

Post-Operative Complications After Cataract Surgery in Patients with Rheumatoid Arthritis and/or Sjögren's Syndrome

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Purpose: To determine the frequency and types of postoperative complications following cataract surgery in patients with rheumatoid arthritis (RA) and/or Sjögren's syndrome (SS).

Patients and Methods: A retrospective review was conducted of consecutive patients with RA and/or SS who underwent cataract surgery between 2006 and 2018.

Results: A total of 100 eyes from 75 patients (mean age 73.1 ± 9.3 years) were included: RA (n=81), SS (n=11), and both RA and SS (n=8). Twenty-nine eyes had preoperative keratoconjunctivitis sicca. Postoperatively, 4% of eyes showed reduced best-corrected visual acuity. Cystoid macular oedema developed in 6 eyes (6%), and 3% experienced prolonged anterior chamber inflammation. One patient with SS developed a paracentral corneal melt without perforation, and another with SS developed postoperative endophthalmitis resulting in complete vision loss.

Conclusion: Patients with RA, particularly those with SS and pre-existing dry eye, are at increased risk of postoperative complications after cataract surgery. Careful preoperative assessment and close postoperative monitoring are recommended in this population.

Keywords: phacoemulsification, autoimmune, post-operative inflammation, dry eye

Introduction

Connective tissue diseases such as rheumatoid arthritis (RA) and Sjögren's Syndrome (SS) are autoimmune disorders most frequently seen in older adults.¹ Cataract formation is common in these patients, particularly posterior subcapsular cataracts in those with a history of long term systemic corticosteroid treatment.² Both RA and SS can lead to several ocular complications, including: keratoconjunctivitis sicca,³ sterile corneal ulcers,⁴⁻⁶ scleritis,⁷ and retinal vasculitis.^{8,9} These ocular sequelae may be initiated or potentiated when these patients undergo ocular surgery and/or are placed on corticosteroid or nonsteroidal anti-inflammatory drug (NSAID) eye drops. These comorbidities not only threaten vision but may also complicate otherwise routine ocular procedures. In particular, the complications of surgically induced corneal melting and scleritis may be sight or eye threatening and have been described in case reports following cataract surgery.¹⁰⁻¹⁸ While isolated case reports have described severe complications such as corneal melt or scleritis following cataract surgery in RA/SS patients, the true frequency of these events remains unclear.¹⁹ Notably, there is a lack of large cohort studies in the era of small-incision phacoemulsification to quantify complication rates in this high-risk group.

Furthermore, dry eye disease is a ubiquitous risk factor in RA and SS, and may further predispose patients to postoperative complications and poorer visual outcomes, which is less thoroughly investigated in the current literature.

Therefore, the purpose of this study was to determine the frequency and spectrum of postoperative complications after phacoemulsification cataract surgery in patients with RA and/or SS, and to assess the influence of preoperative dry eye disease on visual outcomes.

Materials and Methods

We retrospectively reviewed the medical records of consecutive patients with RA and/or SS who underwent cataract extraction and intraocular lens implantation between 1st June 2004 and 31st August 2018 at the Greenlane Surgical Unit of the Auckland District Health Board, New Zealand. Approval of the conduct of this study was obtained from the Auckland District Health Board Research Review Committee. The requirement for individual patient consent was waived as the study involved only review of existing medical records, posed minimal risk to participants, and all data were anonymized prior to analysis. Patient confidentiality was maintained throughout, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria for this study were: patients undergoing phacoemulsification with intraocular lens implantation and a diagnosis of RA and/or SS confirmed by a rheumatologist. The presence of keratoconjunctivitis sicca was recorded separately as a preoperative clinical variable (previously been given a diagnosis of dry eye or were using lubricating eye drops). Exclusion criteria included: diagnosis of other eye diseases (such as uveitis, herpetic eye disease, glaucoma, age-related macular disease). The post-operative eye drop regimen included chloramphenicol 0.5% four times per day for one to two weeks and prednisolone acetate 1% or dexamethasone 0.1% four times per day for at least 1 month. Alternatively, some patients were prescribed topical dexamethasone/neomycin/polymyxin B four times per day for one month. Patient demographics, clinical characteristics, post-operative outcomes and complications were recorded upon direct chart review. For eyes without a postoperative refraction, postoperative BCVA was estimated by pinhole visual acuity. The Mann–Whitney test was conducted for comparison of post-operative visual acuity. P values of <0.05 were considered statistically significant.

