

Call to action: treating dry eye disease and setting the foundation for successful surgery



Kendall Donaldson, MD, MS, Gregory Parkhurst, MD, Bobby Saenz, OD, MS, Walter Whitley, OD, Blake Williamson, MD, John Hovanesian, MD

Dry eye disease (DED) is a common disease that can reduce the quality of life. Prevalence estimates vary but have been reported to be as high as 60% in some populations. Diagnosis is complicated by a multifactorial etiology and a disconnection between clinical signs and patient-reported symptomatology. Critically, preexisting DED can exacerbate postoperative dry eye symptoms and reduce patient satisfaction after ocular surgery, highlighting the value of thorough evaluation and screening for signs and symptoms of DED in preparation for ocular surgery. This article reviewed predisposing

and exacerbating factors for DED and presented an argument for the importance of adequately treating DED prior to surgery, from the perspective of both the patient and the provider. It briefly reviewed currently available methodologies and emphasized the utility of multimodal diagnosis and treatment algorithms to optimize outcomes and patient satisfaction.

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Dry eye disease (DED) is a common ocular surface disorder (OSD) that can cause discomfort, pain, and fluctuating vision, negatively affecting quality of life and work productivity.¹ The global definition of DED was revised in 2017 by the Tear Film and Ocular Surface Society Dry Eye Workshop II as "... a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, accompanied by ocular symptoms in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."² This definition highlights the multiple causes and risk factors for DED, including environmental triggers such as exposure to pollutants and allergies, nutritional deficiencies, contact lenses, meibomian gland dysfunction (MGD), and frequent digital screen use.^{1,3} Autoimmune diseases, including thyroid disease, rheumatoid arthritis, systemic lupus erythematosus, and Sjogren syndrome are associated with DED.^{1,4,5} In addition, glaucoma can be a risk factor for DED because of the need for a barrage of preserved topical treatments that inflame the vulnerable ocular surface.^{1,6}

The prevalence of DED varies depending on the definition of dry eye and population characteristics; however,

a range of approximately 5% to 60% has been reported in studies evaluating patients with symptoms, with or without signs of DED.^{7,8} Patient-reported symptoms and clinical signs of DED may not always be correlated. Symptoms such as ocular discomfort, fluctuating vision, and grittiness may not be reported by patients despite the detection of ocular surface dysfunction using clinical tests (ie, fluorescein staining, Schirmer test, tear breakup time [TBUT]).^{1,9,10} Indeed, the Prospective Health Assessment of Cataract Patients' Ocular Surface study evaluated the incidence of DED in patients undergoing cataract surgery.¹¹ The study demonstrated that 22.1% of patients were previously diagnosed with dry eye but were not on treatment and that although most patients did not report any symptoms of dry eye (stinging/burning/foreign body sensation), many of them had one or more signs of DED (TBUT ≤5 seconds and positive corneal staining).¹¹ This study and a study by Gupta et al. illustrated that DED is undertreated and underdiagnosed among patients presenting for cataract surgery.^{10,11} Similarly, there is a high prevalence of preoperative DED in patients presenting for corneal refractive surgery, with only a small proportion receiving

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From the Bascom Palmer Eye Institute, Plantation, Florida (Donaldson); Parkhurst NuVision, San Antonio, Texas (Parkhurst, Saenz); Virginia Eye Consultants, Norfolk, Virginia (Whitley); Williamson Eye Center, Baton Rouge, Louisiana (Williamson); Harvard Eye Associates, Laguna Hills, California (Hovanesian).

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Corresponding author: Kendall Donaldson, MD, MS, Bascom Palmer Eye Institute, 8100 Southwest 10th St, 3rd Floor, Plantation, FL 33324.

Email: kdonaldson@med.miami.edu.

treatment for DED.¹² In the Patient-Reported Outcomes With Laser In Situ Keratomileusis (PROWL)-1 and PROWL-2 studies, 45% and 56% of patients, respectively, had symptoms of DED with a mild, moderate, or severe ocular surface disease index (OSDI) score prior to laser in situ keratomileusis (LASIK) surgery.¹³ In addition, a recent study demonstrated that approximately 73% of patients presenting for refractive surgery had some evidence of meibomian gland atrophy, which is correlated with OSDI scores and DED symptoms.^{14,15} Preexisting untreated DED is a known risk factor for postsurgical dry eye symptoms and is a reason why some patients are dissatisfied with their postoperative results.^{16,17}

In this review, we focus on the importance of identifying DED and optimizing the ocular surface prior to ocular surgery to maximize postsurgical outcomes and patient satisfaction. This article was developed in accordance with Good Publication Practice (GPP3) guidelines.

