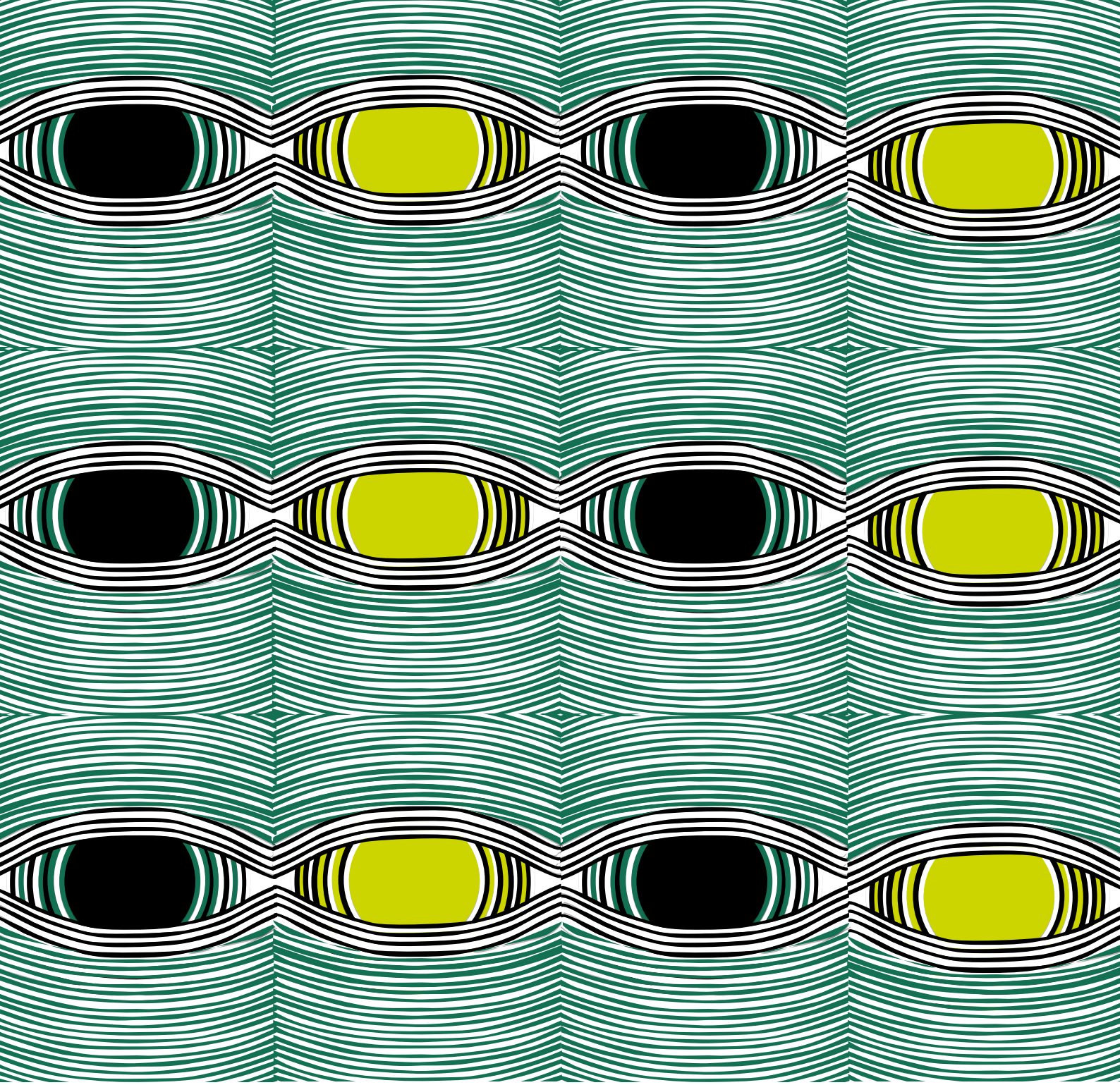

Ocular Surface Disease Diagnosis & Management:

Putting current and emerging treatment options into practice

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The Importance of Treating OSD in Cataract Refractive Practice

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Prevalence of ocular surface disease in the refractive clinic

Ocular surface disease (OSD) is common in patients presenting for cataract surgery as the risk of OSD increases with age.[1] In practice, more than half of patients undergoing cataract surgery have dry eye symptoms,[2] and meibomian gland dysfunction (MGD) is diagnosed in the majority of patients with dry eye disease (DED), and more than half of refractive surgery candidates.[4,5] Women and people of Asian ethnicity are also at increased risk of developing OSD.[3]

