostat prevents normal blinking, thus an even distribution of the TF across the ocular surface[36]; long microscopic light exposure times, which may lead to thermal damage[34]; repeated irrigation of the ocular surface may impact goblet cell density and further impact TF stability[34-37]; and incision location and accuracy, that will be discussed later on in this manuscript. Consistently, studies agree that the surgical procedure increases signs and symptoms of ocular dryness[34,36], with neurogenic inflammation and epithelial (corneal and conjunctival) damage induced by the surgery, being the principal factors acting as DED triggers[38].

Additionally, surgery-induced corneal nerve damage impairs corneal sensitivity[11]. This further affects blink rate and reflex-induced lacrimal secretion[39], which eventually leads to TF instability and increased osmolarity [39]. Tear hyperosmolarity induces epithelial cell hyperosmolarity leading to the liberation of pro-inflammatory CKs, inducing cellular apoptosis and corresponding ocular surface staining.

Previous studies have investigated the pathophysiology of dry eye after cataract surgery[36,38,40-45] (Table 1). These have demonstrated a significant increase in dry eye signs and symptoms, including worse Ocular Surface Disease Index (OSDI) questionnaire scores[36,38], Tear Breakup Time (TBUT)[36,38,40,43,44], Schirmer test[36,38,40], corneal and conjunctival staining[38,40], Tear Meniscus Height (TMH)[36], and corneal sensitivity[41,42,45] until about 2-3 months postoperatively.

Nowadays, a newer technique, called Femtosecond Laser Assisted Cataract Surgery (FLACS) can be used[46] to create the required corneal incisions, capsulotomy and fragmentation of the lens prior to phacoemulsification. This technique is far more accurate than mechanical devices and improved safety and clinical outcomes are expected[46-49]. One drawback of this technique, however, is the pressure to which the peri-limbic conjunctiva is subjected by the suction ring, which has been shown to reduce goblet cell density post-surgery[50,51].

On the contrary, a former cataract surgery technique, extracapsular cataract extraction, requires a larger incision and is expected to induce more corneal sensitivity loss[52] and thus induce more signs and symptoms of dryness post-surgery[53]. Similarly, certain types of IOLs such as accommodative[54] designs require a larger incision for insertion. In this sense, reduced incisions lead to a faster corneal sensitivity recovery (within 1-3 months) compared to larger incisions, and only to a focal diminution of corneal sensation.[44,42] In the same way, micro incisional procedures such as phacoemulsification or the insertion of foldable IOLs are expected to induce less hypoesthesia than conventional techniques[43,44,52,55]. Additionally, incision shape, depth and regularity clearly impact post-surgery healing[42-44].

Finally, potential toxicity of antiseptic agents used during the surgical procedure as well as topical multi-dose eyedrops with preservatives seem to play a role in the onset of dry eye signs and symptoms. Benzalkonium chloride (BAK), is one of the most commonly used preservatives in ocular topical drugs and is recognized to induce, apart from goblet cells apoptosis, conjunctival squamous metaplasia, disruption of the corneal epithelium barrier and TF instability amongst others[35,56].

3.2 CORNEAL REFRACTIVE SURGERY

3.2.1 LASER IN-SITU KERATOMILEUSIS

Laser in-situ keratomileusis (LASIK) is a surgical procedure in which a corneal flap (around 120-160 □m) is created and then reclined (lifted) in order to proceed to the stromal ablation. Flap creation was initially performed using blades (microkeratome), but the emergence of newer technologies such as femtosecond lasers[48] are less invasive, reducing the signs of induced dry eye.[34] Once the flap is reclined, ablation is performed and destroys mid stromal nerves. Consequently, LASIK induces damage to the cornea during both the flap creation where the subbasal nerves are cut, and the excimer laser stromal ablation where stromal nerve trunks are destroyed by the laser[57]. Specifically, it is estimated that there is a 90% reduction of central nerve fiber density in the first month following surgery[58] and some studies report that corneal sensitivity does not return to baseline levels until 2-5 years post-surgery[59].

Consequently, DED is one, if not the most, common adverse effect of LASIK[34,60,61]. When performed on DED patients, the LASIK procedure worsens numerous tear metrics (tear volume[62], tear stability[63-65], osmolarity[66,67]) and staining[63]. (Table 2). In parallel, ocular symptoms of dryness tend to reach a peak between one week and three months after surgery, regardless of preexistent dry eye [48,59,64,65,68,70-80].

LASIK monovision is a valuable option for the presbyopic population[81-83] and other new multifocal LASIK techniques, such as presbyLASIK, for which the excimer laser produces a multifocal corneal ablation profile, have also been developed[84]. Nonetheless, corneal monovision currently offers the highest 'success' rate (reaching 90 % success)[85].

Shoja and Besharati, found a statistically significant effect of age on corneal sensitivity after LASIK[65]; patients developing dry eye after LASIK were significantly more likely to be older in comparison to patients who did not develop dry eye. Kanellopoulus also noted a significant association between age and clinically significant dry eye following LASIK[86]. Similarly, Price et al. in a multivariate model that controlled for dry symptoms at baseline, reported older age as one of the main factors associated with dry eye symptoms 3 years after LASIK[87]. On the contrary, many recent studies discard age as an important risk factor for post-LASIK tear dysfunction or dry eye. For example, Golas and Manche found no statistically significant effect of age on dry eye scores obtained in 51 patients after LASIK[88]. In addition, De Paiva et al. studied 35 adults, aged 24 to 54 years, and found no association between older age and the risk for developing postoperative dry eye[69].

Given the major improvements in safety and efficacy of corneal refractive surgery in recent years, the demand for this type of procedure has considerably increased among the presbyopic population.[83] Albeit LASIK has shown to be successful in correcting refractive errors in presbyopic patients, studies evaluating outcomes of the surgery are still limited and present contradictory results. Nevertheless, the clinician must take into account that given the invasiveness of this technique, due to the flap creation, post-LASIK dry eye will remain a common complication. Given that preoperative tear function is thought to play an important role in long-term ocular surface integrity after LASIK[89], tear function should be assessed in detail for older patients considering this refractive surgery.

3.2.2 PHOTOREFRACTIVE KERATECTOMY

Photorefractive Keratectomy (PRK) is based on removal of the corneal epithelium using an alcohol solution following topical anesthesia (the corneal epithelium is discarded)[90]. The underlying corneal tissue is then reshaped using the excimer laser [more anterior in comparison to LASIK or Laser Assisted Subepithelial Keratectomy (LASEK) procedures]. No flap is created for this procedure.
Recovery takes longer than the LASIK technique, since it takes around a week for epithelial cells to regrow[90]. PRK induces a temporary decrease in subbasal corneal nerve density for up to a year, and complete recovery might take as long as two years[91]. In addition, studies report diminished tear secretion[92-94], tear stability[94,95], and corneal sensitivity[96,97] in patients 3 to 6 months post-surgery. (see Table 3).

As for LASIK, PRK may be performed as a presbyopia correction strategy by inducing monovision. In this regard, while part of the recent literature suggests no effects of age on patient-reported dry eye after PRK[98], other studies advise that the higher prevalence of DED along with corneal changes seen with advancing age may possibly hinder the healing process[99], affecting the final outcome of the surgery[100].

More studies regarding dry eye after corneal refractive surgery in late adulthood are required. Meanwhile, clinicians should pay particular attention to dry eye signs and symptoms before undertaking PRK in older age groups, as the deteriorating effect of the surgery on the ocular surface may worsen an already unbalanced ocular environment.

3.2.3 LASER ASSISTED SUBEPITHELIAL KERATECTOMY

The main difference between LASEK and PRK is that the peeled corneal epithelium, called an epithelial flap (which is discarded in the PRK technique), is repositioned after photoablation (the LASIK procedure uses a stromal flap[101]). Alcohol is used to weaken adhesions between the stroma and epithelium[102]. Factors such as alcohol concentration (usually between 18-25%) and exposure time play a key role in postoperative healing[103]. Autrata et al. compared 184 eyes of 92 patients between PRK and LASEK with 2 years follow-up.[104] The authors concluded that LASEK provided significantly quicker recovery and reduced pain and haze level compared to conventional PRK.[104] (See Table 4).