Results

A total of 101 eyes of 76 individuals with RA and/or SS that underwent cataract surgery were identified. One patient (1 eye) was lost to follow-up due to death from unrelated causes prior to the one-month follow-up appointment and was excluded from analyses. Of the 100 eyes of 75 patients (75% female) included in the study, 81 eyes were from individuals with RA only, 11 with SS only, and 8 with both RA and SS.

Pre-operative clinical characteristics of the patients are summarized in Table 1. Eighty-six cases involved individuals on immunosuppression with prednisone and/or other immunomodulatory medications at the time of surgery. These included methotrexate, azathioprine, leflunomide, sulfasalazine, hydroxychloroquine, adalimumab, etanercept, and rituximab. One patient was also on mesalazine for Crohn's disease at the time of both cataract operations.

Excluding dry eye and previous cataract operation in the other eye, 45 eyes had 1 or more other ocular co-morbidities. These included glaucoma/glaucoma suspect (n=14), meibomian gland dysfunction or blepharitis (n=8), age-related macular degeneration (n=5), epiretinal membrane (n=6), scleritis/scleral thinning (n=4), acute anterior uveitis (n=3), previous peripheral iridotomy for narrow angles (n=3), diabetic retinopathy (n=3), thyroid eye disease (n=2), macular hole (n=3), previous refractive surgery (n=2), pseudoexfoliation (n=2), anterior ischemic optic neuropathy (n=1), previous pterygium surgery (n=1), central serous retinopathy (n=1), corneal guttata (n=1), resolved cystoid macular oedema (CMO) (n=1) and Stevens-Johnson Syndrome (n=1).

Table 1 Pre-Operative Clinical Characteristics of Studied Eyes (n=100)

	All	RA	SS	RA+SS
Average age at the time of operation (\pm standard deviation)	73.1 \pm 9.3 years	72.6 \pm 9.5	73.5 \pm 8.6	78.7 \pm 4.8
Age range at the time of operation - years	42.0–90.4	42.0–90.4	51.7–83.3	69.8–84.9
Oral prednisone therapy	46%	51%	36%	0%
Other immunomodulatory medications	75%	74%	64%	88%
Diabetes mellitus	21%	26%	0%	0%
Keratoconjunctivitis sicca	29%	13%	1%	88%

Abbreviations: RA, Rheumatoid Arthritis; SS, Sjögren's Syndrome.

No eyes had clinically active ocular inflammation at the time of surgery. All cataract operations were performed by consultant ophthalmologists using phacoemulsification. There were two reported intra-operative complications of iris prolapse. All eyes received intracapsular implantation of a single piece intraocular lens (SA60AT, SN60AT, or SN6AT; Alcon Vision LLC, Fort Worth, Texas, USA). Main incisions were made in the cornea for 91 cases, sclera in 9 cases, along with one or two paracentesis incisions at the limbus. There has been no report of posterior capsular ruptures or vitreous prolapse during surgery in any of the cases. Ninety-one eyes received postoperative chloramphenicol eye drops along with a topical corticosteroid (prednisolone 1% or dexamethasone 0.1%) while the remaining 9 eyes received a combination drop of dexamethasone/neomycin/polymyxin B. Three eyes also received post-operative diclofenac 0.1% eye drops 4 times daily for 1 month as CMO prophylaxis.

Post-operative complications of the patients at the one-month follow-up are summarized in Table 2. At the one-month follow-up appointment or later, 91 eyes had improved in final best corrected visual acuity (BCVA) following surgery, 5 eyes had the same BCVA, and 4 eyes had worse BCVA. The causes of worse postoperative BCVA included: CMO (n=2), corneal melt (n=1), and endophthalmitis (n=1). On average, individuals with preoperative dry eye had worse postoperative visual acuity (median 20/30) compared to individuals without dry eye (median 20/25; $p=0.048$).