Asymptomatic patients and the risk of dry eye disease with surgery

Importantly, many routine cataract cases may be asymptomatic for dry eye, yet have abnormal tear osmolarity or central corneal staining (Figure 1).[2] There is ongoing exploration into the neurosensorial factors associated with DED, with evidence suggesting that asymptomatic patients may have higher tolerance of pain, leading to under-reporting of discomfort.[6] Preoperative examination and assessment of tear osmolarity is a key step in understanding the risk of DED and the severity of disease in symptomatic patients.[7] Hyperosmolarity has been identified as the key mechanism that initiates inflammation of the ocular surface in dry eye disease and thus correlates closely with DED severity.[7,8]

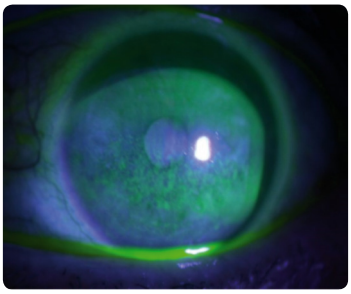


Figure 1. Corneal staining in an eye otherwise asymptomatic for dry eye disease.

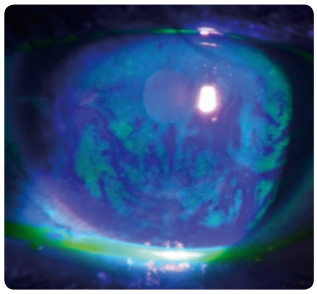


Figure 2. Tear film instability and decreased tear break-up time in a post-surgery eye.

In practice, recognising that patients may have subclinical OSD is important because surgery is likely to expose dry eye symptoms that were unidentified in preoperative examination and exacerbate asymptomatic DED by increasing tear film instability (Figure 2).[9,10] Surgical trauma can increase the production of free radicals, proteolytic enzymes and inflammatory cytokines that can alter the ocular surface,[11,12] and is linked to neuropathy associated with the corneal incision during cataract surgery.

The impact of ocular surface disease on preoperative calculations

Awareness of OSD in cataract surgery candidates is critical to optimising postoperative outcomes, because the tear film is an important component of ocular power. In eyes with a healthy tear film there may be a minimal power difference of 0.1D between blinks. In people with an unstable tear film, there may be variation of more than 1.0D, which can correspond to an error of the same magnitude in lens power calculation and thus significantly impact vision.[13] Dry eye symptoms also affect the repeatability and accuracy of keratometry and topography. Hyperosmolar eyes have been associated with large differences in K cylinder measurements (17% have 1.0D difference) and changes in intraocular lens (IOL) power (10% had > 0.5D change),[13] which can have clinically meaningful impact on the accurate diagnosis and treatment of astigmatism necessary to achieve optimal outcomes with multifocal lenses.

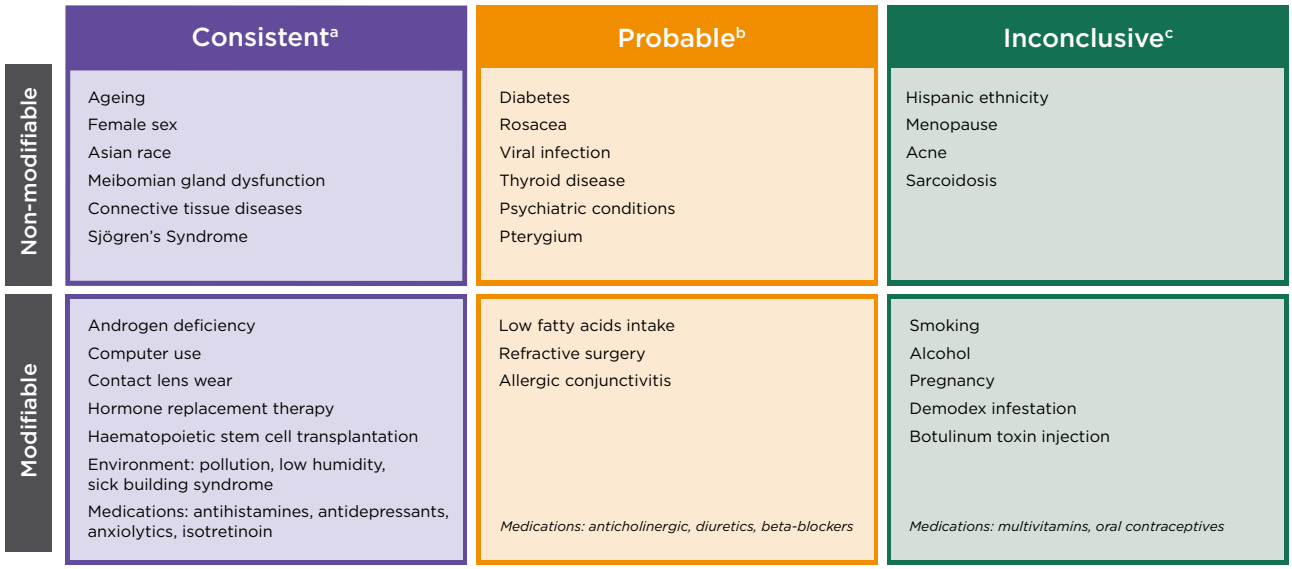
Because an unstable tear film leads to inaccurate or non-repeatable preoperative measurements, robust assessment is recommended in all patients who are candidates for cataract surgery.[14] However, in routine practice, there remains room for improvement in awareness of, and testing for, OSD. The 2018 European Society of Cataract and Refractive Surgeons (ESCRS) Clinical Survey data on ocular surface diseases highlighted that fewer than half of physicians are examining the ocular surface before cataract surgery in all of their patients, and around 20% are only examining when the patient presents with dry eye symptoms.[15] This is despite 90% of respondents agreeing that even mild-to-moderate DED significantly impacts preoperative keratometry and IOL calculations.[15]

