

SYSTEMATIC REVIEW

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Phacoemulsification combined with trabecular meshwork-Schlemm canal-based minimally invasive glaucoma surgery in primary angle-closure glaucoma: a systematic review and meta-analysis

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Abstract

Background To summarize the efficacy and safety of the phacoemulsification with intraocular lens implantation (PEI) ± goniosynechialysis (GSL) + trabecular meshwork-Schlemm canal (TM-SC)-based minimally invasive glaucoma surgery (MIGS) in primary angle-closure glaucoma (PACG).

Methods A comprehensive literature search was conducted across seven electronic databases: PubMed, ScienceDirect, The Cochrane Library, Scopus, Embase, Ovid MEDLINE, and Web of Science. Studies focused on TM-SC-based MIGS with PEI for PACG were included in this review. The efficacy was assessed by the reduction in intraocular pressure (IOP) values and the decrease in the number of anti-glaucoma medications (AGMs), while safety was evaluated by incidence of complications.

Results Out of 5158 studies initially identified, this meta-analysis included 12 articles with a total of 633 eyes with PACG. At 12 months postoperatively, PEI ± GSL + TM-SC-based MIGS yielded an IOP decrease of 10.25 mmHg (95% CI: 7.06 to 13.43), PEI ± GSL + goniotomy yielded an IOP decrease of 13.10 mmHg (95% CI: 7.59 to 18.62), PEI ± GSL + gonioscopy-assisted transluminal trabeculotomy yielded an IOP decrease of 11.54 mmHg (95% CI: 7.18 to 15.90), and PEI ± GSL + trabecular micro-bypass stent yielded an IOP decrease of 3.94 mmHg (95% CI: 2.58 to 5.30). The most common complications were hyphema (16.3%) and IOP spike (7.4%). Specifically, the iStent group had the lowest incidence of each complication.

Conclusions PEI ± GSL + TM-SC-based MIGS is effective in reducing IOP and medication burden while maintaining a favorable safety profile in PACG. More randomized controlled trials are required to support this therapeutic recommendation.

Registration This meta-analysis was registered on PROSPERO (registration number: CRD42024583864).

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Keywords Minimally invasive glaucoma surgery, Angle-closure glaucoma, Meta-analysis

Background

Glaucoma is the leading cause of permanent blindness and a significant public health issue worldwide [1, 2]. Primary angle-closure glaucoma (PACG) is a major subtype of glaucoma that is particularly prevalent in East Asian countries and is estimated to affect over 32 million people by 2024, with more than 5 million affected by blindness [3–5].

In response to the limitations of traditional glaucoma filtering surgery, there has been a shift in treatment strategies. The EAGLE study showed that standalone phacemulsification with intraocular lens implantation (PEI) effectively reduces intraocular pressure (IOP) in PACG patients, particularly in early to moderate stages [6]. A recent Bayesian analysis also revealed that standalone PEI is able to reduce IOP by 3 mmHg or greater in medically controlled PACG, but exhibited a 18% probability of unchanged or even increased postoperative IOP in medically uncontrolled PACG [7]. Notably, this insufficiency in moderate-to-advanced PACG management has been further characterized in a investigation, highlighting the necessity for additional interventions [8].

This challenge has driven the exponential growth of combined PEI with minimally invasive glaucoma surgery (MIGS) as a promising alternative for PACG [9–39]. As a subtype of MIGS, trabecular meshwork-Schlemm canal (TM-SC)-based MIGS for PACG reduce intraocular pressure (IOP) by enhancing aqueous humor outflow through the patient's natural drainage system [15–35]. It is performed with smaller incisions than traditional glaucoma filtering surgeries, resulting in a faster recovery, safer decrease in IOP as well as fewer postoperative visits and complications [18–31]. As the application of PEI ± goniosynechialysis (GSL) + TM-SC-based MIGS in PACG becomes broadly applied, a meta-analysis to analyze its efficacy and safety will provide valuable information for managing patients with PACG.

Methods

Study selection

This meta-analysis adhered to the 2020 Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Table S1) and was registered in the PROSPERO database (registration number: CRD42024583864) on September 7, 2024. The title, abstract screening and article review were independently conducted by two authors (Z. F. and Y. S.) blinded to each other's decisions, with disagreements adjudicated by the senior author (X. Z.).

