REVIEW/UPDATE

Preoperative optimization of ocular surface disease before cataract surgery

Jasmine Chuang, MB BS, Kendrick Co Shih, MB BS, MRes (Med), MRCSEd, Tommy C. Chan, MB BS, FRCSEd, Kelvin H. Wan, MBChB, MRCSEd, Vishal Jhanji, MD, FRCOphth, Louis Tong, MD, PhD, FRCSEd

An impaired ocular surface adversely affects preoperative planning for cataract surgery, including intraocular lens (IOL) calculations, toric IOL axis and magnitude estimates, keratometry, and topography measurements. It also increases surgical difficulty. We performed a review to evaluate the connection between cataract surgery and dry eye and to determine the best management for these patients. Of the 16 papers included in this review, 6 were randomized controlled trials. Cataract surgery was shown to worsen ocular parameters and aggravate dry-eye disease. Physicians should recognize and aggressively treat cataract patients with poor prognostic factors and/or with existing dry-eye disease. Increased incision extent, operation time, irrigation, and microscopic-light exposure time decreased the tear breakup time and mean goblet cell density. Postoperatively, the use of eyedrops was associated with worsening of goblet cell density; hence, these medications should be tapered off when no longer needed.

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Cataract surgery is the most common ophthalmic surgery performed worldwide, and approximately 50% of patients having this procedure have dry-eye disease.[1] Cataract surgery has been shown to worsen or cause dry-eye disease.[2–5] There are several hypotheses as to the mechanism of how cataract surgery leads to dry eye. These include the use of topical eyedrops with or without preservatives, exposure to the operating microscope light, intraoperative sterilization of the surgical field with povidone–iodine solution, transection and denervation of the corneal nerves by corneal incisions, vigorous irrigation intraoperatively, damage to the corneal epithelium, elevation of inflammatory markers from ocular surface damage, and loss of goblet cell density.[5–10]

Although most patients with dry eye are asymptomatic, 87% of cataract surgery patients with dry eye become symptomatic after surgery, with 50% having evidence of ocular surface damage on corneal staining.[2] An impaired ocular surface might also adversely affect preoperative planning, including intraocular lens (IOL) calculations, toric IOL axis and magnitude estimates, keratometry and topography measurements, and increased surgical difficulty. In addition, dry eye will impair healing and visual recovery and thus adversely affect postoperative outcome. In a study of patients having cataract surgery, 35% of patient dissatisfaction was related to dry eye after surgery.[11] Although cataract surgery is one of the most successful operations in ophthalmology, postoperative exacerbation or development of dry eye adversely affects the outcome and quality of life in cataract patients. Therefore, it is imperative for ophthalmologists to recognize, diagnose, and manage dry-eye disease specifically for these patients.

With a variety of treatment options available for dry eye, the International Task Force Guidelines for Dry Eye recommends that treatment be stratified by severity,[12] whereas the Asia Dry Eye Society developed a new strategy called tear film-oriented therapy.[13] The tear film-oriented therapy strategy targets the type of dry eye the patient has. For example, if the patient has mucin-deficient dry eye, a mucin secretagogue should be given. If the lipid layer is affected, as in meibomian gland dysfunction, warm compression, lid hygiene, lubricants, topical lipid formulations, or oral fatty acids can be prescribed according to severity.[14] When the patient has aqueous-deficient dry eye, such as in the case of Sjögren syndrome, tear secretagogues or punctal occlusion can be used to increase tear volume.[15–17]

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From the Li Ka Shing Faculty of Medicine (Chuang) and the Department of Ophthalmology (Shih), University of Hong Kong, the Department of Ophthalmology and Visual Sciences (Chan, Jhanji), Faculty of Medicine, the Chinese University of Hong Kong, Department of Ophthalmology (Wan), Tuen Mun Eye Centre and Tuen Mun Hospital, Hong Kong, China; the Department of Ophthalmology (Jhanjij), University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania USA; the Ocular Surface Research Group (Tong), Singapore Eye Research Institute, the Corneal and External Eye Disease Service (Tong), Singapore National Eye Centre, the Eye-Academic Clinical Program (Tong), Duke-NUS Medical School, and the Department of Ophthalmology (Tong), Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

Corresponding author: Kendrick Co Shih, MB BS, MRes (Medicine), MRCSEd (Ophth), Department of Ophthalmology, Li Ka Shing Faculty of Medicine, University of Hong Kong, 301B Cyberport 4, 100 Cyberport Road, Pokfulam, Hong Kong, China. E-mail: kcshih@hku.hk.

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There is lack of literature reviewing the management of dry eye, specifically in the context of cataract surgery patients. Thus, we performed a systematic review to evaluate the connection between cataract surgery and dry eye and to determine the best management for these patients.

MATERIALS AND METHODS

A search of the online PubMed database was performed on the May 20, 2017, using the search terms "dry eye" AND "cataract surgery" AND "ocular surface"; the search resulted in 44 studies. This was further filtered to include only studies with humans and written in English. Articles were limited to journal articles in which the keywords "dry eye" or "ocular surface" occurred in conjunction with the keyword "cataract surgery" in the text word field of the search. The 44 articles identified were then curated for relevance by 2 coauthors (J.C., K.S.) via abstract or full text of the article. For example, articles that involved only cataract surgery or ocular surface disease/dry eye and not both would be considered irrelevant. The analysis was also limited to original articles; therefore, review papers were also excluded. Initially 17 nonhuman and non-English studies were excluded. From the resultant 27 articles, a further 11 review articles, letters, and commentaries were excluded. Thus, 16 papers were included in this review (Figure 1). Among the 16 papers, 6 were randomized controlled trials (RCTs). These studies were analyzed and summarized in this paper (Tables 1 to 3[4,5,18–31]). Levels of evidence and grades of recommendation were determined using the system outlined by the Scottish Intercollegiate Guidelines Network.[32]

