

BMJ Open Trabeculotomy versus combined trabeculotomy–trabeculectomy for primary congenital glaucoma: study protocol of a randomised controlled trial

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ABSTRACT

Introduction Trabeculotomy and combined trabeculotomy–trabeculectomy (CTT) are major surgical options for primary congenital glaucoma (PCG). However, it is unclear which of these two surgical procedures should be recommended as the optimum first-line treatment for PCG. This trial aims to determine whether the outcomes of trabeculotomy are non-inferior to those of CTT in moderate PCG with a horizontal corneal diameter (HCD) of 12–14 mm.

Methods and analysis This is a 3-year, non-inferiority, prospective, randomised controlled trial. We plan to recruit 248 participants (aged ≤3 years) with PCG with an HCD of 12–14 mm from the Department of Glaucoma, Zhongshan Ophthalmic Center, Guangzhou, China. One eye per participant will be randomly (1:1) assigned to receive trabeculotomy or CTT. The primary outcome is the 3-year postoperative success rate in lowering intraocular pressure (IOP), and the secondary clinical outcomes will include IOP reduction, visual acuity, HCD, central corneal thickness, axial length, cup–disc ratio, refractive error and postoperative complications. Data will be analysed by the intention-to-treat principle.

Ethical approval and dissemination The study protocol has been approved by the ethics committee of Zhongshan Ophthalmic Center (2014MEKY023) and the ‘5010 Plan’ evaluation committee at Sun Yat-Sen University, Guangzhou, China. The results will be disseminated in international academic meetings and published in peer-reviewed journals.

Trial registration number Chinese Clinical Trial Registry, ChiCTR-IOR-14005588; Date registered: 20 November 2014.

INTRODUCTION

Primary congenital glaucoma (PCG) is one of main causes of blindness in children. Liu *et al*¹ reported that congenital glaucoma accounted for 5.1% of all congenital ocular diseases in a Chinese population. It is estimated to account for 0.01%–0.04% of blindness worldwide.² In India, this disease accounts for 4.2% of all childhood blindness.² Haddad *et al*³ evaluated 3210 visually impaired children and found that PCG was responsible for 10.2% of visual impairments. Since

Strengths and limitations of this study

- The trial design is prospective, randomised and controlled with a relatively large sample size, and the follow-up is comparatively long (3 years).
- The study is the first randomised controlled trial to comprehensively evaluate the surgical and visual outcomes of trabeculotomy and combined trabeculotomy–trabeculectomy in patients with primary congenital glaucoma with a horizontal corneal diameter (HCD) of 12–14 mm.
- This study assesses important clinical measurements with significant clinical implications, including HCD, axial length, central corneal thickness, cup–disc ratio, refractive errors and visual acuity. All data will be obtained following standardised protocols and assessed longitudinally.
- The intraocular pressure (IOP) criteria (≤21 mm Hg) used to define glaucoma and surgical success rate may be relatively high for children younger than 3 years old.
- Instead of the gold applanation tonometry, IOP is measured by Tono-Pen tonometry.

at least 50% of eyes with PCG presenting at birth will become legally blind, patients with PCG require prompt treatment and follow-up examinations throughout their lives.⁴

Surgical intervention is the main treatment for PCG. Goniotomy and trabeculotomy are considered initial procedures because of their high success rates.^{5 6} However, clear cornea is a premise for goniotomy but not necessarily for trabeculotomy. Trabeculotomy reduces intraocular pressure (IOP) by tearing the trabecular meshwork into the anterior chamber. Regarding complications, hyphema is more common in trabeculotomy but can resolve spontaneously and cause no additional problems.^{7–9}

