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SYSTEMATIC REVIEW

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Efficacy analysis of microinvasive glaucoma surgery alone or in combination with phacoemulsification in patients with normal tension glaucoma: a systematic review and meta-analysis

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Abstract

Objective To assess the effectiveness of minimally invasive glaucoma surgery (MIGS) as monotherapy, or in combination with phacoemulsification, in the management of normal tension glaucoma (NTG).

Methods A systematic literature review and meta-analysis were conducted. The literature search was performed using four electronic databases, including Pubmed, Embase, Web of science, and Cochrane Central Register of Controlled Trials, to identify studies evaluating the efficacy of MIGS on patients with NTG, published from October 1, 2019 to October 1, 2024. The articles meeting our inclusion criteria were independently screened and assessed by three reviewers. Effect estimates associated with NTG were pooled and evaluated via meta-analysis. The articles retrieved from the databases were systematically analyzed using Citespace 6.2.R3.

Results A total of 11 English-language studies involving 413 eyes from 327 NTG patients were included. Follow-up ranged from 6 to 60 months. MIGS alone reduced IOP by 2.62 mmHg (95% CI: -3.70 to -1.54; $Z=4.77$, $P<0.00001$), while MIGS with cataract surgery reduced IOP by 2.09 mmHg (95% CI: -2.83 to -1.35; $Z=5.53$, $P<0.00001$). The number of IOP-lowering medications decreased by 1.47 with MIGS alone (95% CI: -2.16 to -0.77; $Z=4.07$, $P<0.0001$) and by 1.13 with combined surgery (95% CI: -1.75 to -0.52; $Z=3.63$, $P=0.0003$). No significant differences were observed between the two surgical approaches.

Conclusion The meta-analysis demonstrated that either MIGS alone or combined with phacoemulsification effectively reduced the IOP and the requirement for IOP-lowering medications in NTG patients. MIGS alone or combined with phacoemulsification reduced the IOP most at 12 months, and the lowest IOP-lowering medications at 24 months in postoperative patients with NTG.

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Key messages

Why carry out this study? Normal-tension glaucoma (NTG), a subtype of primary open-angle glaucoma (POAG), is characterized by optic nerve damage despite intraocular pressure (IOP) within the statistically normal range. Microinvasive glaucoma surgery (MIGS), with its minimal invasiveness, safety profile, and compatibility with phacoemulsification, presents a promising alternative for NTG management. However, prior evidence on the efficacy and safety of MIGS in NTG patients was limited and fragmented. This study aimed to systematically evaluate the long-term outcomes of MIGS alone or combined with phacoemulsification in reducing IOP and medication burden in NTG patients, addressing critical knowledge gaps in this understudied population.

What did the study ask? / What was the hypothesis of the study? The hypothesis of this study is that Both MIGS alone and MIGS combined with phacoemulsification would achieve significant reductions in IOP and medication use in NTG patients. Combined surgery was hypothesized to offer additional benefits (e.g., addressing concurrent cataracts) without compromising safety.

What were the study outcomes/conclusions? The meta-analysis demonstrated that MIGS alone or combined with phacoemulsification effectively reduced the IOP and the requirement for IOP-lowering medications in postoperative patients with NTG. MIGS with phacoemulsification failed to improve IOP and IOP-lowering medications more than MIGS alone. MIGS alone or combined with phacoemulsification reduced the IOP most at 12 months, and the lowest IOP-lowering medications at 24 months in postoperative patients with NTG. Both MIGS alone and combined with phacoemulsification effectively reduced IOP and medication requirements in NTG patients, with comparable efficacy. Combined surgery is advantageous for NTG patients with concurrent cataracts, preventing postoperative cataract progression and reducing reoperation risks.

What has been learned from the study? This can be any outcome even if it contradicts the initial study hypothesis. If the data was negative, neutral or purely confirmatory, how might this still affect research and/or treatment in future? This study tells us that phacoemulsification alone or in combination can effectively reduce the IOP and the need for ocular hypotensive drugs in patients after NTG surgery, and reduce the occurrence of complications. This gives us more confidence to use MIGS surgery on NTG patients to achieve the purpose of anti-glaucoma treatment. In addition, the development and upgrading of existing glaucoma filtering devices will benefit more patients.