LITERATURE SEARCH

Three RCTs studied various management for dry eye after cataract surgery. Park et al.[18] compared the use of diquafosol 3.0% with sodium hyaluronate 0.1% in their RCT. They found aggravated symptoms and signs at 1 week after surgery that began to recover significantly 4 weeks after surgery in both groups. The diquafosol group had a statistically significant better tear breakup time (TBUT) ($P < .001$), corneal fluorescein ($P = .045$) and conjunctival staining ($P = .001$), improvement in TBUT, and changes in higher-order aberrations ($P < .001$ and $P = .018$). There was, however, no significant benefit in visual acuity and the Ocular Surface Disease Index (OSDI) score.[18] Diquafosol is a P2Y2 receptor activator that aids the promotion of mucin secretion and tear secretion[33]; only 1 person in their diquafosol study group stopped using diquafosol because of severe irritation. However, their study size (130 eyes of 86 patients) was too small to evaluate drug reactions and they only recruited patients with no to mild dry eye. Thus, their results cannot be applied to those with severe dry-eye disease. In their RCT of the effect of topical cyclosporine 0.05%, Chung et al.[19] found no difference between the cyclosporine group and the normal saline group in Schirmer test I, TBUT, or symptom severity scores. They found, however, a significant improvement in the TBUT with cyclosporine starting at 1 month with further increases at the second and third month as compared with the flatter trend in the normal saline group. The Schirmer test score at 3 months was also statistically significant higher in the cyclosporine group than in the normal saline group ($P = .02$). Both groups had significant improvement in all parameters after treatment postoperatively ($P < .05$). Cyclosporine is an immunomodulatory medication and has been demonstrated to be effective in the management of dry eye.[34–36] This may be the result of the inhibition of activated T-lymphocytes, which in turn reduces the inflammation caused by cataract surgery. There is, however, a transient symptom aggravation in the first few weeks of treatment. It is important that ocular discomfort and irritability were the leading causes for the discontinued use of cyclosporine in Chung et al.'s study.[19] Another study by Sheppard et al.[37] advocated the use of a topical corticosteroid as a pretreatment for 2 to 16 months to reduce this adverse effect.

Four prospective cohort studies that evaluated the association between dry-eye disease and cataract surgery were identified. In Li et al.'s study[5] of 50 eyes of 37 patients, dry-eye symptoms, including ocular discomfort, ocular fatigue, eye redness, and foreign-body sensation, were most significant 1 month after phacoemulsification cataract surgery but diminished with time. The tear meniscus height became shorter, and 3 months postoperatively both the Schirmer test I and TBUT scores were significantly worse compared with baseline values ($P = .01$). They also performed impression cytology and found a statistically significant drop in goblet cell density after surgery ($P < .01$). This finding is consistent with that of Oh et al.,[21] who also found a statistically significant decrease in mean goblet cell density 1 day, 1 month, and 3 months postoperatively

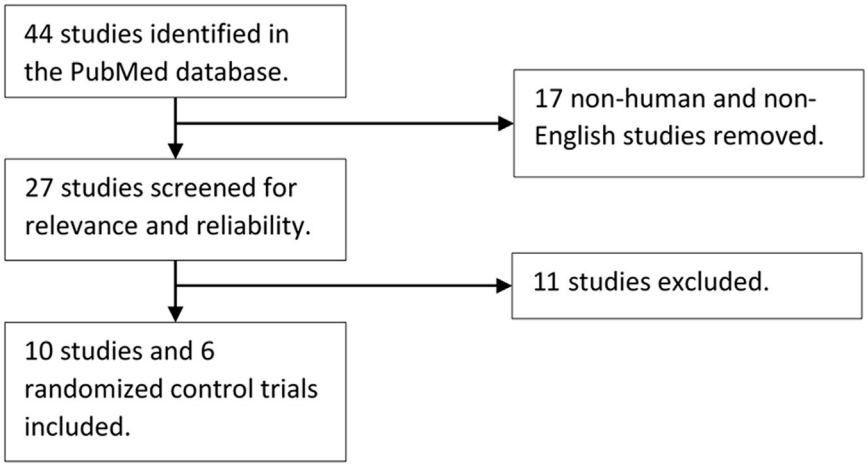

Figure 1. Flow diagram.

Table 1. Randomized controlled trials comparing treatments/interventions on dry eye disease after cataract surgery with at least 3 months of follow-up.

Study*	Level of Evidence	Design	Eyes/ Pts	Blinding	Comparator	Surgical Procedure	Exams
Park[18]	Ib	RCT	94/63	Not specified	Diquafosol ophthalmic solution 3.0% vs HA ophthalmic solution 0.1%	Phaco (2.8 mm CCI)	Baseline; 1 wk, 4 wk, 12 wk postop
Chung[19]	Ib	RCT	64/32	Double-blind	Topical cyclosporine 0.05% vs normal saline 0.9% (placebo)	Phaco (3.0 mm CCI)	Baseline; 1 wk, 1 mo, 2 mo, 3 mo postop
Moon[20]	Ib	RCT	58/58	Not specified	Use of aspirating speculum vs no use of aspirating speculum	Phaco (2.7 mm CCI) alone vs phaco with aspirating speculum	Baseline; 1 d, 1 wk, 1 mo postop

AC = anterior chamber; CCI = clear corneal incision; HA = sodium hyaluronate; HOAs = higher-order aberrations; OSDI = Ocular Surface Disease Index; Pts = patients; RCT = randomized controlled trial; TBUT = tear breakup time; UDVA = uncorrected distance visual acuity
*First author