Similar to LASIK and PRK, LASEK may be applied in older age groups to treat presbyopia using monovision. Increasing age can considerably influence LASEK postoperative outcomes. For example, age has shown to increase the prevalence of postoperative complications[108], reduce predictability[109] and increase healing time[110] after LASEK.

To date, no studies have evaluated the effects of LASEK surgery on TF in late adulthood. Based on the results of studies obtained from the general population, lower postoperative dry eye signs and symptoms compared to other corneal ablation techniques are also expected in prebyopes and elderly patients. Besides this, considering the afore mentioned, older age groups may be more susceptible to post-LASEK dry eye related complications.

3.2.4 SMALL INCISION LENTICULE EXTRACTION

The advent of lasers in the ophthalmic field to perform corneal refractive surgery has led to the concept of lenticule extraction. Recently, Small Incision Lenticule Extraction (SMILE) has been developed to perform corneal reshaping[111]. This refractive procedure uses a femtosecond laser to create a corneal lenticule that is extracted through a small incision.[111]

SMILE no longer requires excimer laser ablation or the creation of a flap, making this technique less invasive than LASIK. The absence of a flap, reduces corneal inflammation and keratocyte damage[112] and resulting in less iatrogenic dry eye[113], compared to other corneal refractive strategies, such as LASIK. Denoyer et al. found that 80% of SMILE patients did not use any eye drops 6 months post-surgery compared to 57% in the LASIK group, with 20% of the LASIK group requiring daily and frequent use of tear substitutes or even gels[58]. Higher tear osmolarity and lower TBUT, Schirmer score and corneal sensitivity were also observed in the LASIK group (see Table 5). Moreover, according to Li et al., SMILE patients reported less DED symptoms and had higher subbasal nerve density three months after surgery in comparison with LASIK patients[114].

SMILE monovision represents an additional corneal refractive surgical technique for presbyopia correction. This technique has shown to be a safe and effective option, yielding predictable outcomes for treating patients with presbyopia[115]. While more studies based on late adulthood are needed, the advantages of this technique in relation to tear function, found in the general population, are also expected to benefit older individual's.

Importantly, older patients tend to have a greater stromal response to SMILE and more unpredictable refractive outcomes[118]. Older age has been identified as a risk factor for residual refractive error following SMILE that requires enhancement procedures (PRK)[116], speculated to result from wound healing and biomechanical characteristics in older corneas[117]. Consequently, as in the previous strategies, the clinician must consider the potentially increased effects of SMILE on the TF and ocular dryness with increasing age.

3.2.5 CORNEAL ONLAYS/INLAYS

The main advantage of corneal onlays/inlays over the previously described techniques is that no tissue removal is needed[119]. Corneal onlays/inlays are optical devices designed to change corneal curvature or modify its optical properties, either by altering the refractive index to induce bifocal optics or by using small aperture optics in order to increase depth of focus[120]. Nowadays, femtosecond laser is widely used as it provides a more dependable flap than a microkeratome[121] and allows for the creation of stromal pockets, improving the accuracy of implantation depth and inlay centration[122].

Dry eye after corneal inlay implantation is mainly due to the flap creation which is basically the same technique as for LASIK surgery[123]. However, since no laser ablation is applied to the corneal stroma, less deep nerve damage is expected to occur in comparison with LASIK. In addition, the stromal pocket technique is less invasive than the flap technique and as such, a reduced incidence of dry eye post-surgery is expected as well as a shorter recovery period[124,125].

Tomita et al. examined the postoperative outcomes of 277 patients after LASIK and small-aperture corneal inlay implantation for hyperopic presbyopia[126]. The authors found no significant effect of age on the rates or severity of subjective symptoms, including dryness. Nevertheless, they underlined that taking age into account might help achieve optimum postoperative outcomes and improved patient satisfaction.[126]

To conclude, the ocular surface should be carefully evaluated, and treated when required, before and after inlay implantation. As pre-existing dry eye is common in the presbyopic population it will likely be exacerbated by the creation of a pocket or a flap. Further studies are needed to assess the long-term outcomes of the lamellar cut and tunnel incision performed for the refractive inlay and small aperture optics implants[127] on dry eye signs and symptoms.

4. CONTACT LENSES

Various CL options for presbyopic correction are available on the market: including single vision (combination of distance correction CLs and reading glasses), monovision, bifocal designs and multifocal designs[128]. However, not every CL wearer is able to achieve acceptable comfort and vision during CL wear and this can eventually lead to discontinuation and dropout; CL Discomfort (CLD) (24%) and dryness (20%) being the primary reasons of discontinuation[129-131]. In this regard, the TFOS International Workshop on CLD has extensively reviewed the problem of CLD and associated dryness.[132] According to recent findings, the mechanisms involved in CLD seem to share common pathways with DED[133-135], initiating a closed loop of inflammation as described by Baudouin et al.[136]

When a CL is fitted on a patient's eye, TF is disturbed leading to an increase in evaporation rate and dewetting[137] and possibly impacting the function of the MGs[129,131,137]. Specifically, DED in CL wearers is associated with a reduction in wearing time[138], increased risk of desiccation[122] (and raised osmolarity)[139] and thus higher rates of infection[140]. Furthermore, CL water content has been associated with CL related dry eye. **In this regard, it is thought that high water content CL alters the lipid layer structure of the TF, possibly due to the affinity of the polar components of the lipid layer to the CL surface, causing disruption of the prelens TF and thus increasing evaporation and/or dewetting[130,133,141]**. Modifying the fit, changing the CL material and wearing schedule, or even prescribing eyedrops are the main solutions available to alleviate dryness signs[141,142].

In addition, discomfort symptoms related to asthenopic eye strain (burning, irritation, ocular dryness and tearing) have been noted to be closely related to symptoms of dry eye[143] and CLD[132]. Consequently, DED-like symptoms may be partially explained by suboptimally corrected refractive error or binocular vision disorders in many CL wearers, particularly in older patients without near vision correction[144].

Additionally, the physiological changes of advancing age on the ocular surface and TF might decrease the tolerance for CLs and increase the risks of complications[130]. In fact, age has shown to be the main factor influencing CL retention rate[145]. Patel et al. suggest that the presbyopic population might be more susceptible to dryness-related comfort problems[146], mainly because of decreased TF stability, eventually leading to CLD and dropout. However, du Toit et al. found no differences in the TF, ocular surfaces and symptoms between younger and older presbyopic patients, after 6 months of CL wear, except for a shorter TBUT in the older group[147]. The authors pointed out that the dry eye signs and ratings obtained were comparable with figures previously reported for all age groups of CL wearers. Hence, they reflected that presbyopes should not be excluded from consideration for CL fitting and that the usual patient care tenets apply. Overall, evidence suggests that using a low rigidity CL on a daily disposable modality, especially hydrogel daily disposable CLs, could be beneficial when fitting patients with presbyopia[148,149].

In addition, over the past decade there has been a resurgence of interest in scleral CLs (SCLs). SCLs are large-diameter rigid gas permeable CLs that vault the cornea and limbus and are supported by the sclera. These characteristics avoid direct mechanical stress to the cornea and enable the protection and continuous sealed hydration of the ocular surface[152]. Consequently, SCLs are considered a good therapeutic approach for the treatment of patients with moderate to severe dry eye[152-154]. In particular, small diameter SCLs, also known as corneo-scleral or mini-scleral lenses, have been reported especially suitable for this population[155].

As mentioned previously, fitting CLs in a presbyopic population is more challenging in comparison with a younger cohort. However, presbyopic patients could benefit from wearing SCLs; multifocal designs present great advantages such as excellent centration and stability along with better optical quality, compared to conventional multifocal CLs[153]. In this sense, SCLs present dual advantages for this population as they can provide a stable optical platform for correcting presbyopia and protect the ocular surface by vaulting the cornea, reducing their impact on the TF.

Moreover, SCLs are considered a suitable option for aiding patients with corneal ectasia, irregularity, and dry eye after PRK and LASIK surgery[156,157]. In this regard, postoperative optical complications following laser surgery have been observed, particularly procedures conducted in the 1990's, when the importance of sufficient residual bed thickness and exclusion of both form fruste and manifest keratoconus were perhaps not appreciated[158]. Thirty years later many of these patients are now presbyopic and may benefit from treatment with SCL's.

