Original Article

Outcome of repeat trabeculectomy with mitomycin C in isolation or combined with phacoemulsification

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Purpose: To evaluate the effectiveness of repeat trabeculectomy with Mitomycin C (MMC) in isolation or combined with phacoemulsification, and to identify risk factors for failure over 1 year. **Methods:** Retrospective review of 113 eyes of 113 patients (49 primary open angle, 27 primary angle closure, 37 secondary glaucoma) who underwent repeat trabeculectomy with MMC (isolated trabeculectomy 75 and phacotrabeculectomy 38). The primary outcome measure was intraocular pressure (IOP) at 1 year follow-up. Three IOP criteria were chosen to measure success A) IOP ≤21 mmHg and ≥20% reduction from baseline. B) IOP ≤17 mmHg and ≥20% reduction from baseline. C) IOP ≤14 mmHg. **Results:** Mean IOP decreased from 24.5 ± 8.8 mmHg to 16.4 ± 7.6 mmHg 1 year after repeat trabeculectomy. The mean number of medications reduced from 2.9 ± 1.0 to 0.6 ± 1.0. Complete success with trabeculectomy versus phacotrabeculectomy for criterion A was 60% vs 55.3%, criterion B 54.7% vs 50.0% and criterion C 40.0% vs 28.9%. IOP ≤14 mmHg was more likely with trabeculectomy than phacotrabeculectomy ($P = 0.047$). On regression analysis, duration between surgeries ≤4 years ($P = 0.018$) and secondary glaucoma ($P = 0.046$) were identified as risk factors for surgical failure with criterion A. Younger age ($P = 0.042$), fornix based flap ($P = 0.058$), and phacotrabeculectomy ($P = 0.042$) for criterion C. **Conclusion:** Repeat trabeculectomy with MMC is successful at lowering IOP and decreasing number of antiglaucoma medications. Low IOP levels are less likely with phacotrabeculectomy.

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Trabeculectomy is the most commonly used surgical intervention for the management of glaucoma. The most common cause of surgical failure is subconjunctival and episcleral fibrosis.[1] The progressive fibrosis of subconjunctival and episcleral tissues has been attributed to the increase in subepithelial conjunctival fibroblasts stimulated after any surgery on the conjunctiva.[2] Although previous filtration surgery is a known risk factor for trabeculectomy failure, repeat trabeculectomy is performed frequently in cases of initial trabeculectomy failure refractory to medical treatment.

There are a few reports in the literature describing the outcome of repeat trabeculectomy[3-7] where success rates had been noted to be between 30 and 80% with reasonable qualified success and few complications. Repeat trabeculectomy has been noted to produce similar IOP reduction to non-valved shunt surgery in the Tube versus Trabeculectomy study[8,9] with higher rates of reoperation in the trabeculectomy group. However, there is no detailed analysis of success rates in different types of glaucoma or comparison between repeat trabeculectomy and phacotrabeculectomy. Since cataract progression is common after a trabeculectomy, many eyes would need cataract surgery along with repeat trabeculectomy.

We analyzed the effectiveness of repeat trabeculectomy and phacotrabeculectomy in different types of glaucoma and risk factors for surgical failure over a follow-up of 1 year.

Methods

Patient data

We performed a retrospective study of patients who had undergone repeat trabeculectomy with Mitomycin C (MMC), with or without phacoemulsification, between 2000 and 2016 at a single centre. Institutional review board approval was obtained before data collection. One hundred and thirteen eyes of 113 patients were included. Exclusion criteria were age less than 18 years at the time of first trabeculectomy, congenital, and developmental glaucoma and patients with less than 1 year follow-up.

The indications for surgery were either inadequately controlled intraocular pressure (IOP) or glaucomatous progression of the visual field or optic disc.

We extracted data regarding age at the time of surgery, gender, laterality, associated systemic comorbidities, family history of glaucoma, prior ocular surgical or laser treatments, type of glaucoma, lens status, preoperative visual acuity (VA), IOP, central corneal thickness, number of antiglaucoma medications (AGM), duration on AGM, cup disc ratio and visual field defect as mean deviation (MD). The duration between the first and second trabeculectomy was noted. Per-operative data collected included type of surgery (trabeculectomy or phacotrabeculectomy- same or separate site), fornix or limbus

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based conjunctival flap, duration of and concentration of MMC used, location of trabeculectomy, and intraoperative complications. We collected postoperative data at 6 weeks, 6 months, and 1 year. This included VA, IOP, bleb morphology, cup disc ratio, and visual field MD. In addition, we recorded postoperative complications, interventions such as needling, the indication and time and IOP when AGM's were restarted, and any surgeries or procedures performed.

