Incidence and management of cataract after glaucoma surgery

Hussain Y. Patel and Helen V. Danesh-Meyer

Purpose of review
This review summarizes the recent literature regarding the incidence and management of cataract following glaucoma surgery.

Recent findings
Half of the total number of phakic patients that have either trabeculectomy or tube shunt surgery will go on to develop visually significant cataract within 5 years. Phacoemulsification following trabeculectomy is significantly associated with bleb failure and loss of intraocular pressure (IOP) control. Recent studies suggest that the risk of bleb failure increases, the earlier cataract surgery is performed, and recommend a delay of at least 1–2 years after trabeculectomy to enable the bleb to stabilize. Bleb failure occurs because of scarring secondary to postoperative inflammation. Evidence suggests that intraoperative subconjunctival 5-fluorouracil (5-FU) may be protective, and repeated postoperative 5-FU injections may have a role in high-risk individuals along with aggressive anti-inflammatory treatment. Phacoemulsification following tube shunt surgery improves vision and does not affect IOP control. Novel glaucoma procedures are emerging, but they are often combined with cataract surgery, and/or clinical studies are at an early stage.

Summary
The development of visually significant cataract is common after glaucoma surgery. Subsequent cataract surgery can affect IOP control following trabeculectomy but not after tube shunt surgery. Measures to minimize the risk of bleb failure and loss of IOP control following trabeculectomy are critical in the management approach to patients who have had trabeculectomy.

Keywords
bleb failure, cataract, trabeculectomy, tube shunt surgery

INTRODUCTION
Coexisting cataract and glaucoma is commonly seen in the aging population. Furthermore, patients that undergo glaucoma surgery have an increased risk of developing visually significant cataract. In primary angle closure glaucoma, cataract surgery alone is often considered the preferred surgical option. However, for primary open angle glaucoma (POAG), the ideal timing of cataract surgery is a challenging issue. For patients with uncontrolled intraocular pressure (IOP) but without a visually significant cataract, a glaucoma surgical procedure alone is indicated. For patients with visually significant cataract and uncontrolled IOP, cataract surgery alone is unlikely to achieve the targeted IOP level. Instead, combined cataract and glaucoma surgery may be performed. Alternatively, glaucoma surgery followed by cataract surgery at a later date may be preferred. This review summarizes the recent literature relating to the incidence and management of cataract in patients who have undergone glaucoma surgery including trabeculectomy, tube shunt surgery, and novel glaucoma procedures.

INCIDENCE OF CATARACT AFTER TRABECULECTOMY
It is well established that patients who are undergoing trabeculectomy surgery have an increased risk of cataract formation and/or progression. In the Advanced Glaucoma Intervention Study [1], the Collaborative Normal Tension Glaucoma Study [2], and the Collaborative Initial Glaucoma Department of Ophthalmology, University of Auckland, Auckland, New Zealand
Correspondence to Professor Helen V. Danesh-Meyer, Department of Ophthalmology, University of Auckland, Private Bag 92019, Auckland 1023, New Zealand. Tel: +64 212291840; e-mail: h.daneshmeyer@auckland.ac.nz

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Department of Ophthalmology, University of Auckland, Auckland, New Zealand
Correspondence to Professor Helen V. Danesh-Meyer, Department of Ophthalmology, University of Auckland, Private Bag 92019, Auckland 1023, New Zealand. Tel: +64 212291840; e-mail: h.daneshmeyer@auckland.ac.nz

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Cataract surgery in the presence of a functioning filtration bleb can have a significant impact on bleb function and IOP control. Timing of cataract surgery after trabeculectomy is an important consideration with the risk of bleb failure decreasing as the time interval increases. Intracorneal subconjunctival 5-FU offers some protection against bleb failure. Clear corneal phacoemulsification through a temporal approach with minimal intraoperative iris manipulation is advised to decrease postoperative inflammation and the risk of bleb scarring.

More aggressive postoperative anti-inflammatory treatment compared with routine cataract surgery is recommended, and for high-risk patients, repeated subconjunctival 5-FU injections should also be considered.

