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24-month prospective randomized comparison of ab externo penetrating canaloplasty versus trabeculectomy in primary angle-closure glaucoma☆

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ABSTRACT

Purpose: To report the 24-month efficacy and safety of ab externo penetrating canaloplasty compared with trabeculectomy in the treatment of primary angle-closure glaucoma (PACG).

Methods: This is a prospective, randomized, controlled trial. Patients with PACG and inadequately controlled intraocular pressure (IOP) were recruited. Patients enrolled were randomized to either ab externo penetrating canaloplasty (PCP group) or trabeculectomy (TRAB group). The main outcome measures were intraocular pressure (IOP), number of glaucoma medications, success rate and ocular surface disease index (OSDI) questionnaire. Surgical success (definition 1) was defined as 6 mm Hg $\leq$ IOP $\leq$ 21 mm Hg with an IOP reduction of $\geq$ 20 % without glaucoma medications (complete success) or regardless of glaucoma medications (qualified success).

Results: A total of 52 eyes (44 patients) were finally enrolled with 25 eyes in PCP group and 27 eyes in TRAB group. PCP group (85.0 %) had a similar qualified success rate compared with TRAB group (87.0 %) with definition 1 at 24 months in intention to treat (ITT) analysis (P = 1.000). In per protocol (PP) analysis, the qualified success with definition 1 were 81.3 % in PCP group and 87.0 % in TRAB group (P = 0.972). But PCP group had a lower success rate in postoperative IOP $\leq$ 15 mm Hg with an IOP reduction of $\geq$ 20 % than in TRAB group, in ITT analysis with complete success (PCP 35.0 % vs TRAB 65.2 %, P = 0.048) and PP analysis with qualified success (PCP 31.3 % vs. TRAB 69.6 %, P = 0.025). The mean OSDI score was equal in PCP group (11.9 $\pm$ 8.5) and TRAB group (16.6 $\pm$ 14.3) (P = 0.302). Hypotony-associated complications were the main complications in PCP group and TRAB group (24.0 % vs. 33.3 %, P = 0.458).

Conclusions: Compared with trabeculectomy, ab externo penetrating canaloplasty had a similar qualified success rate and comparable complications at 24 months. Without frequent bleb interventions, penetrating canaloplasty may be a promising surgery for PACG patients especially with early or mild stages.

1. Introduction

Glaucoma is the leading cause of irreversible blindness worldwide.[1] Primary angle-closure glaucoma (PACG) is a subtype that causes nearly half of all cases of glaucoma-related blindness, especially in Asia.[2,3] The conventional treatment for advanced PACG is trabeculectomy with adjunctive mitomycin C (TRAB). Although trabeculectomy with adjunctive mitomycin C is highly effective in the reduction of IOP, it is associated with significant complications, such as persistent hypotony, choroidal detachment, malignant glaucoma, bleb scarring, and cataract

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progression.[4,5] And frequent postoperative interventions like bleb needling or laser suture lysis are needed for bleb scarring[6,7] and patients with bleb may have ocular discomfort.[8,9] Phacoemulsification with intraocular lens implantation and goniosynechialysis (PEI-GSL) is a new option to treat PACG.[10–12] but the removal of transparent crystals still poses ethical issues that the patients will lose the ability to accommodate. So, trabeculectomy remains the main treatment for PACG.

Ab externo penetrating canaloplasty (PCP) is a bleb-independent glaucoma surgery which is previously reported by our team with promising outcomes in PACG.[13] It combines the procedure of trabeculectomy with ab externo canaloplasty and restores the aqueous outflow pathway in PACG eyes guiding the aqueous into the Schlemm' s canal (SC) directly. With the independence of the filtering bleb and watertight suture of scleral flap, it may have less bleb associated complications, less postoperative bleb management, and better ocular surface.[13–17]

This randomized controlled study aims to compare the efficacy and safety of penetrating canaloplasty versus trabeculectomy with adjunctive mitomycin C in PACG eyes.

2. Materials and methods

The study was a single-centre prospective randomized controlled trial designed to evaluate the efficacy and safety between ab externo penetrating canaloplasty and trabeculectomy in PACG patients. Patients diagnosed with PACG will be randomized by a 1:1 allocation ratio into either PCP group or TRAB group.

This randomized clinical trial was performed at the Eye Hospital, Wenzhou Medical University (WMU). And the trial was registered at Chinese Clinical Trial Registry before recruitment (ChiCTR-IIR-16009009). This study adhered to the principles of the Declaration of Helsinki and received approval from the WMU ethics committee (Y-2016023). Informed consent was obtained from all participants.

2.1. Participants

The inclusion criteria were patients with PACG aged 18–80 years old with peripheral anterior synechia (PAS) $\geq 180^{\circ}$ and who had uncontrolled IOP (IOP $\geq$21 mm Hg) with topical glaucoma medications or inability to tolerate with medications.