($P < .001$). They also found a statistically significant increase in dry-eye symptom scores ($P < .01$) and corneal sensitivity at the corneal center and temporal incision sites ($P = .021$ and $P < .001$, respectively). Contrary to the results of Li et al.,[5] they did not find a statistically significant difference in Schirmer test I and TBUT results 1 month and 3 months after surgery. The Lee et al.[22] article, which studied dry-eye association with not only cataract surgery but also other systemic diseases such as rheumatoid arthritis, diabetes mellitus, and thyroid diseases and factors including smoking and contact lens wearing found statistical significance in cataract surgery and meibomian gland dysfunction, Yamaguchi score, Schirmer test score, and temporal fluorescein staining. Kasetsuwan et al.'s study[4] in Thailand used the OSDI score, TBUT, and Schirmer test for the diagnosis of dry eye, and their results also showed a trend toward dry-eye syndrome with an incidence of dry eye after phacoemulsification of 9.8% (95% confidence interval, 3.8-16.0).

Five studies evaluated the associations of dry eye and cataract surgery in patients with specific diseases including diabetes, graft-versus-host disease (GVHD), and Stevens-Johnson syndrome. Jiang et al.[23] found the incidence of dry eye to be 17.1% in diabetic patients as opposed to 8.1% in nondiabetic patients. In addition, diabetic patients had worse ocular symptom scores and lower TBUT values at 7 days and 1 month ($P < .05$) but not at 3 months ($P > .05$). Sangwan and Burman[24] studied the outcomes of cataract surgery in Stevens-Johnson syndrome in a case series of 2 patients. They showed that cataract surgery can be beneficial and safe in Stevens-Johnson syndrome patients when the underlying ocular surface disease is meticulously controlled. However, being a case series, this study lacked both sample size and level of evidence. Three studies assessed the outcomes of cataract surgery in hemopoietic stem cell transplantation patients with GVHD. Because GVHD has deleterious effects on aqueous tear production, dry eye is one of the most common presentations of GVHD ocular manifestation. The mean visual acuity of patients in all 3 studies significantly improved after cataract surgery. In both the Balaram and Dana[25] and de Melo Franco et al.[26] studies, postoperative complications occurred, albeit meticulous management of dry-eye disease was performed preoperatively. These complications included intraocular pressure (IOP) elevation, worsening of dry-eye syndrome, corneal thinning, cystoid macular edema (CME), corneal ulceration with perforation, and band keratopathy. de Melo Franco et al.[26] also noted that OSDI scores showed a trend toward worsening. In Penn and Soong's study,[27] in which all patients had dry eye preoperatively, aggressive management of dry eyes with artificial tears and lubricant ointments with or without punctal occlusion and prednisolone eyedrops led to no development of corneal ulceration or significant conjunctival inflammation. One out of 7 patients developed CME, which resolved with periocular corticosteroid injections.[27]

In terms of cataract surgery operative technique, Moon et al.[20] evaluated the use of an aspirating speculum during surgery and its association with dry eye. They hypothesized that because the use of an aspirating speculum can lead to conjunctival jamming into suction holes, its use will cause damage to and inflammatory changes on the ocular surface and subsequently dry eye. Indeed, they observed a statistically significant increase in conjunctival staining 1 day

Table 1. (Cont.)

Main Outcome Measures	Results	Comments
OSDI, TBUT, Schirmer I test, corneal fluorescein and conjunctival lissamine green staining scores, serial ocular HOAs/corneal HOAs measurements, UDVA	• Diquafosol group had superior TBUT ($P < .001$), corneal fluorescein ($P = .045$), corneal staining ($P = .045$), conjunctival staining ($P = .001$), quicker improvement in TBUT ($P < .001$) and change in HOAs ($P = .018$). • No overall differences in OSDI ($P = .221$), Schirmer I test ($P = .256$), safety measures (AC inflammation, dropout rate) ($P = .484$).	• Patients with severe dry eye were excluded. • Improvement in dry eye might be confounded by stoppage of preserved eyedrops 4 wk postop. • Sample size too small for evaluating safety and drug reactions.
Schirmer I test without anesthesia, TBUT, OSDI, corneal temperature	• Cyclosporine group had improved Schirmer I test at 3 mo ($P = .02$), TBUT at 2 and 3 mo ($P = .04$, $P < .01$), OSDI scores at 3 mo ($P \leq .02$). • Normal saline group improved less over time. • No differences in corneal temperature noted. • Cyclosporine group had a transient insignificant increase of OSDI score at 2 wk ($P = .18$).	• Sample size small for evaluating drug safety and reactions. • Comparisons made between R eye and L eye in cases of bilateral cataract surgery.
Conjunctival staining, TBUT, Conjunctivochalasis grades, OSDI	• Aspirating speculum group had an increase in conjunctival staining at 1 d ($P = .001$), TBUT and conjunctivochalasis grades at 1 and 7 d ($P < .001$) and OSDI at 7 d ($P = .011$). • Nonaspirating speculum group only showed changes in TBUT and conjunctivochalasis grades 1 d postop ($P < .001$). • All parameters returned to preop values 1 mo postop.	• Impression cytology not performed. • Chronic preoperative dry-eye meds not controlled. • Long-term prevalence and treatment response of dry-eye syndrome not evaluated.

postoperatively ($P = .001$), TBUT and conjunctivochalasis grades at 1 day and 7 days ($P < .001$), and OSDI at 7 days ($P = .011$). The nonaspirating speculum group showed statistical significance only in TBUT and conjunctivochalasis grades 1 day postoperatively ($P < .001$). All these parameters returned to preoperative values by 1 month postoperatively.