Surgical peripheral iridectomy may be a contributing factor due to increased postoperative inflammation [8], as marked postoperative inflammation is significantly associated with increased risk of cataract formation [1]. This situation likely induces subconjunctival or scleral flap interface scarring with consequent loss of function of the filtration bleb [9]. The use of mitomycin C (MMC) with trabeculectomy has reported to increase risk of cataract formation compared with no antimetabolite [10,11], with direct toxicity to the lens being the proposed mechanism. Interestingly, 5-fluorouracil (5-FU) has not been documented to be associated with increased cataractogenesis [6]. Conjunctival manipulation may be another factor [12,13], but this is likely to be less important with phacoemulsification through a clear corneal incision. Postoperative hypotony and shallow or flat anterior chamber may be additional risk factors for cataract formation with several studies reporting a significant association [1,14–16]. Prolonged use of high-dose topical corticosteroids in the postoperative period is another important consideration [7].

The exact mechanism by which cataract surgery leads to trabeculectomy failure is not known. The most likely multifactorial [7]. Several preoperative, intraoperative, and postoperative factors have been implicated. Patient factors that have been documented to be associated with an increased risk of cataract formation following trabeculectomy include pseudoexfoliative glaucoma, myopia, and diabetes [3].

KEY POINTS

- Cataract surgery in the presence of a functioning filtration bleb can have a significant impact on bleb function and IOP control.
- Timing of cataract surgery after trabeculectomy is an important consideration with the risk of bleb failure decreasing as the time interval increases.
- Intracorneal subconjunctival 5-FU offers some protection against bleb failure.
- Clear corneal phacoemulsification through a temporal approach with minimal intraoperative iris manipulation is advised to decrease postoperative inflammation and the risk of bleb scarring.
- More aggressive postoperative anti-inflammatory treatment compared with routine cataract surgery is recommended, and for high-risk patients, repeated subconjunctival 5-FU injections should also be considered.
intrableb reflectivity before phacoemulsification was associated with a higher bleb failure rate [26]. Interestingly, patients who undergo trabeculectomy surgery for primary angle closure glaucoma may actually have improved IOP control, following subsequent phacoemulsification in contrast to patients with open-angle glaucoma [9**]. This is most likely due to the additional effect of drainage angle opening that occurs with cataract extraction.

**MINIMIZING THE RISK OF TRABECULECTOMY FAILURE DUE TO CATARACT SURGERY**

**Preoperative factors**
The timing of cataract surgery after trabeculectomy is perhaps the most important consideration. Published studies indicate that the earlier cataract surgery is performed, the greater the risk of subsequent trabeculectomy failure [9**,17,24*,28,29]. Husain et al. [9**] in a recent study from the Singapore 5-FU trial, determined that the closer the two surgical procedures are to each other, the shorter the time to trabeculectomy failure [hazard ratio: 1.73; 95% confidence interval (CI), 1.05–2.85]. When trabeculectomy failure was compared between patients who had subsequent cataract surgery and those who did not, a declining hazards ratio was observed as the time interval between trabeculectomy and cataract surgery increased [hazards ratio: 3.00 (95% CI, 1.11–8.14) for 6 months, 1.73 (95% CI, 1.05–2.85) for 1 year, and 1.32 (95% CI, 1.02–1.69) for 2 years]. In another recent study, Awaikasoka et al. [24*] determined that phacoemulsification within the year of trabeculectomy was a significant independent risk factor for failure [relative risk 2.87 (95% CI, 1.05–7.82), \( P = 0.04 \)], however, cataract surgery more than 1 year after trabeculectomy was not [relative risk 1.23 (95% CI, 0.23–6.51), \( P = 0.80 \)]. Furthermore, Manoj et al. [18] in an earlier study identified that phacoemulsification 2 or more years after trabeculectomy had no significant effect on IOP control.

Although the optimum timing of cataract surgery after trabeculectomy is not known, these studies indicate that a delay of at least 1–2 years will offer protection against bleb failure. It is likely that this time interval enables the bleb to fully stabilize and develop resistance against the effect of phacoemulsification.

A significant association between a higher IOP prior to cataract surgery and increased risk of bleb failure has been demonstrated in several studies [12,17,22,24*]. It is likely that patients with a higher preoperative IOP have filtering blebs with borderline function that are more susceptible to scarring following cataract surgery [12]. Younger age is another factor that predisposes to bleb failure, with one study reporting that patients less than 50 years of age have a significantly increased risk [17]. The influence of the type of glaucoma on bleb failure after cataract surgery has not been evaluated. It is likely that secondary glaucoma, and in particular uveitic glaucoma, confers increased risk of bleb failure.

It is important to identify patients that are at an increased risk for bleb failure following cataract surgery. It is advisable that more aggressive intraoperative and postoperative measures are taken in these patients to prevent bleb failure.