5. CONCLUSIONS

Aging processes challenge the ocular surface directly by inducing drastic changes to the LFU. Additionally, ocular surface integrity can be jeopardized through surgical interventions involving the cornea and CL fitting, potentially initiating a closed loop of inflammation leading to DED (Table 6). Given that preoperative tear function is thought to play an important role in long-term ocular surface integrity after surgical procedures, the clinician must consider the potentially greater adverse effects of surgery on the TF and ocular dryness with increasing age. More than in any other age group, postoperative ocular dryness is highly dependent on the invasiveness of the surgical technique, mostly related to corneal nerve damage. Similarly, CLD and dryness CL wearing presbyopes may be influenced to some extent by the lens material and wearing schedule. Newer CL designs including SCLs may be particularly useful for presbyopes with DED since they provide a stable optical platform and protection and constant hydration of the ocular surface. Further studies are still needed to assess long-term outcomes of recent advances in refractive surgeries and CL designs on dry eye signs and symptoms in older adults.

6. REFERENCES

1. Stern ME, Beuerman RW, Fox RI, et al. The Pathology of Dry Eye: the interaction between the ocular surface and lacrimal glands. *Cornea* 1998;17:584–589.

2. Sullivan DA (Ed.) Lacrimal gland, tear film and dry eye syndrome: Basic science and clinical relevance. NYC: Springer, 1994.

3. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. *Ocul Surf* 2017;15:276–283.

4. Rocha EM, Alves M, Rios JD, et al. The aging lacrimal gland: changes in structure and function. *Ocul surf* 2008;6:162–174.

5. El-Fadaly AB, El-Shaarawy EA, Rizk AA, et al. Age-related alterations in the lacrimal gland of adult albino rat: a light and electron microscopic study. *Ann Anat* 2014;196:336–351.

6. Obata H, Yamamoto S, Horiuchi H, et al. Histopathologic study of human lacrimal gland. Statistical analysis with special reference to aging. *Ophthalmology* 1995;102:678–686.

7. Chhadva P, McClellan AL, Alabiad CR, et al. Impact of eyelid laxity on symptoms and signs of dry eye disease. *Cornea* 2016;35:531–535.

8. Alghamdi YA, Mercado C, McClellan AL, et al. Epidemiology of meibomian gland dysfunction in an elderly population. *Cornea* 2016;35:731–735.

9. Pult H, Riede-Pult, BH. Impact of conjunctival folds on central tear meniscus height. Invest *Ophthalmol Vis Sci* 2015;56:1459–1466.

10. Gumus K Pflugfelder SC. Increasing prevalence and severity of conjunctivochalasis with aging detected by anterior segment optical coherence tomography. *Am J Ophthalmol* 2013;155:238–242.

11. Chao W, Belmonte C, Castillo JMBD, et al. Report of the inaugural meeting of the TFOS i(2) = initiating innovation series: Targeting the unmet need for dry eye treatment. *Ocul Surf* 2016;14:264–316.

12. Schein OD, Munoz B, Tielsch JM, et al. Prevalence of dry eye among the elderly. *Am J Ophthalmol* 1997;124:723-8

13. Moss SE, Klein R, Klein BE. Long-term incidence of dry eye in an older population. *Optom Vis Sci* 2008;85:668-74

14. The Lancet. Series on Ageing. November 6, 2014. Available at: http://www.thelancet.com/series/ageing. Accessed October 02, 2018.

15. Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II Epidemiology Report. *Ocul Surf* 2017;15:334–365.

16. Papadopoulos PA, Papadopoulos AP. Current management of presbyopia. *Middle East Afr J Ophthalmol*. 2014;21:10–17.

17. Patel I, West SK. Presbyopia: prevalence, impact, and interventions. *Community Eye Health* 2007;20:40–41.

18. American Optometric Association (2010): Care of the patient with presbyopia. St. Louis: American Optometric Association.

19. Frick KD, Joy SM, Wilson DA, et al. The global burden of potential productivity loss from uncorrected presbyopia. *Ophthalmology* 2015;122:1706–1710.

20. Charman WN. Developments in the correction of presbyopia I: spectacle and contact lenses. *Ophthalmic Physiol Opt* 2014;34:8–29.

21. He W, Goodkind D, Kowal PR. An aging world: 2015. United States Census Bureau, 2016.

22. Thylefors B, Negrel AD, Pararajasegaram R, et al: Global data on blindness. *Bull World Health Organ* 1995;73:115–121.

23. Asbell PA, Dualan I, Mindel J, et al. Age-related cataract. *Lancet* 2005;365:599–609.

24. Pescosolido N, Barbato A, Giannotti R, et al. Age-related changes in the kinetics of human lenses: prevention of the cataract. *Int J Ophthalmol* 2016;9:1506–1517.

25. Muller LJ, Pels L, Vrensen GF. Ultrastructural organization of human corneal nerves. *Invest Ophthalmol Vis Sci* 1996;37:476–488.

26. Belmonte C, Nichols JJ, Cox SM, et al. TFOS DEWS II pain and sensation report. *Ocul Surf* 2017;15:404–437.

27. Marfurt CF, Cox J, Deek S, et al. Anatomy of the human corneal innervation. *Exp Eye Res* 2010;90:478–492.

28. Belmonte C, Acosta MC, Gallar J. Neural basis of sensation in intact and injured corneas. *Exp Eye Res* 2004;78:513–525.

29. Trikha S, Turnbull AM, Morris RJ, et al. The journey to femtosecond laser-assisted cataract surgery: new beginnings or false dawn? *Eye* 2013;27:461–473.

30. Grewal DS, Schultz T, Basti S, et al. Femtosecond laser-assisted cataract surgery--current status and future directions. *Surv Ophthalmol* 2016;61:103–131.

31. Brian G, Taylor H. Cataract blindness – challenges for the 21st century. *Bull World Health Org* 2001;79:249–256.

32. Montés-Micó R. Role of the tear film in the optical quality of the human eye. *J Cataract Ref Surg* 2007;33:1631–1635.

33. Montés-Micó R, Alió J, Charman N. Dynamic changes in the tear film in dry eyes. *Invest Ophtalmol Vis Sci* 2005;46:1615–1619.

34. Salomão MQ, Ambrósio R, Wilson SE. Dry eye associated with laser in situ keratomileusis: Mechanical microkeratome versus femtosecond laser. *J Cataract Refract Surg* 2009;35:1756–1760.

35. Walker TD. Benzalkonium Toxicity. *Clin Exp Ophthalmol* 2004;32:657.

36. Cho YK, Kim MS. Dry eye after cataract surgery and associated intraoperative risk factors. *Korean J Ophthalmol* 2009;23:65–73.

37. Nakamori K, Odawara M, Nakajima T, et al. Blinking is controlled primarily by ocular surface conditions. *Am J Ophthalmol* 1997;124:24–30.

38. Kasetsuwan N, Satitpitakul V, Changul T, et al. Incidence and pattern of dry eye after cataract surgery. *PLoS One* 2013;8:e78657.

39. Calonge M, Enriquez-de-Salamanca A, Diebold Y, et al. Dry eye disease as an inflammatory disorder. *Ocul Immunol Inflamm* 2010;18:244–253.

40. Li X-M, Hu L, Hu J, et al. Investigation of Dry Eye Disease and analysis of the pathogenic factors in patients after cataract surgery. *Cornea* 2007;26:16–20.

41. Kohlhaas M, Stahlhut O, Tholuck J, et al. Development of corneal sensitivity after phacoemulsification with scleral tunnel incision. *Klin Monbl Augenheilkd* 1997;211:32–36.

42. Khanal S, Tomlinson A, Esakowitz L, et al. Changes in corneal sensitivity and tear physiology after phacoemulsification. *Ophthalmic Physiol Opt* 2008;28:127–134.

43. Ram J, Gupta A, Brar G, et al. Outcomes of phacoemulsification in patients with dry eye. J *Cataract Refract Surg* 2002;28:1386–1389.