Keywords Microinvasive glaucoma surgery, Normal tension glaucoma, Meta-analysis

Introduction

Glaucoma is the world's leading cause of irreversible blindness, and the number of glaucoma patients is expected to exceed 100 million by 2040 [1]. Intraocular pressure (IOP) is the primary modifiable risk factor used to assess the development and progression of most types of glaucoma. Glaucoma surgery is effective in reducing IOP, which prevents worsening optic nerve damage and visual field defects [2, 3].

Microinvasive glaucoma surgery (MIGS) is a new and innovative surgical approach for the management of mild to moderate glaucoma that bridges the therapeutic gap between glaucoma medications and more invasive filtration surgeries [4]. There are many types of MIGS, including various microsurgical procedures, which can be categorized according to their biomechanical background, including enhancement of blood flow through the trabecular meshwork, shunting of atrial aqueous fluid into the subconjunctival space, and reduction of atrial fluid secretion [5, 6]. The theoretical advantage of this approach is that it can prevent serious impairment of the ocular anatomy, which is particularly important in cases that ultimately require more invasive procedures. MIGS has the potential to treat NTG due to its high safety profile, short operative time, and low incidence of surgical complications compared to filtration or drainage devices, as well as a short postoperative recovery time [7]. Even so, more research and analysis are needed to determine whether MIGS surgery can reduce intraocular pressure and improve medication strategies as effectively as more traditional therapeutic approaches to NTG.

Cataract surgery has improved over the past decade with the development of new micro-incision techniques [8]. Patients with glaucoma are often accompanied by cataracts, which eventually require cataract extraction [9]. MIGS is usually used in conjunction with phacoemulsification [10]. This is revealed in trials combining MIGS surgery with cataract extraction and comparing it with cataract extraction alone. The combined procedure has a unique risk-benefit profile compared with glaucoma surgery alone. For patients with glaucoma and cataracts, combined surgery improves vision and reduces IOP more than cataract extraction alone [11]. Functional intraocular lens(IOL) meet the postoperative refractive needs of cataract patients, and combined surgery can help deepen the peripheral anterior chamber and reduce the incidence of postoperative peripheral anterior synechiae (PAS) [12]. MIGS combined with phacoemulsification can avoid the aggravation of cataract development after MIGS alone. Therefore, this study selected specific post-operative time points to compare long-term IOP measurements at 6 months, 12 months, and 24 months, to demonstrate the effects of MIGS alone and combined phacoemulsification surgery on IOP and on the requirements for IOP-lowering drugs, as a therapeutic strategy for patients with normal tension glaucoma (NTG).

Primary open-angle glaucoma (POAG) is the most frequent form of glaucoma, which typically exhibits the insidious onset and minimal symptoms until advanced stages, resulting in an estimated 50% of individuals unknowing they have been diagnosed with glaucoma and not getting proper treatment [13, 14]. Normal-tension glaucoma (NTG) is a specific type of POAG. NTG is characterized by the presence of optic nerve damage but intraocular pressure (IOP) values within the normal range. Patients with NTG are often underdiagnosed or inappropriately treated due to the subtle clinical presentation and reliance on IOP levels that fall within the statistically normal range, which may delay diagnosis and management. In patients with NTG who have normal IOP values, lowering the IOP is the basis of treatment [15]. IOP can be lowered with medicines or surgery. Treatments range from only topical IOP-lowering medications to more aggressive filtering surgery. This recently introduced surgical approach is changing treatment paradigms, via the feasibility and potential cost-effectiveness of minimally-invasive interventions early in NTG, especially in patients who are willing to undergo surgery and have cataracts [16]. Although there is currently a lack of connection between MIGS and NTG patients, considering that lowering IOP is the main therapeutic strategy in all glaucoma patients, there is promise that NTG patients could also benefit from MIGS.

The focus of this systematic review and meta-analysis is to assess the effectiveness of minimally invasive glaucoma surgery (MIGS) alone or in combination with phacoemulsification as monotherapy, in the management of NTG.