Improving screening and diagnosis in practice

There is a clear need to encourage preoperative assessment of the risk of DED development or worsening in all patients as a routine approach to cataract surgery. In the majority of cases (80%+) presenting for refractive surgery, only an estimated two minutes is required to assess the ocular surface, and only five minutes in patients who are at greater risk of DED or who have existing symptoms.[14] Preoperative diagnosis is essential to anticipate the possible effects of dry eye after surgery, to warn patients of the possible emergence of symptoms and to institute appropriate treatment. Patient symptom assessment and slit-lamp examination are among the most useful diagnostic tools; in selected cases an osmolarity test can identify patients susceptible to worsening DED after surgery and help avoid residual refractive errors. Use of dry eye questionnaires and evaluation of medical history can help identify patients at risk. Attention to current systemic illnesses and to concomitant medical treatment is also key, because anxiolytics, antidepressants and antihistamines are commonly prescribed and are recognised modifiable risk factors for DED (Figure 3).

Unresolved ocular surface disease and post-surgery outcomes

Patient expectations from cataract surgery are higher than ever and most physicians expect DED to contribute to patient satisfaction after a refractive procedure.[15] Unresolved OSD is likely to lead to suboptimal postoperative vision quality and quantity, because preoperative calculations will be inaccurate.[13,14] Persistent DED will contribute to vision instability, fluctuation, glare and fatigue,[15] which will drive both patient and physician dissatisfaction. Surgery in patients with untreated OSD may also be more prone to result in infection.[5]



[a]Implies the existence of at least one adequately powered and otherwise well-conducted study published in a peer-reviewed journal, along with the existence of a plausible biological rationale and corroborating basic research or clinical data; [b]Implies the existence of either inconclusive information from peer-reviewed publications or inconclusive or limited information to support the association, but either not published or published somewhere other than in a peer-reviewed journal; [c]Implies either directly conflicting information in peer-reviewed publications, or inconclusive information but with some basis for a biological rationale.

Figure 3. Modifiable and non-modifiable risk factors for DED.

Adapted from Stapleton F, et al. Ocul Surf 2017;15:334–65.

> ***Importantly, many routine cataract cases may be asymptomatic for dry eye, yet have abnormal tear osmolarity or central corneal staining***

Summary

It is therefore important to detect, diagnose and treat OSD prior to surgery. The benefits of pretreating MGD on keratometry, prior to cataract surgery, have been demonstrated: 88% of patients with well-managed MGD were within 0.25D of refractive target and 92% were within 0.5D.[13] Effective, early management of OSD will improve pre-surgery assessments, increase accuracy of IOL power calculations and help reduce complications associated with surgery. Management of OSD in the pre-, peri- and postoperative phases of cataract surgery will contribute to more stable vision and greater patient satisfaction.