Literature search

The literature search encompassed seven electronic databases: (1) PubMed; (2) ScienceDirect; (3) The Cochrane Library; (4) Scopus; (5) Embase; (6) Ovid MEDLINE; and (7) Web of science. The most recent search was conducted on August 7, 2024. Various terms were employed, including goniotomy (GT), Ab interno trabeculotomy, gonioscopy assisted transluminal trabeculotomy (GATT), trabectome, Ab interno canaloplasty (ABiC), trabecular micro-bypass stent (iStent), iStent inject, Hydrus, PEI, goniosynechialysis (GSL), phacogoniotomy, Kahook dual blade, Tanito microhook, Micro Vitreoretinal blade, needle, Bent Ab interno needle goniotomy (BANG), primary angle closure glaucoma (PACG), angle closure glaucoma, and chronic angle closure glaucoma. The detailed search strategy is outlined in Table S2. Additionally, references from retrieved articles were screened for further eligible studies and only English literature was included, unpublished studies were not sought.

Inclusion and exclusion criteria

The included articles met specific criteria: (1) Intervention: The interventions were characterized as PEI with GSL by viscoelastic material or a blunt device plus TM-SC-based MIGS, for example: GT / Ab interno trabeculotomy, GATT, and iStent, etc.; (2) Outcomes: The efficacy was assessed by the reduction from the baseline in IOP values and the number of anti-glaucoma medications (AGMs), while safety was evaluated by incidence of complications.

The excluded articles met specific criteria: (1) Reviews lacking original data, editorials, case reports, meta-analyses, letters, animal experiments, guidelines, conference abstracts, and opinion articles; (2) Studies presenting combined results for various types of glaucoma without specific data of PACG, angle closure glaucoma, or chronic angle closure glaucoma; (3) Studies with a follow-up period of less than one year; (4) Studies with an overlapping study population; (5) Articles not in English.

Data collection

Data extraction was performed by two investigators (Zige Fang and Yunhe Song), utilizing an Excel spreadsheet. The extracted data included the first author's name, publication year, study design, number of participants and enrolled eyes, participant characteristics [country, age, the ratio of gender: male/female, average mean deviation (MD) of the visual field at baseline], follow-up duration, definitions of different professional terms (e.g., IOP spike, hyphema, surgical failure, and so on), surgical technique, surgical instruments, incision size, method

for biometry measurement, and mean values with standard deviations of IOP and the number of AGM. Pre-operative and postoperative gonioscopic findings are detailed in Table S3. Synechiolysis methods (e.g., viscosynechiolysis, spatula-based synechiolysis) and the angle size of synechiolysis were systematically extracted and summarized in Table S4. Surgical instruments and angle size for PEI±GSL+GT group are listed in Table S5. Types and implantation strategies of iStent are listed in Table S6. Primary outcomes recorded were IOP values and the number of AGMs at baseline and fixed postoperative time points (1, 6, and 12 months). Additionally, all complications (intra- and post-operative) in the included studies were noted. Disputes were resolved by a third investigator (X. Z.).

Quality assessment

Two researchers independently evaluated the quality of the included studies. Randomized controlled trials (RCTs) were assessed using the improved Jadad scale, which includes criteria related to the generation of random sequences, randomization concealment, masking, and accountability of all patients. Studies are considered of high quality if they achieve a score of 4 points or higher [40]. Two reviewers conducted the risk of bias assessment for non-RCTs using the Newcastle-Ottawa Scale (NOS). This scale is structured around three assessment criteria: selection, comparability, and outcome. Studies scoring between 7 and 9 were categorized as “Good”, those scoring between 4 and 6 were deemed “Fair”, and studies with scores below 3 were labeled as “Poor” [41]. Studies with a quality score lower than 4 on the improved Jadad scale or 7 on the NOS were excluded.

Statistical analysis

The meta-analysis was performed using Review Manager (version 5.4 by Cochrane Collaboration) and STATA (version 18.0, Stata Corp). Mean differences with 95% confidence intervals (CI) were calculated for the outcomes of IOP change and the number of AGMs. In cases where complications were not explicitly reported, they were considered as 0. Incidence of the complication were compared between any two groups across all groups using the Chi-square tests or Fisher’s exact tests. Subgroup analysis of TM-SC-based MIGS was conducted to assess differences based on surgical technique and baseline MD. Heterogeneity was assessed using the I^2 statistic and Q test. $I^2 > 50\%$ or P-values of < 0.05 indicated significant heterogeneity, leading to the use of random-effects models. Otherwise, fixed-effects models were employed. Furthermore, leave-one-out sensitivity analyses were conducted to explore sources of heterogeneity and assess result robustness.