Combined trabeculotomy–trabeculectomy (CTT) has been advocated for treating

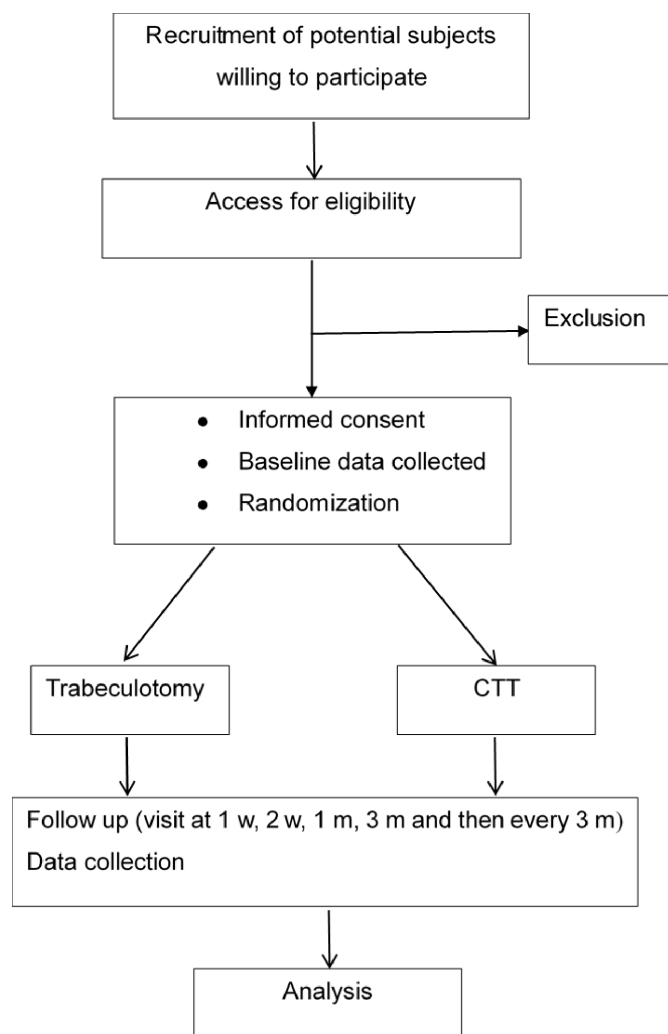


Figure 1 Flow chart of the study. CTT, combined trabeculotomy–trabeculectomy.

moderate-to-severe congenital glaucoma.¹⁰ The rationale for CTT is to gain access to the dual outflow through Schlemm's canal and the trabeculectomy fistula. The application of mitomycin-C (MMC) can improve the surgical success rates of CTT,¹¹ which is, however, disputed by some other studies.^{12 13} Complications after CTT surgery, such as hyphema, bleb-related infections, and choroidal detachment, have been reported.¹⁴

Although some studies have indicated that trabeculotomy and CTT are equally effective in lowering IOP,^{7 9 15} their results were inconsistent with others.^{10 16} There is a paucity of randomised controlled trials with large sample sizes that compare the results of trabeculotomy with CTT for PCG. A randomised trial conducted by Khalil and Abdelhakim⁹ included a cohort of 28 eyes of 28 children younger than 2 years old with a mean follow-up time of 3 years. They concluded that both trabeculotomy and CTT with MMC had similar outcomes. However, due to limitations of sample sizes, it remains inconclusive as which procedure is preferable.¹⁷

The horizontal corneal diameter (HCD) is typically increased in patients with PCG, which serves as an

indication for disease severity and a key factor for surgery selection.¹⁸ In general, angle surgeries are recommended for PCG with an HCD <12 mm.⁸ Trabeculectomy or CTT with or without the use of MMC is usually chosen for advanced cases with an HCD exceeding 14 mm.^{7 19} For moderate PCG with an HCD of 12–14 mm, trabeculotomy and CTT are the two major surgical options. However, it remains unknown whether trabeculotomy, when compared with CTT, yields comparable results and fewer postoperative complications in PCG with an HCD of 12–14 mm. Therefore, we design a study to determine whether the clinical outcomes of trabeculotomy are non-inferior to those of CTT for PCG with an HCD of 12–14 mm.

Study objectives

The primary outcome of our study is to compare the 3-year success rate in lowering IOP between trabeculotomy and CTT in patients with PCG with an HCD of 12–14 mm. The secondary outcome is to assess changes in IOP and the morphometric parameters of the eyeball, visual outcomes and postoperative complications in these two surgical procedures.

METHODS AND ANALYSIS

This protocol is developed in line with the Standard Protocol Items Recommendations for Interventional Trials (SPIRIT). The SPIRIT checklist for the protocol is available as online supplementary file. Protocol of this trial was approved on 25 August 2014.