Four studies had a shorter follow-up time (<3 months); 3 of which were RCTs. Although their short follow-up is inadequate to prove the validity of the study, properly evaluated 1- to 2-month studies are valuable when they give additional information that longer studies do not. Jee et al.[28] evaluated the effects of preservatives by comparing preservative-free eyedrops with preserved sodium hyaluronate 0.1% and fluorometholone 0.1% eyedrops. Consistent with previous studies of the epithelial toxic effects of preservatives, they found that the preservative-free group has statistically better OSDI scores, TBUT, Schirmer I score, fluorescein staining score, impression cytology findings, goblet cell count, interleukin-1β concentrations, and tumor necrosis factor-α concentrations ($P < .05$). Although patients were followed for only 2 months, this is the only study that used objective outcomes, such as human leukocyte antigen-antigen D related (HLA-DR) and cytokines, and the increase in antioxidants and decrease in inflammatory markers are consistent with findings in several other reports, showing that preservative-free eyedrops can reduce ocular surface inflammation and oxidative damage.[38–41] It is hence likely to be beneficial for all patients to use preservative-free eyedrops rather than preserved ones.

Mencucci et al.'s RCT[29] studied the effects of a hyaluronic acid and carboxymethylcellulose ophthalmic solution compared with only topical steroid and antibiotic eyedrops after surgery. They found that dry-eye symptoms (assessed using visual analog scale) statistically significantly improved in the group prescribed the additional artificial tears and that this group also had reduced fluorescein staining starting at 5 weeks ($P < .001$ and $P = .002$, respectively). Sánchez et al.'s RCT[30] studied hydroxypropyl (HP)-guar, a different macromolecular complex that can be added to lubricants. They also found statistically better results in TBUT ($P = .0004$), OSDI ($P = .0002$), ocular symptoms subscale ($P = .0004$), vision-related function subscale ($P = .0004$), CD3 levels ($P = .011$), and HLA-DR levels ($P = .0002$) when HP-guar was used on top of steroid and antibiotic eyedrops compared with steroid and antibiotic eyedrop use alone. However, Mencucci et al.'s[29] and Sánchez et al.'s[30] studies might be biased by the placebo effect of an additional eyedrop to the usual treatment of topical steroids and antibiotics, and the short follow-up makes their studies less valid.

The study by Yu et al.[31] is the only one that evaluated the effect of femtosecond laser–assisted surgery on dry eye. They found that the femtosecond laser–assisted procedure increased operative time significantly ($P < .001$) and resulted in a higher OSDI score at 1 week ($P = .014$). However, no statistically significant difference was found at 1 month ($P = .622$) and both groups had elevated OSDI scores 1 week and 1 month after surgery. The femtosecond group also had a statistically significant higher fluorescein staining score at the 1-month timepoint, with neither group having complete recovery of vital staining of the ocular surface. Both groups had a decrease in noninvasive keratography TBUT and Schirmer I testing values; however, no significant difference was found between the groups. Yu

Table 2. Observational studies of visual and ocular surface outcomes after cataract surgery in dry-eye disease with at least 3 months follow-up.

Study*	Level of Evidence	Design	Eyes/Pts	Blinding	Outcome Measures	Surgery Procedure	Exams
Kasetsuwan[4]	IIb	Prospective cohort	92/92	No	Incidence and pattern of dry eye	Phaco	0 d, 1 wk, 1 mo, 3 mo
Li[5]	IIb	Prospective cohort	50/37	No	Analysis of dry-eye pathogenic factors in patients after cataract surgery	Phaco (CCI)	3 d preop; 1 wk, 1 mo, 3 mo postop
Oh[21]	IIb	Prospective cohort	48/30	No	Changes in tear film and ocular surface	Phaco (2.8 mm CCI)	Baseline (1 d preop); 1 d, 1 mo, 3 mo postop
Lee[22]	IIb	Prospective cohort	510†	No	Associations of systemic diseases, ocular surgeries, contact lens wear, and smoking with dry eye	Not specified	Assessment on prospective recruitment of new referrals
Jiang[23]	IIa	Prospective cohort	648/568	No	Tear-film dysfunction after cataract surgery in diabetic patients	Phaco (3.4–3.8 mm CCI)	Baseline; 7 d, 1 mo, 3 mo postop
Sangwan[24]	III	Case series	3/2	No	Outcomes of cataract surgery in SJS	ECCE with posterior limbal incision	Clinical records from 2 SJS patients with FU from 3-24 mo
Balaram[25]	IIb	Case control	34/19	No	Outcomes of cataract surgery after allogeneic bone marrow transplantation	Phaco	Clinical records from patients with a mean postop FU of 13 mo
de Melo Franco[26]	IIb	Case control	72/41	No	Outcomes of cataract surgery in GVHD	Phaco (CCI)	Clinical records from ocular exams at baseline; every 3 mo for 1st yr and 6–8 mo after
Penn[27]	IIb	Case control	12/å7	No	Outcomes of cataract surgery in GVHD	Phaco (2.7 mm CCI or 3.0 mm scleral tunnel incision)	Clinical records with a mean postop FU of 23 mo

CCI = clear corneal incision; CDVA = corrected distance visual acuity; CI = confidence interval; CME = cystoid macular edema; ECCE = extracapsular cataract extraction; FU = follow-up; GCD = goblet cell density; GVHD = graft-versus-host disease; NEI VFQ-25 = National Eye Institute Visual Function Questionnaire; OSDI = Ocular Surface Disease Index; PCO = posterior capsule opacification; Pts = patients; SJS = Stevens-Johnson syndrome; TBUT = tear breakup time; VA = visual acuity

*First author

†Patients

Table 2. (Cont.)