44. Oh T, Jung Y, Chang D, et al. Changes in the tear film and ocular surface after cataract surgery. *Jpn J Ophthalmol* 2012;2:113–118.

45. Park Y, Hwang HB, Kim HS. Observation of influence of cataract surgery on the ocular surface. *PLoS One* 2016;11:e0152460.

46. Donaldson KE, Braga-Mele R, Cabot F, et al. Femtosecond laser–assisted cataract surgery. *J Cataract Refract Surg* 2013;39:1753–1763.

47. Nagy Z, Takacs A, Filkorn T, et al. Initial clinical evaluation of an intraocular femtosecond laser in cataract surgery. *J Refract Surg* 2009;25:1053–1060.

48. Sugar A. Ultrafast (femtosecond) laser refractive surgery. *Curr Opin Ophthalmol* 2002;13:246–249.

49. Palanker DV, Blumenkranz MS, Andersen D, et al. Femtosecond laser-assisted cataract surgery with integrated optical coherence tomography. *Sci Transl Med* 2010;2:58-85.

50. Friedman NJ, Palanker DV, Schuele G, et al. Femtosecond laser capsulotomy. *J Cataract Refract Surg* 2011;37:1189–1198.

51. Rodriguez-Prats JL, Hamdi IM, Rodriguez AE, et al. Effect of suction ring application during LASIK on goblet cell density. *J Refract Surg* 2007;23:559–562.

52. Hoffman RS, Fine IH, Packer M. New phacoemulsification technology. *Curr Opin Ophthalmol* 2005;16:38–43.

53. Sitompul R, Sancoyo GS, Hutauruk JA, et al. Sensitivity Change in Cornea and Tear layer due to Incision Difference on Cataract Surgery with Either Manual Small-Incision Cataract Surgery or Phacoemulsification. Cornea. 2008;27:13-18.

54. Aristeidou A, Taniguchi EV, Tsatsos M, et al. The evolution of corneal and refractive surgery with the femtosecond laser. *Eye Vis* 2015;14:2–12.

55. Kissner A, Kohlhaas M, Spörl E, et al. Corneal aberrations before and after corneal and corneoscleral small incision cataract surgery. *Klin Monbl Augenheilkd* 2007;224:95–100.

56. Baudouin C, Labbé A, Liang H, et al. Preservatives in eyedrops: The good, the bad and the ugly. *Prog Ret Eye Res* 2010; 29:312–334.

57. Calvillo MP, Mclaren JW, Hodge DO, et al. Corneal Reinnervation after LASIK: prospective 3-Year Longitudinal Study. *Invest Opthalmol Vis Sci* 2004;45:3991–3996.

58. Denoyer A, Landman E, Trinh L. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. *Ophthalmology* 2015;122:669–676.

59. Patel SV, McLaren JW, Kittleson KM, et al. Subbasal nerve density and corneal sensitivity after laser in situ keratomileusis: femtosecond laser vs mechanical microkeratome. *Arch Ophtalmol* 2010;128:1413–1419.

60. Chao C, Golebiowski B, Stapleton F. The role of corneal innervation in LASIK-induced neuropathic dry eye. *Ocul Surf* 2014;12:32–45.

61. Ang RT, Dartt DA, Tsubota K. Dry eye after refractive surgery. *Curr Opin Ophthalmol* 2001;12:318–322.

62. Tao A, Shen M, Wang J, et al. Upper and lower tear menisci after laser in situ keratomileusis. *Eye Contact Lens* 2010;36:81–85.

63. Toda I, Asano-Kato N, Hori-Komai Y, et al. Laser-assisted in situ keratomileusis for patients with dry eye. *Arch Ophthalmol* 2002;120:1024–1028.

64. Vroman DT1, Sandoval HP, Fernández de Castro LE, et al. Effect of hinge location on corneal sensation and dry eye after laser in situ keratomileusis for myopia. *J Cataract Refract Surg* 2005;31:1881–1887.

65. Shoja M, Besharati M. Dry Eye after Lasik for Myopia: Incidence and Risk Factors. *Eur J Ophthalmol* 2007;17:1–6.

66. Battat L, Macri A, Dursun D, et al. Effects of laser in situ keratomileusis on tear production, clearance, and the ocular surface. *Ophthalmology* 2001;108:1230–1235.

67. Chao C, Stapleton F, Zhou X, et al. Structural and functional changes in corneal innervation after laser in situ keratomileusis and their relationship with dry eye. *Graefes Arch Clin Exp Ophthalmol* 2015;253:2029–2039.

68. Mian SI, Li AY, Dutta S, et al. Dry eyes and corneal sensation after laser in situ keratomileusis with femtosecond laser flap creation. *J Cataract Refract Surg* 2009;35:2092–2098.

69. De Paiva CS, Chen Z, Koch DD, et al. The incidence and risk factors for developing dry eye after myopic LASIK. *Am J Ophthalmol* 2006;141:438–445.

70. Pflugfelder SC, Corrales RM, Paiva CSD. T helper cytokines in dry eye disease. *Exp Eye Res* 2013;117:118–125.

71. Erie JC, McLaren JW, Hodge DO, et al. Recovery of corneal subbasal nerve density after PRK and LASIK. *Am J Ophthalmol* 2005;140:1059–1064.

72. Ambrósio R, Tervo T, Wilson SE. LASIK-associated dry eye and neurotrophic epitheliopathy: pathophysiology and strategies for prevention and treatment. *J Refract Surg* 2008;24:396–407.

73. Jagow BV, Kohnen T. Corneal architecture of femtosecond laser and microkeratome flaps imaged by anterior segment optical coherence tomography. *J Cataract Refract Surg* 2009;35:35–41.

74. Tran DB, Sarayba MA, Bor Z, et al. Randomized prospective clinical study comparing induced aberrations with IntraLase and Hansatome flap creation in fellow eyes. *J Cataract Refract Surg* 2005;31:97–105.

75. Durrie DS, Kezirian GM. Femtosecond laser versus mechanical keratome flaps in wavefront-guided laser in situ keratomileusis. *J Cataract Refract Surg* 2005;31:120–126.

76. Tervo T, Vannas A, Tervo K, et al. Histochemical evidence of limited reinnervation of human corneal grafts. *Acta Ophthalmol (Copenh)* 1985;63:207–214.

77. Wei S, Wang Y. Comparison of corneal sensitivity between FS-LASIK and femtosecond lenticule extraction (ReLEx flex) or small-incision lenticule

extraction (ReLEx smile) for myopic eyes. *Graefes Arch Clin Exp Ophthalmol* 2013;25:1645–1654.

78. Xu Y, Yang Y. Dry Eye After Small Incision Lenticule Extraction and LASIK for Myopia. *J Refract Surg* 2014;30:186–190.

79. Mian SI, Shtein RM, Nelson A, et al. Effect of hinge position on corneal sensation and dry eye after laser in situ keratomileusis using a femtosecond laser. *J Cataract Refract Surg* 2007;33:1190–1194.

80. Liu Z, Li Y, Cheng Z, et al. Seven-year follow-up of LASIK for moderate to severe myopia. *J Refract Surg* 2008;24:935–940.

81. Jain S, Ou R, Azar DT. Monovision outcomes in presbyopic individuals after refractive surgery. *Ophthalmology* 2001;108:1430–1433.

82. Miranda D, Krueger RR. Monovision laser in situ keratomileusis for pre-presbyopic and presbyopic patients. *J Refract Surg* 2004;20:325–328.

83. López-Montemayor P, Valdez-García JE, Loya-García D, et al. Safety, efficacy and refractive outcomes of LASIK surgery in patients aged 65 or older. *Int Ophthalmol* 2018;38:1515–1520.

84. Wolffsohn JS, Davies LN. Presbyopia: Effectiveness of correction strategies. *Prog Retin Eye Res* 2019;68:124–143.

85. Levinger E, Trivizki O, Pokroy R, et al. Monovision surgery in myopic presbyopes: visual function and satisfaction. *Optom Vis Sci* 2013;90:1092–1097.

86. Kanellopoulus AJ. Incidence and management of symptomatic dry eye related to LASIK for myopia, with topical cyclosporine A. *Clin Ophthalmol* 2019;13:545–552.

