

BMJ Open Efficacy and safety of trabeculectomy versus peripheral iridectomy plus goniotomy in advanced primary angle-closure glaucoma: study protocol for a multicentre, non-inferiority, randomised controlled trial (the TVG study)

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ABSTRACT

Introduction Primary angle-closure glaucoma (PACG) is a major subtype of glaucoma that accounts for most bilateral glaucoma-related blindness globally. Filtering surgery is a conventional strategy for PACG, yet it has a long learning curve and undesirable disastrous complications. Minimally invasive glaucoma surgery (MIGS) plays an increasing role in the management of glaucoma due to its safer and faster recovery profile; cataract surgery-based MIGS is the most commonly performed such procedure in PACG. However, for patients with a transparent lens or no indications for cataract extraction, incorporation of MIGS into PACG treatment has not yet been reported. Therefore, this multicentre, non-inferiority, randomised controlled clinical trial aims to compare the efficacy and safety of trabeculectomy versus peripheral iridectomy plus an ab interno goniotomy in advanced PACG with no or mild cataracts.

Methods and analysis This non-inferiority, multicentre, randomised controlled trial will be conducted at seven ophthalmic departments and institutes across China. Eighty-eight patients with no or mild cataracts and advanced PACG will be enrolled and randomised to undergo trabeculectomy or peripheral iridectomy plus ab interno goniotomy. Enrolled patients will undergo comprehensive ophthalmic examinations before and after surgery. The primary outcome is intraocular pressure (IOP) at 12 months postoperatively. The secondary outcomes are cumulative success rate of surgery, surgery-related complications and number of IOP-lowering medications. Participants will be followed up for 36 months postoperatively.

Ethics and dissemination The study protocol was approved by the ethical committees of the Zhongshan Ophthalmic Center, Sun Yat-sen University, China (ID: 2021KYPJ191) and of all subcentres. All participants will be required to provide written informed consent. The results will be published in peer-reviewed journals and disseminated in international academic meetings.

Strengths and limitations of this study

- ⇒ Randomisation prevents selection bias and increases comparability between two study arms.
- ⇒ Participants are recruited from multiple centres, which will lead to a shorter study duration and increased generalisability.
- ⇒ An extended follow-up will provide valuable longer-term evidence.
- ⇒ The study only recruits participants aged 45–80 years, which will limit generalisability to younger patients.

Trial registration number NCT05163951.

INTRODUCTION

Primary angle-closure glaucoma (PACG) is an important subtype of glaucoma and is responsible for 50% of glaucoma-related blindness worldwide.^{1 2} PACG has a high prevalence and blindness rate in Asia, especially in China.³ It is of great importance to continuously advance treatment strategy that is safer, easier, faster, more favourable and less complicated.

The routine treatment regimen for advanced PACG is surgery, of which trabeculectomy or phacotrabeculectomy is the most popular.⁴ However, there are many issues associated with trabeculectomy, such as complications of a shallow anterior chamber, persistent hypotony, malignant glaucoma, endophthalmitis and bleb-related complications, a long learning curve for ophthalmologists, and difficulty with postoperative

care; therefore, it is not an ideal surgical method.^{5–8} Lens extraction, for example, phacoemulsification with intraocular lens implantation (PEI), is used as a safer alternative to treat PACG.⁹ The anterior chamber can be deepened and widened to facilitate aqueous humour outflow. Goniosynechialysis (GSL) is combined when extensive peripheral anterior synechia (PAS) exists; however, clinical studies have reported insufficient or no additive intraocular pressure (IOP) reduction of GSL.¹⁰ The diseased trabecular meshwork and the Schlemm's canal due to chronic adhesion, inflammation and fibrous tissue hyperplasia during the progression of angle closure could explain this.^{11 12} Adjunctive antiglaucoma medications or surgeries are needed.