Main Outcome Measures	Results	Comments
OSDI, TBUT, Schirmer I test without anesthesia, Oxford Schema	• Dry-eye incidence 7 d postop 9.8% (95% CI, 3.6-16.0). • Dry-eye severity peaked 7 d postop; improved at 1 and 3 mo. • Postop dry-eye not associated with sex, age or systemic hypertension ($P = .26$, $P = .17$, $P = .73$).	• Did not include subjects without surgery for comparison. • Small sample might have led to nonsignificant results for the associations with pt's sex. • Fluorescein staining not included.
NEI-VFQ-25, OSDI, lacrimal river line, fluorescein staining, TBUT, Schirmer I test, impression cytology for goblet cell density and squamous metaplasia	• No statistically significant change on overall OSDI score from preop to postop. • Tear meniscus height <0.3 mm 3 mo after surgery when majority previously had a normal lacrimal river line. • Number of pts with positive fluorescein staining increased at 1 mo; STI and TBUT significantly worse compared with baseline ($P = .01$). • Impression cytology demonstrated a statistically significant drop in GCD after surgery ($P < .01$)	• Single center study with small sample. • Longest FU 3 mo.
OSDI, Corneal sensitivity test, slitlamp microscopy, fluorescein staining, Schirmer I test without anesthesia, TBUT, impression cytology for metaplasia grading (0–5) and goblet cell density	• Statistically significant decrease in mean GCD at 1 d, 1 mo, and 3 mo postop ($P < .001$). Statistically significant increase in dry-eye symptom scores ($P < .01$) and corneal sensitivity at the corneal center and temporal incision sites ($P = .021$, $P < .001$). • TBUT and ST1 not statistically worse 1 and 3 mo postop ($P = .108$, $P = .098$, $P = .422$, $P = .415$)	• Single center study with small sample. • The FU limited to 3 mo.
Dry-eye symptoms, Schirmer I test without anesthesia, TBUT, corneal fluorescein staining, Meibomian gland status (Yamaguchi grading)	• Association between cataract surgery and meibomian gland dysfunction, Yamaguchi score ($P < .001$), Schirmer score (0.015), and temporal fluorescein staining ($P = .041$). • Association became statistically significant after factoring confounders in multivariate analysis.	• Sjogren syndrome not studied. Cause–effect relationship not established. • Quantification of smoking, habits, duration and type of contact lens wear, and effects of dry-eye management were not done.
OSDI, TBUT, corneal fluorescein staining, Schirmer I test, tear secretion	• Incidence of dry eye is 17.1% in diabetic patients as opposed to 8.1% in non-diabetic patients. • Diabetic patients exhibited worse OSDI scores and lower TBUT values at 7 d and 1 mo ($P < .05$) but not at 3 mo ($P > .05$). • No statistically significant differences in tear secretion, corneal fluorescein staining and Schirmer I test ($P > .05$).	• Meibomian gland function not fully studied. Corneal sensitivity not studied. • Lacked information on blood sugar levels and duration of disease.
CDVA, surgical complications	• CDVA improved in all eyes postop although a drop in CDVA from 20/40 and 20/50 to 20/100 and 20/200 was present on FU. • Otherwise, no evidence of exaggerated conjunctival inflammation, stromal keratolysis, corneal perforation, or symblepharon formation.	• Lacked in sample size (2 case reports) and level of evidence.
Schirmer I test, Snellen VA, TBUT, corneal fluorescein staining, conjunctival rose-bengal staining, management of ocular surface diseases, postop complications	• Management of ocular surface disease preop included frequent lubrication (95%), punctal occlusion (76%), topical steroids (33%), topical immunosuppressive therapies (14%), systemic steroids, and immunosuppressants (63%) • Postop complications included PCO (3 eyes), worsening of dry eye (2 eyes), and corneal thinning (1 eye); VA improved in 97% of eyes at last FU.	• Recurrence of ocular surface disease after immunosuppressive therapy.
CDVA, OSDI, surgical complications	• CDVA showed statistically significant improvement postsurgery ($P < .0001$). • 4 eyes developed cystoid macular edema, 2 eyes ulceration with perforation, 1 eye band keratopathy. • OSDI trended toward worsening but with no statistically significant change ($P = .1743$).	• Small sample might have led to statistically insignificant results in OSDI scores and the spike in CME incidence compared with other studies.
VA, surgical complications, management of ocular surface disease before surgery	• Mean VA improved ($P < .005$). Management of ocular surface disease included oral corticosteroids (100%), lubricants (100%), punctal occlusion (75%), and topical prednisolone acetate (58%) preop. • Conjunctival scarring in 3 eyes, severe blepharitis in 1 pt, CME in both eyes of 1 pt. • No corneal ulceration or significant conjunctival inflammation.	• Small sample.

Table 3. Studies with shorter follow-up (<3 months).

Study*	Level of Evidence	Design	Eyes/Pts	Blinding	Outcome Measures	Surgical Procedure
Jee[28]	Ib	RCT	80/80	NS	Preservative-free vs preserved HA 0.1% and fluorometholone 0.1% eyedrops	Phaco (CCI)
Mencucci[29]	Ib	RCT	282/282	No	Addition of HA and CMC ophthalmic solution on top of topical steroid–antibiotic vs only topical steroid–antibiotic	Phaco (2.2 mm CCI)
Sánchez[30]	Ib	RCT	48/48	No	Addition of preservative-free HP-Guar vs only topical steroid–antibiotic	Phaco
Yu[31]	IIa	Prospective cohort	137/137	No	FLACS vs conventional phaco	FLACS or phaco

CCI = clear corneal incision; CMC = carboxymethylcellulose; FLACS = femtosecond laser–assisted cataract surgery; HA = sodium hyaluronate; HLA-DR = HLA-DR human leukocyte antigen–antigen D related; HP-Guar = hydroxypropy-Guar; IL = interleukin; MFI = mean fluorescence intensity; NIfBUT = noninvasive first tear breakup time; NIavBUT = noninvasive average tear breakup time; NS = not specified; NSAID = nonsteroidal antiinflammatory drug; OSDI = Ocular Surface Disease Index; Pts = patients; SOD2 = superoxide dismutase 2; TBUT = tear breakup time; TNF = tumor necrosis factor; VAS = visual analog scale
*First author

et al.[31] did not evaluate their patients in terms of other factors, including corneal sensitivity, and surgeons should keep in mind that the patients were followed for 1 month only.