**Intraoperative measure to minimize bleb failure**
Each patient should be assessed in regard to the risk of bleb failure. All patients should be advised of this potential risk as part of the consent procedure. Given that there is a clear association between bleb failure and cataract surgery, it is generally advisable to delay cataract surgery if possible. However, often cataract surgery needs to be performed during the ‘high risk for bleb failure’ period. There are several techniques that the surgeon may undertake to minimize the risk of bleb failure. The more atraumatic the cataract surgery, the less risk of bleb failure. Minimal conjunctival manipulation is recommended. Clear corneal phacoemulsification through a temporal approach away from the bleb site is likely to minimize the risk of conjunctival scarring and subsequent bleb fibrosis [25]. Intraoperative iris manipulation has been association with increased risk of bleb failure [17,28], but this is not the case in all studies [12,23]. The role of other possible intraoperative factors such as surgical time, ultrasound power used, and surgical experience have not been studied.

Additional intraoperative procedures may minimize risk of bleb failure. There is evidence to suggest that a single subconjunctival injection of 5 mg 5-FU at the time of cataract surgery has a protective effect on a preexisting functioning trabeculectomy bleb. Sharma et al. [13] in a retrospective study evaluated the role of 5-FU in patients with primary open-angle glaucoma who underwent clear corneal phacoemulsification at least 12 months after trabeculectomy surgery. These patients were compared with a matched control group that did not receive 5-FU. Worsening of IOP control was seen in 13.6% of cases compared with 36.4% of controls (\( P = 0.03 \)) at 12 months postoperatively. Although the mean IOP was comparable between the two
groups, the mean number of glaucoma medication and the proportion of patients requiring additional glaucoma medications were significantly lower in the 5-FU group. Although further confirmation is needed, adjunct subconjunctival 5-FU at the time of cataract surgery should be considered in all patients and definitely used in those at increased risk of bleb failure. Simultaneous phacoemulsification and internal revision of the bleb have previously been described to prevent scarring of the filtering bleb, with bleb preservation in 89% of patients reported [30]. However, the revision of functioning blebs during phacoemulsification is not routinely advised but may be indicated in patients with high preoperative IOP and/or blebs with borderline function [12].

Postoperative factors

It has been demonstrated using laser flare photometry that subclinical low-grade inflammation can persist for up to 6 months following phacoemulsification [27]. This is thought to be due to the release of lens crystallins and lens epithelial cells into the aqueous humour, the effect of ultrasound, and/or the high volume of fluid passing through the eye at the time of surgery. The inflammation leads to an upregulation of fibrogenic cytokines in the aqueous humour and consequent increased risk of bleb failure [27].

More aggressive anti-inflammatory treatment in the postoperative period may, therefore, decrease the risk of bleb failure. Topical steroid treatment for 1 month is a regime commonly used after routine cataract surgery. The findings of the above study suggest that topical steroids should be used for a longer period when cataract surgery is performed on a patient with a functioning trabeculectomy bleb. In addition, topical nonsteroidal anti-inflammatory treatment may also have a role. Unfortunately, there are no studies or published studies that have evaluated this further, hence the optimal postoperative anti-inflammatory treatment regimen is not known at present.

The use of repeated subconjunctival 5-FU injections in the postoperative period is another consideration. The effectiveness of this intervention was recently evaluated by Shahid and Salmon [25]. Using a retrospective study, they investigated the effect of 5-FU subconjunctival injections at 2, 4, and 12 weeks after uncomplicated clear corneal phacoemulsification in 25 consecutive POAG patients with a functioning trabeculectomy bleb. They were compared with a historical series of consecutive patients who underwent cataract surgery in the presence of a filtering trabeculectomy bleb but who did not receive postoperative 5-FU injections. Using Kaplan–Meier survival analysis, the cumulative probability of trabeculectomy survival in the 5-FU group was 96.0% and in the control group 87.5% at 2 years. The authors noted that although this may be clinically significant, the difference did not reach statistical significance ($P = 0.30$), and a larger prospective study is needed to determine the precise role of repeated postoperative subconjunctival 5-FU injections. However, this intervention should be considered in patients who have additional risk factors for bleb failure and who have an early postoperative IOP elevation, which is another factor associated with bleb failure [17]. If conjunctival scarring does lead to bleb failure then bleb needling combined with adjunct subconjunctival 5-FU or MMC will be needed to resuscitate the bleb.