Minimally invasive glaucoma surgery (MIGS) has been successfully incorporated in clinical practice in recent years, and although initially used in primary open-angle glaucoma it has now been attempted in PACG in a PEI-based manner.^{13–15} After PEI, MIGS including goniotomy (GT), implantation of bypass and endocycloplasty can be performed just as in primary open-angle glaucoma with its advantages being having a safe profile, faster recovery and relatively few complications.^{16–18} Additive IOP-lowering is thus obtained for advanced PACG. GT, the most popular type of MIGS, has been successfully adopted for PACG using Kahook Dual Blade,^{19–21} Tanito Microhook,^{22 23} or other microhooks or gonioscopy-assisted transluminal trabeculotomy.^{24–26} However, the evidence was mainly retrospective.²⁷ An ongoing randomised controlled trial (RCT) is comparing phacotrabeculectomy and phacogoniotomy (PEI+GSL+GT) (ClinicalTrials.gov: NCT04878458).²⁸ For patients with no or mild cataracts, removal of the lens remains controversial.²⁹ Theoretically, it is possible to choose surgical peripheral iridectomy (SPI) instead of PEI to eliminate the pupillary block in PACG. The application of a viscoelastic substance can deepen the anterior chamber, facilitating the performance of GSL and GT. On the other hand, SPI, along with postoperative antiglaucoma eye-drops, is a strategy to avoid the complications of filtration surgery, especially in young patients with PACG who have a short axial length.^{30 31} The combined procedure of GT can lower IOP and reduce IOP-lowering medications.

Herein, we intend to conduct a collaboration of seven top-ranked ophthalmic departments and institutes across China and perform a non-inferiority RCT to compare trabeculectomy with SPI+GSL+GT in terms of efficacy and safety for treatment of advanced PACG with no or mild cataracts.

METHODS AND ANALYSIS

Objective

This study aims to compare the efficacy and safety of trabeculectomy with SPI+GSL+GT for treatment of advanced PACG with no or mild cataracts.

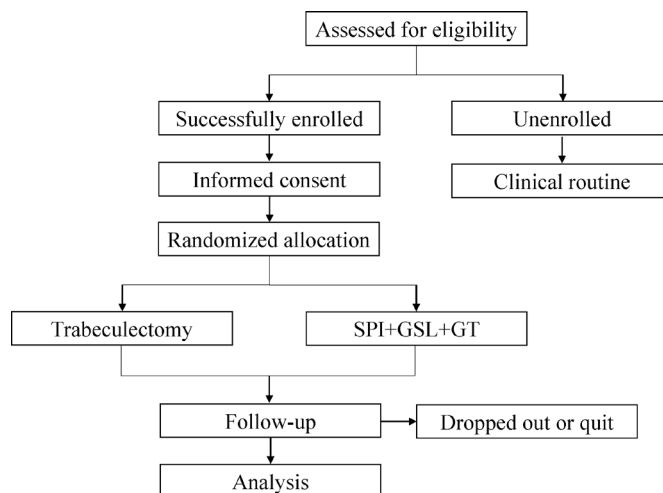


Figure 1 Study flow chart. GSL, goniosynechialysis; GT, goniotomy; SPI, surgical peripheral iridectomy.

Design and setting

This is a multicentre, parallel-assignment, open-labelled, non-inferiority RCT. This study will be conducted at the Zhongshan Ophthalmic Center, Sun Yat-sen University, as the principal centre, in partnership with six other hospitals and eye institutes, as subcentres, including Handan City Eye Hospital (The Third Hospital of Handan); Department of Ophthalmology, West China Hospital of Sichuan University; Department of Ophthalmology, The Second Affiliated Hospital, Harbin Medical University; Department of Ophthalmology, The Third Affiliated Hospital of Chongqing Medical University; Department of Ophthalmology, Shijiazhuang People's Hospital; and Department of Ophthalmology, People's Hospital of Chongqing. **Figure 1** summarises the trial design along with the details of the trabeculectomy versus peripheral iridectomy plus goniotomy (TVG) study.

Eligibility

Inclusion criteria

- ▶ Age 45–80 years.
- ▶ Eyes diagnosed with advanced PACG meeting criteria 1, 2 and 3, or criteria 1, 2 and 4^{29 30}: (1) PAS $\geq 180^\circ$ range, including the nasal and inferior quadrants; (2) IOP > 21 mm Hg with or without antiglaucoma medications (medications include maximally tolerated medications), taken with the Goldmann applanation tonometer; (3) glaucomatous optic neuropathy (cup to disc (C:D) ratio ≥ 0.7 , C:D asymmetry > 0.2 , or rim width at the superior and inferior temporal areas < 0.1 of the vertical diameters of the optic disc); and (4) glaucomatous visual field defects (nasal step, arcuate scotoma and paracentral scotoma on a reliable Humphrey analyser and a mean deviation of ≤ -12 dB).
- ▶ No or mild cataracts and uncorrected visual acuity of ≥ 0.63 (Early Treatment Diabetic Retinopathy Study chart).
- ▶ Axial length of ≥ 20 mm.