Results

Study characteristics

Initially, 5158 potentially eligible studies were identified, and articles not meeting the specified eligibility criteria were excluded. Following the screening process, 12 articles were selected, involving a combined total of 633 eyes for the final analysis. Among these studies, outcomes of PEI±GSL+GT were reported in 5 studies, PEI±GSL+GATT in 4 studies, and PEI±GSL+iStent in 3 studies (Fig. 1) [15–17, 19, 21, 25, 27, 29, 32–35]. The baseline characteristics of the included studies are outlined in Table 1. The quality assessment of the 12 included studies was deemed high, with results categorized by RCT and non-RCT in Tables S7 and Tables S8, respectively.

Reduction of IOP and AGM

The mean reductions in IOP and number of AGMs between baseline and 12 months postoperatively were shown in Fig. 2. PEI±GSL+TM-SC-based MIGS effectively decreased IOP (10.25 mmHg, 95% CI: 7.06 to 13.43) and reduced the number of AGMs (1.89, 95%CI: 1.51 to 2.27). Subgroup analysis was performed to ensure consistency of outcomes across different subgroups. Pooled outcomes were estimated within each category of the following classification variables: surgical technique and baseline MD (Table S9). Subgroup analysis results based on baseline MD indicated that PEI±GSL+TM-SC-based MIGS is effective in advanced glaucoma, with a reduction in IOP of 13.97 mmHg (95% CI: 8.13 to 19.80) and a decrease of 2.20 AGMs (95% CI: 1.55 to 2.86). Outcomes of different surgical techniques were also analyzed respectively. PEI±GSL+GT group exhibited the IOP reduction of 13.10 mmHg (95% CI: 7.59 to 18.62) and a decrease of 2.06 AGMs (95% CI: 1.90 to 2.22). PEI±GSL+GATT group exhibited the IOP reduction of 11.54 mmHg (95% CI: 7.18 to 15.90) and a decrease of 2.38 AGMs (95% CI: 1.51 to 3.25). PEI±GSL+iStent group exhibited the IOP reduction of 3.94 mmHg (95% CI: 2.58 to 5.30) and a decrease of 1.21 AGMs (95% CI: 0.99 to 1.42).

Safety

The most common complications (hyphema and IOP spike) are individually detailed for each included study in Table 2. Among the 633 eyes, hyphema occurred in 103 eyes (16.3%) and IOP spike in 47 eyes (7.4%). Chi-square tests were conducted for the various surgical techniques in terms of complications (Table S10). Concerning hyphema, the most prevalent complication, PEI±GSL+GATT group (33.2%) has the highest incidence (all P s < 0.01), while there was no significant difference between PEI±GSL+GT group (10.1%) and PEI±GSL+iStent group (6.1%) ($P = .242$). The incidence