The exclusion criteria included previous history of glaucoma surgery, existence of retinal vascular lesions, such as diabetic retinopathy, central or branch retinal vein occlusion, etc., having previous cataract surgery, pregnant or nursing women, unwillingness, or inability to provide voluntary consent, and inability to adhere to the scheduled follow-up visits. All patients enrolled had preoperative and postoperative examinations such as slit-lamp photography, IOP (mean of at least two Goldmann applanation readings), best corrected visual acuity (BCVA), gonioscopy, visual field by Humphrey visual field examination, surgical complications, postoperative interventions required for complications or IOP-controlled.

2.2. Surgical procedure

Experienced glaucoma surgeons (LYB, ZSD) performed all surgeries alone without combined with phacoemulsification. The surgical procedures were standardized to ensure consistency.

2.2.1. Ab externo penetrating canaloplasty (PCP)

The ab externo PCP procedure was reported previously and described briefly here.[14,15] With a fornix-based conjunctival dissection and a 4.0 × 3.5 mm partial thickness (50 %) scleral flap, a 1.5 × 2.0 mm inner scleral flap was dissected with the outer wall of Schlemm's canal (SC) unroofed. Then the microcatheter (iTrack, Ellex iScience, Inc., Fremont, CA, US) had the circumferential catheterization of SC and a 10–0 polyprolene suture was guided into the canal with a small amount of high molecular weight hyaluronic acid (Healon GV, Johnson & John Surgical Vision, Inc., Santa Ana, CA, US) injections at two-hour intervals. The suture was then tied tightly to distend the TM inwards, placing the tissues in tension. A 1.0 × 0.5 mm block of corneal limbus tissue anterior to the suture was subsequently excised following the removal of peripheral iris (2.5 ×1.0 mm). Finally, water tight closure of the scleral flap and conjunctiva flap was achieved; neither mitomycin C (MMC) nor 5-fluorouracil (5-FU) were used during the procedure.

2.2.2. Trabeculectomy with mitomycin C (TRAB)

The procedure of TRAB was performed as follows.[18] A fornix-based conjunctival flap and a corneal-based scleral flap (approximately half scleral thickness) were dissected. Then two fluid-retaining sponges soaked with MMC (0.4 mg/ml) were applied beneath the conjunctive flap and scleral flap for 3–4 min. After irrigation with balanced saline solution (BSS) completely, a block of limbal tissue was excised under the scleral flap followed by an iridectomy. The scleral flap was sutured to the scleral bed with 10–0 nylon suture as a visible leak was present around the scleral flap without a shallow anterior chamber. The dimensions of the scleral flap, the size of the inner block, and the number and tension of the scleral flap sutures were at the surgeon's discretion. Then the conjunctival flap was closured water-tightly.

Patients were prescribed topical antibiotics (levofloxacin) for 1–2 weeks in both groups and steroids (dexamethasone) four times daily for a period of 2–4 weeks in PCP group depending on the ocular surface congestion and intraocular inflammation[14,15] and 4–8 times daily for 8–12 weeks or longer in TRAB group depending on the ocular surface congestion, intraocular inflammation, and bleb status.[19] In PCP group, glaucoma medications were prescribed when IOP was higher than 25 mm Hg on two consecutive measurements in case transient IOP elevation occurred within three months. In TRAB group, if signs of bleb scarring, such as flat bleb and increased IOP, occurred persistently, ocular massage or subconjunctival injections of 5-FU or bleb needling would be administered. In case of flat blebs which inflate after ocular massage, laser suture lysis was carried out to increase outflow. If the above treatment failed, topical glaucoma medications were added, or further glaucoma surgeries were performed.

2.3. Outcomes measures

The outcome measure was the ocular surface disease index (OSDI) score, objective scattering index (OSI), IOP, the number of glaucoma medications taken, success rate with different definitions (detailed in the following), postoperative complications, and interventions.

Surgical success was defined by the following criteria: (1) 6 mm Hg $\leq$ IOP $\leq$ 21 mm Hg and IOP reduction $\geq$ 20 % (definition 1); (2) 6 mm Hg $\leq$ IOP $\leq$ 18 mm Hg and IOP reduction $\geq$ 20 % (definition 2); (3) 6 mm Hg $\leq$ IOP $\leq$ 15 mm Hg and IOP reduction $\geq$ 20 % (definition 3). Success was subsequently specified as complete success (without glaucoma medications) and qualified success (regardless of glaucoma medications).

Surgical failure was defined as persistent IOP $>$ 21 mm Hg with maximum glaucoma medications at two consecutive follow-up visits, having postoperative glaucoma reoperations for IOP uncontrolled, or bleb interventions like bleb needling or bleb massage for IOP uncontrolled in PCP group. Bleb interventions in TRAB group were defined only as postoperative management but not surgical failure.

With the attainment of informed consent from the participants, their baseline demographic and clinical information were collected. Postoperatively, study visits were scheduled at 1 day, 1 week, 1 month, 3 months, 6 months, and then every 6 months for at least 2 years, with documentation of IOP (mean of least 2 Goldmann applanation readings), number of glaucoma medications, best corrected visual acuity (BCVA), bleb status by ultrasound biomicroscopy (UBM) and slit-lamp photography, visual field by Humphrey visual field examination, complications, postoperative interventions required for complications or IOP-controlled.