Exclusion criteria

- ▶ History of ocular surgery or trauma.
- ▶ Retinal disease that influences the collection of ocular parameters or other types of glaucoma, including open-angle glaucoma, secondary angle-closure glaucoma, steroidal glaucoma, angle recession glaucoma, neovascular glaucoma, nanophthalmos and pseudo-exfoliation syndrome.
- ▶ Monophthalmia (best-corrected visual acuity of <0.01 in the non-study eye).
- ▶ An international standardised ratio of >3.0 for patients receiving warfarin or anticoagulant therapy before surgery.
- ▶ Patients with serious systemic diseases.
- ▶ Pregnant or lactating women.

If both eyes are eligible for the study, the eye with the worse visual field or optic nerve will be included.

Recruitment

This is a multicentre study. All the subcentres are tertiary hospitals in China. The first screening will be conducted at the outpatient clinics of all subcentres. Once the eligibility criteria are met, the trial will proceed further.

Intervention allocation

A central randomisation system will be used to generate a random allocation sequence with a block size of four patients for each subcentre. The participants in each block unit will be evenly assigned (1:1) to the control group (trabeculectomy) and the experimental group (SPI+GSL+GT).

Masking

This study has an open design because the experimental and control groups have been assigned different surgical interventions and the doctors and patients cannot be masked. The examiners will be blinded to the groups during the screening, allocation and follow-up. The statisticians will be unaware of the randomisation results until completion of the statistical analysis.

Intervention methods

Professors or senior attending physicians who have more than 10 years' training will perform the same standard surgical technique designed for each group.

Preoperative medication

- ▶ Topical IOP-lowering medications will be used until the day of surgery.
- ▶ Osmotic agents such as mannitol will be used before surgery, if needed.
- ▶ Antibiotic drops such as levofloxacin eye-drops will be used 3 days before surgery to minimise the risk of endophthalmitis.

Anaesthesia

Either local anaesthesia or general anaesthesia will be used according to the standard clinical routine.

Control group (trabeculectomy with mitomycin C)

All patients in the control group will undergo standard trabeculectomy. The incision will be made along the corneal limbus (11–1 o'clock position) to raise a curved fornix-based conjunctival flap. A superficial (12 o'clock position) scleral flap of 4×3 mm and a half or two-third thickness will be raised, and mitomycin-soaked sponges (0.2–0.5 mg/mL) will be applied under the flap and conjunctiva for 1–5 min. The area will be subsequently rinsed thoroughly with 200 mL of balanced salt solution. Trabeculectomy involving the excision of a trabecular block measuring approximately 1×2 mm in size is performed, followed by an SPI with an area of approximately 1.5×1.5 mm. The scleral flap will then be replaced and closed with two 10-0 nylon sutures. The anterior chamber will be constructed using balanced salt solution with the appropriate filtered volume, and the bulbar conjunctiva will be closed using 10-0 interrupted sutures.

Intervention group (SPI+GSL+GT)

SPI will be performed. A conjunctival incision of approximately 2 mm will be made superior-nasally along the corneal limbus, and a full-thickness self-sealing corneal incision will be made with a 15° scalpel. To press the posterior lip of the corneal incision for herniation of the peripheral iris tissue from the corneal incision, a full-thickness iris tissue with an area of approximately 1.5×1.5 mm will be cut using corneal scissors. A main transparent corneal incision of approximately 2.2 mm will be made at the temporal quadrant or superior temporal quadrant, and the viscoelastic agent (eg, IVIZ, Bausch & Lomb; DisCoVisc, Alcon) will be injected to deepen the anterior chamber. The patient's head will be rotated 35° – 45° away from the surgeon, and the microscope will be tilted at an angle of 35° – 45° towards the operator. Following this, the viscoelastic agent will be applied on the corneal surface. A close observation of the angle, and in particular the trabecular meshwork, can be made using a surgical gonioscope placed on the cornea. GSL will be completed by separating all the PAS down gently as much as possible with a chopper. A microhook or microblade will then be inserted through the main incision of the cornea into the anterior chamber, with the tip embedded into the Schlemm's canal to scratch and incise the inner wall of the Schlemm's canal and trabecular meshwork at a range of at least 120° . After aspirating the viscoelastic material and the blood, the corneal incision will be sealed by stromal hydration. [Figure 2](#) presents the schematic of the two manners of SPI+GSL+GT.