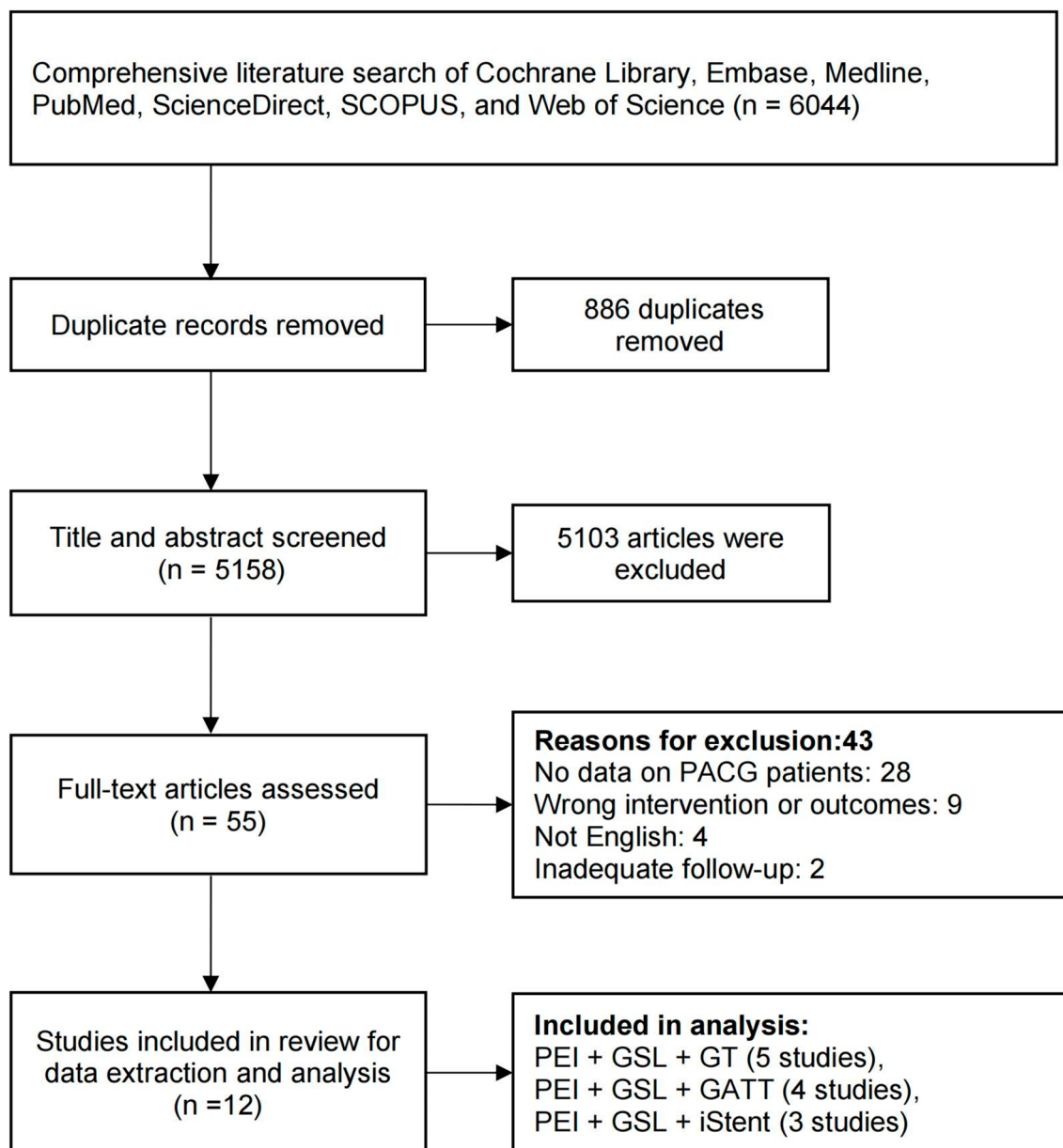


Fig. 1 Flow chart of study selection. GSL: goniosynechiysis; GT: goniotomy; GATT: gonioscopy-assisted transluminal trabeculotomy; PACG: primary angle closure glaucoma; PEI: phacoemulsification with intraocular lens implantation

of IOP spike was relatively low across the three groups, with rates of 6.8%, 2.2%, and 11.9%, respectively. The PEI ± GSL + GATT group exhibited a significantly higher incidence of IOP spike compared to both the PEI ± GSL + GT group ($P = 0.031$) and the PEI ± GSL + iStent group ($P < 0.01$). Incidence of all complications were summarized in Table S11.

IOP and AGMs within 1 year postoperative follow-up

Figure 3 shows the mean IOP values and the number of AGMs across various visit periods (baseline, 1 month, 6 months, and 12 months) revealing the efficacy of

PEI ± GSL + TM-SC-based MIGS or its different subtypes in treating PACG. This approach at baseline, postoperative month (POM) 1, POM6 and POM12 yielded IOPs of 25.85 mmHg (95% CI: 22.25 to 29.46), 13.74 mmHg (95% CI: 13.10 to 14.38), 13.71 mmHg (95% CI: 13.28 to 14.13), and 14.10 mmHg (95% CI: 13.49 to 14.71), respectively. The number of AGMs at these time points were 2.50 (95% CI: 2.06 to 2.94), 0.65 (95% CI: 0.11 to 1.18), 0.62 (95% CI: 0.18 to 1.06), and 0.60 (95% CI: 0.23 to 0.98), respectively. Simultaneously, IOP and the number of AGMs were also recorded for the three groups at the same time points based on different surgical techniques: PEI ± GSL + GT