2.4. Randomization

The eyes were randomized to either PCP group or TRAB group with 1:1 by a randomized digital table. Only research assistants responsible for participant assignment had the access to the random allocation sequence. Other relevant investigators, surgeons and assistants were not able to get the sequence.

The study was conducted in the Glaucoma Center at the Eye Hospital of WMU. The random allocation sequence of the present study was generated by the statistical specialist at the Clinical and Epidemiological Eye Research Center, WMU. Two research assistants were responsible for the enrollment of participants. Another two research assistants assigned participants for interventions at the Clinical and Epidemiological Eye Research Center, WMU. And for blinding, the surgeons for the patients and participants were blinded before the surgery until the treatment was assigned to the participants. And the follow-up examiners were masked to the randomization assignment.

2.5. Statistical methods

All statistics were calculated using the Statistical Package for the Social Sciences 24.0 for Windows (SPSS Inc., Chicago, IL). Continuous data were expressed in mean ± standard deviation and compared using mixed-effects modeling. Models were fitted with age, glaucoma medications, OSDI score, and ocular measurements (IOP, BCVA, AL (axial length), MD of visual fields, and PAS) as the response variable and study eye and the treatment groups as fixed effects. Participant deviation and intercept were introduced as random effects. The categorical variables like gender, study eye, surgical success rate with different definitions, and postoperative complications between groups were expressed in percentages and analyzed by the Pearson $\chi 2$ test or Fisher exact test as appropriate. A P value of < 0.05 was considered statistically significant.

3. Results

During the study recruitment period from July 2016 to January 2020, 52 eyes of 44 patients were recruited. Of these 52 eyes, 25 eyes were randomized into PCP group, whereas 27 eyes were randomized into TRAB group.

3.1. Baseline characteristic

Fig. 1 shows the flow of patient enrollment in intention to treat (ITT) analysis. In PCP group, five eyes had a failure of 360° canalization of Schlemm's canal and had trabeculectomy instead. And in TRAB group, one eye was incorrectly enrolled with the misdiagnosis of POAG. So, those had exactly trabeculectomy in PCP group and the incorrect enrollment of POAG eye in TRAB group was excluded in the PP analysis.

Table 1
Patient demographics of the treatment groups in ITT analysis.

Treatment allocation	PCP, n = 25	TRAB, n = 27	P value*
Age (yrs)			**0.032**
Mean ± SD	54.0 ± 5.4	58.3 ± 7.6	
Range	45–65	41–74	
Gender, n, (%)			0.133*
Male	17 (70.8)	13 (50.0)	
Female	7(29.2)	13 (50.0)	
Study eye, n, (%)			0.158*
Right	16 (64.0)	12 (44.4)	
Left	9 (36.0)	15 (55.6)	
IOP (mmHg)			0.362
Mean ± SD	37.3 ± 14.8	34.8 ± 10.0	
Glaucoma medications			0.172
Mean ± SD	3.4 ± 1.0	2.7 ± 1.1	
Glaucoma stage			0.110*
Early	0(0.0)	1(3.7)	
Mild	1(4.0)	5(18.5)	
Advanced	24(96.0)	21(77.8)	
BCVA (LogMAR)			0.330
Mean ± SD	1.0 ± 1.4	0.6 ± 1.1	
Humphrey visual field, mean ± SD			
MD, dB	−27.9 ± 6.1	−20.2 ± 8.8	**0.001**
PSD, dB	6.2 ± 3.4	8.4 ± 2.6	0.194
C/D, mean ± SD	0.9 ± 0.1	0.8 ± 0.1	**0.017**
AL, mm, mean ± SD	22.6 ± 0.8	22.6 ± 0.7	0.950
PAS, hours, mean ± SD	10.5 ± 2.3	8.6 ± 3.7	**0.016**
Type of Prior laser treatment			0.420*
LPI	4(16.0)	6(22.2)	
ALPI	1(4.0)	0(0.0)	

AL, axial length; BCVA, best corrected visual acuity; C/D, cup/ disc ratio; ITT, intention to treat; MD, mean deviation; PAS, peripheral anterior synechia; PCP, penetrating canaloplasty; SD, standard deviation; TRAB, trabeculectomy.

* Chi-square test was used for data analysis. The mixed effects model was used for the rest; Bold present a significant difference.