Postoperative management

- ▶ Topical 1% prednisone acetate eye-drops will be administered four times a day and steroid ointment will be administered once at bedtime for 1 month for the trabeculectomy group. For the SPI+GSL+GT group, 1% prednisone acetate eye-drops will be administered for 1 week, followed by non-steroidal anti-inflammatory eye-drops for 3 weeks, and 1%

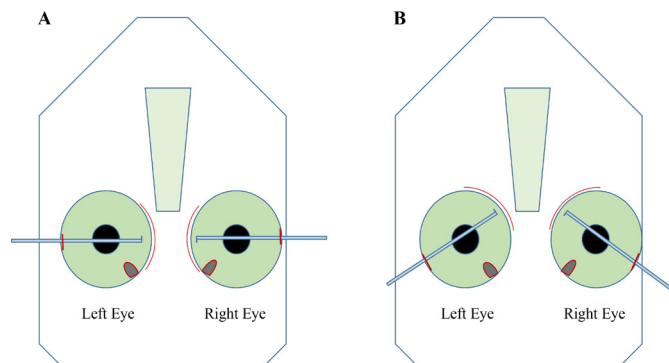


Figure 2 Schematic of the two manners of SPI+GSL+GT. SPI at the superior nasal quadrant of the corneal limbus will be carried out, where an oval shadow indicates SPI; the incision is made at the temporal (A) or superior temporal (B) quadrant. GSL and GT will be carried out within a 120° range at the nasal (A) or inferior nasal (B) quadrant of the angle, where a short red line indicates the corneal incision and an arc line indicates an incision range (a chopper is used for GSL; a microhook or microblade is used for GT). GSL, goniosynechialysis; GT, goniotomy; SPI, surgical peripheral iridectomy.

pilocarpine eye-drops will be administered four times a day for 1 month.

- ▶ An intramuscular injection of 2 KU hemocoagulase will be administered to individuals in both groups before and after surgery.
- ▶ If glucocorticoids cause increased IOP, the participant will be assessed and non-steroidal anti-inflammatory eye-drops will be administered for 1 week, along with stoppage of steroid medications. If the IOP remains uncontrolled for more than 1 week, the participant will be excluded from the study.
- ▶ If the IOP is >18 mm Hg after surgery, topical antiglaucoma medication will be administered. In the trabeculectomy group, ocular massage, releasable suture lysis or laser suture lysis will be performed by the attending ophthalmologist, if needed.
- ▶ The topical medication will consist of eye-drops according to local practice from the following list of medications: prostaglandin, beta-blocker, carbonic anhydrase inhibitor and alpha-2 agonist. A maximum of four drugs with different mechanisms will be used.
- ▶ After medical antiglaucoma therapy fails to control IOP for 3 months, glaucoma surgery will be performed. The need for glaucoma surgery will be qualified as a 'failure' of the intervention/control care to control the disease. Patients will be excluded from the study.
- ▶ If an intervention/control procedure is not performed successfully intraoperatively, the patient will be excluded from the study and receive further treatment after assessment.

The schematic of the postoperative management is shown in figure 3.

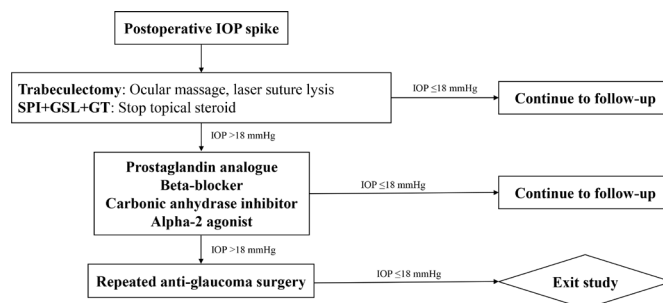


Figure 3 Flow chart showing the postoperative management. GSL, goniosynechialysis; GT, goniotomy; IOP, intraocular pressure; SPI, surgical peripheral iridectomy.

Outcome measurement

Primary outcome

- ▶ IOP at 12 months after surgery.