Surgical technique

Three experienced surgeons performed all surgeries. After peribulbar anesthesia with 2% lignocaine and 0.5% bupivacaine, the eye was prepped and draped. Either a limbus or fornix based conjunctival flap was fashioned. A thin cellulose sponge soaked in 0.4 mg/ml of MMC was placed under the conjunctiva for 1–3 min. The duration of MMC application was based on the preoperative evaluation of each patient's risk factors for failure. The MMC treated area was irrigated with balanced salt solution. Light wet field cautery was applied to the areas of bleeding and the flap area. A 3 × 3 mm partial thickness triangular scleral flap was made which we then dissected into clear cornea. The trabeculectomy fistula was then trephined using Kelly's punch. A peripheral iridectomy was done through the sclerectomy. The scleral flap was sutured with fixed and releasable sutures. The site and number of releasable sutures were adjusted according to the patient's risk profile. The conjunctiva and Tenon's capsule were closed in a water tight fashion.

All patients who underwent phacotrabeculectomy had a single site cataract surgery and trabeculectomy.

Postoperatively patients were treated with a tapering course of topical steroids. Postoperative injections of 5- fluorouracil, removal of releasable sutures and argon laser suturolysis were done as and when needed.

Outcome measures

The main outcome measure was intraocular pressure at 1 year follow-up (IOP). We chose three IOP criteria to measure success A) IOP ≤21 mmHg with ≥20% reduction from baseline B) IOP ≤17 mmHg with ≥20% reduction from baseline and C) IOP ≤14 mmHg.

We defined complete success as when these criteria were met without any AGM and qualified success with or without medical therapy. Failure was defined as IOP >21 mm Hg or <6 mm Hg or glaucoma surgery was required again.

The secondary outcome measure was the number of AGM's.

We evaluated outcome measures separately for trabeculectomy and phacotrabeculectomy and different types of glaucoma.

All continuous data are presented as Mean ± SD. Means were compared using t test. A *P* value of <0.05 was considered significant. We performed logistic regression analysis keeping success by different criteria as the outcome measure and assessing the risk factors listed to analzse risk factors for failure.

These included age, gender, history of diabetes, hypertension or prior ocular surgery, preoperative IOP, type of glaucoma, lens status, number of AGM's, duration between first and repeat trabeculectomy, fornix vs limbus based flap, MMC duration, site of trabeculectomy, trabeculectomy versus phacotrabeculectomy, postoperative complications, and postoperative needling.

Results

We included 113 eyes (113 patients), of whom 92 were men and 21 women who had all undergone a trabeculectomy earlier. Seventy five eyes underwent a trabeculectomy and 38 eyes a phacotrabeculectomy. Table 1 summarizes the baseline characteristics, preoperative and surgical details.

The mean IOP at baseline was 24.5 ± 8.8 mm Hg and at 1 year after repeat trabeculectomy IOP was 16.4 ± 7.6 mm Hg.

Isolated trabeculectomy produced greater statistically significant reduction in IOP (10.0 mm Hg/30.73%) compared to phacotrabeculectomy (3.7 mm Hg/12.33%) (*P* = 0.033) [Fig. 1]. Four eyes with secondary glaucoma (three inflammatory and one neovascular glaucoma) had IOP more than 40 mm Hg at the 1 year follow-up. One eye with primary open angle glaucoma (POAG) eye had IOP of 5 mm Hg at the 1 year follow up.

The mean number of medications reduced from 2.9 ± 1.0 to 0.6 ± 1.1. Seventy five eyes (66. 4%) were not on any AGM after repeat trabeculectomy. The mean number of AGM reduced significantly in the trabeculectomy group from 3.2(SD: 0.8) to 0.5(SD: 0.1) (*P* < 0.0001) and in the Phacotrabeculectomy group from 2.3(SD: 1.0) to 0.8(SD: 1.3) (*P* < 0.0001). This reduction in AGM was greater with trabeculectomy than phacotrabeculectomy (*P* = 0.046).