Table 1 Characteristics of enrolled patients

Years, Author	Country	Study design	No. of eyes at Baseline	Age, mean \pm SD (years)	Follow-up (months)	Baseline IOP, Mean \pm SD (mm Hg)	No. of Baseline AGM, Mean \pm SD
PEI \pm GSL + GT							
2024, Song	China	RCT	65	65.90 \pm 9.30	12	40.30 \pm 10.60*	2.00 \pm 1.20
2023, Tan	China	Non-RCT	72	67.10 \pm 8.07	12	23.40 \pm 8.10	2.60 \pm 1.30
2022, Song	China	Non-RCT	83	64.10 \pm 9.30	12	27.40 \pm 7.30	NA
2021, Gupta	India	Non-RCT	46	58.06 \pm 28.26	12	21.44 \pm 6.60	3.28 \pm 1.01
2019, Dorairaj	Vietnam, USA	Non-RCT	42	66.50 \pm 15.55	12	25.50 \pm 4.73	2.33 \pm 0.65
PEI \pm GSL + GATT							
2023, ElSayed	Egypt	RCT	36	60.69 \pm 9.58	12	28.92 \pm 4.74	NA
2022, Fontana	Italy	Non-RCT	15	70.00 \pm 10.00	12	30.27 \pm 4.20	3.50 \pm 0.50
2021, Sharkawi	Switzerland	Non-RCT	103	69.90 \pm 11.75	24	21.40 \pm 7.40	2.50 \pm 1.10
2021, Chira-Adisai	Japan	Non-RCT	39	73.60 \pm 9.00	12	21.80 \pm 5.40	3.50 \pm 1.40
PEI \pm GSL + iStent							
2021, Salimi	Canada	Non-RCT	79	69.20 \pm 8.00	12	17.60 \pm 3.20	2.20 \pm 1.20
2020, Chen	Singapore	RCT	16	65.00 \pm 4.69	12	18.60 \pm 4.70	1.50 \pm 1.48
2019, Hernstadt	Australia	Non-RCT	37	68.70 \pm 6.39	12	17.50 \pm 3.82	1.49 \pm 0.77

Abbreviations: AGM: anti-glaucoma medication; GSL: goniosynechiysis; GT: goniotomy; GATT: gonioscopy-assisted transluminal trabeculotomy; IOP: intraocular pressure; iStent: trabecular micro-bypass stent; NA: not available; PEI: phacoemulsification with intraocular lens implantation; RCT: randomized controlled trial; SD: standard deviation; USA: United States of America

*Showed as the highest preoperative IOP

group, PEI \pm GSL + GATT group, and PEI \pm GSL + iStent group, yielding similar outcomes across these subgroups.

Sensitivity analysis

Given the significant heterogeneity found in the analyses of IOP and AGM, the outcomes at 12 months postoperatively served as indicators for leave-one-out sensitivity analysis (Figure S1). The evaluation considered the impact of each study on the reliability and consistency of the overall outcome. Collectively, the above findings suggest that this study may be considered reliable and stable.

Discussion

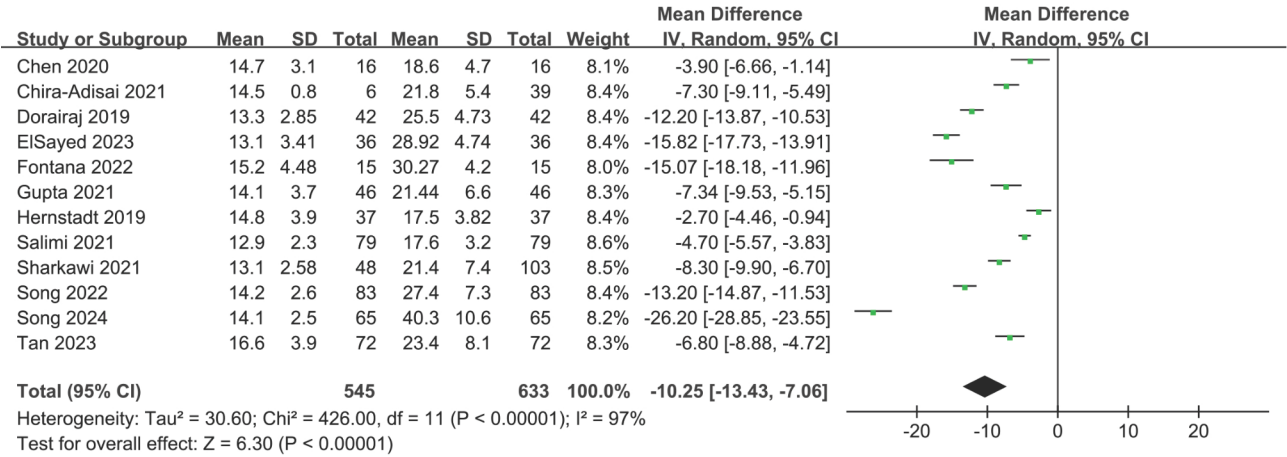
The role of PEI and MIGS in treating PACG has gained more and more attention [9–39]. This meta-analysis is the first to focus on PEI \pm GSL + TM-SC-based MIGS for treatment of PACG. We found the approach of PEI \pm GSL + TM-SC-based MIGS achieving satisfactory IOP control and a reduction in the number of AGMs within one year postoperative follow-up.

