

# Outcomes and risk factors for failure of trabeculectomy in glaucomatous patients in Southwest China: a 325 eyes analysis

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## Abstract

• **AIM:** To evaluate the outcomes and elucidate the failure factors for trabeculectomy with mitomycin C (MMC) in Southwest Chinese patients.

• **METHODS:** A retrospective correlational study was conducted on the glaucomatous patients who underwent initial trabeculectomy with MMC in Southwest Hospital and had been followed up for 1-3y. A complete success for surgery is defined as a postoperative intraocular pressure (IOP) >5 and ≤21 mm Hg and 20% reduction of IOP compared to preoperative, without IOP-lowering medications. A qualified success for surgery is defined as the abovementioned postoperative IOP with or without IOP-lowering medications. The primary outcomes were IOP, the number of IOP-lowering medications, and cumulative success rate. The secondary outcomes included best corrected visual acuity (BCVA), mean deviation (MD) of visual field, major complications, and risk factors for surgical failure.

• **RESULTS:** A total of 325 eyes of 261 glaucomatous patients had been included in our study. Both the mean IOP and the number of IOP-lowering medications were significantly decreased from 32.9±12.0 to 16.4±5.7 mm Hg ( $P<0.0001$ ) and 3.0±0.9 to 0.9±1.0 ( $P<0.0001$ ), respectively, at the last visit. The cumulative complete success rate and qualified success rate were 77.8% and 92.0% at 1-year follow-up, and 47.2% and 77.7% at 3-year follow up. There

were no significant differences in surgical outcomes between primary angle-closure glaucoma (PACG) and primary open angle glaucoma (POAG). In PACG patients, the success rates of trabeculectomy were comparable with those of phacotrabeculectomy. Hypertension (HR=1.904,  $P=0.011$ ), encapsulated bleb (HR=2.756,  $P<0.001$ ), and more preoperative topical medications (HR=2.475,  $P=0.008$ ) were risk factors for surgical failure.

• **CONCLUSION:** The qualified success rate of trabeculectomy with MMC in glaucomatous patients in the cohort is 92.0% at 1-year, and 77.7% at 3-year follow up. Hypertension, encapsulated bleb, and more preoperative topical medications are associated with surgical failure.

• **KEYWORDS:** glaucoma; trabeculectomy; outcomes; risk factors

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## INTRODUCTION

Glaucoma is an irreversible optic neuropathy that considered to be one of the leading causes of blindness worldwide. More than 90% of patients are unaware of their vision loss and many risk factors are associated with physiopathology of glaucoma. Among them, intraocular pressure (IOP) remains the main modifiable risk factor, and surgical treatment is the standard care for glaucomatous patient aiming to lower IOP if not controlled by pharmacological agents.

Nowadays, minimally invasive glaucoma surgeries are blooming<sup>[1-2]</sup>. Recent studies of the American Glaucoma Society have demonstrated a rise in the proportion of using tube shunts and a decline in the popularity of trabeculectomy<sup>[3-4]</sup>. Nevertheless, trabeculectomy still remains the most effective procedure<sup>[5]</sup> for glaucoma management in China since most patients suffer from primary angle-closure glaucoma (PACG).

The success rate of trabeculectomy has been increasing along with innovation of intraoperative techniques such as wide application of antifibrotics and placement of adjustable sutures. It is believed that the postoperative interventions, for instance, removal of adjustable sutures or laser suture lysis, ocular massage, and bleb needling, have reduced complications and improved outcomes of trabeculectomy<sup>[6-7]</sup>.

The success rate of trabeculectomy is lower in non-Caucasian individuals than it is in Caucasians which is probably related to differences in disease type and soft tissue characteristics between these populations<sup>[8]</sup>. There are some studies report the efficacy and safety of trabeculectomy in Asian. The 5-year success rate was 87.3% according to the Japanese Collaborative Bleb-Related Infection Incidence and Treatment Study (CBIITS)<sup>[9]</sup>. A research in Taiwan described a cumulative qualified success rate of 67.1% in a 10-year follow-up period<sup>[10]</sup>. A retrospective study on mitomycin C (MMC)-augmented trabeculectomy revealed that the qualified success rate was 75% after a follow-up period of 21.8mo in Hong Kong<sup>[11]</sup>. However, studies on trabeculectomy in mainland Chinese patients are lacking. To evaluate the efficiency and safety for trabeculectomy, we retrospectively review 325 eyes of 261 glaucomatous patients who underwent trabeculectomy with MMC and elucidate the success and failure factors for trabeculectomy in Southwest Chinese patients.

## **SUBJECTS AND METHODS**

**Ethical Approval** The study was approved by the human research ethics committee of the Southwest Hospital (KY2020206). Informed consent was obtained from all patients. All methods were performed in accordance with the relevant guidelines and regulations adhered to the tenets of the Declaration of Helsinki.

**Study Design** The medical records of patients who were diagnosed with glaucoma and underwent trabeculectomy with MMC in Southwest Hospital of China were retrospectively reviewed from January 2016 to December 2018.

All patients enrolled in this study had uncontrollable glaucoma and were on maximal tolerable medication therapy. Types of glaucoma include PACG, primary open angle glaucoma (POAG), secondary glaucoma and congenital glaucoma. The inclusion criteria were as follows. Patients were over 18 years old, diagnosed of glaucoma, and underwent initial trabeculectomy with MMC. The surgery includes trabeculectomy concomitantly performed with cataract surgery or anterior vitrectomy. Patients had no previous intraocular surgeries except laser peripheral iridotomy (LPI) and selective laser trabeculoplasty (SLT), and had been followed up for minimum 1y. The exclusion criteria were patients of less than 18 years old, history of cataract surgery or trabeculectomy, and less than 1-year follow-up period.