Trial design and setting

This study is a 3-year, prospective, randomised, single-centre, non-inferiority trial comparing clinical outcomes and postoperative complications between trabeculotomy and CTT in treating PCG with an HCD of 12–14 mm. Eligible patients will be enrolled and randomly assigned to receive either trabeculotomy or CTT (figure 1). The trial is being conducted at the Zhongshan Ophthalmic Center, Guangzhou, China.

Participant selection

Inclusion criteria

Participants will be included if they meet all of the following criteria: (1) diagnosis of PCG in either eye, (2) equal to or under 3 years of age, (3) HCD between 12 and 14 mm and (4) no previous intraocular surgery or laser treatment.

PCG is defined as follows²⁰:

1. Age ≤3 years old.
2. IOP >21 mm Hg.
3. Absence of other ocular or systemic diseases.
4. Combined with one or more of the following clinical signs: (1) corneal findings: Haab's striae, corneal oedema, corneal diameters >11 mm in the newborns, >12 mm in children younger than 1 year old, and >13 mm in children older than 1 year old; (2) increased (>0.3)

or asymmetric (>0.2) cup–disc (C/D) ratio; and (3) abnormally increased axial length (AL).

Normal AL is as follows: 3 months–3 years: 19–22 mm.²¹

Only one eye per patient will be enrolled. If both eyes of a patient are eligible for the study, the eye with the higher baseline IOP will be selected. The treatment for the fellow eye will be determined at the physician's discretion.

Exclusion criteria

Patients will be excluded if they meet any of the following criteria:

- ▶ Inability of the patients' legal guardian to give informed consent.
- ▶ Inability of the patient to return to the clinic for the scheduled study visits.
- ▶ Contraindications to anaesthesia or surgery for ocular disease.
- ▶ Severe corneal cloudiness precluding anterior chamber visualisation.
- ▶ Secondary congenital glaucoma.
- ▶ Other coexisting ocular diseases such as an abnormal cornea, congenital iris abnormality, congenital cataract or retinopathy of prematurity.

Withdrawal criteria

1. Failure to locate or dissect Schlemm's canal by 120°.
2. The presence of any of the following issues during the operation: severe anaesthesia accident, suprachoroidal haemorrhage, or a change in the operative procedure according to the patient's condition.
3. A desire to quit the trial.

The withdrawal criteria described above have been established to ensure that the outcomes of the two procedures (trabeculotomy and CTT) will be effectively analysed for the full 3-year duration of the study.

Interventions

All surgeries will be performed under general anaesthesia by three attending surgeons (XL, MBY and MKL) who specialised in both types of surgery.

Trabeculotomy

This technique has been previously described.⁸ In brief, a superior quadrant fornix-based flap will be created. A 3 mm × 3 mm superficial (12 o'clock) scleral flap of three-quarters thickness will be made. A 2 mm radial incision will be made starting from the grey zone up to the white zone, followed by entering Schlemm's canal externally. An incision will be slowly deepened until the outer wall of Schlemm's canal is opened and seeping aqueous humour is observed. Schlemm's canal will be dissected by 120° in both directions using a trabeculotome probe. The scleral flap will then be replaced with three interrupted 10–0 nylon sutures. The conjunctival flap will also be replaced with 8–0 absorbable sutures.

Combined trabeculotomy–trabeculectomy

In the superior quadrant, CTT with MMC will be performed. A fornix-based conjunctival flap will be

dissected. After dissection of a superficial (12 o'clock) scleral flap measuring 4×3 mm², MMC (0.3 mg/ mL) soaked pieces of micro sponge will be applied under the scleral flap and the conjunctiva for 3 min, and the area will then be washed thoroughly with 30 mL of balanced salt solution. Then, trabeculotomy will be performed as described above. Trabeculectomy will be performed by cutting a 1 mm × 2 mm deep scleral flap, followed by a peripheral iridectomy. The scleral flap and conjunctiva will then be replaced. Finally, the anterior chamber will be reformed with balanced salt solution.