Six eyes (5 RA, 1 SS) developed postoperative CMO which resolved with subsequent topical corticosteroid and NSAID treatment. Of these, two had prior scleritis, one of which also had intraoperative iris prolapse, and both had received an increase in their oral prednisone perioperatively as directed by their uveitis specialist and immunologist. None of the patients had acute necrotizing scleritis as a result of surgery. None of the patients with CMO had a background of diabetes.

Three patients experienced persistent anterior chamber inflammation beyond the one-month postoperative appointment and required prolonged topical corticosteroid treatment. One of these patients had a history of uveitis which had previously required a subtenon's triamcinolone injection. Another patient, who also had a prior diagnosis of sarcoidosis, received an extended course of corticosteroid eye drops following surgery. A third patient with prior necrotizing scleritis required a 3-month oral and topical corticosteroid taper for postoperative inflammation, with no reactivation of the scleritis. None of the 3 eyes that received routine planned (according to surgeon preference) topical NSAID eye drops experienced a complication related to NSAID use.

One patient developed a paracentral corneal melt as a result of severe dry eye secondary to SS with visual acuity of counting fingers at one month follow up. This patient was not on any immunosuppression at the time of cataract surgery or 3 months after surgery. Management with preservative free lubricants, oral doxycycline, and punctal occlusion with plugs initially followed later by thermocautery resulted in closure of the epithelial defect. Best corrected visual acuity at approximately 5 years post-operatively was 6/18 due to corneal scarring.

Table 2 Post-Operative Complications at One Month for All Cases and According to Pre-Operative Dry Eye Status

Parameter	All Cases (n=100)	Dry Eye (n=29)	No Dry Eye (n=71)
Worse post-operative BCVA	4	4	0
Cystoid macular oedema	6	4	2
Persistent AC inflammation	3	2	1
Corneal ulceration	1	1	0
Scleritis	0	0	0
Infection	1	1	0

Abbreviations: BCVA, Best Corrected Visual Acuity; AC, Anterior chamber.

One eye developed endophthalmitis. This patient had SS and was using ocular lubricants as needed pre-operatively. She was not on any immunomodulating medications and had no other systemic diseases that would be expected to increase her risk of infection. She presented six days post-operatively with symptoms of pain and reduced vision. Anterior chamber and vitreous samples grew *Streptococcus pneumoniae*. Treatment included anterior chamber washout, vitrectomy, and intravitreal/topical/IV/oral antibiotics. This eye subsequently developed a persistent corneal epithelial defect and corneal haze requiring a prolonged course of topical corticosteroid eye drops, antibiotic ointment and lubricants. Ten months post-operatively, the patient developed microbial keratitis in the operative eye (corneal scrape cultured *Staphylococcus epidermidis*) and was treated with intravitreal/topical/oral antibiotics. The patient remained on long-term dexamethasone eye drops and lubricants. Visual acuity at approximately 2 years post-operatively was hand movements as a result of band keratopathy and retinal damage.

Discussion

This study examined the postoperative outcomes and complication rates of cataract surgery in patients with RA and/or SS. The most common postoperative complication, CMO, occurred in 6% of eyes in our study. In comparison, only 3.2–3.7% of eyes developed CMO in four prospective studies of 500 consecutive eyes each (2000 total eyes) conducted within the same ophthalmology department between the years 2000 and 2017.^{20–23} The use of prophylactic postoperative topical NSAIDs was low in our study (3%). However, this is unlikely to account for the difference in CMO rates as the reported rates of NSAID use in two of the comparative studies (other 2 not reported) were also low at 0% and 5.4%.^{22,23} Topical NSAIDs must be used with caution in patients with RA/SS due to reports of spontaneous corneal melting precipitated by the NSAID use.^{15,18,24,25}

One potential explanation for increased CMO is a higher propensity to inflammation in patients with RA and/or SS, as these are chronic inflammatory conditions. In particular, eyes with prior ocular inflammation such as uveitis or scleritis from any cause are known to be associated with increased postoperative inflammation and CMO.^{26,27} Matsuo et al¹⁴ measured the titers of rheumatoid factor and C-reactive protein one week prior to cataract surgery in 33 eyes and found that post-operative aqueous inflammation tends to persist in patients with higher titer of rheumatoid factor, although no cases of CMO were identified. However, another study of 23 eyes did not identify any correlation between the extent of postoperative inflammation and pre-operative RA disease activity or medical management of RA.¹⁶