87. Price MO, Price DA, Bucci FA Jr, et al. Three-Year Longitudinal Survey Comparing Visual Satisfaction with LASIK and Contact Lenses. *Ophthalmology* 2016;123:1659–1666.

88. Golas L, Manche EE. Dry eye after laser in situ keratomileusis with femtosecond laser and mechanical keratome. *J Cataract Refract Surg* 2011;37:1476–1480.

89. Konomi K, Chen LL, Tarko RS, et al. Preoperative Characteristics and a Potential Mechanism of Chronic Dry Eye after LASIK. *Invest Ophthalmol Vis Sci* 2008;49:168–174.

90. Browning AC, Shah S, Dua HS, et al. Alcohol debridement of the corneal epithelium in PRK and LASEK: an electron microscopic study. *Invest Ophthalmol Vis Sci* 2003;44:510–513.

91. Erie JC. Corneal wound healing after photorefractive keratectomy: a 3-year confocal microscopy study. *Trans Am Ophthalmol Soc* 2003;101:293–333.

92. Lee JB, Ryu CH, Kim J, et al. Comparison of tear secretion and tear film instability after photorefractive keratectomy and laser in situ keratomileusis. *J Cataract Refract Surg* 2000;26:1326–1331.

93. Nejima R, Miyata K, Tanabe T, et al. Corneal barrier function, tear film stability, and corneal sensation after photorefractive keratectomy and laser in situ keratomileusis. *Am J Ophthalmol* 2005;139:64–71.

94. Ozdamar A, Aras C, Karakas N, et al. Changes in tear flow and tear film stability after photorefractive keratectomy. *Cornea* 1999;18:437–439.

95. Hong JW, Kim HM. The changes of tear break up time after myopic excimer laser photorefractive keratectomy. *Korean J Ophthalmol* 1997;11:89–93.

96. Ishikawa T, Park SB, Cox C, et al. Corneal sensation following excimer laser photorefractive keratectomy in humans. *J Refract Corneal Surg* 1994:10;417–422.

97. Perez-Santonja JJ, Sakla HF, Cardona C, et al. Corneal sensitivity after photorefractive keratectomy and laser in situ keratomileusis for low myopia. *Am J Ophthalmol* 1999;127:497–504.

98. Murakami Y, Manche EE. Prospective, Randomized Comparison of Self-reported Postoperative Dry Eye and Visual Fluctuation in LASIK and Photorefractive Keratectomy. *Ophthalmology* 2012;119:2220–2224.

99. Gipson IK. Age-related changes and diseases of the ocular surface and cornea. *Invest Ophthalmol Vis Sci* 2013;54:ORSF48– ORSF53.

100. Hersh PS, Schein OD, Steinert R. Characteristics influencing outcomes of excimer laser photorefractive keratectomy. Summit Photorefractive Keratectomy Phase III Study Group. *Ophthalmology* 1996;103:1962–1969.

101. Ambrósio R, Wilson S. LASIK vs LASEK vs PRK: Advantages and indications. *Semin Ophthalmol* 2003;18:2–10.

102. Shah S, Doyle SJ, Chatterjee A, et al. Comparison of 18% ethanol and mechanical debridement for epithelial removal before photorefractive keratectomy. *J Refract Surg* 1998;14(2 Suppl):S212–214.

103. Kim SY, Sah WJ, Lim YW, et al. Twenty percent alcohol toxicity on rabbit corneal epithelial cells: electron microscopic study. *Cornea* 2002;21:388–392.

104. Autrata R, Rehurek J. Laser-assisted subepithelial keratectomy for myopia: two-year follow-up. *J Cataract Refract Surg* 2003;29:661–668.

105. Herrmann WA, Shah CP, Mohrenfels CWV, et al. Tear film function and corneal sensation in the early postoperative period after LASEK for the correction of myopia. *Graef Arch Clin Exp Ophthalmol* 2005;243:911–916.

106. Dooley I, Darcy F, Okeefe M. Comparison of dry-eye disease severity after laser in situ keratomileusis and laser-assisted subepithelial keratectomy. *J Cataract Refract Surg* 2012;38:1058–1064.

107. Horwath-Winter J, Vidic B, Schwantzer G, et al. Early changes in corneal sensation, ocular surface integrity, and tear-film function after laser-assisted subepithelial keratectomy. *J Cataract Refract Surg* 2004;30:2316–2321.

108. Galindo J, Fadlallah A, Robinson S, et al. Risk factors for loss of epithelial flap integrity in laser-assisted subepithelial keratectomy surgery. *J Cataract Refract Surg* 2016;42:591–595.

109. Garcia-Gonzalez M, Gros-Otero J, Rodrifuez-Perez I, et al. Effect of age on visual and refractive results after laser-assisted subepithelial keratomileusis (LASEK) with adjuvant use of mitomycin C. *J Optom* 2019;12:92–98.

110. Rhim JH, Kim JH, Yeo EJ, et al. Caveolin-1 as a novel indicator of wound-healing capacity in aged human corneal epithelium. *Mol Med* 2010;16:527–534.

111. Reinstein DZ, Archer TJ, Gobbe M. Small incision lenticule extraction (SMILE) history, fundamentals of a new refractive surgery technique and clinical outcomes. *Eye Vis (Lond)* 2014;1:1.

112. Dong Z, Zhou X, Wu J, et al. Small incision lenticule extraction (SMILE) and femtosecond laser LASIK: comparison of corneal wound healing and inflammation. *Br J Ophthalmol* 2014;98:263–269.

113. Moshirfar M, McCaughey MV, Reinstein DZ, et al. Small-incision lenticule extraction. *J Cataract Refract Surg* 2015;41:652–665.

114. Li M, Niu L, Qin B, et al. Confocal Comparison of Corneal Reinnervation after Small Incision Lenticule Extraction (SMILE) and Femtosecond Laser In Situ Keratomileusis (FS-LASIK). *PLoS One* 2013;8:e81435.

115. Luft N, Siedlecki J, Sekundo W, et al. Small incision lenticule extraction (SMILE) monovision for presbyopia correction. *Eur J Ophthalmol* 2018;28:287–293.

116. Liu YC, Rosman M, Mehta JS. Enhancement after Small-Incision Lenticule Extraction: Incidence, Risk Factors, and Outcomes. *Ophthalmology* 2017;124:813–821.

117. Hjortdal JØ, Vestergaard AH, Ivarsen A, et al. Predictors for the outcome of small incision lenticule extraction for myopia. *J Refract Surg* 2012;28:865–871.

118. Netto MV, Mohan RR, Ambrósio Jr R, et al. Wound healing in the cornea: a review of refractive surgery complications and new prospects for therapy. *Cornea* 2005;24:509–522.

119. Lindstrom RL, Macrae SM, Pepose JS, et al. Corneal inlays for presbyopia correction. *Curr Opin Ophthalmol* 2013;24:281–287.

120. Arlt EM, Krall EM, Moussa S, et al. Implantable inlay devices for presbyopia: The evidence to date. *Clin Ophthalmol* 2015;9:129–137.

121. Callou TP, Garcia R, Mukai A, et al. Advances in femtosecond laser technology. *Clin Ophthalmol* 2016;10:697–703.

122. Waring GO, Klyce SD. Corneal inlays for the treatment of presbyopia. *Int Ophthalmol Clin* 2011;51:51–62.

123. Yilmaz ÖF, Alagöz N, Pekel G, et al. Intracorneal inlay to correct presbyopia: Long-term results. *J Cataract Refract Surg* 2011;37:1275–1281.

124. Binder P. New femtosecond laser software technology to create intrastromal pockets for corneal inlays. *ARVO* 2010;51:2868.

125. Limnopoulou AN, Bouzoukis DI, Kymionis GD, et al. Visual Outcomes and Safety of a Refractive Corneal Inlay for Presbyopia Using Femtosecond Laser. *J Refract Surg* 2013;29:12–19.

126. Tomita M, Waring GO 4th. One-year results of simultaneous laser in situ keratomileusis and small-aperture corneal inlay implantation for hyperopic presbyopia: comparison by age. *J Cataract Refract Surg* 2015;41:152–161.