**Data Collection** Preoperative data including the patients' demographic information, glaucoma type, IOP, number of IOP-lowering medications, best corrected visual acuity (BCVA), mean deviation (MD) of visual field, vertical cup to disc ratio, and surgery type were collected. IOP was measured by non-contact or rebound tonometer. At least 3 consecutive readings were recorded for each patient at each follow-up point. BCVA measurements were converted to logarithm of the minimum angle of resolution (logMAR) equivalents for the purpose of data analysis<sup>[12]</sup>. Postoperative data included BCVA, IOP, number of IOP-lowering medications, complications, and surgical interventions.

According to the World Glaucoma Association Guidelines, a complete success for surgery is defined as a postoperative IOP of  $>5$  and  $\leq 21$  mm Hg and 20% reduction of IOP compared to preoperative without IOP-lowering medications. A qualified success for surgery is defined as the abovementioned postoperative IOP with or without IOP-lowering medications<sup>[10]</sup>. The primary outcomes were IOP, the number of IOP-lowering medications, and cumulative success rate. The secondary outcomes included BCVA, MD of visual field, major complications, and risk factors for surgical failure.

**Surgical Procedure** The surgeries were performed by highly skilled glaucoma specialists (Ying X and Tan L). Topical anesthesia or general anesthesia were tailored to the best experience for the patients and their specific needs. After applying a corneal traction suture, a fornix-based conjunctival flap was created. The subconjunctival tissue was then dissected to expose the sclera in an appropriate size. After bipolar coagulation hemostasis and a rectangular partial-thickness scleral flap was made, a sponge soaked with MMC (0.4 mg/mL) was placed on the scleral bed and subconjunctival area for 2-5min at the surgeon's discretion. The area was then irrigated thoroughly with balanced salt solution. A paracentesis was then performed to lower IOP and an anterior ostium was created, followed by peripheral iridectomy. After the scleral flap was sutured, the conjunctiva flap was closed separately to make a watertight closure. Prednisolone and antibiotics were administrated topically immediately post-surgery. Complications such as encapsulated bleb, shallow anterior chamber, hyphema, wound leak, malignant glaucoma, and choroidal effusion were closely observed. Personalized interventions such as removal of adjustable sutures, laser suture lysis, massage, bleb needling, and antifibrotic injection were performed based on the surgeon's clinical judgement.

**Statistical Analysis** Statistical analysis was performed by SPSS software (version 20.0, IBM, USA). Continuous variables were presented as mean $\pm$ SD. *t*-test was used to compare the measurements of IOP, the number of topical medications, BCVA (logMAR), visual field MD. Kaplan

Meier survival analysis was applied to draw the survival curves and calculate success rates. Comparison of success rate between groups was performed using the Log rank test. Cox proportional hazards regression analysis was used to identify factors associated with surgical failure. A  $P \leq 0.05$  was considered statistically significant.

**RESULTS**

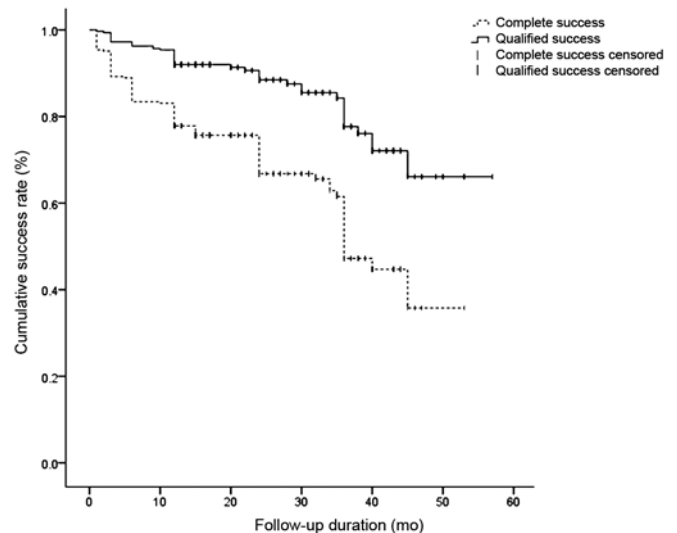
**Eye Characteristics** A total of 325 eyes of 261 patients were observed in the study, including 116 males (44.4%) and 145 females (55.6%). The mean follow-up time was  $22 \pm 12$  mo, ranging from 12 to 57 mo. The average age was  $59.3 \pm 12.8$  (19-90) years old, and 189 (58.2%) patients were over 60 years old. PACG was the main type of glaucoma, which accounted for 64.6% of patients. The mean preoperative IOP was  $32.9 \pm 12.0$  mm Hg, and the mean number of topical IOP-lowering medications before surgery was  $3.0 \pm 0.9$ . In these patients, 245 (75.4%) underwent trabeculectomy alone, and 80 (24.6%) received trabeculectomy combined with cataract surgery. The demographic characteristics of the patients and preoperative ocular characteristics are presented in Table 1. Information about visual field MD was unavailable in 40 cases.

**Surgical Outcomes and Success Rate** The IOP and the number of topical IOP-lowering medications at each follow-up time are shown in Table 2. The mean IOP and glaucoma medications were significantly decreased from  $32.9 \pm 12.0$  to  $16.4 \pm 5.7$  mm Hg ( $P < 0.0001$ ) and  $3.0 \pm 0.9$  to  $0.9 \pm 1.0$  ( $P < 0.0001$ ), respectively, at 3-year follow-up. The IOP values and the number of topical medications were consistently lower than those observed at baseline throughout the follow-up period.