Secondary outcomes

- ▶ Cumulative success rate of the surgery: (1) complete success will be defined as a postoperative IOP of ≥ 5 mm Hg or ≤ 18 mm Hg and a 20% reduction from baseline without antiglaucoma medications; and (2) qualified success will be defined as a postoperative IOP of ≥ 5 mm Hg or ≤ 18 mm Hg and a 20% reduction from baseline with antiglaucoma medications.
- ▶ Intraoperative and postoperative complications (eg, shallow anterior chamber, malignant glaucoma, hyphema, persistent hypotony, corneal endothelium decompensation, endophthalmitis and bleb-related complications).
- ▶ Number of antiglaucoma medications.

Other prespecified and exploratory outcomes

- ▶ Visual acuity.
- ▶ Degree of PAS.
- ▶ Corneal endothelial cell counting.
- ▶ Visual field.
- ▶ Optic nerve head and retinal parameters derived from optical coherence tomography (OCT).
- ▶ Quality of life.
- ▶ Filtering bleb classification using the Indiana Bleb Appearance Grading Scale.³²
- ▶ Surgical time and cost.

Examinations

The following are the baseline data and follow-up examination parameters:

- ▶ Demographic data, including name, identity number and sex.
- ▶ Medical history, surgical history and current medication.
- ▶ Vital signs, height and weight.
- ▶ Optometry and visual acuity: using the Early Treatment Diabetic Retinopathy Study logarithm of the minimum angle of resolution visual acuity chart (Precision Vision, Villa Park, Illinois, USA), in accordance with the Refractive Error Study in Children research protocol.³³

- ▶ Slit lamp and fundus examinations (BQ-900, Haag Streit, Koeniz, Switzerland).
- ▶ Fundus photography using a fundus camera.
- ▶ IOP measurement: each visit requires IOP evaluations in both eyes and the average of the two measurements will be taken using Goldmann applanation tonometry (AT900, Haag Streit).
- ▶ Endothelial cell count using endokeratoscope (SP-2000P, Topcon, Japan).
- ▶ Gonioscope: a single-mirror gonioscope (Ocular Instruments, Bellevue, Washington, USA) will be used for grading according to the Shaffer classification method.
- ▶ Ultrasound biomicroscopy examination to visualise the morphology of the anterior segment.
- ▶ A spectral domain OCT (Cirrus 5000, Carl Zeiss Meditec, USA; or Heidelberg SPECTRALIS OCT, Heidelberg, Germany) will be used (each subcentre can choose the instrument).
- ▶ Visual field examination will be performed using the Swedish interactive threshold algorithm standard 24-2 program by Humphrey Field Analyzer (Mark 2/3, Carl Zeiss Meditec, Dublin, California, USA). It is required to report a false positive rate of <15%, false negative rate of <15% and fixation loss of <20%. The mean deviation and pattern SD values will be recorded.
- ▶ Quality of life assessment using the 5-level EQ-5D version (EQ-5D-5L, simplified Chinese, EuroQol Research Foundation, registered).
- ▶ Anterior OCT examination will be performed using CASIA OCT (Tomey, Tokyo, Japan) to examine the angle structure and measure the depth of the anterior chamber.
- ▶ Pentacam examination (Oculus, Germany) will be performed to measure the biological parameters of the patient's corneal curvature, corneal spherical aberration, corneal astigmatism, etc.

Table 1 Follow-up schedule

Visit number	0	1	2	3	4	5	6	7	8	9
Inspection items	-7 to 1 day	7 days	1 month	3 months	6 months	12 months*	18 months	24 months	30 months	36 months
Informed consent	X									
Demographic data and medical history	X									
Vital signs	X					X	X	X	X	X
Medication record	X	X	X	X	X	X	X	X	X	X
Optometry	X					X		X		X
Visual acuity	X	X	X	X	X	X	X	X	X	X
Slit lamp biomicroscopy	X	X	X	X	X	X	X	X	X	X
Fundus photo	X					X		X		X
Intraocular pressure	X	X	X	X	X	X	X	X	X	X
Endokeratoscope	X					X		X		X
Gonioscopy	X			X		X		X		X
UBM	X					X		X		X
Anterior segment OCT†	X					X		X		X
Posterior segment OCT	X					X		X		X
Visual field	X				X	X	X	X	X	X
Pentacam†	X					X		X		X
Quality of life questionnaire	X					X		X		X
Adverse events	X	X	X	X	X	X	X	X	X	X

X indicates data need to be collected during the visit.

*End-of-study follow-up showed that the main study outcome had been achieved; from the second visit, the time window of each visit was ± 7 days.

†The inspection subcentres shown can choose by themselves.