127. Dexl AK, Ruckhofer J, Riha W, et al. Central and peripheral corneal iron deposits after implantation of a smallaperture corneal inlay for correction of presbyopia. *J Refract Surg* 2011;27:876–880.

128. Bennett ES. Contact lens correction of presbyopia. *Clin Exp Optom* 2008;91:265–278.

129. Richdale K, Sinnott LT, Skadahl E, et al. Frequency of and Factors Associated With Contact Lens Dissatisfaction and Discontinuation. *Cornea* 2007;26:168–174.

130. Dumbleton K, Woods CA, Jones LW, et al. The Impact of Contemporary Contact Lenses on Contact Lens Discontinuation. *Eye Contact Lens* 2013;39:92–98.

131. Young G, Veys J, Pritchard N, et al. A multi-centre study of lapsed contact lens wearers. *Ophthalmic Physiol Opt* 2002;22:516–527.

132. Nichols JJ, Willcox MD, Bron AJ, et al. The TFOS International Workshop on Contact Lens Discomfort: executive summary. *Invest Ophthalmol Vis Sci* 2013;54:TFOS7–TFOS13.

133. Dogan AS, Gurdal C, Arslan N. Corneal confocal microscopy and dry eye findings in contact lens discomfort patients. *Cont Lens Anterior Eye* 2018;41:101–104.

134. Wagner H, Chalmers RL, Mitchell GL, et al. Risk factors for interruption to soft contact lens wear in children and young adults. *Optom Vis Sci* 2011;88:973–980.

135. Robertson DM. The effects of silicone hydrogel lens wear on the corneal epithelium and risk for microbial keratitis. *Eye Contact Lens* 2013;39:67–72.

136. Baudouin C, Aragona P, Messmer E, et al. Role of hyperosmolarity in the pathogenesis and management of dry eye disease: proceedings of the OCEAN group meeting. *Ocul Surf* 2013;11:246–258.

137. Dumbleton K, Caffery B, Dogru M, et al. The TFOS International Workshop on Contact Lens Discomfort: report of the subcommittee on epidemiology. *Invest Ophthalmol Vis Sci* 2013;54:TFOS20–36.

138. Harknett T, Bowden T, Shadbolt H, et al. Five years after dispensing — are contact lenses a success? *Contact Lens Ant Eye* 2001;24:127–128.

139. Nichols JJ, Sinnott LT. Tear film, contact lens, and patient-related factors associated with contact lens–related dry eye. *Invest Ophthalmol Vis Sci* 2006;47:1319–1328.

140. Bruinsma GM, van der Mei HC, Busscher HJ. Bacterial adhesion to surface hydrophilic and hydrophobic contact lenses. *Biomaterials* 2001;22:3217–3224.

141. Fonn D, Situ P, Simpson T. Hydrogel lens dehydration and subjective comfort and dryness rating in symptomatic and asymptomatic contact lens wearers. *Optom Vis Sci* 1999;76:700–704.

142. Efron N. Contact lens wear is intrinsically inflammatory. *Clin Exp Optom* 2016;100:3–19.

143. Sheedy JE, Hayes JN, Engle J. Is all asthenopia the same? *Optom Vis Sci* 2003;80:732–739.

144. Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. *BMJ Open Ophthalmol* 2018;3:e000146.

145. Sulley A, Young G, Hunt C. Factors in the success of new contact lens wearers. *Cont Lens Anterior Eye* 2017;40:15–24.

146. Patel S, Boyd KE, Burns J. Age, stability of the precorneal tear film and the refractive index of tears. *Cont Lens Anterior Eye* 2000;23:44–47.

147. du Toit R, Situ P, Simpson T, et al. The effects of six months of contact lens wear on the tear film, ocular surfaces, and symptoms of presbyopes. *Optom Vis Sci* 2011;78:455–462.

148. Guillon M, Dumbleton K, Theodoratos P, et al. Objective Assessment of Ocular Surface Response to Contact Lens Wear in Presbyopic Contact Lens Wearers of Asian Descent. *Eye Contact Lens* 2018;44:182–189.

149. Hickson-Curran SB, Chalmers RL, Keay L, et al. Patient-Reported Wearing Experience From Hydrogel Daily Disposable Wearers Older Than 40 Years From the TEMPO Registry. *Eye Contact Lens* 2017;43:313–317.

150. Nau CB, Harthan J, Shorter E, et al. Demographic Characteristics and Prescribing Patterns of Scleral Lens Fitters: The SCOPE Study. *Eye Contact Lens* 2018;44 Suppl 1:S265-s272.

151. Vincent SJ. The rigid lens renaissance: A surge in sclerals. *Cont Lens Anterior Eye* 2018;41:139-143.

152. Schornack MM, Pyle J, Patel SV. Scleral Lenses in the Management of Ocular Surface Disease. *Ophthalmology* 2014;121:1398–1405.

153. van der Worp E, Bornman D, Ferreira DL, et al. Modern scleral contact lenses: a review. *Cont Lens Anterior Eye* 2014;37:240–250.

154. La Porta Weber S, Becco de Souza R, Gomes JÁP, et al. The Use of the Esclera Scleral Contact Lens in the Treatment of Moderate to Severe Dry Eye Disease. *Am J Ophthalmol* 2016;163-167–173

155. Lafosse E, Romín DM, Esteve-Taboada JJ, et al. Comparison of the influence of corneo-scleral and scleral lenses on ocular surface and tear film metrics in a presbyopic population. *Cont Lens Anterior Eye* 2018;41:122–127.

156. Mian SZ, Agranat JS, Jacobs DS. Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) Treatment for Complications After LASIK. *Eye Contact Lens* 2016;42:371–373.

157. Nguyen MTB, Thakrar V, Chan CC. EyePrintPRO therapeutic scleral contact lens: indications and outcomes. *Can J Ophthalmol* 2018;53:66–70.

158. Seiler T, Koufala K, Richter G. Iatrogenic keratectasia after laser in situ keratomileusis. *J Refract Surg* 1998;14:312–317.

Table 1. Dry eye and ocular surface-related signs and symptoms after cataract surgery.

Authors	Sample	Objectives	Surgical Procedure	Tests performed	Results
[Kasetsuwan et al. 2013][38]	92	**Evaluate the incidence and severity of dry eye after phacoemulsification.**	**Phacoemulsification with 2.75 mm incision and foldable IOL implantation.**	-OSDI -Oxford Staining -Schirmer I -TBUT	DED incidence 7 days postoperatively: -OSDI: 9.8% -Oxford Staining: 58.7% -Schirmer I: 11.9% -TBUT: 68.4%
[Li et al. 2007][40]	37 (50 eyes)	**Evaluate the pathogenic factors relevant to the occurrence of dry eye after cataract surgery.**	**Phacoemulsification with small incision (size not specified).**	-NEI-VFQ25 -OSDI -TBUT -Schirmer I	-NEI-VFQ25: Improvement in functional indices and ocular pain aggravated before/after surgery. -OSDI did not show any changes. -TBUT significantly worse ($P<0.01$).

				-Fluorescein staining (Oxford and van Bijsterveld) -Impression Cytology -TMH with fluorescein	-Fluorescein staining: Increase of staining at one-month post-surgery. -OSDI did not show difference before/after surgery. -TMH diminished significantly 70% >0.3mm pre-surgery and 70% post-surgery maintained at 1 month and 3 months after surgery.
[Ram et al. 2002][43]	23 (25 eyes)	**Evaluate the outcomes of phacoemulsification in patients with dry eye.**	**Phacoemulsification with 3.4 to 3.8 mm corneal incision and foldable IOL implantation.**	-Schirmer test with anesthesia -TBUT	-The mean preoperative Schirmer score was 4.80 mm ± 2.01 (SD) and the mean postoperative score, 3.80 ± 2.40 mm. -The mean preoperative TBUT was 4.00 ± 1.87 s (range 0 to 9 s) and the mean score at the last follow-up, 3.40 ± 1.60 s.