The Kaplan-Meier survival plot of success rate for included patients is demonstrated in Figure 1. The cumulative complete success rate was 77.8%, 66.8%, and 47.2% at 1-, 2-, and 3-year follow-up visits, respectively. The cumulative qualified success rate was 92.0%, 88.5%, and 77.7% at 1-, 2-, and 3-year follow-up visits, respectively.

We compared the surgical outcomes between PACG and POAG patients (Figure 2). Before the surgery, both the IOP values and the number of medications in PACG group were higher. However, after the surgery, both IOP and the number of glaucoma medications were comparable between PACG and POAG throughout 3-year follow-up. The 3-year complete success rates of PACG and POAG were 54.6%, 46.4%, while the qualified success rates were 78.7%, 71.5%, respectively. The cumulative success rates of two groups were similar.

For PACG patients who underwent with trabeculectomy alone or phacotrabeculectomy, there was no significant difference in IOP control between the two surgical procedures. There was no significant difference with respect to IOP-lowering medications between the two surgical procedures at all follow

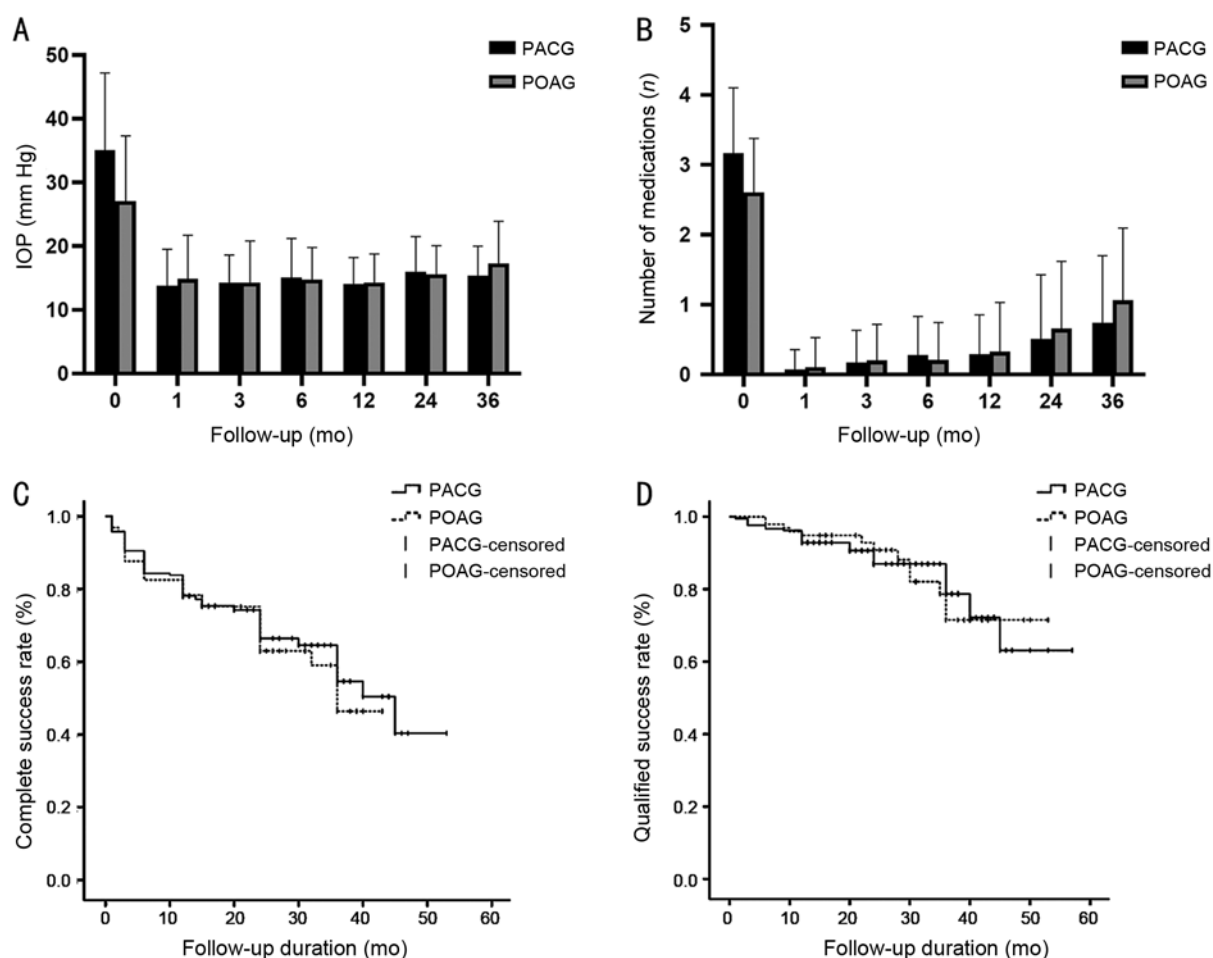


**Figure 1** Kaplan-Meier survival plot of the cumulative probability of success until the last follow-up visit based on the criteria of complete success and qualified success definitions.