Method

We searched according to the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines and recommendations after registering this review with the International Prospective Register of Systematic Reviews (CRD42023387519). Institutional Review Board/Ethics Committee approval was not required for this study. Informed consent was not required due to the retrospective nature of this study. All studies adhered to the tenets of the Declaration of Helsinki. All included studies reported obtaining ethical approval or adhered to institutional ethical standards.

For research hotspots and trends, all the literature were searched from the Web of Science Core Collection (WoSCC) database in SSCI and SCI-EXPANDED.

Search strategy

We conducted systematic electronic database searches for RCTs, prospective nonrandomized studies, and observational studies in Pubmed, Embase, Web of science, and the Cochrane Central Register of Controlled Trials. A complete search strategy containing keywords and index terms was used in these databases (Appendix 1). We used the Cochrane Database of Systematic Reviews and the JBI Database of Systematic Reviews and Implementation Reports and found no current or ongoing systematic reviews on this topic. The reference lists of all studies selected for critical appraisal were screened for additional studies. The database searches were last conducted on October 1, 2024.

All literature was validated by searching the Web of Science Core Collection (WoSCC) database at SSCI and SCI-EXPANDED. The search strategy was 'Glaucoma Surgery' and 'normal tension glaucoma'. The year of publication was between 2019 and 2024, the language category was English, and the article type was article or review was included in this study.

Study selection

At the end of the database search, all screened citations were organized and uploaded into reference management software (Endnote 20, Clarivate Analytics) with the aim of removing duplicate citations. Two authors independently screened the search results by title, abstract, and keywords and then by full text against the eligibility criteria, as required by the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Disagreements between authors regarding whether a study met the inclusion criteria were resolved through discussion.

Inclusion criteria

The types of studies included were single-center and multicenter retrospective study, single-center and multicenter prospective study, single-center and multicenter case series. Only studies published in English were included. As surgical techniques have been continuously advanced and improved in recent years, studies published between January 1, 2019 to October 1, 2024 were included to maintain the relevance of the studies.

The studies considered in this review included only people with normal-tension glaucoma (NTG). There were no restrictions based on geographical location, environment, or demographic factors. We included most MIGS, such as iStent, XEN, endoscopic cyclophotocoagulation, Kahook Dual Blade, or Trabectome. Glaucoma interventions such as laser treatment and peripheral iridotomy and participants with ocular diseases (e.g. corneal and fundus diseases) were excluded.

Comparators

We compared glaucoma surgery alone or in combination with cataract surgery (phacoemulsification) with the patients' preoperative and postoperative IOP and the IOP-lowering medications. Unfortunately, most studies have used MIGS surgery combined with phacoemulsification as the surgical method, thus we cannot directly compare the advantages of MIGS surgery alone and MIGS combined with phacoemulsification.

Outcomes

The primary outcomes reviewed were changes in IOP and IOP-lowering medications at 6, 12, and 24 months compared with baseline.

Quality assessment

We assessed the methodological quality of the studies according to the Newcastle-Ottawa Scale (NOS) guidelines. The study quality rating mainly consisted of three parts. The first part was the representativeness of the selection of exposed and non-exposed cohorts. The second part was comparability, which was assessed based on the study design and analysis, and whether any confounding variables were adjusted. The third part was the outcome, which was determined by independent blinded assessment, recorded contact, or self-report based on the follow-up period and cohort retention.

Statistical analysis

The data analysis was performed using RevMan (Review manager V5.4) in accordance with the requirements of the Cochrane Collaboration and meta-analysis reporting quality guidelines. The odds ratio (OR) was calculated using the random-effects model, and heterogeneity was quantified using the I2 and X2 statistics with the corresponding p-values. IOP, medications were compared between preoperative and postoperative patients.

Results

Search results

There were no significant differences in gender or age of glaucoma patients. Figure 1 shows a flow chart of the included and excluded studies in this review. Of the 212 studies identified by the search, 83 were reviewed in full text after assessing the titles and abstracts. 32 studies met the predefined inclusion criteria. A total of 11 studies were included in the quantitative analysis (Fig. 1). Countries included Canada, China, Japan, Germay, and the United States. Four of the studies were from Japan [17–20], 3 were from United States [21–23], 1 was from Australia [24], 1 were from Canada [25], 1 were from Germany [26], and 1 were from China [27]. The sample size of patients ranged from 11 to 91.