[Khanal et al. 2008][42]	18	**Identify changes in corneal sensitivity and tear physiology after phacoemulsification.**	**Phacoemulsification with 4.1 corneal incision and foldable IOL implantation**	-Corneal sensitivity (NCCA) -Osmolarity (freezing point depression) - TTR (automated scanning fluorophotometer)	-A significant decrease was seen postoperatively in central corneal sensitivity at 3 days (p<0.001), 2 weeks (p<0.001), 1 month (p=0.003) and 3 months (p=0.009). -Osmolarity significantly rises 3 days after surgery but decreases across the 3 months post-surgery (no statistical differences with preoperative values). -Significant increase in evaporation at 3 days and 2 weeks post-surgery. -Significant reduction in TTR at 3 days until two weeks post-surgery.
[Park et al. 2016][45]	34 (8 eyes)	**Evaluate changes of lacrimal tears and ocular surface parameters and tear inflammatory**	**Phacoemulsification with 2.85 mm corneal incision.**	-Ocular symptoms -TBUT -Schirmer I	-Significantly worse symptoms at 1 day, 1 month, 2 months post-surgery for the dry eye group compared to the no dry eye group.

		mediators following cataract surgery. Patients were divided into 2 groups with those who had preexisting dry-eye before cataract surgery and those who did not.		-Corneal fluorescein staining (NEI scale) -Corneal sensitivity (Cochet-Bonnet aesthesiometer) -Multiplex immunoassay kits	-TBUT was more significantly worsened in the dry eye group compared to the no dry eye group and recovery was significantly slower. -No statistically significant differences in recovery for Schirmer I in both groups. - Corneal staining more significantly worsened in the dry eye groups compared to the no dry eye group. -Corneal sensitivity threshold was more slowly recovered in the dry eye group than in the no dry eye group. -Significant increase in CKs levels at 1 month/2 months in contrast with day 1 post-surgery in both groups.

IOL, Intraocular Lens; OSDI, Ocular Surface Disease Index; TBUT, Tear Breakup Time; NEI VFQ-25, National Eye Institute Visual Function Questionnaire; TMH. Tear Meniscus Height; NCCA, Non-Contact Corneal Aesthesiometer; TTR, Tear Evaporation Turnover Rate; CKs, Cytokines.

Table 2. Dry eye and ocular surface-related signs and symptoms after LASIK.

Authors	Sample	Objectives	Tests performed	Results
[Vroman et al. 2005][64]	94 eyes from 47 patients	**Evaluate the effects of a superior or nasal hinge location on corneal sensation and dry eye after LASIK**	-Corneal sensitivity (Cochet-Bonnet) -Schirmer with anaesthesia -TBUT -Ocular surface staining (NEI scale) -OSDI	For both hinge locations: -Central corneal sensitivity significantly diminished at 1 week/1 month/ 3 months/ 6 months (p<0.001). -Schirmer values were significantly reduced only at 1 week post-surgery (p<0.05). -TBUT significantly reduced at 3 months post-surgery (p<0.01). -No difference in ocular surface staining. -Significant increase in OSDI score at 1 week/1 month/ 3months/ 6 months (p<0.01).
[Mian et al. 2009][68]	66 eyes from 33 patients	**Determine whether hinge position (superior vs**	-Corneal sensitivity (Cochet-Bonnet)	-Significant reduction in corneal sensitivity at 1 week/1 month/3 months/ 6months/ 12 months (p<0.0001).

		temporal) has an effect on corneal sensation and dry-eye symptoms after myopic LASIK.	-Schirmer test with anaesthesia -TBUT -Corneal fluorescein staining -Lissamine green staining with Oxford scale -OSDI	-Increase in Corneal fluorescein at 1 week post-surgery (p=0.01). -No difference of corneal sensation between superior-hinged and temporal-hinged flaps at any time. -TBUT/Schirmer test and conjunctival staining did not show significant changes after surgery. -Increase in OSDI score at 1 week and one month (p<0.0001) that stabilized at 3 months.
[Shoja et Besharati 2007][65]	190 eyes	**Determine the incidence and risk factors of dry eye after LASIK.**	-TBUT -Schirmer I -Corneal fluorescein staining -Central corneal sensitivity -Symptomatology	-Significant decrease of Schirmer and TBUT at 1 month/ 3 months/ 6 months (p<0.05). -Corneal sensitivity reduced at 1 month and 3 months but returned back to preoperative values at 6 months. **-There was a statistically significant effect of age, sex and mean spherical equivalent refraction on corneal sensitivity after LASIK.**

[Battat et al. 2001][66]	48 eyes	**Evaluate components of the ocular surface and the LFU before and after LASIK.**	-Questionnaire evaluating character and severity of ocular irritation symptoms -Snellen visual acuity -Tear Fluorescein Clearance -Schirmer I -Corneal/conjunctival sensibility -Corneal surface regularity	-Symptom severity scores were significantly increased at 1 week/ 12 months/ and 16 months postoperatively ($p<0.007$). -Corneal and conjunctival sensitivity significantly decreased at 1 week/ 1 month/ 12 months/ 16 months postoperatively. -Schirmer I test scores decreased from 24 ± 14 mm preoperatively to 18 ± 14 mm 1 month postoperatively.
[De Paiva CS et al. 2006][69]	**35 eyes**	**Determine the incidence of dry eye and its risk factors after myopic LASIK**	**-Corneal fluorescein staining** **-Aberrometry** **-TBUT** **-Corneal sensitivity (Belmonte non-contact esthesiometer)**	**-No differences obtained in corneal staining, TBUT, Schirmer or HOA RMS** **-Symptomatology significantly increased at 1 week and 1 month post-LASIK** **-Degree of preoperative myopia and depth of laser treatment were significantly correlated with dry eye risk.**

			-Schirmer I **-Symptomatology**	**- Age showed no significant correlation with postoperative dry eye.**

TBUT, Tear Breakup Time; OSDI, Ocular Surface Disease Index; **LFU, Lacrimal Functional Unit.**

Table 3. Dry eye and ocular surface-related signs and symptoms after PRK.

Authors	Sample	Objectives	Tests performed	Results
[Ishikawa et al. 1994][96]	17 eyes from myopic subjects	**Evaluate corneal sensation in different regions of the cornea following PRK at varying depths.**	-Corneal sensitivity with two group of patients: -Shallow photoablation (0 to 30 µm) -Deep photoablation (31 to 70 µm)	-Superior corneal sensation loss in the deep ablation group with no recovery within one month of the surgery. -Corneal fluctuations in sensations present up to 6 months post-surgery in this group
[Ozdamar et al. 1999][94]	32 (64 eyes)	**Investigate the changes in tear flow and tear film stability after PRK for myopia.**	-Schirmer test -TBUT	-Significant decrease in Schirmer/TBUT values post-surgery in comparison with the fellow eye (control) ($p=0.0001$) 6 weeks after the surgical procedure.
[Perez-Santonja et al. 1999][97]	18	**Evaluate the recovery of corneal sensitivity after PRK for low myopia.**	-Corneal sensitivity (Cochet-Bonnet aesthesiometer): Central zone and 2 mm from that central zone (nasal, inferior, temporal, and superior)	-Return to preoperative values at 3 months for central cornea and 1 month for the other corneal areas evaluated ($p>0.05$).

[Lee et al. 2000][92]	21 (36 eyes) eyes from 21 patients	**Evaluate tear secretion and tear film stability after PRK.**	-Schirmer with anesthesia/TBUT	-Significant decrease in Schirmer values at 3 months (p=0.0011) which tend to come back to normal values at 6 months (p=0.3080) and TBUT at 3 (p<0.01) and 6 months (p=0.07).

PRK, Photorefractive Keratectomy; TBUT, Tear Breakup Time.

Table 4. Dry eye and ocular surface-related signs and symptoms after LASEK.

Authors	Sample	Objectives	Tests performed	Results
[Herrmann et al. 2005][105]	20 eyes from 10 patients	**Evaluate tear film function, corneal sensation and subjective symptoms of dry eye in the early postoperative period after LASEK for the correction of myopia**	-Schirmer with anaesthesia -Schirmer I (without anesthesia) -TBUT -Fluorescein staining of the cornea -Corneal aesthesiometry (Cochet-Bonnet) -Symptomatology	-Schirmer test with anesthesia was reduced at 3 months post-surgery ($p<0.05$). -Schirmer test without anesthesia was reduced at 2 and 3 months after surgery ($p<0.05$). -TBUT was reduced at 1 week and 1 month after surgery ($p<0.05$). -Corneal staining was increased at 3 days and one week after surgery ($p<0.05$). -Symptomatology was increased after surgery ($p<0.05$) excepted at 3 months.
[Dooley et al. 2012][106]	35 eyes	**Evaluate the effects of LASEK on dry eye disease markers**	-OSDI -Schirmer test with anesthesia -Osmolarity (TearLab)	-OSDI values did not change during the follow-up period. -Schirmer values changed significantly at 12 months. -Osmolarity did not change across the follow-up period.