DISCUSSION

Of the 16 studies included in this systematic review, 6 were RCTs and the rest were prospective or retrospective, with 1 being a case series. Most of the studies had a limited follow-up (up to 3 months). At most, current studies are effective in showing a return of ocular surface status to the baseline status quo in the intermediate term after treatment. Long-term studies are needed for a more complete understanding of the longitudinal changes in the ocular surface after cataract surgery as well as the effect of interventions in the long run. Such studies might benefit from the inclusion of newer corneal imaging techniques in the planning phase, such as the measurement of corneal subbasal nerve plexus density via confocal microscopy.

Studies included in this review were also limited in sample size, especially those examining patients with specific diseases such as Sjögren syndrome, GVHD, and Stevens-Johnson syndrome. In the RCTs of various topical ophthalmic solutions, the sample sizes were not sufficient to safely evaluate the medications. In addition, results in these studies might have been confounded or limited by interpersonal and intercenter differences in diagnosis, operation techniques such as incision extent, and operation time as well as by different recruitment inclusion and exclusion criteria. There is also inconsistency in that treatment methods improve only certain parameters but not others.

Table 3. (Cont.)

Exams	Main Outcome Measures	Results	Comments
Baseline; 1 and 2 mo postop	OSDI, TBUT, Schirmer I test (without anesthesia), corneal fluorescein staining, conjunctival impression cytology (goblet cell density), inflammatory cytokines and antioxidants (IL-1β, TNF-α, Catalase (MFI), SOD 2 (MFI)	• Preservative-free group had improved OSDI score at 1 and 2 mo ($P = .03$, $P = .02$), TBUT at 2 mo ($P = .04$), Schirmer I test at 2 mo ($P = .04$), fluorescein staining at 2 mo ($P = .03$), impression cytology grade and goblet cell density at 2 mo ($P = .04$, $P = .03$), decrease in inflammatory cytokines IL-1β, TNF-α, and increase in antioxidants catalase (MFI), SOD 2 (MFI)	• Pts followed up for 2 mo only. • This study includes outcomes like inflammatory cytokines and oxidants that are more objective and are not in the longer studies.
Baseline; 1 wk and 5 wk postop	TBUT, VAS, OSDI, corneal fluorescein staining	• Study group had improved VAS-assessed dry-eye symptoms and reduced inferior and nasal corneal fluorescein staining starting at 5 wk ($P < .001$, $P = .05$, $P = .002$). • No differences seen 1 wk postop. • OSDI scores improved in both groups from 1 to 5 wk ($P < .0001$) but differences between groups not statistically significant ($P > .05$). • No adverse events reported.	• Pts were followed up for only 5 wk only. • Mean TBUT score significantly lower in study group than control group preop. • Addition of artificial tears might have resulted in placebo effect.
Baseline; 1 mo postop	Corneal fluorescein staining, conjunctival lissamine green staining, TBUT, Schirmer I test with anesthesia and tear clearance, conjunctival impression cytology for CD3, CD11b and HLA-DR, OSDI score	• HP-Guar group had improved TBUT ($P = .0004$), overall OSDI ($P = .0002$), CD3 ($P = .011$), HLA-DR ($P = .0002$), no differences in fluorescein and lissamine staining ($P = .741$, $P = .880$), Schirmer I test ($P = 0.615$), tear clearance ($P = .120$), CD11b ($P = .768$). • No adverse events reported	• Pts were followed up for 1 mo only. • HP-Guar group given additional eyedrops, perhaps causing placebo effect.
Baseline; 1 d, 1 wk, 1 mo postop	OSDI, Tear meniscus height, NIfBUT, NIavBUT, Schirmer I test, fluorescein staining	• FLACS group had increased operative time ($P < .001$), higher OSDI score at 1 wk ($P = .014$), higher fluorescein staining score at 1 d, 1 wk, and 1 mo ($P = .011$, $P = .047$, $P = .025$). • No differences between groups were in NIfBUT, NIavBUT, Schirmer I test at all timepoints and OSDI at 1 mo.	• Pts were followed for 1 mo only. • Study might be confounded by addition of 1 d of topical NSAID in FLACS group. • Factors such as corneal sensitivity, goblet cell density, etc., not evaluated.

Thus, the treatments mentioned are shown to be potentially, and not definitely, beneficial.

Pathophysiology of Postoperative Dry-Eye Disease in Cataract Surgery

The association between dry eye and cataract surgery is multifactorial. Cataract surgery worsens OSDI scores, TBUT, and the Schirmer I score; increases fluorescein staining; and decreases mean goblet cell density and corneal sensitivity at the corneal center and temporal incision sites. Symptoms can occur as early as 1 day after surgery, and ocular changes generally peak 1 week to 1 month postoperatively and then taper off with time.[4,5,21,22] These parameters, however, might not return to baseline 3 months postoperatively.[5] Comparing Oh et al.'s findings[21] of decreased corneal sensitivity with the study by Khanal et al.,[3] a smaller incision (2.8 mm versus 4.1 mm) might have led to improvement in corneal sensitivity. This might be the result of less diffuse sensory nerve damage by the transection and denervation made by corneal incisions.

A longer operation time, as evident in femtosecond laser–assisted surgery and in Oh et al.'s study[21] comparing operation time with goblet cell density loss, also worsens dry eye in cataract surgery patients. This might be a result of increased microscopic-light exposure time and increased irrigation, leading to increased inflammatory response from the surgery. Li et al.[5] also found a more obvios decrease in goblet cells on the lower lid region than on the upper and exposed regions. This is likely a result of eyedrop use after surgery. Hence, one should taper or discontinue prescribed eyedrops once they are no longer necessary.