**Table 1** Demographic and ocular characteristics of patients with trabeculectomy at baseline

Parameters	n (%)
Gender	
Female	145 (55.6)
Male	116 (44.4)
Age (y), mean±SD	59.3±12.8
<60	136 (41.8)
≥60	189 (58.2)
Hypertension	
Yes	54 (16.6)
No	271 (83.4)
Diagnosis	
PACG	210 (64.6)
POAG	97 (29.8)
Secondary glaucoma	10 (3.1)
Congenital glaucoma	8 (2.5)
BCVA (logMAR), mean±SD	0.77±0.94
≤1	254 (78.2)
>1	71 (21.8)
IOP (mm Hg), mean±SD	32.9±12.0
Medications, mean±SD	3.0±0.9
Visual field MD (dB), mean±SD	-19.73±10.03
>-15	100 (30.8)
≤-15	185 (57.0)
Missing data	40 (12.2)
Preoperative C/D, mean±SD	0.8±0.2
Surgery type	
Trabeculectomy	245 (75.4)
Phacotrabeculectomy	80 (24.6)

PACG: Primary angle-closure glaucoma; POAG: Primary open angle glaucoma; BCVA: Best corrected visual acuity; logMAR: Logarithm of the minimal angle of resolution; IOP: Intraocular pressure; SD: Standard deviation; MD: Mean deviation; dB: Decibels; C/D: Vertical cup to disc ratio.



**Figure 2 Surgical outcomes between PACG and POAG patients** The mean IOP (A) and the number of glaucoma medications (B) at baseline and each follow-up visit of the PACG and POAG patients. There were no significant differences in IOP control and need for glaucoma medications between the PACG group and POAG group after surgery. Error bars represent SD. The complete success rate (C) and qualified success rate (D) of the PACG and POAG patients are displayed by the Kaplan-Meier survival curve plot. The cumulative success rates of two groups were similar. PACG: Primary angle-closure glaucoma; POAG: Primary open angle glaucoma; IOP: Intraocular pressure.

up times except 1mo after surgery. The success rates of two surgical procedures were comparable (Figure 3).

**Visual Acuity and Visual Field Test** The changes of BCVA (logMAR) and visual field MD are shown in Table 3. The mean BCVA (logMAR) was 0.77±0.94 before surgery and 0.67±0.83 at the last follow-up. There was no significant difference between baseline and last follow-up ( $P=0.14$ ). At the last follow-up, the mean visual field MD was -16.80±11.47 dB, which was slightly improved compared with that at baseline ( $P=0.04$ ).

**Postoperative Complications** In our study, a total of 62 (19.1%) eyes developed postoperative complications in the follow up period. Of these, 33 (10.2%) had encapsulated bleb, 10 (3.1%) had shallow anterior chamber, 5 (1.5%) had wound leak, and 4 (1.2%) had malignant glaucoma. Postoperative complications during follow-up visits are displayed in Table 4. Encapsulated bleb was treated with massage, needling, or antifibrotic injection based on surgeon’s clinical judgement.

**Table 2 IOP and the number of glaucoma medications for patients at baseline and follow-up**

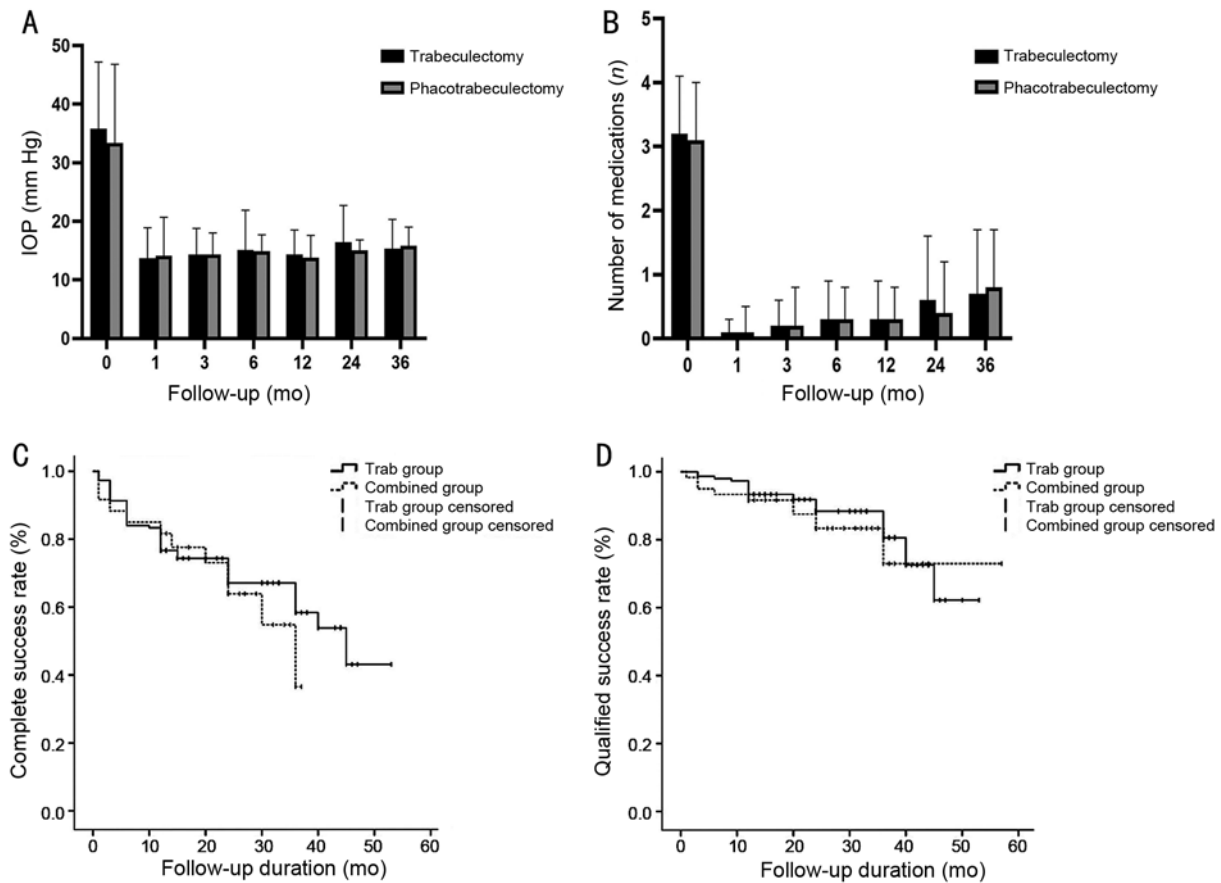
Follow-up	IOP (mm Hg)	<i>P</i>	No. of medications	<i>P</i>
Baseline	32.9±12.0		3.0±0.9	
1mo	14.2±6.3	<0.0001	0.1±0.4	<0.0001
3mo	14.4±5.2	<0.0001	0.2±0.5	<0.0001
6mo	14.9±5.5	<0.0001	0.3±0.5	<0.0001
12mo	14.2±4.3	<0.0001	0.3±0.6	<0.0001
24mo	16.0±5.3	<0.0001	0.6±0.9	<0.0001
36mo	16.4±5.7	<0.0001	0.9±1.0	<0.0001