Overall complete success (CS) rates were 58.4%, 53.1%, and 36.3% for criterion A, B, and C, respectively. Qualified success (QS) were 85.8%, 75.2%, and 47.8%, respectively. Table 2 shows the success rates with trabeculectomy and phacotrabeculectomy.

Low IOP levels of ≤14 mm Hg were more likely with trabeculectomy than phacotrabeculectomy (*P* = 0.047).

Fig. 2 shows overall success rates in different types of glaucoma for each IOP criteria.

There were no significant intraoperative complications. In the postoperative period four eyes (2 of each group) had a choroidal detachment associated with hypotony and were treated conservatively. One eye in trabeculectomy group had a bleb leak and treated with bandage contact lens.

One patient in the trabeculectomy group underwent needling with 5 fluorouracil and IOP remained under control with one AGM at the 1 year follow-up.

Of the 18 eyes with surgical failure, 13 eyes underwent a repeat glaucoma procedure, of which 6 had a third trabeculectomy, 5 an Ahmed glaucoma valve and 2 underwent

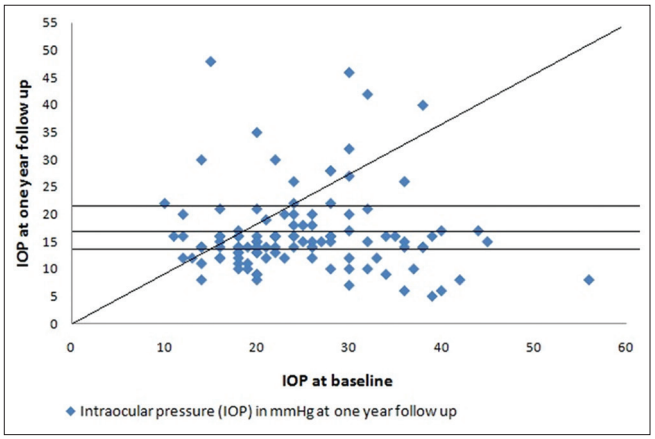

Figure 1: Scatter plot demonstrating change from preoperative intraocular pressure (IOP) to one year follow-up. Points indicate IOP in mmHg at one year follow up

Table 1: Baseline characteristics, preoperative and surgical details

	Total	Trabeculectomy	Phacotrabeculectomy
Number of eyes (*n*)	113	75	38
Age (years)			
Mean±SD	52±13	50±14	55±11
Range	19-77	19-77	20-72
Median	54	52	56
Gender, *n* (%)			
Male/female	92 (81.4%)/21 (18.6%)	60 (80%)/ 15 (20%)	32 (84.2%)/6 (15.8%)
Laterality, *n* (%)			
Right/left	57 (50.4%)/56 (49.6%)	36 (48%)/39 (52%)	21 (55.3%)/17 (44.7%)
Diagnosis, *n* (%)			
POAG	49 (43.3%)	35 (46.7%)	14 (36.8%)
PACG	27 (23.9%)	13 (17.3%)	14 (36.8%)
Secondary glaucoma	37 (32.7%)	27 (36%)	10 (26.3%)
Inflammatory	11	9	2
Traumatic	6	4	2
Neovasular	5	2	3
Post vitreoretinal surgery	5	4	1
Post keratoplasty	1	1	0
Raised episcleral venous pressure	4	2	2
Iridocorneal endothelial syndrome	5	5	0
Preoperative IOP (mm Hg)			
Mean±SD	24.5±8.8	26.1±9.1	21.3±7.0
Number of preoperative medications			
Mean±SD	2.9±1.0	3.2±0.8	2.3±1.0
Preoperative Lens status, *n* (%)			
Phakic	78 (69%)	40 (53.3%)	38 (100%)
Pseudophakic	35 (31%)	35 (46.7%)	0
Duration between first and second trabeculectomy (years)			
Mean±SD	4.1±3.7	4.3±4.2	3.4±2.0
Systemic illness, *n* (%)			
Diabetes	42 (56%)	24 (32%)	18 (47.3%)
Hypertension	36 (31.8%)	20 (26.7%)	16 (42.1%)
Fornix/limbus based flap, *n* (%)	56 (49.6%)/ 57 (50.4%)	24 (32%)/ 51 (68%)	38 (100%)/0
Duration of MMC in min, *n* (%)			
1	38 (33.6%)	20 (26.7%)	18 (47.3%)
2	34 (30.08%)	27 (36%)	07 (18.4%)
3	41 (36.3%)	28 (37.3%)	13 (34.2%)
Location of trabeculectomy, *n* (%)			
Superior	31 (27.4%)	17 (22.7%)	14 (36.8%)
Superonasal	29 (25.7%)	23 (30.7%)	06 (15.8%)
Superotemporal	53 (46.9%)	35 (46.7%)	18 (47.4%)
Intraoperative complications, (*n*)			
Posterior capsular rent	1	0	1
Zonular dialysis	1	0	1
Opening of previous trabeculectomy stoma	1	1	0
Conjunctival buttonholing	1	1	0