IMPORTANCE OF ASSESSING DED PRIOR TO OCULAR SURGERY

Many patients presenting for ocular surgery have baseline preoperative DED. A comprehensive medical history, with an emphasis on any underlying illness or medication that might predispose patients to DED, is essential, together with identification of other risk factors (Table 1).^{1,6,18–20} Particular attention should be paid to the possibility of systemic diseases such as collagen vascular disease, rheumatoid arthritis, Graves disease and other thyroid disorders, Sjogren syndrome, or diabetes mellitus, which may also exacerbate or be a primary cause of DED. A thorough medication history, with an interest in antihistamines, tricyclic antidepressants, selective serotonin reuptake inhibitors, diuretics, and beta-blockers, can

reveal contributing underlying causes of dry eye.^{1,4,18,19} In addition, dry eye symptoms are more likely to be reported in women than in men and are prevalent and need to be evaluated in perimenopausal or postmenopausal female patients.^{21,22}

Dry eye symptoms may become more noticeable after ocular surgery, and patients may interpret this as a complication of the surgery if this preexisting condition is not diagnosed, discussed, and treated preoperatively. LASIK surgery has been shown to be safe and effective; however, postoperative dry eye is a frequent early complaint by patients.¹⁷ The PROWL-1 and PROWL-2 studies demonstrated that approximately 27% (PROWL-1 and PROWL-2) and 19.5% (PROWL-2) of patients developed dry eye symptoms at postoperative months 3 and 6, respectively. However, most of the patients in the study had baseline dry eye symptoms, and it is interesting that among the patients who had baseline OSDI scores worse than normal, approximately 59% (PROWL-1 and PROWL-2) and 65% (PROWL-2) had resolution of their dry eye symptoms at postoperative months 3 and 6, respectively.¹³ Patients were, therefore, 3.33 times more likely to have resolution of their preoperative DED than they were to develop new symptoms of dry eye at 6 months after LASIK (PROWL-2). Patient satisfaction score with the surgery was greater than 90% at months 3 and 6, with lower satisfaction associated with dry eye symptoms.¹³ In another study that evaluated patients with no baseline dry eye symptoms, only 0.8% of patients undergoing LASIK developed chronic dry eye 12 months postoperatively.²³ In another study that evaluated patient satisfaction after LASIK surgery, Price et al. demonstrated strong satisfaction with the corrective surgery for 3 years in patients who had previously worn contact lenses. The proportion of patients who had no dry eye symptoms decreased from 44% at baseline to 42% at

Table 1. Risk Factors Associated With Dry Eye Disease.^{1,6,18–20}

High evidence	Moderate evidence	Low evidence
Older age	Asian race	Cigarette smoking
Female sex	Medication (beta-blockers, diuretics, isotretinoin, selective serotonin reuptake inhibitors, and tricyclic antidepressants)	Hispanic ethnicity
Postmenopausal estrogen therapy	Diabetes mellitus	Medication (anticholinergics, antipsychotics, and anxiolytics)
Low dietary intake of omega-3 fatty acid	Human immunodeficiency virus/human T-cell lymphotropic virus infection	Alcohol use
Medication (antihistamines)	Systemic chemotherapy	Menopause
Connective tissue disease	Large-incision extracapsular cataract extraction and penetrating keratoplasty	Botulinum toxin injection
LASIK and refractive excimer laser surgery	Low humidity environments	Acne
Radiation therapy	Sarcoidosis	Gout
Hematopoietic stem cell transplantation	Ovarian dysfunction	Oral contraceptives
Vitamin A deficiency		Pregnancy
Parkinson disease (reduced blinking rate)		
Glaucoma and treatment		
Screen use		