For research hotspots and trends, the country and institution co-occurrence information for the literature search between 2012 and 2024 is as follows (Supplemental Figure 1 A & B). We also analyzed the keyword clustering information and arranged it according to the timeline (Supplemental Figure 2).

Subgroup analysis

Figures 2 and 3 shows subgroup analysis of surgical prognostic indicators. Postoperative and preoperative patients' IOP and medications were compared at 6 months, 12 months, 24 months, and time endpoints. Postoperative patients' IOP decreased by 2.08 ($P<0.01$), 3.28 ($P<0.01$), 2.50 ($P<0.01$) and 2.62 ($P<0.01$) at 6 months, 12 months, 24 months and time endpoints (Fig. 2A-D). Postoperative patients' medications decreased by 1.34 ($P<0.05$), 1.58 ($P<0.01$), 1.68 ($P<0.01$) and 1.47 ($P<0.01$) at 6 months, 12 months, 24 months and time endpoints (Fig. 3A-D).

Figures 4 and 5 shows subgroup analysis of MIGS combined with cataract surgery. Postoperative patients' IOP decreased by 1.93 ($P<0.01$), 2.11 ($P<0.01$), 1.98 ($P<0.01$) and 2.09 ($P<0.01$) at 6 months, 12 months, 24 months and time endpoints (Fig. 4A-D). Postoperative patients' medications decreased by 0.85 ($P<0.05$), 0.95 ($P<0.05$), 1.32 ($P<0.01$) and 1.13 ($P<0.01$) at 6 months, 12 months, 24 months and time endpoints (Fig. 5A-D).

A total of 18 complications were mentioned in the statistical studies (Table 1). The highest incidence was device malposition, including EXPRESS filter device with or without Phacoemualsification and Intraocular lens implantation (P/I) (13.5%) and iStent injection with P/I (20.3%). In addition, complications with an incidence of more than 10% include Contact with the iris and device (13.5%), Hyphema (10.7% and 10.8%), Hypotony (10.7%), Elevated IOP (10.9%) and Choroidal detachment (13.5%) (Table 2).

Discussion

With the development of science and technology, MIGS has gradually been integrated into the diagnosis and treatment methods of ophthalmology. The term 'MIGS' was coined by Dr. Ike Ahmed in 2009. It is a type of ultra-minimally invasive surgery that operates from a small corneal limbus incision through the anterior chamber without damaging the bulbar conjunctiva and sclera. Its characteristics include minimal wound and tissue destruction, high safety, and easy combination with