The studies that included fluorescein staining as a parameter found a significant increase in staining.[5,22] This increase indicates damage to the ocular surface from cataract surgery, which can be a factor leading to elevation of inflammatory markers and ocular surface disease. Several

studies also found an increase in the Schirmer I score postoperatively.[4,5,22] This indicates that cataract surgery aggravates or induces a mixture of evaporative and aqueous-deficient type of dry eye.

Recommendation for Preoperative Assessment and Optimization

To minimize ocular surface complications after cataract surgery, dry eye in patients should be recognized before surgery. The Asia Dry Eye Society recommends that dry-eye disease be diagnosed when there is a combination of symptoms of discomfort or visual disturbance and tear-film instability.[13] This is especially true for patients with poor prognostic factors. Although the studies in GVHD and Stevens-Johnson syndrome patients did not find complete elimination of complications with aggressive management of dry eye before surgery, they all concluded that it is imperative to recognize and aggressively treat any concurrent ocular surface diseases and dry-eye disease in these patients. Treatment included artificial tears, lubricant ointments, punctal occlusion, and prednisolone eyedrops; their patients achieved good visual outcomes postoperatively.[24–27] Other poor prognostic factors of dry-eye disease in cataract surgery include diabetes mellitus,[22,23] rheumatoid arthritis, laser in situ keratomileusis surgery, and smoking.[22] Surprisingly, in Lee et al.'s study,[22] contact lens wearers had improved dry-eye symptoms over noncontact lens wearers. This result might have been biased as a result of the avoidance of contact lenses in patients with more severe dry eye.

Recommendation for Intraoperative Surgical Techniques

Increased incision extent, operation time, irrigation, and microscopic-light exposure time decreases TBUT and mean goblet cell density.[21] It is thus important to shorten operative time and reduce other stimuli. In terms of surgical techniques, cataract surgery can be split into phacoemulsification and extracapsular cataract extraction (ECCE), which can be further subdivided into classic ECCE and the newer small-incision cataract surgery (SICS). As its name implies, SICS is differentiated from classic ECCE by a smaller incision. Although phacoemulsification is the current gold standard for cataract surgery, ECCE remains an important and cost-effective technique, especially in the developing world.[42] Several studies have explored the differences between the 3 main cataract surgical techniques. In general, studies including 2 metaanalyses by Gogate et al.[43,44] and Zhang et al.[45] and 2 RCTs conducted by Gogate et al.[46] and Ruit et al.[47] concluded that SICS and phacoemulsification are comparable in terms of visual outcomes (corrected distance visual acuity) and complication rates. However, classic ECCE, which requires the use of sutures to close the larger incision, has higher rates of postoperative astigmatism and complications than both SICS and phacoemulsification.[42,48,49] Based on the effect of the corneal incision on postoperative dry eye, phacoemulsification with the smallest incision size (1.8 to 3.8 mm) has a significant advantage over both classic ECCE (9.0 to 13.0 mm) and SICS (5.0 to 8.0 mm). On the contrary, SICS has been shown to have a shorter operation time (3.75 to 9.00 minutes) than phacoemulsification (15.0 to 15.5 minutes).[44,46,47,50,51] Based on these combined factors, SICS and phacoemulsification might be comparable in terms of their effects on the ocular surface whereas classic ECCE theoretically results in a higher rate of postoperative dry eye. Unfortunately, we found no published paper specifically comparing dry-eye disease in phacoemulsification versus classic ECCE versus SICS.

Regarding different techniques in phacoemulsification, Yu et al.[31] showed that femtosecond laser–assisted surgery has a higher risk for staining and dry-eye symptoms than conventional phacoemulsification. Surgeons should be reminded that both had an adverse effect on dry-eye parameters. It is thus suggested that conventional phacoemulsification might be more beneficial for patients prone to dry eye. Nonetheless, earlier evaluation and treatment of dry eye should be offered to patients regardless of whether the patient had femtosecond laser–assisted surgery or conventional surgery. In their RCT, Moon et al.[20] found the use of an aspirating speculum aggravated dry-eye parameters. This is likely a result of conjunctival damage leading to decreased mucin secretion from the epithelial cells and increased inflammation, altering tear-film components and destabilizing the tear film. In addition, mechanical forces from the speculum can lead to increased conjunctivochalasis, causing dysfunctional tear distribution. Cataract surgeons who intend to use an aspirating speculum should consider the possibility that it will induce or aggravate dry-eye disease.

Recommendation for Postoperative Management

A variety of dry-eye treatments are available on the market for postoperative treatment of dry eye. These include artificial tears, antiinflammatory agents, tetracycline, cyclosporine, punctal plugs, secretagoges, and autologous serum.

Typical postoperative care involves the use of a topical nonsteroidal antiinflammatory drugs (NSAIDs) and a topical steroids and antibiotics. Eyedrop use is associated with worsening of goblet cell density[5]; hence, these medications should be tapered to discontinuation when no longer needed. No single agent has been shown to be significantly superior to other agents. The addition of lubricants containing a macromolecular complex,[29,30] diquafosol 3.0% ophthalmic solution,[18] and topical cyclosporine 0.05%[19] have been shown through 2 separate RCTs to be potentially beneficial to postsurgery dry-eye patients and should be considered as an adjuvant therapy after cataract surgery. In patients with GVHD or Stevens-Johnson syndrome and severe ocular surface disease, complications such as IOP elevation, worsening of dry-eye syndrome, corneal thinning, CME, corneal ulceration with perforation, and band keratopathy might arise even with meticulous control before surgery.[24–27] Thus, it would be prudent for surgeons to monitor these patients for complications and earlier management.