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Making Treatment Decisions For Dry Eye Disease

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The challenges of ocular surface disease in refractive surgery

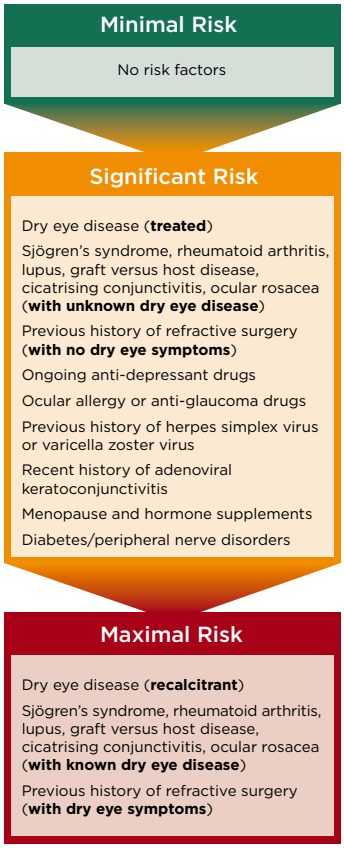
Unresolved ocular surface disease (OSD) represents a major risk factor for suboptimal outcomes in refractive surgery.[1] Untreated preoperative dry eye disease (DED) and meibomian gland dysfunction (MGD) can impact the accuracy of refractive calculations and contribute to poor vision outcomes.[1] Existing DED, both asymptomatic and symptomatic, can be exacerbated during surgery and lead to postoperative patient dissatisfaction with their cataract procedure.[1] Untreated MGD also increases the risk of infection during and post-procedure.[2]

Given the relatively common incidence of OSD in patients presenting for cataract surgery – approximately half have DED symptoms and half of these people have symptomatic MGD – an effective management strategy for OSD is vital.[1,3–5]

Effective stratification of dry eye disease risk

In practice, the foundations of management are in accurate risk assessment and stratification, and in accurate diagnosis. These steps are particularly important considering that many patients may have asymptomatic OSD. It is estimated that the prevalence of asymptomatic MGD may be much greater than that of symptomatic dysfunction,[1,5] and that only a quarter of people with subclinical DED experience dry eyes.[6] There is a paucity of consensus and clear direction on how physicians should stratify, diagnose and work up cases of OSD prior to cataract surgery.

A practical approach to stratification in the pre-refractive surgery setting could identify patients at minimal, significant or maximal risk of OSD (Figure 4). A common factor associated with significant risk of underlying, symptomatic or postoperative DED is the use of concomitant medication for depression, menopause or hormonal conditions and intraocular pressure-lowering drugs and anti-inflammatory medication in patients with glaucoma. Existing DED that is currently being managed remains at risk of being exacerbated during surgery. Patients with certain autoimmune conditions (Sjögren's syndrome, rheumatoid arthritis and lupus) are also at elevated risk of DED. Patients with these autoimmune conditions, or with existing cicatrising conjunctivitis or ocular rosacea, in conjunction with current DED undergoing management are at the greatest risk of OSD-related complications during refractive surgery. The highest risk category also includes those with recalcitrant and treatment refractory DED or those who have previously had refractive surgery and have ongoing DED. The OSD diagnostic procedure in the refractive clinic required to make this stratification is not time-intensive in most patients and, given the potential impact of untreated disease on surgical outcomes, this approach is recommended in all preoperative candidates.[1]

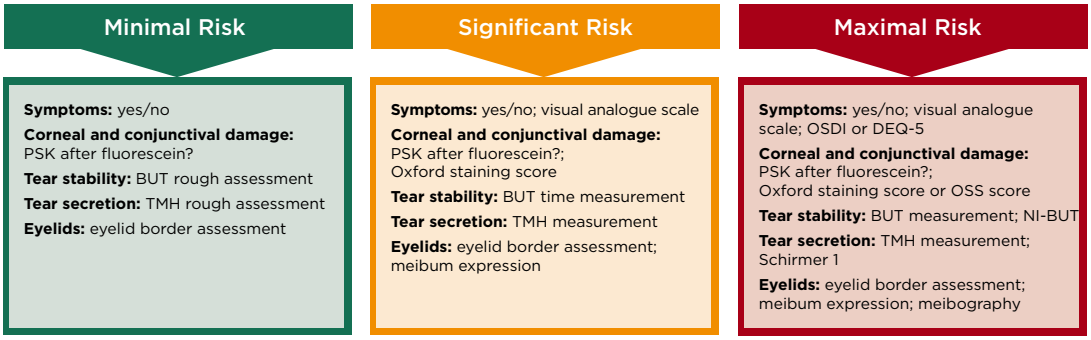


Adapted from Labetoulle M, et al. Journal français d'ophtalmologie 2019;42:907–12.

Figure 4. DED risk stratification prior to refractive surgery.