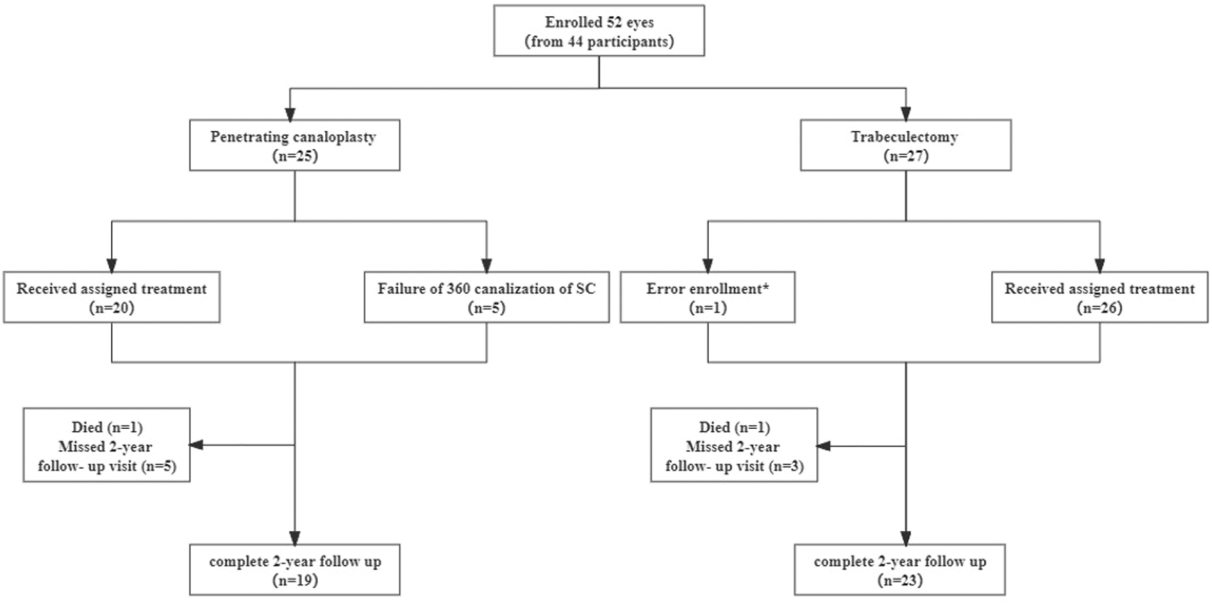

Fig. 1. The participant flow of the study in two treatment groups.

Table 1 summarizes the patients' demographics. There was no statistically significant difference (P > 0.05) between the two treatment groups, except age, MD (mean deviation) of Humphrey visual field, cup/disc ratio (C/D) and range of peripheral anterior synechia (PAS).

3.2. Outcome measures

3.2.1. Intraocular pressure and glaucoma medications

Fig. 2 summarizes the mean IOP at various time points of follow-up for the two treatment groups. Both PCP group and TRAB group had postoperative IOPs at each follow-up time decreased statistically significantly compared with preoperative IOP in each group (P < 0.001). There were no significant differences in the mean IOP between two treatment groups preoperatively and postoperatively except postoperative 1 week (P = 0.013). At 24 months, the mean IOP was 14.3 ± 3.0 mm Hg in PCP group and 13.8 ± 2.1 mm Hg in TRAB group (P = 0.720). And for ITT analysis, the two-year IOP reduction in PCP group was 53.3 % (21.9 ± 14.8 mm Hg) compared with TRAB group (48.9 %, 16.7 ± 11.7 mm Hg), which had no significant difference (P = 0.468) and it was also consistent in PP analysis (P = 0.456). Table S1 summarizes the mean IOP at each follow-up in the PP analysis.

Fig. 2 demonstrates the baseline and postoperative number of glaucoma medications at 1 week, 1 month, 3 months, 6 months, 12 months, 18 months, and 24 months in ITT analysis. There were no statistically significant differences in the mean number of topical glaucoma medications between two treatment groups, except at 1 month (P = 0.012). At 24 months, the mean medications were 0.5 ± 0.9 in PCP group and 0.2 ± 0.6 in TRAB group (P = 0.262). And for ITT analysis, the two-year medication reduction in PCP group was 86.9 % (2.8 ± 1.1) compared with TRAB group (84.1 %, 2.4 ± 1.3), which had no significant difference (P = 0.892).

3.3. Surgical success rate

Table 2 and Table S2 compared the surgical success rate between TRAB group and PCP group with different definitions in both ITT and PP analysis, respectively. According to definition 1 (6 mm Hg ≤ IOP ≤ 21 mm Hg and IOP reduction ≥20 %) and definition 2 (6 mm Hg ≤ IOP ≤ 18 mm Hg and IOP reduction ≥20 %), no statistically significant differences were observed between two treatment groups in both ITT and PP analysis with qualified success and complete success at 12 and 24 months, respectively. In ITT analysis, qualified success with definition 1 was 85.0 % in PCP group and 87.0 % in TRAB group at 24 months (P = 1.000).60.0 % of eyes in PCP group and 78.3 % of eyes in TRAB group achieved complete success with definition 1 (P = 0.193).

With definition 3 (6 mm Hg ≤ IOP ≤ 15 mm Hg and IOP reduction ≥20 %), the complete success rate in TRAB group (65.2 %) was significantly higher than it in PCP group (35.0 %) in ITT analysis (P = 0.048).

Table 2
Surgical success of two treatment groups in ITT analysis.