IOP: Intraocular pressure.

**Risk Factors for Surgical Failure** The risk factors for surgical failure were investigated using Cox proportional hazard analysis (Table 5). Hypertension (HR=1.904,  $P=0.011$ ), encapsulated bleb (HR=2.756,  $P<0.001$ ), and preoperative more topical medications (HR=2.475,  $P=0.008$ ) were associated with a higher risk of surgical failure.

**DISCUSSION**

Our study is designed to evaluate the effect of trabeculectomy



**Figure 3 Surgical outcomes of PACG patients between the two surgical procedures** The mean IOP (A) and the number of glaucoma medications (B) at baseline and each follow-up visit of the PACG patients who underwent solo trabeculectomy or phacotrabeculectomy. There were no significant differences in IOP control between the two groups after surgery. There were no significant differences for the need for glaucoma medications between the two groups at all time points except 1mo after surgery. Error bars represent SD. The Kaplan-Meier survival curve plot showing complete success rate (C) and qualified success rate (D) of the two groups. There were no significant differences in the cumulative success rates between the trabeculectomy group and phacotrabeculectomy group after surgery. PACG: Primary angle-closure glaucoma; POAG: Primary open angle glaucoma; IOP: Intraocular pressure; SD: Standard deviation.

**Table 3 Visual acuity and visual field results at the last follow-up visit**

Items	Mean±SD	P
BCVA (logMAR)		0.14
Baseline (n=325)	0.77±0.94	
Last follow-up (n=325)	0.67±0.83	
MD of VF (dB)		0.04 <sup>a</sup>
Baseline (n=285)	-19.73±10.03	
Last follow-up (n=66)	-16.80±11.47	

BCVA: Best corrected visual acuity; logMAR: Logarithm of the minimal angle of resolution; SD: Standard deviation; MD: Mean deviation; VF: Visual field; dB: Decibels. <sup>a</sup>Not all patients at baseline returned for perimetry follow up.

**Table 4 Postoperative complications during follow-up visits**

Complications	n (%)
Encapsulated bleb	33 (10.2)
Shallow anterior chamber	10 (3.1)
HypHEMA	8 (2.5)
Wound leak	5 (1.5)
Malignant glaucoma	4 (1.2)
Choroidal effusion	2 (0.6)
Total	62 (19.1)

with MMC in glaucomatous patients in Southwest China. We retrospectively reviewed the medical records of glaucomatous patients underwent trabeculectomy in Southwest Hospital from January 2016 to December 2018. The cumulative success rate, visual function, postoperative complications, and risk factors for surgical failure were analyzed.

Several lines of studies had evaluated the efficiency of trabeculectomy<sup>[13-23]</sup>. The success rate of trabeculectomy appeared to be lower in Asian than that of in Caucasians. A multicenter retrospective study conducted in the United Kingdom showed that the complete and qualified success rates were 80% and 87% respectively at the 2-year follow-up<sup>[24]</sup>. Ng *et al*<sup>[11]</sup> conducted a study on MMC-augmented trabeculectomy in Hong Kong and revealed that the complete and qualified success rates were 47.9% and 75%, respectively, after a mean follow-up period of 21.8mo. In the present study, the IOP decreased from 32.9±12.0 mm Hg to 16.4±5.7 mm Hg at 3-year follow up, with a mean 50.2% IOP reduction. The complete and qualified success rates were 47.2% and 77.7%

Table 5 Cox proportional hazard ratio of risk factors for failure

Factor	Complete success		Qualified success	
	HR (95%CI)	P	HR (95%CI)	P
Gender	1.265 (0.808-1.981)	0.304	0.985 (0.479-2.206)	0.966
Age	0.971 (0.602-1.565)	0.902	1.326 (0.632-2.781)	0.455
Hypertension	1.904 (1.156-3.136)	0.011 <sup>a</sup>	1.742 (0.815-3.723)	0.152
Glaucoma type	1.288 (0.781-2.123)	0.321	1.261 (0.558-2.850)	0.577
Preoperative medications	1.189 (0.767-1.846)	0.439	2.475 (1.267-4.835)	0.008 <sup>a</sup>
Preoperative BCVA	0.771 (0.453-1.314)	0.339	1.491 (0.739-3.008)	0.265
Encapsulated bleb	2.756 (1.592-4.770)	<0.001 <sup>a</sup>	1.679 (0.662-4.260)	0.275
Surgery type	1.034 (0.628-1.703)	0.896	1.159 (0.550-2.442)	0.698