year 1 postoperatively; however, the proportion of patients who had no dry eye symptoms increased at years 2 and 3 to 45% and 50%, respectively, after LASIK compared with preoperative levels.²⁴ In patients who continued to wear contact lenses, only 29% reported no feeling of dry eye at baseline and at year 3; thus, more patients had no dry eye with LASIK compared with contact lenses.²⁴ When comparing patients with and without DED prior to surgery, Toda et al. demonstrated that, despite no statistically significant differences in refractive outcomes and patient satisfaction in those with pre-LASIK DED and those without, patients with definite preoperative DED had significantly more dry eye symptoms at 3 months, 6 months, and 12 months post-LASIK compared with those without preoperative DED.²⁵ These studies show that it is not uncommon to evaluate and treat patients with preoperative dry eye symptoms with corneal refractive surgery. In fact, after having surgery, these patients typically have fewer dry eye symptoms than contact lens wearers and report higher satisfaction. If preoperative dry eye symptoms are present, treating the ocular surface prior to surgery is important. A retrospective study showed that dry eye symptoms were significantly lower in patients who were treated before, during, and after LASIK surgery, further highlighting the importance of managing the ocular surface.²⁶ Taken together, DED is common in preoperative patients, and it is important that patients with dry eye are identified and treated appropriately before proceeding with surgery to optimize visual outcomes and patient satisfaction.

Cataract surgery is commonly associated with favorable postoperative visual outcomes.²⁷ In a retrospective study, although visual outcomes after cataract surgery in patients with DED were satisfactory, preexisting keratopathy was the main reason for suboptimal visual outcomes.²⁸ Thus, achieving the desired refractive target is highly correlated with higher levels of patient satisfaction.²⁹ A healthy/stable tear film is needed for accurate intraocular lens (IOL) calculations including axial length, anterior chamber depth, and keratometry magnitude and axis.^{7,16} Incorrect IOL power calculations can result from inaccurate corneal power measurements, which ultimately can lead to unsatisfactory outcomes after cataract surgery.⁷ As demonstrated by Epitropoulos et al., patients with DED can have IOL power calculations that vary as much as 0.5 D between visits, highlighting that treatment of dry eye preoperatively is crucial for achieving the best refractive results.³⁰ In a study by Hovanesian et al., preoperative treatment of DED improved the accuracy of anterior corneal power measurements, resulting in better postoperative outcomes.⁷ Similarly, preoperative and postoperative treatment with cyclosporin 0.05% was shown to alleviate dry eye signs and improve visual quality and patient satisfaction after multifocal IOL implantation.³¹ It is important to recognize that aberrations induced by DED compromise visual quality through the more complex optics associated with multifocal technology.³¹ Through the years, patient expectations from their cataract surgery have been high, and premium

lens technology has increased the bar to new levels through higher patient costs.^{32,33} Most cataract patients (even if asymptomatic) likely have significant tear film disturbances that can affect their preoperative measurements and postoperative satisfaction with cataract surgery. If not addressed, tear film problems can lead to decreased predictability in IOL power selection, slow down healing and visual recovery, and reduce postoperative satisfaction and quality of vision. The degree of dissatisfaction is magnified in refractive cataract surgery with a premium IOL.³⁴ By routinely screening for OSDs—even in the absence of complaints—surgeons will be able to improve outcomes with premium IOLs.³⁴

The American Academy of Ophthalmology published their Dry Eye Syndrome Preferred Practice Pattern in 2018, recommending that DED should be evaluated and managed prior to LASIK or cataract surgery.¹⁸ In 2019, the ASCRS Cornea Clinical Committee outlined a consensus-based practical diagnostic algorithm for efficiently evaluating the corneal surface, to assist surgeons with the diagnosis and treatment of any visually significant OSD prior to refractive surgery.³ Addressing DED proactively is essential, despite adding time to the preoperative workup and occasionally delaying the actual surgery for optimization of the ocular surface. By not diagnosing and treating DED prior to surgery, the risk for patient dissatisfaction is increased because of potential errors in the power and axis of the IOL and postoperative discomfort and issues with fluctuations in vision and overall poor-quality vision.