SD=Standard deviation; POAG=Primary open angle glaucoma; PACG=Primary angle closure glaucoma; MMC=Mitomycin C

diode cyclophotocoagulation. One eye post-trabeculectomy had persistent hypotony.

Risk factors for surgical failure were analyzed using logistic regression analysis for various IOP criteria [Table 3].

On regression analysis, duration between surgeries ≤4 years ($P = 0.018$) and secondary glaucoma ($P = 0.046$) were identified as risk factors for surgical failure with lenient IOP criteria of ≤21 mm Hg. Younger age ($P = 0.042$), fornix based flap ($P = 0.058$), and phacotrabeculectomy ($P = 0.042$) were identified as risk factors for failure with strict IOP criteria of ≤ 14 mm Hg.

Discussion

There is no consensus on the choice of glaucoma surgery in an eye with a previously failed trabeculectomy. As a repeat trabeculectomy with MMC is found to be less successful at achieving a robust IOP reduction[3,4] and technically more challenging than a primary trabeculectomy, alternative management approaches have been suggested.[8-10] The tube versus trabeculectomy (TVT) study indicated that tubes provided better IOP control than trabeculectomies.

Table 2: Comparison of success rates of repeat trabeculectomy and phacotrabeculectomy

	Complete success (%)		Qualified success (%)	
	Trabeculectomy	Phacotrabeculectomy	Trabeculectomy	Phacotrabeculectomy
Criteria A	60.0	55.3	89.3	79.0
Criteria B	54.7	50.0	77.4	71.1
Criteria C	40.0	28.9	54.7	34.2

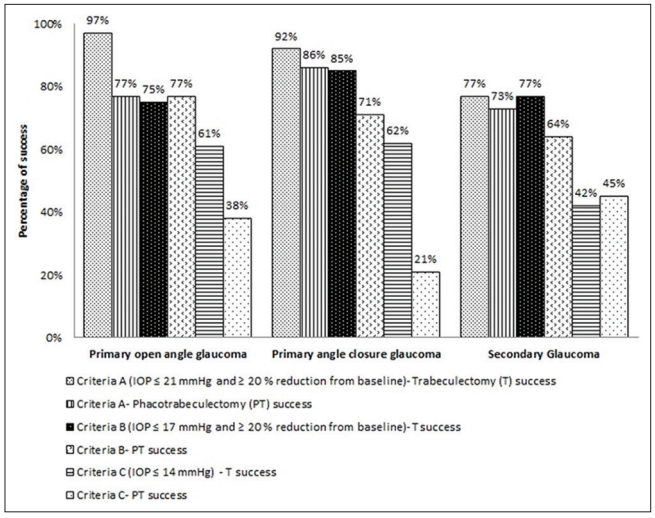

Figure 2: Bar graph showing overall success rates in percentage for criteria A (IOP ≤21 mmHg and ≥20% reduction from baseline), criteria B (IOP ≤17 mmHg and ≥20% reduction from baseline) and criteria C (IOP ≤14 mmHg) with repeat trabeculectomy and phacotrabeculectomy in primary open angle glaucoma, primary angle closure glaucoma and secondary glaucoma

The present study demonstrates that repeat trabeculectomy with MMC can be an effective treatment option in reducing IOP. In developing countries, cost plays a major role in the choice of treatment. Devices and ophthalmologists trained in valve surgeries are not uniformly available. Repeat trabeculectomy is a useful option. Titrating the dose and duration of MMC used, close postoperative monitoring and appropriate postoperative intervention as and when needed, can ensure good postoperative results. Since more ophthalmologists are familiar with the technique, this becomes a viable alternative.