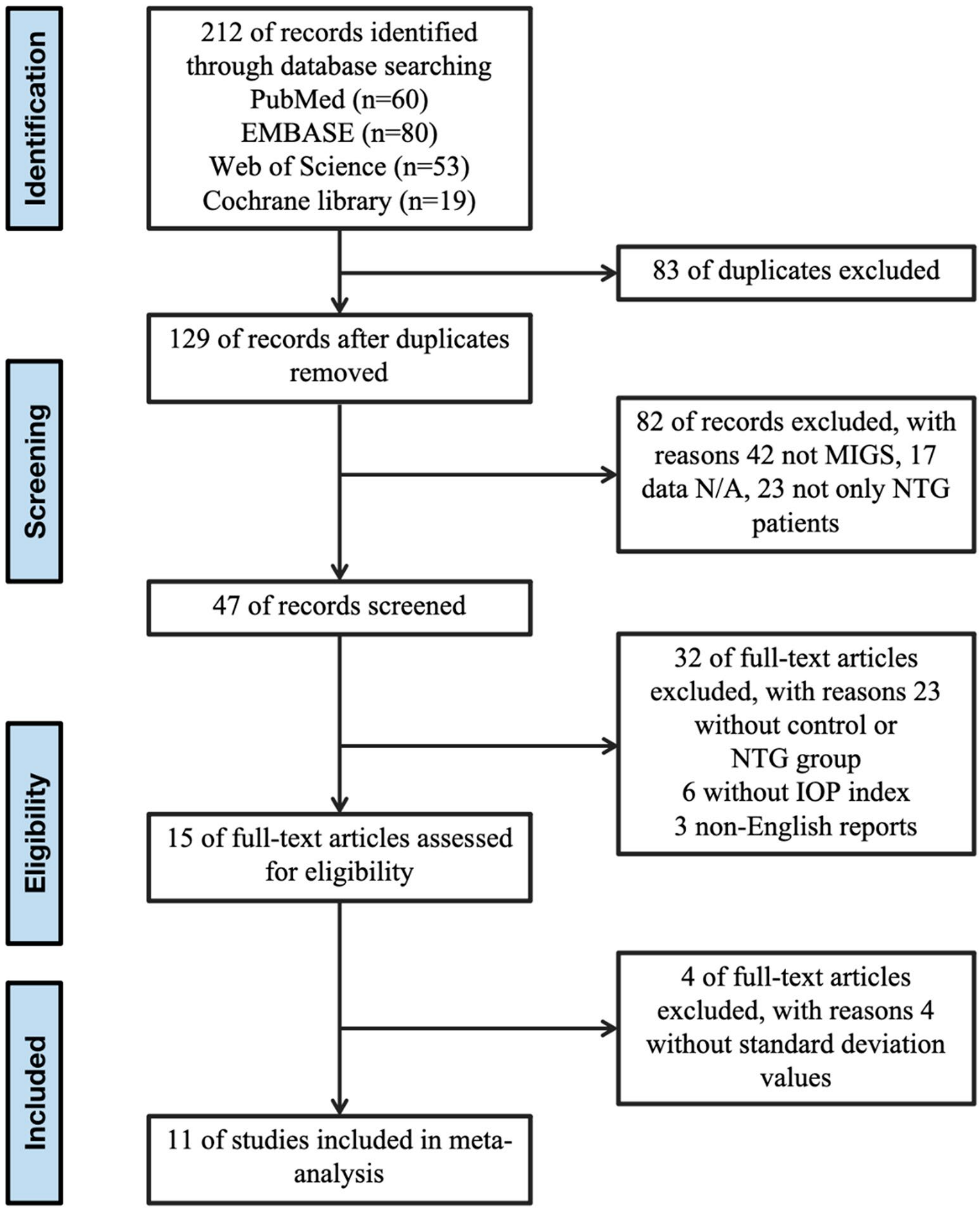

Fig. 1 Flowchart of studies included in systematic review. Flowchart summarizing included and excluded studies, based on Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines

cataract surgery. Its postoperative characteristics include short recovery time, good preservation of residual vision, relatively good curative effect, and IOP can usually be dropped to the normal range. There are many classifications of MIGS, including outflow through the trabecular meshwork/Schlemm canal, suprachoroidal outflow, subconjunctival filtration and reduction of aqueous humor production, including Trabectome, Kahook Dual Blade, XEN [28, 29]. It is mainly used in patients with early POAG, mild to moderate POAG, secondary glaucoma, and patients with both cataract and glaucoma.

NTG is a specialized type of POAG. Its characteristics are that the IOP is within the normal range (10-21mmHg), the difference between the two eyes is not >5mmHg, and the 24-hour IOP range is not >8mmHg. Such patients may have visual field defects, including paracentral scotoma in the early stages. As the disease progresses, the visual field may gradually become restricted, and finally a tubular visual field (central visual field) may remain. The optic disc will have corresponding depressions, and the optic nerve will also have corresponding damage, which is often accompanied by some vascular diseases, such as migraine, ischemic disease, hypotension, etc [30].