Summary of Recommended Clinical Approach to Ocular Surface Disease in Cataract Surgery

Figure 2 summarizes the recommendations in a simple flow chart.

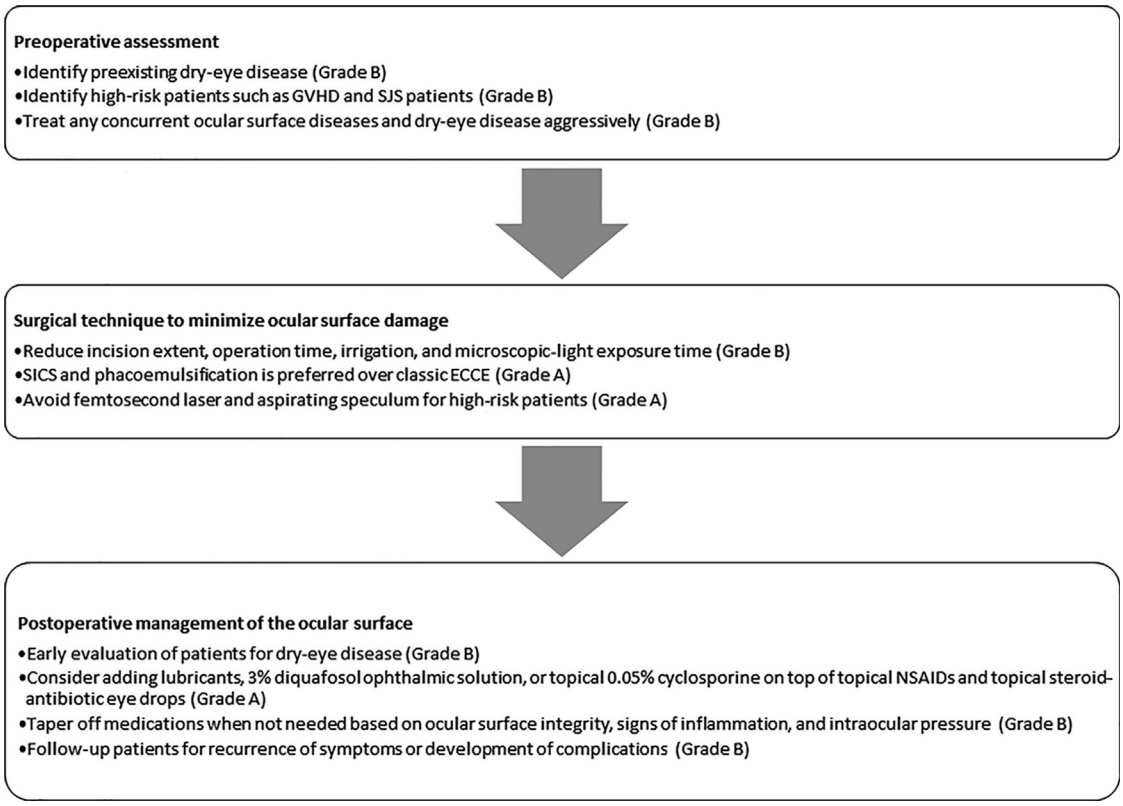

Figure 2. Algorithm with grade of recommendation (ECCE = extracapsular cataract extraction; GVHD = graft-versus-host disease; NSAIDs = nonsteroidal antiinflammatory drugs; SJS = Stevens-Johnson syndrome; SICS = small-incision cataract surgery).

To predict exacerbation of preexisting ocular surface or dry-eye disease, patients should be screened for preexisting dry-eye disease before any cataract surgery and treated accordingly.[21–27] Intraoperatively, surgeons should reduce incision extent, operation time, irrigation, and microscopic-light exposure time.[3,5,21,22,31] Small-incision cataract surgery and phacoemulsification should be preferred over classic ECCE[42–51] and surgeons should keep in mind that the femtosecond laser and aspirating speculum might lead to a higher risk for dry-eye disease.[20]

Patients should be screened early for dry-eye disease and ocular surface complications after surgery. This is especially true for high-risk patients such as those with GVHD or Stevens-Johnson syndrome who are at higher risk for complications including CME, corneal ulceration with perforation, and band keratopathy.[24–27] Treatment options and length can be guided by dry-eye type (tear film–oriented therapy strategy) and/or severity.[2,13] Lubricants, diquafosol 3.0% ophthalmic solution, or topical cyclosporine 0.05% can be considered as an additive to typical topical NSAIDs and topical steroid and antibiotic eyedrops.[18,19,28] These should be tapered to discontinuation when not needed based on ocular surface integrity, signs of inflammation, and IOP.[5] Patients should be followed for recurrence of symptoms or development of complications after treatment.[24–27]

In conclusion, cataract surgery is an ocular surface–damaging procedure that will induce or aggravate dry-eye disease through many different pathophysiologic pathways. Although these changes are usually temporary, it would prove beneficial for the cataract surgeon to consider ocular surface diseases preoperatively and postoperatively in the era of refractive cataract surgery. Preoperative identification allows for optimization of the ocular surface as well as improved visual outcomes after surgery. Postoperative management can be guided by the mechanism behind the dry-eye disease using the tear film–oriented therapy strategy or stratified by severity following the International Dry Eye WorkShop/International Task Force Guidelines for Dry Eye.[2] Ultimately, although dry-eye disease is mostly a transient complication of cataract surgery, its effect on short-to-intermediate term visual outcomes is highly significant and can result in patient dissatisfaction. To avoid postoperative conflicting explanations to the patient and his or her family, the presence of dry-eye disease and its risk factors should be thoroughly investigated before cataract surgery.

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First author:
Jasmine Chuang, MB BS

Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong, China