OCT, optical coherence tomography; UBM, ultrasound biomicroscopy.

Participant schedule

The follow-up schedule is listed in [table 1](#).

Sample size calculation

This will be a non-inferiority trial. The sample size is estimated based on the primary outcome, that is, IOP 12 months after surgical treatment. Previous studies have reported that the average IOP after trabeculectomy at 12 months is approximately 14 mm Hg.^{30 34} An IOP of 18 mm Hg or lower will be defined as successful surgery; therefore, the non-inferiority margin (Δ) will be specified as 4.0 mm Hg, which will be acceptable in clinical practice. A common SD (σ) of 5 mm Hg will be employed for both treatment groups, as previously reported.^{30 34} To achieve a power of 90%, at a one-sided significance level (α) of 2.5%, a sample size of 34 eyes from 34 participants per group will be required. Allowing for a 20% loss to follow-up, a sample size of 88 eyes from 88 participants will be necessary. The sample size was calculated using PASS V.16.0 (NCSS, USA).

Monitoring

Data monitoring

Data monitoring will be performed by a professional data administrator at the clinical research centre of Zhongshan Ophthalmic Center and will be independent of the researchers.

Interim analysis

Interim analyses will not be performed.

Harms

The risks include uncontrolled IOP, occurrence or aggravation of cataract, endophthalmitis and hyphema, and adverse effects of general anaesthesia and topical medications, which are common risks in clinical practice.

Auditing

The study will be conducted by the supervisor of the trial, will not involve new drugs or devices, and will be conducted under the guidance of the ethics committees of all subcentres.

Data collection and management

All the original data will be stored in the electronic data capture system, and only the centres will have access to their data. All raw data must be kept by the researcher in the participant's file. Any changes in the raw data will be documented in the electronic data capture system.

Statistical analysis plan

All statistical analyses will be performed using a commercially available software package (Stata V.16). Histogram and Shapiro-Wilk tests will be employed to check the normality of continuous data. Continuous variables will be described as mean (SD) with normal distribution and median (IQR) without normal distribution. Categorical variables will be presented as frequencies (percentages).

The baseline characteristics of the two study groups will be compared first. A two-sample t-test will be employed for continuous variables if normally distributed, otherwise using the Mann-Whitney U test. The χ^2 test or Fisher's exact test will be employed to compare categorical outcomes.

Analyses of the primary and secondary outcomes will be based on the principles of intent to treat and will include all participants who are randomised and receive surgery, where the missing data will be imputed by multiple imputations, regardless of complications or further surgical interventions.

Primary outcome analysis

The mean difference in IOP at 12 months between the control and study groups and the 95% CI will be estimated using univariable and multivariable linear regression models. For the non-inferiority test, the hypothesis of inferiority will be rejected when the upper limit of the one-sided 97.5% CI (equal to two-sided 95%) of the difference in IOP is less than the prespecified non-inferiority margin (4 mm Hg). Variables that will be significantly associated with the difference in IOP between both groups ($p < 0.2$) will be included in the multivariate linear regression analysis.

Secondary outcome analysis

The cumulative rate of surgical success and complications between both groups will be assessed using the χ^2 test or Fisher's exact test. The stratified Kaplan-Meier survival curves and log-rank test will also be employed to show the cumulative probability and the time to the incidence of unsuccessful surgery over time in each group. Unsuccessful surgery will be defined as an IOP of >18 mm Hg or $<20\%$ reduction below the baseline during two consecutive follow-up visits after 3 months, an IOP of ≤ 5 mm Hg during two consecutive follow-up visits after 3 months, reoperation for glaucoma or loss of light perception vision.³⁴ Other secondary outcomes will be assessed using two-sided tests. The detailed method will be as mentioned above in the baseline data analysis. Statistical significance will be set at $p < 0.05$.

Study completion and termination

Criteria of completion

The primary outcome endpoint will be 1 year, although when the study is completed the investigator will hold a clinical study report meeting and revise and sign the final clinical study report. The investigator will report the completion of the study to the ethics committee.

Participants will be withdrawn from the study for the following reasons: safety, participation in other clinical trials, severe adverse events occurring during the study and surgical failure.

Patient and public involvement

There is no patient or public involvement.