Optimising examination and diagnosis

Once the likely risk of DED has been determined, an optimised approach to examination and diagnosis can be followed (Figure 4). For patients judged to be at the lowest risk, an appropriate examination would include vital staining, approximation of tear secretion and stability, as well as assessment of eyelid inflammation, crusting and obstruction. Examination of patients at more significant risk of DED would also include a scoring scale for fluorescein staining, more accurate measurements of tear properties and more thorough assessment of the eyelids, including meibum expression to determine the presence of MGD. In the highest risk patients, quantification of symptoms should be performed using a validated questionnaire and indexing system (for example, the ocular surface disease index [OSDI]).[1] Patients with specific medical histories (previous surgery, autoimmune DED or



BUT, break-up time; DEQ-5, dry eye questionnaire; OSDI, ocular surface disease index questionnaire; OSS, ocular surface score; NI-BUT, non-invasive break-up time; PSK, punctate superficial keratitis; TMH, tear meniscus height.

Figure 5. Appropriate examination protocols for patients stratified by risk of DED.

Adapted from Labetoulle M, et al. Journal français d'ophtalmologie 2019;42:907–12.

graft versus host disease) may require more comprehensive investigation, such as meibography or a Schirmer I test.

Treatment decisions for preoperative ocular surface disease

Management strategies for OSD are driven by disease severity. In routine practice, this approach is complicated by the lack of consensus defining stages of DED severity. A simplified, practical assessment of disease state has been proposed to classify patients as having 'severe' DED (OSDI ≥33 and corneal fluorescein staining [CFS] ≥3/5) or not having severe DED.[7] There is no universally accepted delineation between a 'mild' and a 'moderate' DED patient, and consequently physicians are encouraged to use clinical experience and judgment to optimally manage OSD.

A practical approach to treatment (Figure 5) should start with patient education and modifiable lifestyle factors, along with assessment of concomitant medication that can cause eye dryness or inflammation. Additional therapy will typically involve artifical tear eye drops, which should be preservative-free to avoid complications or corneal toxicity,[8] and then be tailored to address the underlying OSD. Where inflammation is worsening a patient's DED, short-term preservative-free corticosteroids may be used; in moderate cases lifitegrast may provide benefit and cyclosporine has been associated with good outcomes in more severe moderate disease.[1] Patients frequently have MGD as a component of their DED, and this is typically treated with optimised lid hygiene, warm compresses and antibiotics.[1,2] The potential role of MGD in DED should not be underestimated: the 2018 European Society of Cataract and Refractive Surgeons (ESCRS) Clinical Survey data on ocular surface diseases revealed that over half of physcians believed that MGD was a component of ≤40% of their patients' DED.[9] While the prevalence of MGD varies markedly between different age groups and ethnicities, it is the most common cause of evaporative DED, and may play a role in aqueous DED also.[10] A practical recommendation is never to leave any diagnosed MGD untreated in the management of OSD, and especially prior to refractive surgery. Progression to more invasive procedures to treat DED should be based on the physician's evaluation of the individual case, with appropriate evaluation of the risk-benefit profile for that patient.

In cases of severe OSD, it may be advisable to delay surgery until symptoms are well managed and a patient no longer qualifies as having severe DED.[1]

Practical considerations for managing dry eye disease with refractive surgery

Cataract surgery increases the risk of postoperative DED and MGD via several mechanisms: pupillary dilation, antiseptic application and the nature of the incision and phacoemulsification. Consequent postoperative OSD can persist for three months or longer, and therefore it is critical to manage existing disease preoperatively and manage risk of disease throughout the refractive procedure.[1]

Prior to surgery, drug-associated corneal toxicity can be mitigated by avoiding nonsteroidal anti-inflammatory drugs (NSAIDs) and benzalkonium chloride (BAK)-containing eye drops. Antibiotics should be substituted for antiseptics, which are less toxic to the corneal epithelium. Bacterial cleaning, to reduce the risk of infection, can be effectively performed with antiseptics and povidone-iodine cleansing. Immediately before surgery, intracameral injection of anaesthetics and mydriatics, rather than an eye drop regimen, can significantly reduce short-term ocular surface damage. Surgery can be optimised to reduce risk of DED by avoiding large incisions, limiting microscope light intensity and exposure and not using an aspirating speculum. Immediately post-surgery, applying viscoelastic substances, in place of immediate steroids and antibiotics, may provide benefit. In terms of lens selection, caution is advised with multifocal lenses due to the potential inaccuracy of refractive power calculations in patients with more severe DED. Following surgery, continued avoidance of BAK-containing agents and NSAIDs is advisable, as is limiting exposure to epitheliotoxic antibiotics.

Increasing the frequency of follow-up, post-surgery, can help determine patient progress and assess any need for adjustments to the treatment strategy. Short-term, preservative-free topical steroids may be prescribed to patients who experience post-procedure inflammation. For patients who develop DED immediately following surgery, symptom control may be achieved with topical cyclosporine.[1]

Summary

Treatment of existing OSD is crucial prior to refractive surgery. This can be facilitated with accurate risk stratification, appropriate examination and optimised management. Simple practical considerations during surgery and in the follow-up period can further minimise the impact of DED. Routine monitoring and evaluation for OSD are encouraged for all patients who are undergoing cataract procedures.