ASSESSMENT AND MANAGEMENT

Assessing DED

The ASCRS Guidelines recommend implementation of a consensus-based algorithm for the preoperative diagnosis of DED, with an emphasis and reliance on objective, point-of-care tests performed by technicians, which can reduce surgeon chair time while increasing the preoperative diagnosis of potentially visually significant OSD.³ The algorithm was designed primarily for lens-based and corneal-based refractive surgeries, with cataract and LASIK being the most common procedures.³ DED assessment usually begins with a questionnaire to assess the patient's symptoms. The 2 most common questionnaires are the OSDI and the Standard Patient Evaluation of Eye Dryness (SPEED).^{3,16} The ASCRS Guidelines recommend the use of a modified SPEED questionnaire in patients with preoperative OSD (SPEED II questionnaire). Although symptom evaluation is an integral aspect of the algorithm, many patients with DED perform normally in traditional DED questionnaires, and symptoms and signs have been shown to correlate poorly.³ Therefore, all surgical patients should also be assessed for signs of OSD.

Symptom screening should be followed by noninvasive objective evaluation of OSD signs, which can be performed by a technician. These tests evaluate refractive and IOL measurements and signs of OSD. The refractive and IOL measurements include noncontact optical biometry,

keratometry, tomography, topography, and aberrometry. There are a variety of point-of-care diagnostic tests for OSD, and the recommended essential screening tests by the ASCRS Cornea Clinical Committee are the tear osmolarity and inflammation (matrix metalloproteinase-9) tests.³ Tear osmolarity greater than 308 mOsmol/L or a difference greater than 8 mOsmol/L between eyes is considered abnormal.¹⁶ Matrix metalloproteinase-9 is an inflammatory response enzyme that is involved in the breakdown of the ocular surface, and levels ≥ 40 ng/mL are considered abnormal.^{3,16} If any of the essential screening tests show abnormalities, additional diagnostic testing can be pursued, with noninvasive tests preferred by the ASCRS Cornea Clinical Committee to minimize disruption to the tear film. These noninvasive adjunctive tests can be helpful in determining OSD and the subtype of DED.³ Meibomian gland imaging can be used to identify MGD, which can lead to tear film irregularities and result in inaccurate IOL power calculations.^{3,16} Topography is also another valuable tool that can be used to evaluate noninvasive tear breakup time, corneal astigmatism, and surface regularity. Ocular scatter index, measured using optical quality analysis devices (HD Analyzer, Visiometrics SL), can provide useful measures of visual quality, ocular surface, and tear film.³ Using the terms Look, Lift, Pull, and Push, the ASCRS Cornea Clinical Committee emphasized the need for a thorough clinical examination of the ocular surface—regardless of the results of the screening tests—to confirm the type, severity, and visual effect of OSD in preoperative patients. The final phase of the algorithm involves corneal staining and TBUT to help distinguish between visually significant OSD and nonvisually significant OSD.³ Visually significant OSD refers to the implication of

preoperative and postoperative effect on visual quality and the potential of postoperative infections such as endophthalmitis. To reduce the risk for these postoperative effects, prior to any preoperative refractive measurements and surgery, treatment is needed until the visually significant OSD is converted to nonvisually significant OSD.³

Managing DED

Treatment goals include the reduction of inflammation and the restoration of tear film homeostasis, which, in turn, would optimize preoperative measurements, maximize postoperative outcomes, and improve patient satisfaction.³ Several treatment options are available for DED regardless of whether patients are undergoing surgery or not. To reach treatment goals, a combination of these options may be the best approach. Treatments such as procedural/devices, anti-inflammatory medications, supplements, and lifestyle modifications can be considered.¹⁶ Figures 1 to 3 show various preoperative treatments of dry eye and the postoperative outcomes.