ETHICS AND DISSEMINATION

Ethics approval

Ethical approval has been obtained from the ethical committees of the Zhongshan Ophthalmic Center, Sun Yat-sen University, China (ID: 2021KYPJ191; version 20211124) and of all subcentres. The registration identifiers of other centres are listed as follows: Handan City Eye Hospital (The Third Hospital of Handan) (ID: 2021007); West China Hospital of Sichuan University (ID: 2022(39)); the Second Affiliated Hospital, Harbin Medical University (ID: KY2021-395); Shijiazhuang People's Hospital (ID: 2022(009)); The Third Affiliated Hospital of Chongqing Medical University (ID: 2022(2)); and People's Hospital of Chongqing (ID: KYS2022-001-01).

Informed consent

Researchers must obtain signed informed consent to confirm that the participants fully understand the content of the study and participate voluntarily before the trial begins (online supplemental material 1).

Confidentiality

The contents of this clinical study are confidential. Any information about this study, including study design, methods, results, etc, is within the scope of confidentiality and cannot be discussed with persons outside the study.

Dissemination policy

The results will be published in peer-reviewed journals and disseminated in international academic meetings.

Study status

Recruitment of the study began on 5 January 2022 and the planned recruitment completion date is June 2023. The study completes in June 2026.

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Contributors XZhang, SF, LT, HY, XN, GT and LX participated in the study design. XG and AL cowrote the protocol draft. LJ and WS helped with sample size calculation and were the statistical consultants. FL, HZ, YZ, YS, PL, XZhu, KH, YingZ, YP and ML helped review the protocol draft. The authors from all centres agreed to publish the protocol on behalf of the 'trabeculectomy versus peripheral iridectomy plus goniotomy (TVG) study group'.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

- Sun X, Dai Y, Chen Y, *et al*. Primary angle closure glaucoma: What we know and what we don't know. *Prog Retin Eye Res* 2017;57:26–45.
- GBD 2019 Blindness and Vision Impairment Collaborators, Vision Loss Expert Group of the Global Burden of Disease Study. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to vision 2020: the right to sight: an analysis for the global burden of disease study. *Lancet Glob Health* 2021;9:e144–60.
- Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006;90:262–7.
- Lai J, Choy BNK, Shum JWH. Management of primary angle-closure glaucoma. *Asia Pac J Ophthalmol* 2016;5:59–62.
- Jampel HD, Musch DC, Gillespie BW, *et al*. Perioperative complications of trabeculectomy in the Collaborative initial glaucoma treatment study (CIGTS). *Am J Ophthalmol* 2005;140:16–22.
- Al-Haddad C, Abdulaal M, Al-Moujahed A, *et al*. Fornix-based versus limbal-based conjunctival trabeculectomy flaps for glaucoma. *Cochrane Database Syst Rev* 2015;11:CD009380.
- Sawchyn AK, Slabaugh MA. Innovations and adaptations in trabeculectomy. *Curr Opin Ophthalmol* 2016;27:158–63.
- Hansapinyo L, Choy BNK, Lai JSM, *et al*. Phacoemulsification versus phacotrabeculectomy in primary angle-closure glaucoma with cataract: long-term clinical outcomes. *J Glaucoma* 2020;29:15–23.
- Espandar L, Kassem J. Phacotrabeculectomy meta-analysis. *Ophthalmology* 2011;118:2096.
- Husain R, Do T, Lai J, *et al*. Efficacy of phacoemulsification alone vs phacoemulsification with Goniosynechialysis in patients with primary angle-closure disease: a randomized clinical trial. *JAMA Ophthalmol* 2019;137:1107–13.
- Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA* 2014;311:1901–11.