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How to Decide When to Delay Surgery in Patients With OSD

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Ocular surface disease and surgery postponement

In routine practice, many people presenting for cataract and refractive surgery have some degree of ocular surface disease (OSD).[1-4] Physicians are encouraged to investigate, diagnose and comprehensively manage OSD before surgery,[1,5] in order to increase the accuracy of pre-surgery measurement, reduce exacerbation of dry eye post-surgery and improve patient satisfaction with their refractive procedure.[1] In some cases, when a patient has severe unresolved OSD, it is advisable to postpone surgery until dry eye disease (DED) and any meibomian gland dysfunction (MGD) are well-managed.[1]

Considerations in candidates with dry eyes

There are several situations that require the physician to consider delaying cataract and refractive surgery (Figure 7). People with eyes demonstrating extensive corneal staining, which is indicative of persistent dry eye symptoms, impaired tear-film production or rapid tear-film breakup, represent one of the most common groups of patients in whom delay of invasive procedures should be considered. Similarly, patients with corneal damage should be carefully monitored and managed until they are more suitable for surgery, otherwise severe complications could occur. When considering surgery in patients with dry eye symptoms, environmental factors should also be assessed – dryness, inflammation and allergic reactions may all be exacerbated in late spring and summer. Surgery can be undertaken following control of DED symptoms, typically by avoiding medication that can contribute to dryness (non-steroidal anti-inflammatory drugs [NSAIDs] and benzalkonium chloride-containing eye drops) and using preservative-free artificial tears.[6,7]

> *"The consequences of proceeding with surgery in a patient with severe, unresolved OSD include exacerbation of existing symptoms and suboptimal satisfaction outcomes*

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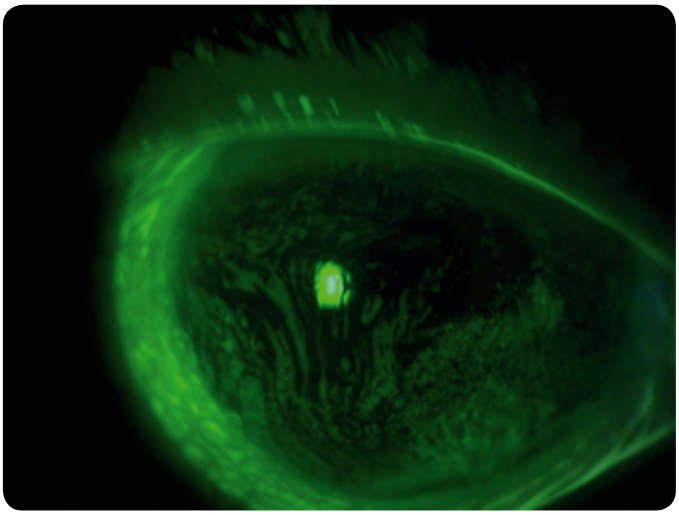

Figure 6. Severe dry eye in a patient with Sjögren's syndrome, with corneal staining and major tear film instability.

Risks in patients with autoimmune conditions

Surgery in patients with Sjögren's syndrome should be considered as high risk; these patients are prone to severe DED and tear-film instability (Figure 6). Treatment prior to surgery should typically include preservative-free tear substitutes and, in more severe cases, topical cyclosporine to improve tear production and decrease dry eye symptoms. Sjögren's syndrome may present concomitant with rheumatoid arthritis, which is also independently associated with dry eyes and should be considered as a risk factor for complications with refractive surgery.[8]

Neurotrophic factors that affect surgery

Nerve damage, for example from persistent neurotrophic keratopathy or postoperative ulceration, also represents a decision point in the pathway to surgery. If surgery is undertaken in a sub-optimally managed eye, there is risk of worsening damage to the trigeminal nerve, reducing corneal sensitivity and potentially resulting in corneal melting.

Meibomian gland dysfunction and infection risk

Delay of surgery should be considered in patients with active, unresolved MGD, primarily owing to the increased risk of bacterial infection during the surgery. Meibum secreted from obstructed meibomian glands can contain high densities of bacteria such as *Staphylococcus epidermidis, S. aureus* and *Propionibacterium acnes* (Figure 8). Prior to surgery, lid hygiene should be improved and maintained, and topical antibiotic treatment initiated, as appropriate. A warm compress may also help improve preoperative MGD, in conjunction with established management strategies.[9] Treatment with LipiFlow® (Johnson & Johnson Vision) or a similar procedure can improve meibomian gland activity and both reduce microorganism build-up and alleviate dry eye symptoms.