Our meta-analysis demonstrated that IOP and AGM were effectively controlled by PEI \pm GSL + TM-SC-based MIGS at 12 months postoperatively and yielded similar results in different surgical techniques. Subgroup analysis outcomes indicated that despite PEI \pm GSL + GT group (13.10 mmHg, 95% CI: 7.59 to 18.62) seems to achieve the highest IOP reduction, there was no statistically significant difference between PEI \pm GSL + GT group and PEI \pm GSL + GATT group (11.54 mmHg, 95% CI: 7.18 to 15.90). Previous studies compared the effects of different GT sizes with or without PEI on the efficacy

of primary open-angle glaucoma and found that 120° GT has a similar effect on controlling IOP and reducing AGMs as 240° or 360° GT, which could explain this result [42, 43]. Although the IOP-lowering effect of the PEI \pm GSL + iStent group (3.94 mmHg, 95% CI: 2.58 to 5.30) was significantly lower than the other two groups, all three subgroups exhibited similar 12-month postoperative IOP values. That may be due to clinical situation where glaucoma surgeons more frequently select iStent for eyes with lower baseline IOP value. However, these comparisons are not based on individual participant data, further research comparing different subtypes of TM-SC-based MIGS for patients with PACG, particularly with larger RCTs and longer-term follow-up, is warranted to clarify this variation. Washout is usually not performed for patients with high IOP due to practical and ethical reasons, which may affect the accuracy of the IOP-lowering effects of MIGS. However, since the average IOP and the number of AGMs are reduced after surgery, the collective results demonstrate that PEI \pm GSL + TM-SC-based MIGS provides satisfactory IOP control.

The most common postoperative complications observed were hyphema (16.3%) and IOP spikes (7.4%). This observation aligns with findings from prior research on PEI \pm GSL + TM-SC-based MIGS for PACG [21, 27, 29]. Specifically, the incidence of hyphema in the PEI \pm GSL + GATT group is notably higher than in the other groups, possibly attributable to the enhanced exposure of collector channels and episcleral venous connections in GATT [32–35]. Furthermore, the PEI \pm GSL + GATT group demonstrates the

A



B

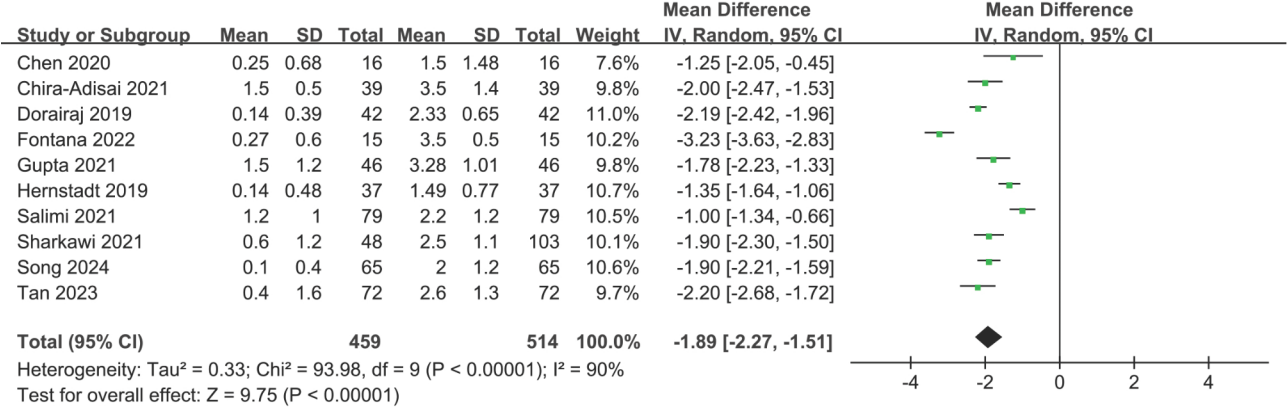


Fig. 2 Mean differences in (A) IOP and (B) number of AGMs at 12 months following PEI ± GSL + TM-SC based MIGS compared to preoperative baseline
AGM: anti-glaucoma medication; IOP: intraocular pressure