Our results of trabeculectomy with IOP ≤21 mmHg (CS 60% QS 89.3%) are comparable to the outcome of repeat trabeculectomy in Tube versus trabeculectomy (TVT) study 1 year follow up results (CS 63% QS 87%).[8]

While the TVT study included eyes that had cataract surgery as the primary intervention, our series included only eyes with a previously failed trabeculectomy and still report comparable results despite being at higher risk for failure.

Persistent hypotony with trabeculectomy in the TVT study was 2.8% (3 out of 105 eyes), probably because of the longer duration of MMC used (0.4 mg for 4 min). In our study hypotony was seen in 0.8% (one eye of isolated trabeculectomy). This could be related to the shorter duration of MMC use (1–3 min), which was titrated based on the risk factors for surgical failure. We can speculate that with the higher risk of scarring in these eyes with failed glaucoma surgery hypotony would be less likely.

Olali *et al*.[7] have reported CS of 82% and QS of 88% for IOP ≤21 mmHg in 50 eyes with repeat trabeculectomy at the 1 year follow-up. The difference in the success rates would be due to the variation in the type of glaucoma included (more POAG) and patients race (whites).

Cankaya *et al*.[4] found that difference between the outcomes for qualified success of the initial (59 eyes) and repeat trabeculectomy (28 eyes) in POAG/pseudoexfoliation at around 19 months follow-up was minimal (Primary group CS 64.4% QS 83.1% repeat group CS 39.3% QS 82.1%). While complete success was significantly more common in the primary group, a greater proportion of eyes in the repeat group needed postoperative anti-glaucoma medications.

Law *et al*.[3] retrospectively evaluated the outcome of repeat trabeculectomy with MMC (50 eyes) in POAG as compared with primary trabeculectomy (50 eyes) at 3 years follow-up. In their study significantly lesser success rate for repeat trabeculectomy with more stringent success criteria (52% success with initial trabeculectomy 32% with repeat trabeculectomy, $P = 0.021$) were seen. With less stringent IOP reduction criteria, the difference between the 2 groups was not statistically significant (68% success with initial trabeculectomy 54.6% with repeat trabeculectomy, $P = 0.131$).

Comparison between the studies available[3-10] on repeat trabeculectomy outcomes is limited, given the variable criteria used for success, follow-up duration, type of glaucoma, surgical techniques, and patient populations.

To our knowledge, no previous studies on the comparison between repeat trabeculectomy and phacotrabeculectomy are available. Studies on primary trabeculectomy versus phacotrabeculectomy with MMC have showed a greater IOP reduction with trabeculectomy than phacotrabeculectomy.[11,12]

In our study a final IOP of ≤14 mm Hg was more likely with trabeculectomy than phacotrabeculectomy ($P = 0.047$). Repeat trabeculectomy produced a greater reduction in IOP ($P = 0.033$) and reduction in the number of AGM ($P = 0.046$) than phacotrabeculectomy.

There was considerable difference in surgical success between the groups with more lenient IOP criteria and a more significant difference using the more stringent criteria.

In eyes with advanced glaucoma, that required very low target pressures and secondary glaucoma with uveitis or neovascularisation, trabeculectomy had higher success rates than phacotrabeculectomy. The inflammatory response associated with secondary glaucoma is expected to be more than in primary glaucoma and the different pathogenesis would be the possible reason for the high rate of surgical failure in this group. The breakdown of the blood-aqueous barrier and the release of inflammatory mediators that accompanies phacoemulsification lead to a heightened inflammatory response which may cause increased scarring of the bleb resulting in poorer long term filtration. In addition, there are other potential complications associated with cataract surgery, such as vitreous loss, that can predispose to bleb failure. It may be advisable, therefore, to avoid simultaneous cataract surgery in favour of isolated trabeculectomy in eyes with advanced glaucoma where cataract surgery can be postponed.