HR: Hazard ratio; CI: Confidence interval; BCVA: Best corrected visual acuity. <sup>a</sup>P<0.05.

respectively at 3-year follow-up. The success rate is consistent with that of Hong Kong, but lower than that of European and American. This could be explained by the fact that the Chinese patients tend to show a more robust inflammatory response than Caucasians after trabeculectomy. This will lead to scarring and will therefore lower the success rate<sup>[25]</sup>. Nevertheless, it is difficult to compare the surgical results among different studies, due to differences in ethnicity, definition of success, and follow-up periods. We assume that the differences in study design, intraocular surgical history, and glaucoma subtypes have contributed to the disparity in success rate among different studies.

There are limited studies to compare the surgical outcomes after trabeculectomy in PACG versus POAG. We suppose this is partly due to POAG is the main glaucoma type in European and American patients. While in China, PACG is the most common type of glaucoma. We find that there is no significant difference in surgical outcomes between the two types of glaucoma. Although both types of glaucoma are characterized by aqueous humor outflow obstruction and progressive irreversible optic nerve degeneration, the pathophysiology of PACG is different from POAG. PACG is characterized by apposition of the peripheral iris against the trabecular meshwork and closure of an already narrow angle of the anterior chamber. While POAG is caused by increased resistance to aqueous outflow through the trabecular meshwork and the angle is open. For both types of glaucoma, the aim of trabeculectomy is to reconstruct the aqueous humor outflow pathway and will have similar outcomes to lower IOP.

It's known that trabeculectomy, cataract surgery, or combined surgeries of these two are the three options for PACG patients, depending on the patient's severity of glaucoma and visual compromise from a cataract. Previous studies have compared the effectiveness of these surgical modalities<sup>[16,26-29]</sup>. It is noteworthy that cataract or clear lens removal has been advocated as initial treatment for PACG<sup>[30]</sup>. In China, the doctors prefer to perform cataract surgery only for PACG

patients with peripheral angle synechiae less than 180 degrees. So, the patients who underwent solo cataract surgery were not included in this study. The results show that both IOP control and the success rates of trabeculectomy are comparable to those of phacotrabeculectomy, which indicate that cataract surgery has poor IOP-lowering efficacy in PACG patients with angle closed totally.

At the last follow-up, BCVA was slightly better than that at baseline. One possible reason is that some patients had acute attack of PACG before surgeries. Owing to the very high IOP, the recorded preoperative vision was worse than their real vision. After surgery, the lowering of the very high initial IOP released the mechanical pressure on the axons at the level of the lamina cribrosa and this spared the axons that were at the brink of extinction. Another explanation is some patients underwent trabeculectomy together with cataract surgery which will result in better postoperative vision due to clear lens. The mean visual field MD was improved at the last follow-up visit when compared with before surgeries. However, it's not conclusive that trabeculectomy can improve visual field, because visual field is difficult to restore once damaged. Kashiwagi *et al*<sup>[31]</sup> reported that visual function may deteriorate, despite effective control of IOP after trabeculectomy. Studies have shown that IOP is not the specific factor responsible for glaucomatous optic nerve damage, but rather some circulating and metabolic factors. We presume that visual function may be maintained when the IOP is controlled at the target level by surgery or topical medications<sup>[32]</sup>.

The rate of postoperative encapsulated bleb was 7.7% to 12% in previous studies<sup>[22,24]</sup>. The incidence of postoperative encapsulated bleb in our study is 10.2%, similar to those reports. The incidences of shallow anterior chamber (3.1%) and hyphema (2.5%) were lower in our study. We think this is due to the retrospective nature of our study, which may lead to underestimation of these postoperative complications. In addition, interventions including removal of adjustable sutures or laser suture lysis were performed beforehand to reduce early

postoperative complications. The low incidence of malignant glaucoma (1.2%) and choroidal effusion (0.6%) may be attributed to trabeculectomy combined with anterior vitrectomy for those high-risk patients, such as PACG with short axial length or several fundus diseases. Anterior vitrectomy can reduce these complications through balancing the pressure of anterior chamber and vitreous cavity.

In further, we did Cox proportional hazard plots and identified that hypertension, encapsulated bleb, and more preoperational topical medications were associated with high risk of surgical failure. To the best of our knowledge, this is the first study to reveal the effect of hypertension on trabeculectomy. Previous studies had shown that hypertension may increase the risk of glaucoma because the common pathogenetic mechanisms in ciliary and renal tubular epithelia<sup>[33]</sup>. To a certain extent, the hypertensive patients were more likely to have more pre-operation drops, higher IOP and higher incidence of diabetes which has shown to be a risk factor for antiglaucoma operation failure<sup>[34]</sup>. Long-term topical IOP-lowering medications has been shown to induce subclinical ocular inflammation with proliferation of fibroblasts, lymphocytes, and macrophages. This will significantly lower trabeculectomy success rate<sup>[35]</sup>. Encapsulated bleb is the main cause of failure in glaucoma filtering surgery. For a successful filtration surgery, an appropriate amount of filtration might be necessary, especially in the early stage of post-operation. In addition, there are many other factors affecting the outcomes of trabeculectomy<sup>[36]</sup>, which need to be further confirmed in future studies.