Table 2 The main complications

Years, Author	Hyphema	IOP spike
Total	103 (16.3%)	47 (7.4%)
PEI ± GSL + GT	31 (10.1%)	21 (6.8%)
2024, Song	4 (6.2%)	4 (6.2%)
2023, Tan	5 (6.9%)	5 (6.9%)
2022, Song	9 (10.8%)	9 (10.8%)
2021, Gupta	13 (28%)	3 (6.5%)
2019, Dorairaj	0	0
PEI ± GSL + GATT	64 (33.2%)	25 (11.9%)
2023, ElSayed	25 (69%)	2 (5.6%)
2022, Fontana	0	0
2021, Sharkawi	4 (3.9%)	22 (21.4%)
2021, Chira-Adisai	35 (100%)	1 (2.6%)
PEI ± GSL + iStent	8 (6.1%)	3 (2.2%)
2021, Salimi	0	3 (4%)
2020, Chen	1 (6.3%)	0
2019, Hernstadt	7 (18.9%)	0

Abbreviations: GATT: gonioscopy-assisted transluminal trabeculotomy; GSL: goniosynechiysis; GT: goniotomy; IOP: intraocular pressure; iStent: trabecular micro-bypass stent; PEI: phacoemulsification with intraocular lens implantation

highest incidence of IOP spikes (11.9%), followed by the PEI ± GSL + GT group (6.8%) and the PEI ± GSL + iStent group (2.2%). These results may be due to steroid induced IOP spike. With different degrees of the opening of trabecular meshwork and the inner wall of Schlemm’s canal after TM-SC-based MIGS surgery, the contact area between glucocorticoids and target cells increases to different extent, leading to different outflow resistances in steroid-sensitive individuals [44–46]. Among the various surgical subgroups, the PEI ± GSL + iStent group exhibited the lowest incidence of all AEs, indicating its superior safety profile. iStent procedure only involves implanting stent(s) into the trabecular meshwork rather than creating a large incision, potentially resulting in less inflammation and complications [47, 48].

This meta-analysis has several limitations. First, the longest follow-up of the studies we included was 2 years, leading to the combined analyses providing results within one year follow-up. Second, our study’s sample size was limited, encompassing only 633 eyes. Furthermore, the predominant inclusion of observational studies may lead