Table 3: Regression analysis for various IOP criteria

Variable	For success ≤21 mmHg				For success ≤17 mmHg				For success ≤14 mmHg			
	95% CI				95% CI				95% CI			
	OR	LL	UL	*P*	OR	LL	UL	*P*	OR	LL	UL	*P*
Age	0.971	0.937	1.007	0.117	0.985	0.956	1.015	0.335	0.971	0.944	0.999	**0.042**
Female	1.013	0.261	3.929	0.985	1.273	0.44	3.677	0.656	2.089	0.772	5.651	0.147
Diabetes	0.518	0.155	1.723	0.283	0.92	0.378	2.238	0.854	1.177	0.547	2.53	0.677
Hypertension	0.265	0.057	1.234	0.091	0.644	0.245	1.691	0.371	0.633	0.285	1.403	0.26
PACG	1.406	0.291	6.805	0.672	0.881	0.288	2.691	0.824	1.785	0.689	4.625	0.233
Secondary Glaucoma	3.616	1.017	12.86	**0.046**	1.142	0.431	3.027	0.79	1.611	0.682	3.807	0.277
Preoperative IOP	1.016	0.958	1.077	0.602	1.001	0.954	1.051	0.963	1.018	0.975	1.063	0.412
Preoperative number of AGM	1.11	0.649	1.897	0.703	1.254	0.789	1.995	0.339	0.954	0.649	1.404	0.811
Preoperative lens status pseudophakia	1.418	0.485	4.146	0.523	1.186	0.492	2.858	0.703	0.806	0.374	1.737	0.582
Duration between trabeculectomies ≤4 years	11.944	1.517	94.044	**0.018**	1.478	0.599	3.646	0.397	1.156	0.542	2.465	0.707
Phacotrabeculectomy	2.233	0.766	6.514	0.141	1.39	0.574	3.369	0.466	2.319	1.032	5.212	**0.042**
Fornix based Flap	1.398	0.481	4.057	0.538	1.871	0.782	4.473	0.159	2.072	0.974	4.408	0.058
MMC - Duration - 1 Minute	2.089	0.559	7.803	0.273	2.242	0.774	6.489	0.137	1.158	0.478	2.802	0.745
MMC - Duration - 2 Minute	1.595	0.393	6.479	0.514	1.749	0.574	5.33	0.326	1.87	0.742	4.716	0.184
Trabeculectomy Location - Superonasal	2.955	0.521	16.755	0.221	1.937	0.543	6.91	0.308	1.664	0.571	4.853	0.351
Trabeculectomy Location - Superotemporal	2.721	0.545	13.581	0.222	1.38	0.432	4.413	0.587	2.107	0.826	5.379	0.119
Postoperative Complication - Yes	1.519	0.164	14.067	0.713	0.464	0.055	3.915	0.48	0.667	0.176	2.527	0.551
Needling	2.089	0.204	21.423	0.535	3.192	0.428	23.798	0.257	2.839	0.286	28.154	0.373

CI=Confidence interval; OR=Odds ratio; LL=Lower limit; UL=Upper limit; PACG=Primary angle closure glaucoma; IOP=Intraocular pressure; AGM=Antiglaucoma medications; MMC=Mitomycin C, significant *P* values are made bold

However, this has to be balanced against the risk in these eyes of a transient rise of IOP post cataract surgery whenever surgery is planned as a second stage procedure.

The longer the duration between repeat surgeries, older the age, eyes with primary glaucoma, and trabeculectomy alone rather than phacotrabeculectomy lesser the inflammatory changes and lesser the risk of surgical failure.

In eyes that have had multiple surgeries or have significant scarring and in eyes that require a combined procedure, fornix-based flaps tend to provide better surgical exposure for dissection of the scleral flap and better access to the trabeculectomy performed at the iris root. In our series a fornix based flap was found to have poorer surgical outcomes with strict IOP criteria. One possible explanation is that fornix based flaps were uniformly used with phacotrabeculectomy which had poorer outcomes, and this could be a confounder.

The strength of our study is that it is, to the best of our knowledge, the first study to compare a repeat trabeculectomy outcome with phacotrabeculectomy. However, longer term outcomes of repeat trabeculectomy still need to be studied. The retrospective nature of the study and short duration of follow-up are the limitations in our study.

Conclusion

Repeat trabeculectomy with MMC is successful at lowering IOP and the number of antiglaucoma medications. Low IOP levels are less likely with phacotrabeculectomy. Repeat trabeculectomy can be an effective treatment option in eyes with failed filtration surgery.

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Conflicts of interest

There are no conflicts of interest.

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