- 12 Hamanaka T, Kasahara K, Takemura T. Histopathology of the trabecular meshwork and Schlemm's canal in primary angle-closure glaucoma. *Invest Ophthalmol Vis Sci* 2011;52:8849–61.
- 13 Saheb H, Ahmed IK. Micro-invasive glaucoma surgery: current perspectives and future directions. *Curr Opin Ophthalmol* 2012;23:96–104.
- 14 Gillmann K, Mansouri K. Minimally invasive glaucoma surgery: where is the evidence? *Asia Pac J Ophthalmol* 2020;9:203–14.
- 15 Wu Z, Huang C, Zheng C, et al. The safety and efficacy of modified minimally invasive trabeculectomy for the treatment of primary chronic angle-closure glaucoma. *Eye Sci* 2015;30:160–6.
- 16 Chen DZ, Sng CCA, Sangtam T, et al. Phacoemulsification vs phacoemulsification with micro-bypass stent implantation in primary angle closure and primary angle closure glaucoma: a randomized single-masked clinical study. *Clin Exp Ophthalmol* 2020;48:450–61.
- 17 Pathak-Ray V, Choudhari N. Phaco-endocycloplasty versus phacotrabeculectomy in primary angle-closure glaucoma: a prospective randomized study. *Ophthalmol Glaucoma* 2020;3:434–42.
- 18 Minckler D, Mosaed S, Dustin L, et al. Trabectome (trabeculectomy-internal approach): additional experience and extended follow-up. *Trans Am Ophthalmol Soc* 2008;106:149–59.
- 19 Barry M, Alahmadi MW, Alahmadi M, et al. The safety of the Kahook dual blade in the surgical treatment of glaucoma. *Cureus* 2020;12:e6682.
- 20 Dorairaj S, Tam MD, Balasubramani GK. Twelve-month outcomes of excisional goniotomy using the Kahook Dual Blade® in eyes with angle-closure glaucoma. *Clin Ophthalmol* 2019;13:1779–85.
- 21 Dorairaj S, Tam MD. Kahook dual blade excisional goniotomy and Goniosynechialysis combined with phacoemulsification for angle-closure glaucoma: 6-month results. *J Glaucoma* 2019;28:643–6.
- 22 Tanito M, Sano I, Ikeda Y, et al. Short-Term results of microhook ab interno trabeculectomy, a novel minimally invasive glaucoma surgery in Japanese eyes: initial case series. *Acta Ophthalmol* 2017;95:e354–60.
- 23 Tanito M, Sugihara K, Tsutsui A, et al. Midterm results of Microhook ab Interno trabeculectomy in initial 560 eyes with glaucoma. *J Clin Med* 2021;10:814.
- 24 Dorairaj S, Tam MD, Balasubramani GK. Two-Year clinical outcomes of combined phacoemulsification, Goniosynechialysis, and excisional goniotomy for angle-closure glaucoma. *Asia Pac J Ophthalmol* 2020;10:183–7.
- 25 Gupta S, Sethi A, Yadav S, et al. Safety and efficacy of incisional goniotomy as an adjunct with phacoemulsification in primary angle-closure glaucoma. *J Cataract Refract Surg* 2021;47:504–11.
- 26 Shokoohi-Rad S, Karimi F, Zarei-Ghanavati S, et al. Phacoemulsification, visco-goniosynechialysis, and goniotomy in patients with primary angle-closure glaucoma: a comparative study. *Eur J Ophthalmol* 2021;31:88–95.
- 27 Gedde SJ, Chen PP, Muir KW, et al. Primary angle-closure disease preferred practice Pattern®. *Ophthalmology* 2021;128:P30–70.
- 28 Song Y, Song W, Zhang Y, et al. Efficacy and safety of phacotrabeculectomy versus phacogoniotomy in advanced primary angle-closure glaucoma: study protocol for a multicentre non-inferiority randomised controlled trial (PVP study). *BMJ Open* 2021;11:e056876.
- 29 European Glaucoma Society Terminology and Guidelines for Glaucoma, European Glaucoma Society Terminology and Guidelines for Glaucoma, 4th Edition - Chapter 2: Classification and terminology Supported by the EGS Foundation: Part 1: Foreword; Introduction; Glossary; Chapter 2 Classification and Terminology. *Br J Ophthalmol* 2017;101:73–127.
- 30 Tham CCY, Kwong YYY, Baig N, et al. Phacoemulsification versus trabeculectomy in medically uncontrolled chronic angle-closure glaucoma without cataract. *Ophthalmology* 2013;120:62–7.
- 31 Roberti G, Oddone F, Agnifili L, et al. Steroid-Induced glaucoma: epidemiology, pathophysiology, and clinical management. *Surv Ophthalmol* 2020;65:458–72.
- 32 Cantor LB, Mantravadi A, WuDunn D, et al. Morphologic classification of filtering blebs after glaucoma filtration surgery: the Indiana bleb appearance grading scale. *J Glaucoma* 2003;12:266–71.
- 33 Negrel AD, Maul E, Pokharel GP, et al. Refractive error study in children: sampling and measurement methods for a multi-country survey. *Am J Ophthalmol* 2000;129:421–6.
- 34 Gedde SJ, Feuer WJ, Lim KS, et al. Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 3 Years of Follow-up. *Ophthalmology* 2020;127:333–45.