Glaucoma treatment and refractive surgery

Postponement of glaucoma surgery is advised in patients with uncontrolled inflammation. Long-term medical therapy for glaucoma often includes several classes of eye drops (prostaglandin analogues, beta-blockers, carbonic

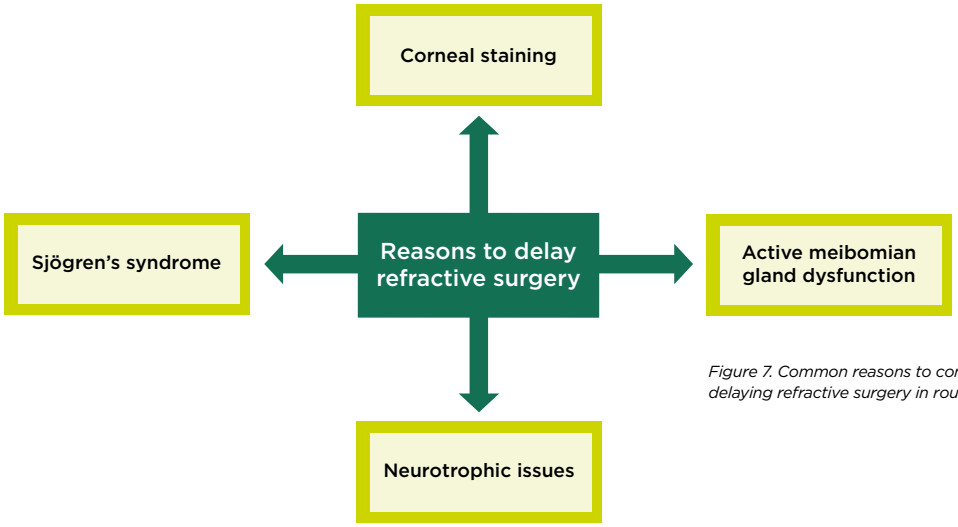

Figure 7. Common reasons to consider delaying refractive surgery in routine practice.

Images courtesy of Prof C. Baudouin

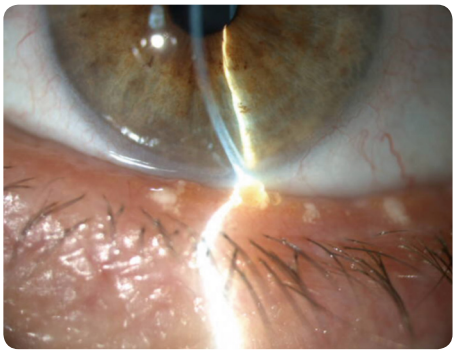

Figure 8. Obstructive meibomian gland dysfunction can elevate the risk of postoperative infection.

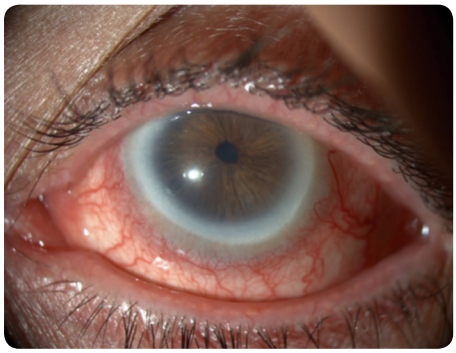

Figure 9. Severe inflammation related to long-term glaucoma treatment. Inflammation will increase the risk of postoperative fibrosis and should be treated before surgery.

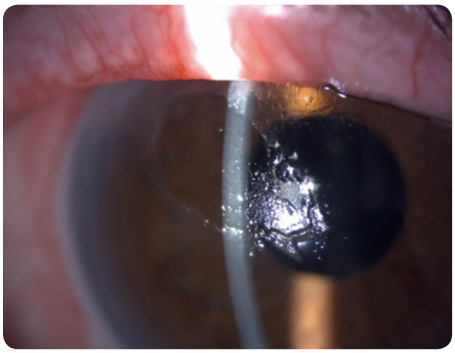

Figure 10. Postoperative corneal ulcer in a dry eye patient. The risk of corneal melting and perforation is particularly high in patients with rheumatoid arthritis or Sjögren's syndrome.

anhydrase inhibitors and alpha agonists) that can result in an ocular surface that is dry, inflamed and allergic (Figure 9). It is recommended that, at least one month prior to surgery, efforts are made to improve the ocular surface, for example by ceasing the use of any pro-inflammatory drugs.