Intraoperative data, including the duration of surgery, the same doses and duration of MMC used during the operation, anaesthesia accidents, intraoperative complications, such as hyphema, iris/vitreous damage, and trabeculotomy-related problems, such as failure to identify Schlemm's canal or an inability to dissect Schlemm's canal by 120°, will be collected.

Postoperative treatment and patient follow-up

Patients will be treated with prednisolone acetate 1% (Allergan, Parsippany-Troy Hills, New Jersey, USA) six times daily in combination with topical antibiotics (tobramycin 0.3%, s.a. ALCON-COUVREUR n.v) and pilocarpine 1% (Bausch & Lomb, Rochester, New York) four times daily for the first 4 weeks after the surgery.

Postoperative follow-up visits will be performed in the paediatric glaucoma clinic at week 1, week 2, week 4, month 3 and then every 3 months (± 1 weeks) for 3 years. The scheduled examinations of the follow-up visits are summarised in table 1. Chloral hydrate 10% (0.8 mL/kg, oral or rectal administration, the maximum dose is 10 mL per day) will be applied to patients not compliant for examinations.

If IOP is found to be high at a scheduled visit, topical anti-glaucoma medication will be prescribed and the scheduled follow-up interval (if longer than 2 weeks) will be shortened to 2 weeks. Additional surgery will be performed if the IOP is > 21 mm Hg on maximum antiglaucoma medications (including pilocarpine 1%, brinzolamide 1% and latanoprost 0.005%) in two consecutive study visits.

Outcome assessment

Primary outcome

The primary outcome is the success rate in lowering IOP at 3 years after surgery. Success is defined as:

1. IOP ≥ 5 mm Hg and ≤ 21 mm Hg on two consecutive follow-up visits with or without antiglaucoma medications.^{5 22}
2. The absence of severe vision-threatening postoperative complications, such as suprachoroidal haemorrhage, retinal detachment or endophthalmitis.
3. No need for additional surgical intervention to control the IOP.

Complete success is defined as meeting success criteria without the need for antiglaucoma medications. Qualified success is defined as meeting success criteria with the use of antiglaucoma medications.

Table 1 Scheduled examinations of follow-up visits

Visit number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Examination	Baseline	Procedure	1 w ±2 d	2 w ±2 d	1 m ±7 d	3 m ±7 d	6 m ±7 d	9 m ±7 d	12 m ±7 d	15 m ±7 d	18 m ±7 d	21 m ±7 d	24 m ±7 d	27 m ±7 d	30 m ±7 d	33 m ±7 d	36 m ±7 d
Informed consent	x																
Demographic data	x																
Medical history	x																
Physical examination	x																
IOP	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
AL	x					x	x		x		x		x		x		x
HCD	x	x			x	x	x	x	x	x	x	x	x	x	x	x	x
Slit lamp examination	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Fundus photography*	x					x	x		x		x		x		x		x
B-scan ultrasound†	x					x	x		x		x		x		x		x
Refraction*	x					x	x		x		x		x		x		x
VA	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Corneal transparency	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
CCT	x																x
Medications	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Reoperation					x	x	x	x	x	x	x	x	x	x	x	x	x

In the event of non-visibility of the fundus,.

*Fundus photography and refraction will not be performed.

†B-scan ultrasound will be used to measure cupping.

AL, axial length; CCT, central corneal thickness; HCD, horizontal corneal diameter; IOP, intraocular pressure; VA, visual acuity.

Secondary outcomes

The secondary outcomes will be evaluated by IOP reduction and changes in the morphometric and functional parameters of eyeball: HCD, corneal transparency, CCT, C/D ratio, AL, VA and refraction. Postoperative complications, including hyphema, shallow anterior chamber, hypotony, surgery-related iridodialysis, complicated cataract, retinal or choroidal detachment, bleb complications (leakage or infection) and endophthalmitis, will be evaluated and recorded.