Although the pathogenesis of NTG is unclear, several hypotheses have been proposed. Some studies suggest

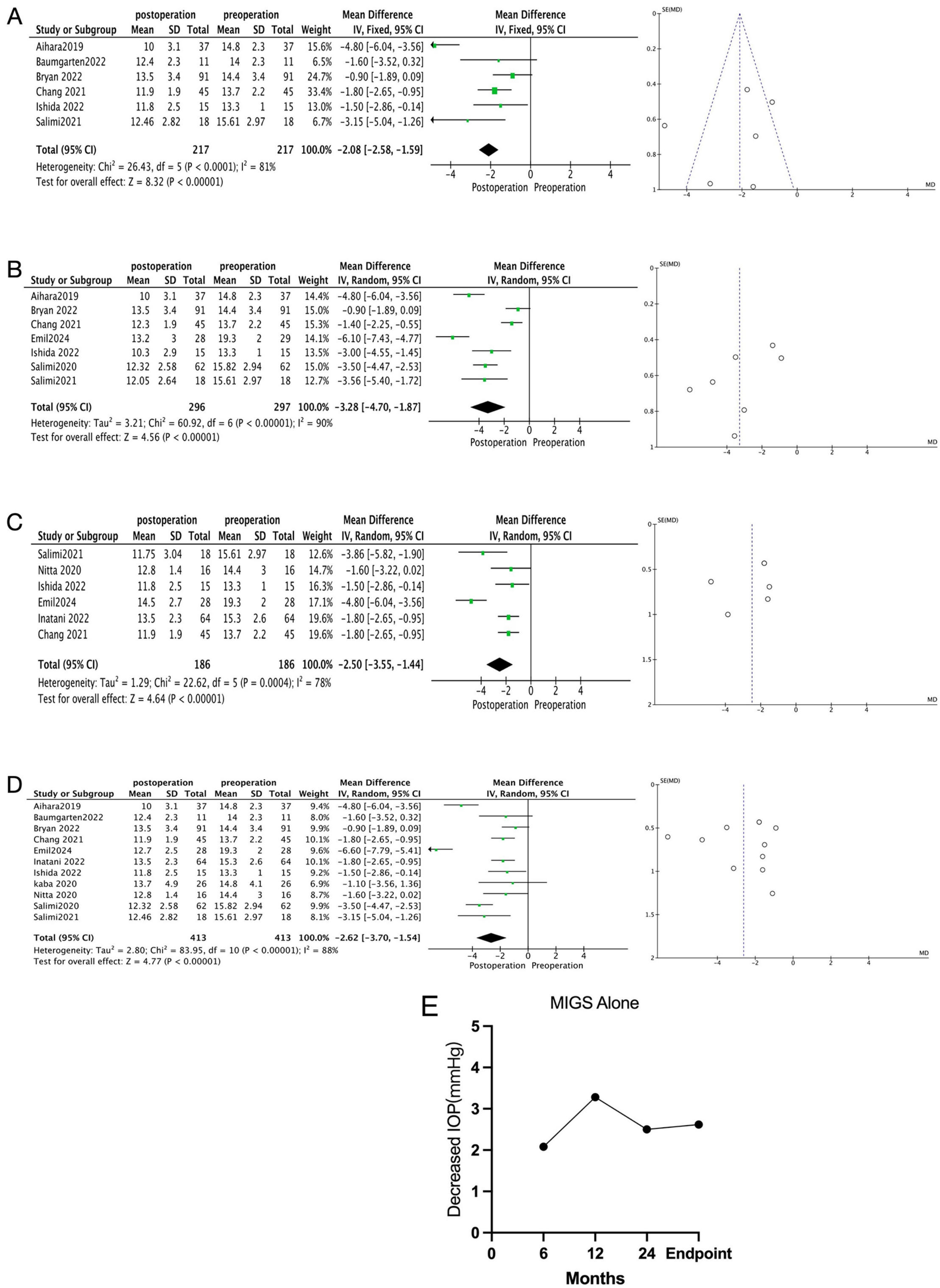

Fig. 2 Forest plots, funnel plots, the median changes (**E**) of microinvasive glaucoma surgery (MIGS) alone showing postoperative and preoperative patients' IOP at 6 (**A**), 12 (**B**), 24 (**C**), and endpoints (**D**). CI = confidence interval; IV = inverse variance; SD = standard deviation