There are also some limitations in the present study. First, the study is designed as a retrospective study. Some key statistics cannot be measured. Researchers cannot control exposure or outcome assessments, but instead must rely on others for accurate recordkeeping. Second, patients are reviewed from a single tertiary referral center, which would limit the application of the data to other centers. Third, the operations are performed by three skilled surgeons. Different surgeons have their inherent deviations and might affect the surgical outcomes. Fourth, we exclude the patients who are followed up for less than 1 year, which would lead to selective bias of the cohort.

In conclusion, our study reports the clinical outcomes of trabeculectomy with MMC in glaucomatous patients in Southwest China. The complete and qualified success rates are 47.2% and 77.7% at 3-year follow up. There are no significant differences in surgical outcomes between PACG and POAG. For PACG patients with peripheral angle synechiae more than 180 degrees, the success rates of trabeculectomy and phacotrabeculectomy are comparable. Hypertension, encapsulated bleb, and more topical preoperative medications are associated with surgical failure. Therefore, glaucoma professionals should choose the appropriate glaucoma surgical

approach based on the patient's disease condition. Intensive proactive preoperative and postoperative management is essential to prevent the deterioration of visual function.

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**Authors' contributions:** Qin ZX and Ying X conceived and designed the study. Han Q, Wang L, Tan L, You QX and Xu YF contributed to the data acquisition and analysis. Qin ZX, Wu N and Liu Y drafted and revised the manuscript. All authors read and approved the manuscript.

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#### REFERENCES

- 1 Francis BA, Singh K, Lin SC, Hodapp E, Jampel HD, Samples JR, Smith SD. Novel glaucoma procedures. *Ophthalmology* 2011; 118(7):1466-1480.
- 2 Chang TC, Vanner EA, Parrish RK 2nd. Glaucoma surgery preferences when the surgeon adopts the role of the patient. *Eye (Lond)* 2019; 33(10):1577-1583.
- 3 Arora KS, Robin AL, Corcoran KJ, Corcoran SL, Ramulu PY. Use of various glaucoma surgeries and procedures in medicare beneficiaries from 1994 to 2012. *Ophthalmology* 2015;122(8):1615-1624.
- 4 Ramulu PY, Corcoran KJ, Corcoran SL, Robin AL. Utilization of various glaucoma surgeries and procedures in Medicare beneficiaries from 1995 to 2004. *Ophthalmology* 2007;114(12):2265-2270.
- 5 Vinod K, Gedde SJ, Feuer WJ, Panarelli JF, Chang TC, Chen PP, Parrish RK 2nd. Practice preferences for glaucoma surgery: a survey of the American glaucoma society. *J Glaucoma* 2017;26(8):687-693.
- 6 Khaw PT, Chiang M, Shah P, Sii F, Lockwood A, Khalili A. Enhanced trabeculectomy: the moorfields safer surgery system. *Dev Ophthalmol* 2017;59:15-35.
- 7 Stalmans I, Gillis A, Lafaut AS, Zeyen T. Safe trabeculectomy technique: long term outcome. *Br J Ophthalmol* 2006;90(1):44-47.
- 8 Schlenker MB, Gulamhusein H, Conrad-Hengerer I, Somers A, Lenzhofer M, Stalmans I, Reitsamer H, Hengerer FH, Ahmed IIK. Efficacy, safety, and risk factors for failure of standalone ab interno gelatin microstent implantation versus standalone trabeculectomy. *Ophthalmology* 2017;124(11):1579-1588.
- 9 Sugimoto Y, Mochizuki H, Ohkubo S, Higashide T, Sugiyama K, Kiuchi Y. Intraocular pressure outcomes and risk factors for failure in the collaborative bleb-related infection incidence and treatment study. *Ophthalmology* 2015;122(11):2223-2233.
- 10 Chiu HI, Su HI, Ko YC, Liu CJ. Outcomes and risk factors for failure after trabeculectomy in Taiwanese patients: medical chart reviews from 2006 to 2017. *Br J Ophthalmol* 2022;106(3):362-367.
- 11 Ng PWC, Yeung BYM, Yick DWF, Yu CBO, Lam DSC. Fornix-based trabeculectomy with Wise's suture technique in Chinese patients. *Ophthalmology* 2000;107(12):2310-2313.