Sample size calculation

The sample calculation was based on the hypothesis that the 3-year success rate of trabeculotomy will be non-inferior to that of CTT. Published studies have shown that the success rate at the third year after CTT ranges from 72.6% to 87%.^{1 9 23 24} We assume that the 3-year success rate of CTT will be approximately 80%. Therefore, 224 subjects (112 per group) will be needed to provide the trial with a power of at least 80% to demonstrate the non-inferiority (−15% margin) of trabeculotomy to CTT (one-sided α value: 0.025). Assuming a 10% loss to follow-up, a sample size of 248 participants is required for this study, with 124 participants in each group.

Patient recruitment and baseline data collection

All subjects will first be assessed for potential participation in the study by the primary investigator. Patients who gave consent to the study will be invited to undergo enrolment examinations to determine enrolment status.

Examinations

IOP: IOP will be measured with a Tono-Pen Avia (Reichert, Depew, New York, USA) under sedation with chloral hydrate 10% and topical anaesthesia. Although the use of anaesthetic agents during examination under anaesthesia may influence IOP and affect the accuracy of IOP documentation, chloral hydrate has been shown to have a minimal effect on IOP in paediatric ophthalmic examinations.¹⁸

Slit-lamp examination: the condition of the anterior segment, including corneal clarity, corneal oedema, Haab's striae, anterior chamber depth, iris, pupil and lens, will be evaluated using a hand-held slit lamp (Keeler, Bucks, England).

Corneal clarity will be recorded as mild (iris texture clearly seen), moderate (iris seen but texture not clearly visible) and severe (iris not visible).

HCD: a calliper will be used to measure the HCD (white to white) by ophthalmologists. Participants with an HCD less than 12 mm or greater than 14 mm will be excluded.

CCT: CCT will be measured using ultrasound pachymetry (IOPac, Heidelberg Engineering, Heidelberg, Germany). Topical anaesthetic will be used prior to the application of the ultrasonic probe to the corneal surface. All measurements were taken with the child in the supine position. Ten measurements will be taken for each eye, and the lowest reading will be recorded.

C/D ratio: the C/D ratio will be evaluated using direct ophthalmoscopy (66 Vision, Suzhou, China) as permitted by the media clarity. Images showing the C/D ratio will be obtained using a hand-held retinal camera (Kowa nonmyd-a-D III; Kowa Optimed Inc, Aichi, Japan) through a dilated pupil. For children with hazy media, whose fundus cannot be visualised, fundus photography will not be performed, and a B-scan ultrasound (Quantel Medical, CF, France) will be used to rule out any intraocular pathology and to detect excavation of the optic nerve head.

Ocular biometry: ocular biometry, including AL, anterior chamber depth, lens thickness and vitreous chamber depth, will be measured using A-scan ultrasound (Quantel Medical, CF, France). Ten repeated measurements will be taken and averaged for analysis.

Visual acuity (VA): VA will be measured using suitable procedures. Teller acuity cards (Vistech Consultants, Dayton, Ohio, USA) will be used at a distance of 55 cm in non-verbal children. The Lea symbols (Precision Vision, La Salle, Illinois, USA) with a test distance of 3 m and the Early Treatment of Diabetic Retinopathy Study LogMAR E chart (Precision Vision, Villa Park, Illinois, USA) with a test distance of 4 m will be employed for verbal children. Monocular VA will be assessed in the right eye followed by the left eye. For children who cannot complete the quantified VA examinations mentioned above, the ability to fix and follow light will be evaluated.

Refractive error: refraction will be measured by retinoscopy after cycloplegia. Cycloplegia will be induced with two drops of cyclopentolate 1% instilled 5 min apart, with a third drop administered after 20 min. Cycloplegia will be then evaluated after an additional 15 min. Cycloplegia is considered complete if the pupil dilates to ≥ 6 mm and a light reflex is absent.²⁵ Refractive error will not be evaluated when attempts to improve the view were not successful.

All ophthalmological examinations described above will be performed in both eyes. Chloral hydrate 10% will be applied to patients not compliant for examinations.

Written informed consent will be collected from each eligible participant's legal guardian prior to inclusion in the study. For eligible participants, demographic data (sex, date of birth and laterality), family history of PCG and medical history (age of onset, initial syndrome, age at diagnosis and medical treatment) will be recorded. Pregnancy and delivery information (gestational weeks, delivery mode, maternal drug intake and infection during pregnancy) will also be ascertained and recorded.