ITT analysis	PCP, n = 25	TRAB, n = 27	P Value
Qualified success			
6 mmHg ≤ IOP ≤ 21 mmHg and IOP reduction ≥ 20 %			
12 months	81.8 (18/22)	78.3 (18/23)	1.000
24 months	85.0 (17/20)	87.0 (20/23)	1.000
6 mmHg ≤ IOP ≤ 18 mmHg and IOP reduction ≥ 20 %			
12 months	68.2 (15/22)	73.9 (17/23)	0.672
24 months	80.0 (16/20)	87.0 (20/23)	0.840
6 mmHg ≤ IOP ≤ 15 mmHg and IOP reduction ≥ 20 %			
12 months	50.0 (11/22)	73.9 (17/23)	0.098
24 months	45.0 (9/20)	69.6 (16/23)	0.103
Complete success			
6 mmHg ≤ IOP ≤ 21 mmHg and IOP reduction ≥ 20 %			
12 months	68.2 (15/22)	69.6 (16/23)	0.920
24 months	60.0 (12/20)	78.3 (18/23)	0.193
6 mmHg ≤ IOP ≤ 18 mmHg and IOP reduction ≥ 20 %			
12 months	59.1 (13/22)	65.2 (15/23)	0.672
24 months	60.0 (12/20)	78.3 (18/23)	0.193
6 mmHg ≤ IOP ≤ 15 mmHg and IOP reduction ≥ 20 %			
12 months	40.9 (9/22)	65.2(15/23)	0.102
24 months	35.0 (7/20)	65.2 (15/23)	**0.048**

Chi- square test or Fisher exact test were used for data analysis for appropriate.
IOP, intraocular pressure; ITT, intention to treat; PCP, penetrating canaloplasty; TRAB, trabeculectomy.

3.4. OSDI score

Table 3 summarizes the OSDI score of participants in two treatment

Table 3
OSDI score in PCP group and TRAB group in ITT analysis.

OSDI score	PCP, n = 25	TRAB, n = 27	P-Value*
12 months	14.4 ± 10.3	12.8 ± 11.4	1.000
24 months	11.9 ± 8.5	16.6 ± 14.3	0.302

ITT, intention to treat; OSDI, ocular surface disease index; PCP, penetrating canaloplasty; TRAB, trabeculectomy.
* Mixed effects model was analyzed for repeated measures.

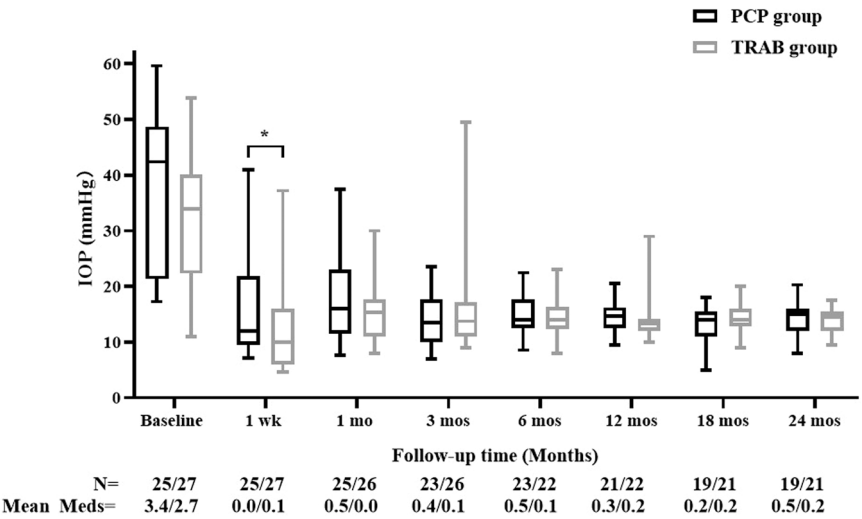

Fig. 2. IOP before and after surgery in two treat groups in ITT analysis (*P < 0.05). IOP, intraocular pressure; wk, week; mo, month; mos, months; PCP, penetrating canaloplasty; TRAB, trabeculectomy.

groups with ITT analysis. No statistically significant difference was seen in the mean score between groups at both 12 and 24 months. At 24 months, the OSDI score in patients of PCP group was 11.9± 8.5 compared with it (16.6± 14.3) in TRAB group (P = 0.302). And five eyes (18.5 %) reported a score ≥ 33 in TRAB group while PCP group (0 %) had none at 24 months (P = 0.277). Table S3 compared the OSDI score in two groups with PP analysis.

3.5. Postoperative complications and interventions

Table 4 summarizes the postoperative complications in two groups. Within the PCP group, the frequency of hyphema (24.0 %) was statistically significantly higher than it was in TRAB group (0.0 %, P = 0.009). The other complications had no significant difference between two groups (P > 0.05). Among them, hypotony or combined with shallow anterior chamber occurred more in TRAB group (33.3 %) than PCP group (24.0 %) without significant difference (P = 0.458). In PP analysis, the frequency of shallow anterior chamber was 5.0 % (1/20) in PCP group and 33.3 % (9/27) in TRAB group (P = 0.047).

The interventions for complications were included as follows. One eye in PCP group and one eye in TRAB group underwent conjunctival repaired for wound leakage. One eye with Descemet membrane detachment during the procedure of trabeculectomy had sterile air injected into anterior chamber, and it recovered within 1 month. One eye with postoperative malignant glaucoma in TRAB group was performed with low-dose laser cycloplasty.[20] One eye in PCP group had anterior chamber reforming for hypotony and shallow anterior chamber within 3 months postoperatively. An anterior chamber reforming with air was also performed on one eye with hypotony and shallow anterior chamber (degree of III) in TRAB group due to postoperative bleb needling at around 6 months. Other complications recovered naturally or by conservative treatments.