[Horwath-Winter et al. 2004][107]	37 eyes from 21 patients	**To investigate the changes in corneal sensation, ocular surface integrity, and tear-film function after LASEK**	-Symptoms -Corneal sensitivity (Cochet-Bonnet) -TBUT -Schirmer I -Fluorescein staining of the cornea	-No statistical difference in symptomatology was found. -Corneal sensation reduced up to one month after the surgical procedure ($p<0.05$). -TBUT was significantly reduced at 1 week and 1 month ($p<0.05$ respectively). -No changes in Schirmer results. -Significant increase in corneal staining at one week ($p<0.05$). -No changes in lissamine green staining.
TBUT, Tear Breakup Time; OSDI, Ocular Surface Disease Index.				

Table 5. Comparison of dry eye and ocular surface-related signs and symptoms after SMILE and other corneal refractive surgeries.

Authors	Sample	Objectives	Tests performed	Results
[Denoyer et al. 2015][58]	30 (60 eyes SMILE) 30 (60 eyes LASIK)	**Compare SMILE vs LASIK post-refractive DED.**	-OSDI -Schirmer I -TBUT -Oxford Staining -Osmolarity (TearLab) -Corneal esthesiometry (Cochet-Bonnet) -Subbasal nerve imaging using in vivo confocal microscopy	-OSDI LASIK> OSDI SMILE at 1/6 months (P<0.09 and 0.01 respectively). -Schirmer I LASIK< Schirmer I SMILE but no significant (P>0.05). -TBUT LASIK< TBUT SMILE significant at 6 months (p=0.01). -No significant differences for staining between techniques (P>0.05). -Osmolarity LASIK> Osmolarity SMILE at 1/6 months (P<0.01). -LASIK eyes showed lower sensibility at 1 month (P<0.05). -Nerve density significantly superior for SMILE eyes at 1/6 months (p<0.05 and P<0.01 respectively).

[WeietWang. 2013][77]	27 (54 eyes) FS-LASIK 32 (61 eyes) SMILE	**Compare the effect on corneal sensitivity between FS-LASIK and ReLEx smile surgery.**	-Cochet-Bonnet esthesiometry at 1 week 1 and 3 months after surgery.	-A higher corneal sensitivity after ReLEx SMILE surgery was observed in every quadrant at 1 week and 1 and 3 months compared with FS-LASIK surgery (P<0.01). -SMILE group did not show statistical differences in the superior and temporal quadrants at 1 month postoperatively compared with preoperatively (p=0.198 and p=0.330 respectively) and no significant differences in any quadrant at 3 months. -FS-LASIK group showed significant decrease in central corneal sensitivity in every quadrant at 1 week and 1 and 3 months postoperatively compared with preoperatively (P < 0.05).
[Xu et Yang. 2014][78]	176 (338 eyes)	**Compare the effects of SMILE and LASIK with either femtosecond laser**	-McMonnies questionnaire -Schirmer I -TBUT	-The mean McMonnies score in the SMILE group was better than other groups. -LASIK group was significantly lower than SMILE other group at 3 and 6 months.

		or mechanical microkeratome on dry eye	-Preoperatively and at 1, 3, and 6 months postoperatively.	-TBUT decreased significantly after surgery and did not return to preoperative levels within 6 months; the SMILE group presented significantly longer TBUT than the LASIK group at 1 month.

OSDI, Ocular Surface Disease Index; TBUT, Tear Breakup Time; LASIK, Laser Assisted In Situ Keratomileusis; **DED, Dry Eye Disease**; ReLex, Refractive Lenticule Extraction; SMILE, Small Incision Lenticule Extraction; FS-LASIK, Femtosecond Laser In Situ Keratomileusis; FLEX, Femtosecond Lenticule Extraction; AS-OCT, Anterior Segment Optical Coherence Tomography.

Table 6. Summary of the dry eye-related main outcomes up to date in an ageing population after the different procedures addressed in this review.

Procedure	Main Outcomes and Important Considerations
Cataract surgery	- Worsen tear film metrics[34-36,38,40,43,44], reduce corneal sensitivity[41,42,45] and decrease goblet cell density[34-37] up to 3 months post-surgery. - Larger corneal incisions for lens insertion are expected to induce more nerve damage and thus, sign and symptoms of dryness post-surgery[42,44]. - FLACS offers a more accurate cutting edge, better safety and improved clinical outcomes[46-49]. However conjunctival pressure by the suction ring reduces goblet cell density and contributes to postoperative DED[50,51]. - Dry eye risk factors after the surgery are related to disruption of corneal nerves and harm to the epithelia through the surgical procedure[34-38]. Incision shape, depth and regularity clearly impact post-surgery healing[42-44]. -Toxicity of antiseptic agents used during the surgical procedure and topical multi-dose eyedrops with preservatives seem to play a role in the onset of dry eye signs and symptoms[35.56].
LASIK	- Successful in correcting refractive errors in presbyopic patients[81-83]. - No consensus that older age impacts post-LASIK dry eye.

	- The LASIK surgical process induces double damage to the cornea; during the flap creation and during the excimer laser stromal ablation, increasing the probability of postoperative dry eye[34,60,61]. - Detailed assessment of tear film and ocular surface should be carried out before performing this surgery in older age groups. -Given the probability of post-LASIK dry eye, LASIK should only be applied in presbyopic patients with a good quality ocular surface and tear film.
PRK	- Recent studies report no effects of age on patient-reported dry eye after PRK[98]. - Older age, however, may possibly hinder the healing process affecting the outcome of the surgery[99]. - More studies regarding dry eye after PRK in the late adulthood are required. - Particular attention should be taken in older age groups before undertaking PRK as the surgery may worsen an already unbalanced ocular surface environment.
LASEK	- Age increases the prevalence of postoperative complications[108], reduces predictability[109] and increases healing time[110] after LASEK. - To date no studies have evaluated the effects of LASEK surgery on tear film in late adulthood. - Quicker recovery, reduced pain and less postoperative dry eye compared to other corneal refractive surgeries in the general population[104].

	- Lower postoperative dry eye signs and symptoms compared to other corneal ablation techniques are expected in the elderly as well.
SMILE	- A safe and effective option, yielding predictable outcomes for treating patients with presbyopia[115]. - Reduced corneal inflammation and keratocyte damage[112] and less iatrogenic dry eye[113], compared to other corneal refractive strategies, mainly due to the absence of a flap. -Older age is thought to increase the risk of enhancement[116]. -Older patients tend to have more stromal response and unpredictable outcomes[118].
CORNEAL ONLAYS/INLAYS	- Dry eye symptoms after inlay implantation in presbyopes are mostly mild to moderate[124-126]. - Less deep nerve damage is expected to occur in comparison with LASIK due to the absence of corneal ablation. - Stromal pocket may offer reduced dry eye symptomatology in comparison to corneal flap[124,125]. -No significant differences on symptom severity has been obtained between groups of different ages[126].
CLs	- Age has shown to be the main factor influencing CL retention rate[145]. - Presbyopic population might be more susceptible to dryness-related comfort problems, eventually leading to CLD and dropout[146].

	- Using a low rigidity CL on a daily disposable modality seems to be the most beneficial option for this group of patients[148,149]. - SCLs can be a good optical platform for multifocality and a protection mechanism for the ocular surface, with reduced impact on the tear film[150-153].
FLACS, Femtosecond Laser Assisted Cataract Surgery; DED, Dry Eye Disease; LASIK, Laser in Situ Keratomileusis; PRK, Photorefractive Keratectomy; LASEK, Laser Assisted Subepithelial Keratectomy; SMILE, Small Incision Lenticule Extraction; CLs, Contact Lenses.	