**TUBE SHUNT SURGERY**

As with trabeculectomy, tube shunt surgery increases cataract incidence and progression. The development of cataract is a significant cause of visual loss following tube shunt surgery. In the Tube versus Trabeculectomy Study [31], 54% of phakic patients who underwent tube shunt surgery developed visually significant cataract, requiring phacoemulsification within the first 5 postoperative years. This was a similar rate to that seen with trabeculectomy. Reassuringly, published studies indicate that in most cases, phacoemulsification in glaucomatous eyes with a functioning tube shunt device improves vision and does not have a detrimental effect on IOP control [32–35]. Some patients, however, will need additional glaucoma medication to maintain IOP control [34], and a minority will have to undergo repeat glaucoma surgery [35]. Optimal phacoemulsification technique and postoperative care in patients having cataract surgery in the presence of a tube shunt device have not been reported on in the recent literature.

**NOVEL GLAUCOMA PROCEDURES**

A range of novel glaucoma procedures has emerged in recent years. These include: the Ex-PRESS miniature glaucoma device (Alcon, Inc., Hunenberg, Switzerland), SOLX Gold Shunt (SOLX Ltd., Boston, Massachusetts, USA), trabeculotomy by internal approach with Trabectome (NeoMedix, Inc., Tustin, California, USA), trabecular microbypass stent (iStent, Glaukos Corporation, Laguna Hills, California, USA), and canaloplasty (iScience Interventional Corp., Menlo Park, California, USA) [36].

The Ex-PRESS miniature device was developed as an alternative filtration procedure to trabeculectomy.
[37,38]. Proposed advantages include less intraocular manipulation, postoperative inflammation, and hypotony [39]. It follows that postoperative cataract formation may also be less common compared with trabeculectomy. de Jong et al. [40], in a prospective randomized clinical trial did report fewer patients requiring cataract surgery following Ex-PRESS than trabeculectomy at 5-year follow-up, however, the difference was minimal, and further investigation is needed. As Ex-PRESS surgery requires formation of a filtering bleb, the effect on bleb function with subsequent cataract surgery is likely to be similar to that seen with trabeculectomy and the same considerations apply.

The incidence of cataract with other novel glaucoma procedures is difficult to ascertain as clinical studies are still in the early stages and/or have combined the new technique with phacoemulsification. These novel procedures aim to improve aqueous outflow through the trabecular meshwork, Schlemm’s canal and outflow channels (Trabectome, iStent, and Canaloplasty) or uveoscleral outflow pathway (SOLX gold shunt), and therefore aim to avoid the formation of an external filtering bleb [36]. They are, therefore, not subject to the risk of failure due to bleb scarring that is seen with cataract surgery after trabeculectomy or the Ex-PRESS device.

CONCLUSION

The coexistence of glaucoma and cataract is common and can be challenging to manage. Approximately half of phakic patients who undergo trabeculectomy will require cataract surgery within the first 5 postoperative years. Cataract surgery in the presence of a functioning filtration bleb can have a significant impact on bleb function and IOP control, with an increased risk of bleb failure well recognized. Timing of cataract surgery after trabeculectomy is an important consideration with the risk of bleb failure decreasing as the time interval increases. The optimum timing of cataract surgery after trabeculectomy is not known, but a delay of at least 1–2 years is protective against bleb failure, allowing the bleb to fully develop and stabilize. Younger age and high preoperative IOP are some of the factors identified that predispose patients to an increased risk of bleb failure. Intraoperative subconjunctival 5-FU offers some protection against bleb failure. Clear corneal phacoemulsification through a temporal approach with minimal intraoperative iris manipulation is advised to decrease postoperative inflammation and the risk of bleb scarring. Revision of the bleb at the time of cataract surgery should be considered in patients with high preoperative IOP and/or borderline bleb function.

More aggressive postoperative anti-inflammatory treatment compared with routine cataract surgery is recommended and for high-risk patients, repeated subconjunctival 5-FU injections should also be considered.

Approximately half of phakic patients undergoing tube shunt surgery will develop visually significant cataract and will need cataract surgery within the first 5 postoperative years. However, in most cases, cataract surgery in glaucomatous eyes with a functioning tube shunt device improves vision and does not have a detrimental effect on IOP control. A range of novel glaucoma procedures has recently emerged. The relationship between cataract and these new procedures is difficult to ascertain, as clinical studies are still in the early stages and/or have combined the new technique with phacoemulsification.

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Conflicts of interest

The authors have no conflicts of interest or financial disclosure to report.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

* of special interest
** of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 80).

Cataract surgery and lens implantation

25. This study evaluates the effect of preoperative IOP and early cataract surgery on trabeculectomy survival.
32. This study presents recent data regarding cataract formation after trabeculectomy versus tube insertion.