For bleb interventions with ITT analysis, frequent bleb massage was common in TRAB group (13/27,48.1 %). In PCP group, three eyes (12.0 %) had trabeculectomy actually and one eye (4.0 %) with postoperative IOP uncontrolled (defined as a surgical failure in PCP group) had bleb massage (4/25,16.0 %). In TRAB group, five eyes (18.5 %) had postoperative laser suture lysis during 2-year visits, while only two eyes (8.0 %) with final trabeculectomy in PCP group had the manipulation. For bleb needling with an injection of 5-FU, there were 40.7 % eyes (11/27) in TRAB group and 8.0 % eyes (2/25) with assigned treatment in PCP group. For the eyes with bleb needling in PCP group, one eye with postoperative IOP uncontrolled had needling following laser suture lysis, and another eye had 1 time of needling accidentally at postoperative 2 weeks, which was defined as surgical failure in both ITT and PP analysis. Among eyes with bleb needling, 45.5 % (5/11) eyes had over 3 times in the TRAB group. The total intervention rate of bleb needling or laser suture lysis was 44.4 % (12/27) in TRAB group.

Table 4
Postoperative complications in two treatment groups in ITT analysis.

	PCP, n = 25	TRAB, n = 27	P Value
Intraoperative complications			
Suture cheese-wiring through TM	1 (4.0)	-	-
Descemet membrane detachment	0 (0.0)	1 (3.7)	1.000
Early complications (≤ 90 days)			
Hyphema	6 (24.0)	0 (0.0)	**0.009**
Transient IOP elevation			
21 mm Hg < IOP ≤ 25 mm Hg	2 (8.0)	-	-
25 mm Hg < IOP ≤ 30 mm Hg	0 (0.0)	-	-
IOP > 30 mm Hg	5 (20.0)	-	-
Hypotony or with shallow AC	6 (24.0)	9 (33.3)	0.458
Ciliary body detachment	0 (0.0)	1 (3.7)	1.000
Choroidal detachment	2 (8.0)	2 (7.4)	1.000
Wound leakage	1 (4.0)	2 (7.4)	1.000
Retinal detachment	0 (0.0)	1 (3.7)	1.000
Malignant glaucoma	0 (0.0)	1 (3.7)	1.000
Late complications (>90 days)			
Hypotony combined with III shallow AC	0 (0.0)	1 (3.7)	1.000
Choroidal detachment	0 (0.0)	1 (3.7)	1.000

Chi-square test or Fisher exact test were used for data analysis for appropriate. Bold present a significant difference.
AC, anterior chamber; IOP, intraocular pressure; ITT, intention to treat; PCP, penetrating canaloplasty; TRAB, trabeculectomy.

4. Discussions

This was the first study to directly compare the efficacy and safety of penetrating canaloplasty and trabeculectomy in PACG management. We failed to demonstrate that patients after penetrating canaloplasty had better IOP control and a more comfortable ocular surface compared with trabeculectomy. However, this study suggested that penetrating canaloplasty had a similar qualified success rate and comparable complications compared with trabeculectomy at 24 months postoperatively.

The IOP, number of medications and the majority of surgical success rate had no significant difference between two groups. From 3 months onward, the difference in mean postoperative IOP between the two groups were no longer statistically significant. This can be figured out. The PCP group had a period of transient IOP elevation within 3 months, which contributed to a higher early postoperative IOP, and the TRAB group had more eyes with hypotony at an early postoperative period which led to much lower at 1 week. After the period, the mean IOP in PCP group decreased, and it in TRAB group increased, which may result in a nonsignificant difference in the following visits. Considering glaucoma medications, TRAB group had less medications than PCP group without a significant difference. Only two eyes (2/21,9.5 %) in TRAB group and five eyes (5/19,26.3 %) in PCP group depended on glaucoma medications with IOP controlled at 24 months. Bleb interventions observed in TRAB group may have contributed to the results with less medications. The surgical success rate with definitions 1 and 2 were comparable in two groups with both qualified and complete success. Although no statistically significant difference was seen in most analyses of success rate, the significant outcome in PP analysis with qualified success of definition 3 suggested that TRAB group did have an advantage in the percentage of postoperative target IOP ≤ 15 mm Hg with IOP reduction ≥ 20 %. PCP, as an inner drainage surgery, could be limited to the episcleral venous pressure with higher postoperative IOP.[21,22] So, moderate, and advance glaucoma patients may need more medications after PCP to maintain the target IOP and trabeculectomy may be a better alternative for advance patients.