Refractive surgery with unresolved ocular surface disease

The consequences of proceeding with surgery in a patient with severe, unresolved OSD include exacerbation of existing symptoms and suboptimal satisfaction outcomes.[1] In some patients, there is risk of ulceration or corneal melting, which may progress to corneal perforation (Figure 10); this complication is more likely in cases of severe immune-mediated OSD associated with Sjögren's syndrome or rheumatoid arthritis.[10]

Summary

All patients can benefit from preoperative ocular surface preparation, and there is a clear case for surface optimisation in people with DED, MGD and conjunctival inflammation. Physicians should be aware of the degree of unresolved OSD and feel confident and validated in any decision to delay a surgery to allow more time for preparation of the ocular surface. Thorough preoperative preparation with timely surgery increases the likelihood of avoiding complications, improving outcomes and increasing patient satisfaction.

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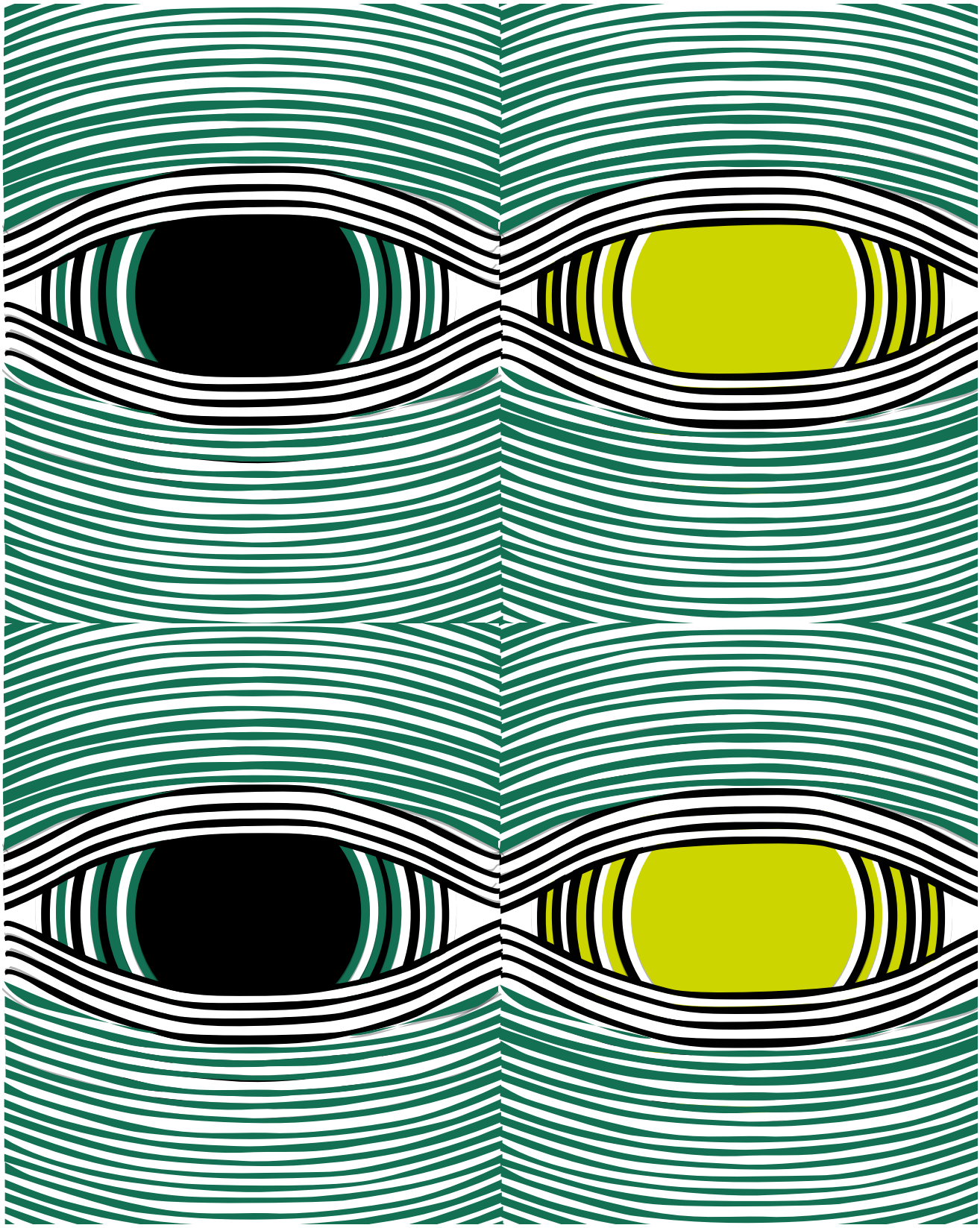

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