A paracentral corneal melt occurred in one patient following surgery in our cohort. Corneal melt is a rare complication of cataract surgery.²⁸ Corneal ulceration in patients with RA and/or SS following cataract surgery has been reported in several other case reports.^{10,12,13,15,18,29} Dry eye disease (DED) is a potential contributing factor in the development of complications in these patients as DED is a common manifestation of RA and SS.^{4–6,29,30} Other proposed mechanisms mediating corneal thinning include: the presence of corneal collagenase as a result of the inflammatory cascade triggered by autoantibodies,^{13,31–34} deficiency in $\alpha 2$ -macroglobulin (an inhibitor of collagenase),³⁵ and surgical interruption of conjunctival and episcleral vasculature resulting in ischaemia aggravating the pathophysiological process associated with RA and SS.^{36,37}

Endophthalmitis developed in one eye in our series. As this patient was not on any immunosuppressive medications, any increased propensity to infection must be presumed to be due to the SS or the associated ocular surface disease.^{38,39}

We identified one other similar study that examined complications following cataract surgery in patients with RA. Reported in 1992, that study described 86 eyes that underwent cataract surgery, primarily by extracapsular or intracapsular cataract extraction, with only 4 eyes having undergone phacoemulsification. There were no cases of scleritis, ulcerative keratopathy, or infection. Three patients with preoperative keratoconjunctivitis sicca developed increased diffuse superficial punctate keratopathy and/or filamentary keratitis postoperatively, suggesting dry eye was the key factor in this complication.

Our analysis comparing patients with DED compared to no DED found that visual acuity improvements were greater in the group without pre-operative DED. Furthermore, four out of 29 eyes (13.8%) with pre-operative dry eye had worse post-operative BCVA compared to none of the eyes without pre-operative DED. A study that examined complications of cataract surgery in 21 eyes with marked DED identified more complications and worse visual outcomes in those patients with an underlying connective tissue disease as the cause of dry eye, underscoring the worse prognosis in this subpopulation.⁴⁰ A review study by Venkateswaran et al also identified that prophylactic ocular surface optimization

before surgery may reduce the likelihood of severe complications. In particular, aggressive dry eye management may be warranted in patients with RA/SS, including the use of preservative-free lubricants, punctal occlusion (plugs or cautery), autologous serum tears, and topical anti-inflammatory therapy where appropriate.⁴¹

This study has several limitations related to the retrospective nature of the study. As this was a retrospective study, we were unable to use standardized criteria to accurately determine the severity of preoperative DED, and patients were classified as having dry eye on a clinical, binary basis (present/absent). This limitation may underestimate the impact of DED on postoperative complications and final visual outcomes, given the known correlation between DED severity, ocular surface stability, and surgical recovery. Future prospective studies with validated DED grading would provide greater clarity. Given the possibility of a spectrum of disease, it may be useful in future studies to look at whether the degree of DED has an effect on visual outcomes and complication rates. Furthermore, the retrospective design introduces the possibility of selection bias and unmeasured confounders, which may affect the generalizability of the findings. In addition, systemic disease activity in RA and SS was not quantified using standardized indices (eg, DAS-28 for RA, ESSDAI for SS). Future prospective studies incorporating validated measures of ocular surface disease and systemic disease activity are needed to better define their impact on surgical risk and outcomes.

The main strength of this study was the sample size which, compared to similar previous studies that have examined cataract surgery outcomes in RA and SS, is the largest number of eyes analyzed. However, because significant complications are rare, determination of accurate rates of these complications is difficult without even higher study numbers.

Conclusion

In summary, the results of this study are clinically significant in demonstrating that patients with connective tissue diseases are at higher risk for both mild and severe postoperative complications. Individuals with preoperative DED are at risk for worse postoperative visual outcomes. Clinicians should be aware of the increased risk in this population and adopt a proactive approach to preoperative ocular surface optimization. Furthermore, given that both cases of the most vision-threatening complications in our series (corneal melt and endophthalmitis) occurred in SS patients, separate and more detailed counseling is recommended for this subgroup to ensure patients are informed of their elevated risk profile.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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