The advantages of IOP control of the TRAB group should be weighed against postoperative complications and interventions. There were no statistical differences between two groups in the risk of postoperative complications except hyphema, which only occurred in PCP group as in previous reports[23] and shallow anterior chamber in PP analysis. Although hyphema only occurred in the PCP group, it recovered within one week without intervention and adverse consequences. And compared with TRAB group, it suggested that hyphema in PCP group may mainly result from the blood reflux from the distal aqueous outflow pathway.[23–25] Bleb associated complications like hypotony or combined with a shallow anterior chamber in two treatment groups had significant differences in PP analysis. The TRAB group could have complications associated with hypotony and shallow anterior chamber even after postoperative bleb management, which was consistent with previous studies.[26,27] As for postoperative bleb management, the TRAB group had many postoperative bleb management like bleb massage (48.1 %), laser suture lysis (18.5 %), and bleb needling with an injection of 5-FU (40.7 %) to control postoperative IOP in patients. Previous studies of trabeculectomy also presented a high percentage of 63.9 %-87.8 % bleb interventions after trabeculectomy.[6,7,28] In this study, we did observe that bleb management was frequent and could also lead to interventions associated with late complications after trabeculectomy. This study and previous studies both suggested patients after trabeculectomy required

more clinic visits and potential costs in the postoperative period, partly to handle complications and partly to maintain the filtration for surgical success.

For the outcome of OSDI, no significant difference in OSDI score was observed between two groups in this study. But the PCP group had a low score compared with TRAB group, and no patients reported a score ≥ 33 at 24 months. Because of the limitations of this study, ocular surface associated evaluation criteria like tear break-up time (TBUT), conjunctival hyperemia, and function of the Meibomian gland were not considered,[29] and baseline OSDI questionnaire was not collected. A solid conclusion of the ocular surface after two treatment groups remained for further investigations. Meanwhile, a previous study reported that the OSDI scores were associated with medications in glaucoma patients.[30,31] In this study, PCP group had more glaucoma medications taken at baseline and follow-up visits, which could be relevant to higher mean OSDI scores. So, the nonsignificant outcome of OSDI score in the study could also be comprised by ignoring the medications taken. To investigate this outcome, further studies are needed.

There are inherent weaknesses in our study. First, this sample size in the study may be small, with limited power to appropriately investigate some outcomes. But, it suggested a comparable efficacy between penetrating canaloplasty and trabeculectomy. Secondly, the outcome of OSDI score failed to report the significant difference between two groups, which could be influenced by various factors such as postoperative medications taken. Further studies with objective indicators like TBUT should be conducted. Thirdly, patients enrolled and surgeons in this study were not blinded to the surgery assigned, which may introduce bias for this study. As surgeons in this study were difficult to be blinded, surgeons were not responsible for data collection, which can minimize the bias. Last, this was a single-centre study. The generalizability of the research results needed to be further verified.

5. Conclusions

Both penetrating canaloplasty and trabeculectomy are effective in reducing IOP in PACG eyes with comparable complications. Trabeculectomy has a higher percentage of postoperative IOP ≤ 15 mm Hg assisted with frequent bleb interventions. If the target pressure requirement is not stringent, penetrating canaloplasty can be considered as a good option.

Abbreviations

PACG, Primary angle-closure glaucoma; IOP, intraocular pressure; PCP, penetrating canaloplasty; TRAB, trabeculectomy; PAS, peripheral anterior synechia OSDI, ocular surface disease index; SC, Schlemm's canal; MMC, mitomycin C; 5-FU, 5-fluorouracil; BSS, balanced saline solution; ITT analysis, Intention to treat analysis; PP analysis, per protocol analysis; BCVA, best corrected visual acuity; UBM, ultrasound biomicroscopy; AL: axis length; MD: mean deviation.

Ethics approval and consent to participate

This study was approved by the Ethics committee of the eye hospital of Wenzhou Medical University (Y-2016023). This study was done in accordance with the tenets set forth in the Declaration of Helsinki and was registered at http://www.chictr.org/.

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Consent for publication

Not applicable.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interest

The authors declare that they have no competing interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.apjo.2025.100167.