Randomisation

A randomisation list was generated with the SAS V.9.3 software package (SAS Institute) by a biostatistician who will not participate in data management. The 1:1 randomisation procedure will be performed using varying block sizes. To ensure concealment, the block size will not be disclosed. The allocation of patients will be concealed using sequentially numbered, opaque sealed envelopes. A total of 248 envelopes will be prepared by two researchers not involved in the study. For each recruited patient, his/her group assignment will be revealed in the operating room on the day of surgery. Surgical management and intraoperative data will be collected.

Postoperative follow-up will be performed by investigators who will not participate in patient care and are trained to follow-up patients prior to the study. The surgeon(s) and investigator(s) will not communicate with each other while collecting data.

Data management and monitoring

All data collected at the scheduled follow-up visits (table 1) will be recorded in the case report forms and entered into a digital database by trained researchers. The soft copies of digital data will be stored in these devices and then in a server at the end of each visit day. The completed case report forms and hardcopy data forms will be kept in locked cabinets in the research centre. The implementation of the trial will be monitored by the principal investigator. Access to the final dataset will be limited to the trial administrator and the statistician.

Statistical analysis

All statistical analyses will be performed using SPSS V.22.0 (SPSS). Continuous variables conformed to the normal distribution will be expressed as the mean (SD). Dichotomous and nominal variables will be expressed as frequencies, ordinal and discrete variables as median and IQR.

The primary analysis will be based on the principle of intention to treat and will include all subjects who underwent randomisation, with data censored at the last scheduled visit. We will perform a sensitivity analysis of the post hoc worst case scenario, in which subjects who did not complete follow-up were considered failed outcomes, and a sensitivity analysis of a post hoc complete-case scenario, in which only subjects who had complete data all through the trial will be included. We calculated 95% CI for the estimates of the absolute differences between the two treatment groups regarding the 3-year success rate using the Cochran-Mantel-Haenszel method. Non-inferiority would be met if the lower limit of the 95% CI of the absolute difference did not cross the prespecified non-inferiority margin (-15%). The survival data (time-to-IOP controlled) will be analysed using the Kaplan-Meier method. The log-rank test will be employed to compare curves in the trabeculotomy and CTT groups.

Secondary outcomes will be assessed with two-sided tests. Comparisons of continuous variables distributed normally, such as the IOP, HCD, AL and central corneal



thickness (CCT) will be performed between the two groups using Student's t-test. Considering that the normal IOP in children is lower than that of adults, we will use 18 mm Hg as a cut-off and compare the surgical outcomes between two groups after 3 years of follow-up using the Kaplan-Meier method. For continuous variables not distributed normally and for discrete variables (including the C/D ratio, number of antiglaucoma drugs and distribution of refractive errors) between the two groups comparison will be performed using Mann-Whitney U test. The Chi-square test or Fisher's exact test will be used to compare the proportions of the visual outcomes, and complications between the two surgical groups.

Safety consideration

The safety evaluations of the study will include complications associated with surgeries as well as drugs adverse events. The procedures and drugs used in the study are routinely administered in daily practice. Thus, the trial has risks not exceeding usual clinical care that the patients would otherwise receive. Throughout the study, all adverse events will be recorded and managed.

Drug-related complications include unanticipated events caused by cycloplegia, antiglaucoma drugs and chloral hydrate. Dilation will be established following a slit lamp examination. Doctors will closely monitor the patients' pupil reflexes and vital signs after administering the medications.

Vision-threatening complications, such as suprachoroidal haemorrhage, retinal detachment and endophthalmitis, will constitute major adverse events.

Trial status

Recruitment began in the first quarter of 2015. Currently, 75% of the sample size has been attained. It is anticipated that the study will reach the recruitment target of 248 participants by the fourth quarter of 2019. There are no plans for interim analysis.

Patient and public involvement

Patients and public were not involved in the design of the study.

ETHICS AND DISSEMINATION

The study results will be presented at national and international meetings on ophthalmology.