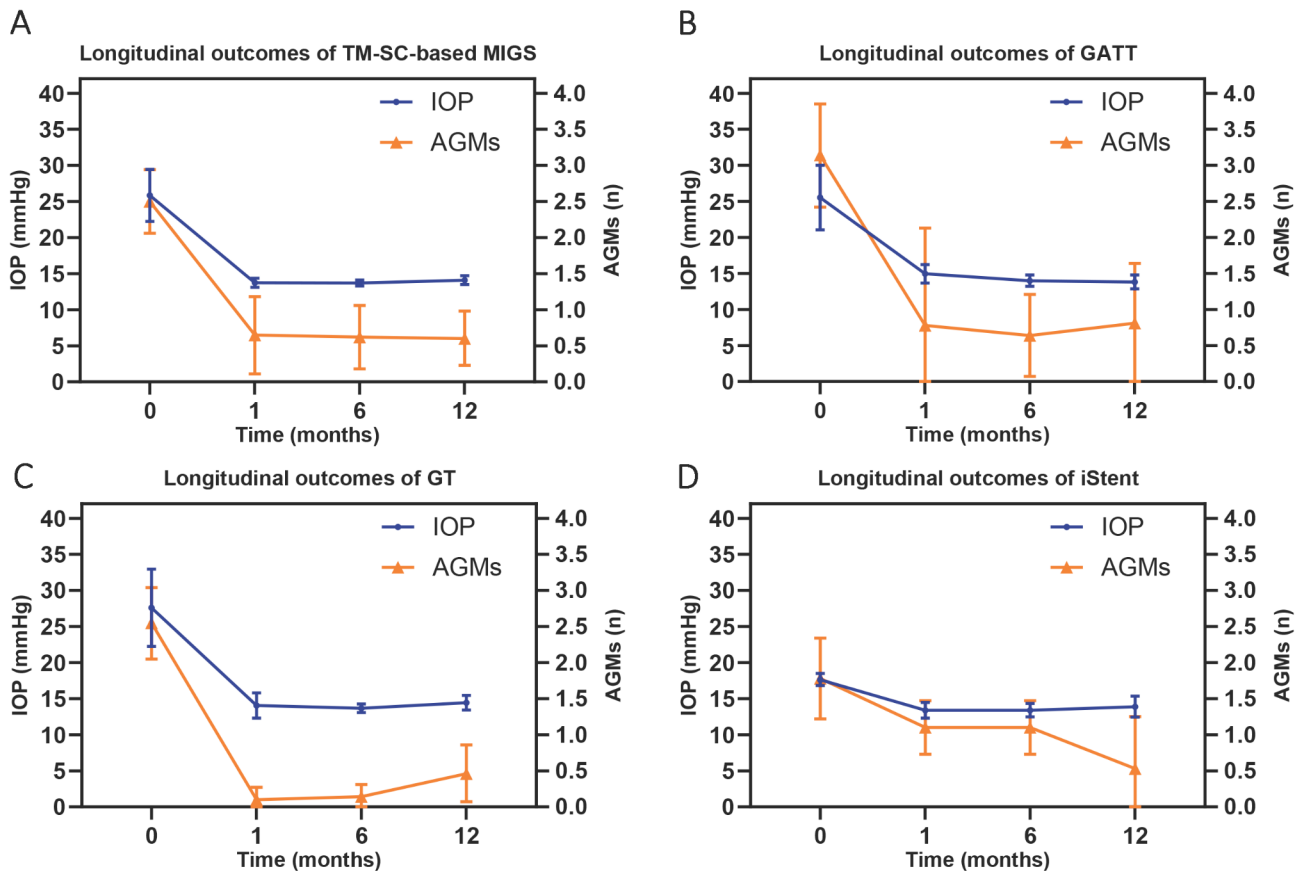


Fig. 3 IOP and AGMs within 1 year postoperative follow-up of PEI combined with (A) SC-TM based MIGS, (B) GT, (C) GATT, and (D) iStent. Each group received PEI ± GSL + MIGS intervention. Error bars represent 95% confidence intervals. AGM: anti-glaucoma medication; GSL: goniosynechiysis; GT: goniotomy; GATT: gonioscopy-assisted transluminal trabeculotomy; IOP: intraocular pressure; iStent: trabecular micro-bypass stent; SC-TM based MIGS: Schlemm's canal-trabecular meshwork based minimally invasive glaucoma surgery

to bias despite careful data analysis planning. Future high-quality RCTs with extended follow-up periods and larger cohorts will test the conclusions.

Conclusion

In conclusion, PEI ± GSL + TM-SC-based MIGS decreased both IOP and the number of AGMs while providing a favorable safety profile in treating patients with PACG. The subgroup analysis revealed no significant difference between GATT and GT in terms of IOP-lowering effect, and iStent appears to offer superior safety. Longer follow-up and high-quality RCTs are needed to support this conclusion.

Abbreviations

ABiC	Ab interno canaloplasty
AGMs	Anti-glaucoma medications
BANG	Bent Ab interno needle goniotomy
CI	Confidence intervals
GATT	Gonioscopy-assisted transluminal trabeculotomy
GSL	Goniosynechiyalysis
GT	Goniotomy
IOP	Intraocular pressure
iStent	Trabecular micro-bypass stent
MIGS	Minimally invasive glaucoma surgery

NOS	Newcastle-ottawa scale
PACG	Primary angle-closure glaucoma
PEI	Phacoemulsification with intraocular lens implantation
POM	Postoperative month
PRISMA	Preferred reporting items for systematic review and meta-analysis
MD	Mean deviation
TM-SC	Trabecular meshwork-Schlemm canal

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12886-025-04005-y>.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

Not applicable.

Author contributions

Study design: X. Z.; Data collection: Z. F., and Y. S.; Data analysis and interpretation: Z. F., Y. S., and L. J.; Original draft: Z. F.; Review and editing: Y. H., and X. Z. All authors revised the work, approved the submitted version, and agreed to be personally accountable for their contributions and to ensure that questions related to the accuracy or integrity of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Data availability

Data for this meta-analysis were sourced from publicly available databases and published articles. The following databases were used: PubMed, ScienceDirect, The Cochrane Library, Scopus, Embase, Ovid MEDLINE, and Web of Science. The data and materials that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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