References

1. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA*. 2014;311:1901–1911.
2. Quigley HA. Number of people with glaucoma worldwide. *Br J Ophthalmol*. 1996;80:389–393.
3. Liang Y, Friedman DS, Zhou Q, et al. Prevalence and characteristics of primary angle-closure diseases in a rural adult Chinese population: the Handan Eye Study. *Invest Ophthalmol Vis Sci*. 2011;52:8672–8679.
4. Tham CC, Lai JS, Poon AS, et al. Results of trabeculectomy with adjunctive intraoperative mitomycin C in Chinese patients with glaucoma. *Ophthalmic Surg Lasers Imaging*. 2006;37:33–41.
5. AGIS (Advanced Glaucoma Intervention Study) Investigators. The advanced glaucoma intervention study: 8. Risk of cataract formation after trabeculectomy. *Arch Ophthalmol*. 2001;119:1771–1779.
6. King AJ, Rotchford AP, Alwitry A, et al. Frequency of bleb manipulations after trabeculectomy surgery. *Br J Ophthalmol*. 2007;91:873–877.
7. Schlenker MB, Gulamhusein H, Conrad-Hengerer I, et al. Standalone ab interno gelatin stent versus trabeculectomy: postoperative interventions, visual outcomes, and visits. *Ophthalmol Glaucoma*. 2018;1:189–196.
8. Lee SY, Wong TT, Chua J, et al. Effect of chronic anti-glaucoma medications and trabeculectomy on tear osmolarity. *Eye (Lond)*. 2013;27:1142–1150.
9. Meng J, Wang X, Wen L, et al. Tear film stability after trabeculectomy and its relationship with bleb morphology. *Chin J Ophthalmol*. 2019;55:214–219.
10. Wright C, Tawfik MA, Waisbourd M, et al. Primary angle-closure glaucoma: an update. *Acta Ophthalmol*. 2016;94:217–225.
11. Lee CK, Rho SS, Sung GJ, et al. Effect of goniosynechialysis during phacoemulsification on IOP in patients with medically well-controlled chronic angle-closure glaucoma. *J Glaucoma*. 2015;24:405–409.
12. Tham CC, Leung DY, Kwong YY, et al. Effects of phacoemulsification versus combined phaco-trabeculectomy on drainage angle status in primary angle closure glaucoma (PACG). *J Glaucoma*. 2010;19:119–123.
13. Zhang S, Hu C, Cheng H, et al. Efficacy of bleb-independent penetrating canaloplasty in primary angle-closure glaucoma: one-year results. *Acta Ophthalmol*. 2022;100:e213–e220.
14. Cheng H, Ye W, Zhang S, et al. Clinical outcomes of penetrating canaloplasty in patients with traumatic angle recession glaucoma: a prospective interventional case series. *Br J Ophthalmol*. 2023;107:1092–1097.
15. Deng Y, Zhang S, Ye W, et al. Achieving inner aqueous drain in glaucoma secondary to iridocorneal endothelial syndrome: one year results of penetrating canaloplasty. *Am J Ophthalmol*. 2022;243:83–90.
16. Hu JJ, Lin HS, Zhang SD, et al. A new bleb-independent surgery namely penetrating canaloplasty for corticosteroid-induced glaucoma: a prospective case series. *Int J Ophthalmol*. 2022;15:1077–1081.
17. Le R, Xie Y, Cheng H, et al. Outcomes of penetrating canaloplasty in childhood glaucoma. *J Glaucoma*. 2023;32:34–39.
18. Tham CC, Kwong YY, Baig N, et al. Phacoemulsification versus trabeculectomy in medically uncontrolled chronic angle-closure glaucoma without cataract. *Ophthalmology*. 2013;120:62–67.
19. Panarelli JF, Nayak NV, Sidoti PA. Postoperative management of trabeculectomy and glaucoma drainage implant surgery. *Curr Opin Ophthalmol*. 2016;27:170–176.
20. Lin HS, Xu XP, Zheng XL, et al. Malignant glaucoma treated by low-dose laser cycloplasty: a 1-year multicenter prospective non-comparative study. *Int J Ophthalmol*. 2024;17:1248–1254.
21. Phelps CD, Armaly MF. Measurement of episcleral venous pressure. *Am J Ophthalmol*. 1978;85:35–42.
22. Sit AJ, McLaren JW. Measurement of episcleral venous pressure. *Exp Eye Res*. 2011;93:291–298.
23. Matlach J, Dhillon C, Hain J, et al. Trabeculectomy versus canaloplasty (TVC study) in the treatment of patients with open-angle glaucoma: a prospective randomized clinical trial. *Acta Ophthalmol*. 2015;93:753–761.

24. Lin ZJ, Xu S, Huang SY, et al. Comparison of canaloplasty and trabeculectomy for open angle glaucoma: a meta-analysis. *Int J Ophthalmol*. 2016;9:1814–1819.
25. Riva I, Brusini P, Oddone F, et al. Canaloplasty in the treatment of open-angle glaucoma: a review of patient selection and outcomes. *Adv Ther*. 2019;36:31–43.
26. Edmunds B, Thompson JR, Salmon JF, et al. The national survey of trabeculectomy. III. Early and late complications. *Eye (Lond)*. 2002;16:297–303.
27. Baker ND, Barnebey HS, Moster MR, et al. Ab-externo microshunt versus trabeculectomy in primary open-angle glaucoma: one-year results from a 2-year randomized, multicenter study. *Ophthalmology*. 2021;128:1710–1721.
28. Reiter C, Wimmer S, Schultheiss A, et al. Corneal epitheliopathy following trabeculectomy with postoperative adjunctive 5-fluorouracil. *Klin Monbl Augenheilkd*. 2010;227:887–891.
29. Verjee MA, Brissette AR, Starr CE. Dry eye disease: early recognition with guidance on management and treatment for primary care family physicians. *Ophthalmol Ther*. 2020;9:877–888.
30. Guarnieri A, Carnero E, Bleau AM, et al. Relationship between OSDI questionnaire and ocular surface changes in glaucomatous patients. *Int Ophthalmol*. 2020;40:741–751.
31. Lajmi H, Chelly Z, Choura R, et al. Relationship between OSDI score and biomicroscopic ocular surface damages in glaucomatous patients treated with preserved antiglaucomatous eye drops. *J Fr Ophtalmol*. 2021;44:1326–1331.