DISCUSSION

This is a prospective, randomised, controlled intervention trial that aims to provide evidence for clinicians for better judgement regarding surgical options for patients with PCG. To the best of our knowledge, this trial is the largest clinical trial in the field of paediatric glaucoma. The findings are expected to provide evidence indicating whether trabeculotomy is non-inferior to CTT in treating PCG with an HCD of 12–14 mm.

For PCG with an HCD less than 12 mm, the anatomic abnormality of Schlemm's canal is usually not significant,

facilitating its identification during the operation. As a result, angle surgery alone is sufficient to lower IOP in these patients. Sampaolesi *et al*²⁶ proposed that trabeculotomy is suitable for children with PCG in whom the corneal diameter is less than 13 mm and the AL is less than 23 mm. Advanced PCG with an HCD greater than 14 mm is usually associated with a significant anatomic anomaly of the anterior drainage angle. The abnormally stretched anatomy of the limbus in these patients frequently makes it difficult to clearly identify the lumen of Schlemm's canal that has to be cannulated for the trabeculotomy. Thus, the success rate of trabeculotomy is lower in advanced PCG cases. Quigley²⁷ reported the results of trabeculotomy in 28 eyes with congenital glaucoma. The success rate in eyes with an HCD greater than 14 mm was 67% compared with 100% in eyes with a smaller HCD. Both of the conditions described above will lead to biases in the results. Moreover, most PCG cases in China have an HCD ranging from 12 mm to 14 mm,^{7 28} and these patients have a good chance of preserving useful VA if treated correctly.

No unified guideline is currently available to determine PCG severity based on corneal diameter. Cronemberger *et al*²⁹ confirmed that a higher HCD will trigger higher HCD and AL at final follow-up. Kiskis *et al*³⁰ studied the HCD and AL in patients with PCG and concluded that HCD measurement was a more reliable guide than AL in the assessment of PCG. Currently, we are unaware of any studies that compared long-term outcomes between CTT and trabeculotomy in patients with PCG who exhibited homogeneity in terms of disease severity. After considering the above information, we selected an HCD of 12–14 mm as an inclusion criterion. However, selection of surgical methods for the treatment of PCG and the evaluation of PCG severity based on HCD alone are issues requiring further investigation and improvement.

With regard to IOP, we selected an IOP value of ≤ 21 mm Hg as a success criterion based on the previous reports.^{5 23 31} In this study, IOP will be measured with Tono-Pen which has been widely used in clinic for many years. We chose Tono-Pen as the measurement by referring to the previous studies.^{32–34} On the other hand, Tono-Pen is particularly useful with corneal scars or oedema,³⁵ which are often seen in PCG eyes. We used Tono-Pen for all patients at each scheduled visit, which eliminated any possibility of bias due to the use of different tonometry techniques in different patients.

In conclusion, this is a large clinical trial aiming to provide evidence for the optimum first-line surgery for patients with PCG with an HCD of 12–14 mm. If the trabeculotomy group is associated with comparable surgical success and fewer postoperative complications compared with CTT group, trabeculotomy should be recommended as a primary surgical treatment for PCG with an HCD of 12–14 mm, saving trabeculectomy for future intervention. In addition, complications associated with trabeculectomy will be reduced. The visual outcome in this trial may help provide insight into the effects of surgical methods on VA. The findings of our study are expected to provide guidance

to clinicians weighing the benefit and risk of trabeculotomy compared with CTT for the treatment of PCG.

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Contributors XL conceived the study and is the project leader for the trial. XL, XG, YY, JH, YZ, XC, JH and LF participated in the study design and recruited the patients. LF wrote the manuscript. XL, XG, YZ and XX critically revised the manuscript. JZ designed the database system and performed the statistics-related design. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the ethics committee of Zhongshan Ophthalmic Center (reference number 2014MEKY023). The study protocol was also reviewed by the "5010 Plan" evaluation committee at Sun Yat-sen University, Guangzhou, China. Every year, the evaluation committee will examine the study progress and its adherence to the study protocol. Any important modifications to the protocol will be documented in the study protocol as formal amendments. These amendments will be submitted to the ethics committee of Zhongshan Ophthalmic Center and the "5010 Plan" evaluation committee of the Sun Yat-sen University for a review. The project leader will ensure that this study is conducted in accordance with the principles of the World Medical Association Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

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