- 12 The Fluorouracil Filtering Surgery Study Group. Five-year follow-up of the fluorouracil filtering surgery study. *Am J Ophthalmol* 1996;121(4):349-366.
- 13 Duman F, Waisbourd M, Faria B, Addis V, Hsieh M, Ekici F, Hark LA, Spaeth GL. Trabeculectomy in patients with glaucoma over 80 years of age: relatively short-term outcomes. *J Glaucoma* 2016; 25(3):e123-e127.
- 14 Wilson MR, Mendis U, Paliwal A, Haynatzka V. Long-term follow-up of primary glaucoma surgery with Ahmed glaucoma valve implant versus trabeculectomy. *Am J Ophthalmol* 2003;136(3):464-470.
- 15 Tham CCY, Kwong YYY, Baig N, Leung DYL, Li FCH, Lam DSC. Phacoemulsification versus trabeculectomy in medically uncontrolled chronic angle-closure glaucoma without cataract. *Ophthalmology* 2013;120(1):62-67.
- 16 Song BJ, Ramanathan M, Morales E, Law SK, Giaconi JA, Coleman AL, Caprioli J. Trabeculectomy and combined phacoemulsification-trabeculectomy: outcomes and risk factors for failure in primary angle closure glaucoma. *J Glaucoma* 2016;25(9):763-769.
- 17 Shigeeda T, Tomidokoro A, Chen YN, Shirato S, Araie M. Long-term follow-up of initial trabeculectomy with mitomycin C for primary open-angle glaucoma in Japanese patients. *J Glaucoma* 2006;15(3):195-199.
- 18 Sen M, Midha N, Sidhu T, Angmo DW, Sihota R, Dada T. Prospective randomized trial comparing mitomycin C combined with ologen implant versus mitomycin C alone as adjuvants in trabeculectomy. *Ophthalmol Glaucoma* 2018;1(2):88-98.
- 19 Hoang TKH, Kim YK, Jeoung JW, Park KH. Relationship between age and surgical success after trabeculectomy with adjunctive mitomycin C. *Eye (Lond)* 2018;32(8):1321-1328.
- 20 Takihara Y, Inatani M, Ogata-Iwao M, Kawai M, Inoue T, Iwao K, Tanihara H. Trabeculectomy for open-angle glaucoma in phakic eyes vs in pseudophakic eyes after phacoemulsification: a prospective clinical cohort study. *JAMA Ophthalmol* 2014;132(1):69-76.
- 21 Panarelli JF, Banitt MR, Gedde SJ, Shi W, Schiffman JC, Feuer WJ. A retrospective comparison of primary baerveldt implantation versus trabeculectomy with mitomycin C. *Ophthalmology* 2016;123(4): 789-795.
- 22 Gedde SJ, Feuer WJ, Lim KS, Barton K, Goyal S, Ahmed IIK, Brandt JD, Primary Tube Versus Trabeculectomy Study Group. Treatment outcomes in the primary tube versus trabeculectomy study after 3 years of follow-up. *Ophthalmology* 2020;127(3):333-345.
- 23 Gedde SJ, Schiffman JC, Feuer WJ, Herndon LW, Brandt JD, Budenz DL, Group TVTS. Treatment outcomes in the Tube Versus Trabeculectomy (TVT) study after five years of follow-up. *Am J Ophthalmol* 2012;153(5):789-803.e2.
- 24 Kirwan JF, Lockwood AJ, Shah P, MacLeod A, Broadway DC, King AJ, McNaught AI, Agrawal P, Trabeculectomy Outcomes Group Audit Study Group. Trabeculectomy in the 21st century: a multicenter analysis. *Ophthalmology* 2013;120(12):2532-2539.
- 25 Husain R, Clarke JK, Seah SL, Khaw PT. A review of trabeculectomy in East Asian people—the influence of race. *Eye (Lond)* 2005;19(3): 243-252.
- 26 Tsai HY, Liu CJ, Cheng CY. Combined trabeculectomy and cataract extraction versus trabeculectomy alone in primary angle-closure glaucoma. *Br J Ophthalmol* 2009;93(7):943-948.
- 27 Tham CCY, Kwong YYY, Leung DYL, Lam SW, Li FCH, Chiu TYH, Chan JCH, Lam DSC, Lai JSM. Phacoemulsification versus combined phacotrabeculectomy in medically uncontrolled chronic angle closure glaucoma with cataracts. *Ophthalmology* 2009;116(4):725-731, 731.e1-731.e3.
- 28 Hansapinyo L, Choy BNK, Lai JSM, Tham CC. Phacoemulsification versus phacotrabeculectomy in primary angle-closure glaucoma with cataract. *J Glaucoma* 2020;29(1):15-23.
- 29 Choy BNK. Comparison of surgical outcome of trabeculectomy and phacotrabeculectomy in Chinese glaucoma patients. *Int J Ophthalmol* 2017;10(12):1928-1930.
- 30 Azuara-Blanco A, Burr J, Ramsay C, Cooper D, Foster PJ, Friedman DS, Scotland G, Javanbakht M, Cochrane C, Norrie J. Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial. *Lancet* 2016; 388(10052):1389-1397.
- 31 Kashiwagi K, Kogure S, Mabuchi F, Chiba T, Yamamoto T, Kuwayama Y, Araie M, Collaborative Bleb-Related Infection Incidence and Treatment Study Group. Change in visual acuity and associated risk factors after trabeculectomy with adjunctive mitomycin C. *Acta Ophthalmol* 2016;94(7):e561-e570.
- 32 Yuasa Y, Sugimoto Y, Hirooka K, Ohkubo S, Higashide T, Sugiyama K, Kiuchi Y. Effectiveness of trabeculectomy with mitomycin C for glaucomatous eyes with low intraocular pressure on treatment eye drops. *Acta Ophthalmol* 2020;98(1):e81-e87.
- 33 Langman MS, Lancashire RJ, Cheng KK, Stewart PM. Systemic hypertension and glaucoma: mechanisms in common and co-occurrence. *Br J Ophthalmol* 2005;89(8):960-963.
- 34 Mariotti C, Dahan E, Nicolai M, Levitz L, Bouee S. Long-term outcomes and risk factors for failure with the EX-press glaucoma drainage device. *Eye (Lond)* 2014;28(1):1-8.
- 35 Broadway DC, Chang LP. Trabeculectomy, risk factors for failure and the preoperative state of the conjunctiva. *J Glaucoma* 2001;10(3): 237-249.
- 36 Zhu JD, Xie LL, Li ZY, Lu XH. The prognosis of trabeculectomy in primary angle-closure glaucoma patients. *Int J Ophthalmol* 2019; 12(1):66-72.