Thermal pulsation treatment can be considered for patients with MGD to relieve gland obstructions and restore meibomian gland function.^{3,16} A pilot study by Matossian evaluated thermal pulsation in patients with MGD who were undergoing cataract surgery and found that thermal pulsation treatment prior to cataract surgery significantly changed ΔK (difference in horizontal and vertical keratometry values) compared with prethermal pulsation, potentially resulting in a change in the planned magnitude or axis of astigmatism correction. Postoperatively, 60% of eyes had no deviation from refractive target.³⁵ Thermal pulsation was also shown to improve not only gland scores but also patient-reported outcomes up to 9 months

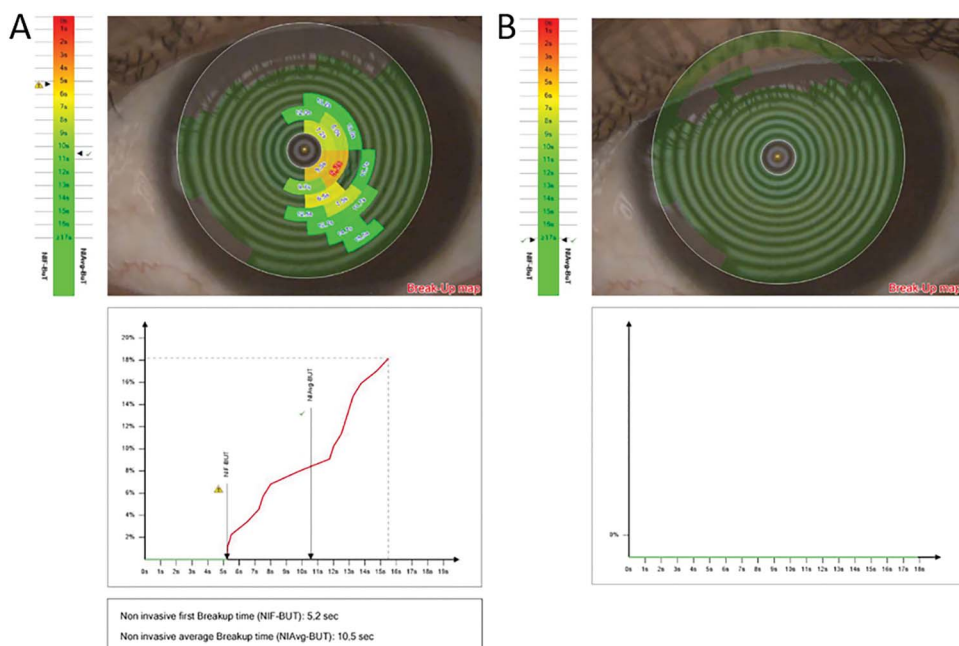


Figure 1. (A) Noninvasive tear breakup time of a preoperative refractive surgery patient before (A) and after (B) an open-eye wearable thermal energy therapy. After dry eye treatment and LASIK, this patient reported no dry eye symptoms 3 months postoperatively.

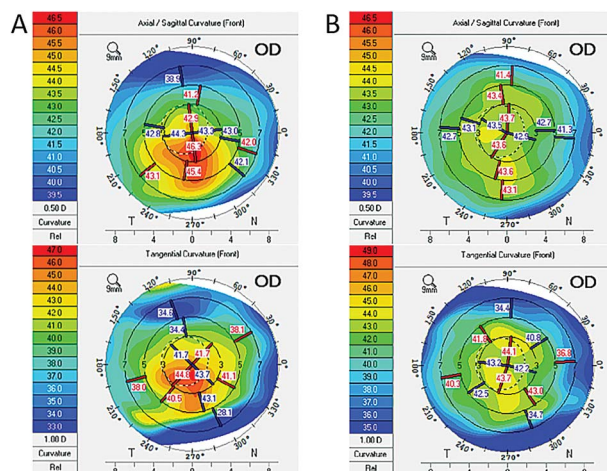


Figure 2. Cataract consultation of a patient with pretreatment corneal tomography (A) and was treated with cyclosporine, loteprednol, and vector thermal pulsation. Six weeks later (B), a significantly improved corneal tomography of the same patient who underwent successful laser refractive cataract surgery with multifocal IOLs was noted.

posttreatment,³⁶ with sustained improvement in dry eye symptoms at 3 years posttreatment.³⁷ Another option is blepharoxfoliation, which is the rigorous debridement of the lid margin using a rotary brush, such as the BlephEx treatment.³ Controlling inflammation should be considered, with the use of topical steroids and anti-inflammatory drugs such as cyclosporin A and lifitegrast, respectively, which are approved in the United States and Europe.³ Other medications include diquafosol ophthalmic solution and rebamipide ophthalmic suspension 2%, which are approved in Japan.^{3,38} A recent prospective, open-label study by Hovanesian et al. demonstrated that lifitegrast 5% significantly improved the accuracy of preoperative corneal surface measurement in patients with confirmed dry eye who were scheduled for cataract surgery and significantly reduced dry eye symptoms (SPEED scores). In addition, the ocular surface benefits were maintained for 56 days postoperatively, demonstrating positive postoperative outcomes.⁷ Dietary intake of omega-3 fatty acids, linoleic acid, and gamma-linolenic acid has also been suggested to be beneficial in treating the signs and symptoms of DED.^{3,19,39} Lifestyle changes, such as reducing or interrupting digital screen use and lubrication with preservative-free artificial tears to improve corneal staining are also recommended treatments for patients with DED.³ Additional treatments that may be effective in improving signs and symptoms of DED are currently in clinical trials. For example, results from a phase 2a study on recombinant human nerve growth factor suggest that it is safe and effective in improving signs and symptoms of DED; however, randomized clinical trials are ongoing.⁴⁰

Patients can be reevaluated for repeat biometry 4 to 6 weeks after initiating DED treatment to determine whether to proceed with surgery. Optimizing the ocular

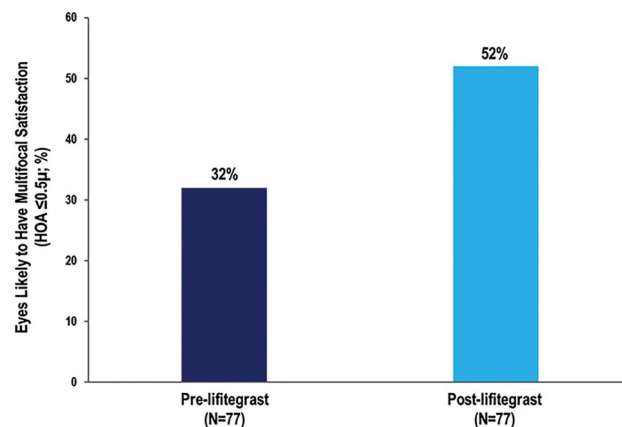


Figure 3. HOAs $\leq 0.5 \mu$ threshold identifying 25 eyes (32%) from 77 patients as candidates for a multifocal lens before lifitegrast vs 40 eyes (52%) after the first course of preoperative lifitegrast.⁷ HOA = higher-order aberration

surface for reproducible keratometry and topography is needed to ensure maximal postoperative refractive outcomes.¹⁶ In addition, just as managing DED prior to surgery is important for a positive postoperative experience for the patient, so are perioperative, intraoperative, and postoperative management considerations. Several of the medicinal drops given to the patient on the day of surgery may contain preservatives (eg, benzalkonium) affecting the epithelium; therefore, alternative drops with less toxic preservatives may be considered in vulnerable patients. For routine ocular surgery, the eyelids are fixated with a speculum during the procedure, and frequent re-wetting with a balanced solution is required to reduce prolonged exposure during the surgical procedure.³ Postoperatively, eyedrop regimens, preferably without preservatives, are recommended. Alternatively, antibiotics and steroids administered at the conclusion of the surgical procedure in an intracameral, subconjunctival, or sub-Tenon approach may limit the toxicity associated with postoperative topical medications.³

CONCLUSION

In conclusion, the identification of underlying DED is an important facet of both preoperative and postoperative care to ensure that the ocular surface is optimized and to achieve the best possible outcome for the patient. An unevenly distributed tear film and/or a reduction in the quantity or quality of tears (eg, increased osmolarity) can affect visual acuity and lead to patient dissatisfaction with surgery, although the symptoms they experience are likely because of undiagnosed and untreated DED. The goal of identifying and managing DED is to ensure that the very best preoperative data are acquired to help optimize the patient's postoperative refractive outcome while ensuring they remain comfortable without exacerbating any underlying DED. Ultimately, this results in the best surgical experience, leading to the highest levels of both patient and surgeon satisfaction.

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First author:

Kendall Donaldson, MD, MS

Bascom Palmer Eye Institute, Plantation, Florida

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