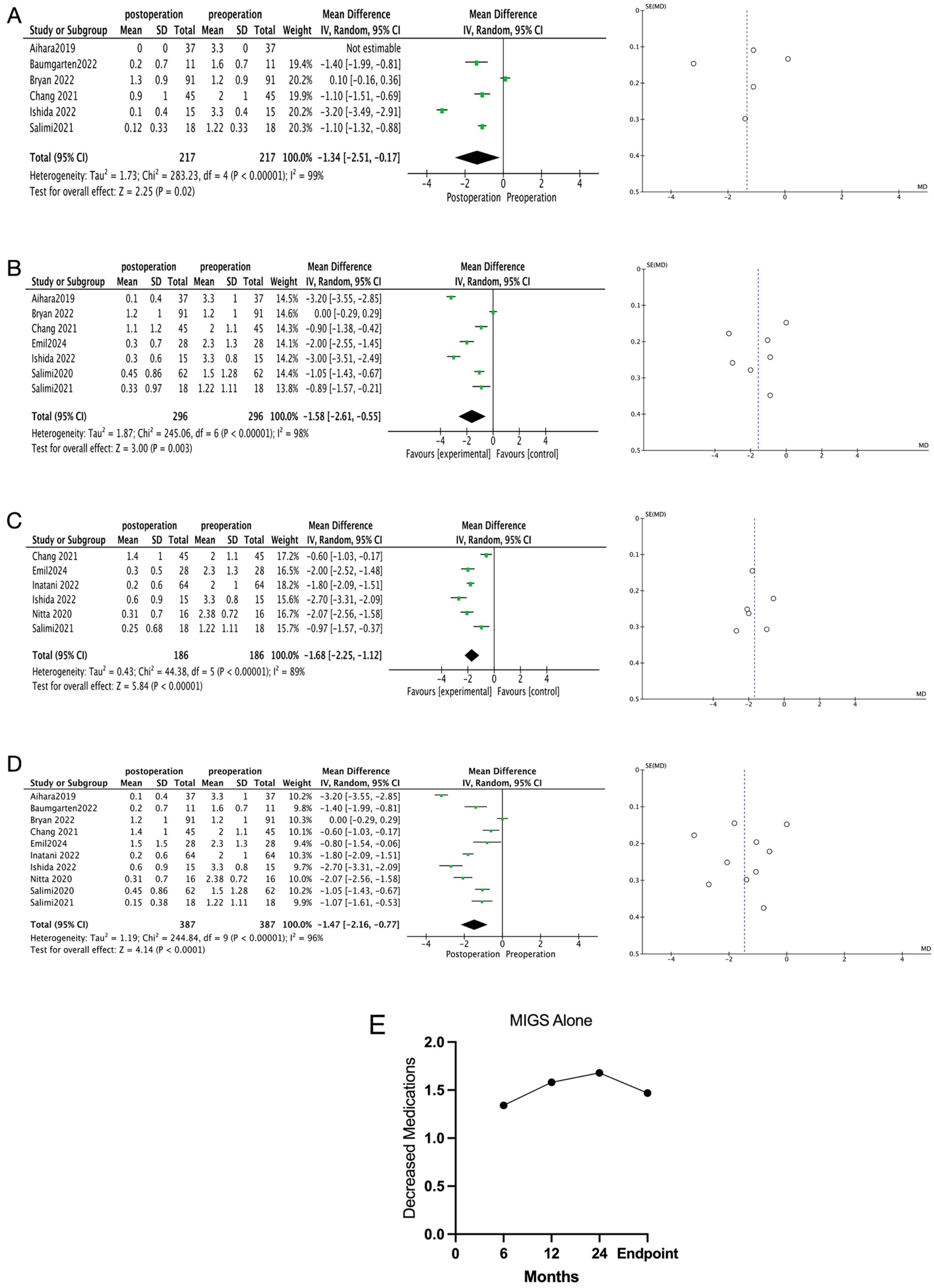

Fig. 3 Forest plots, funnel plots, the median changes (**E**) of microinvasive glaucoma surgery (MIGS) alone showing postoperative and preoperative patients' medications at 6 (**A**), 12 (**B**), 24 (**C**), and endpoints (**D**). CI = confidence interval; IV = inverse variance; SD = standard deviation

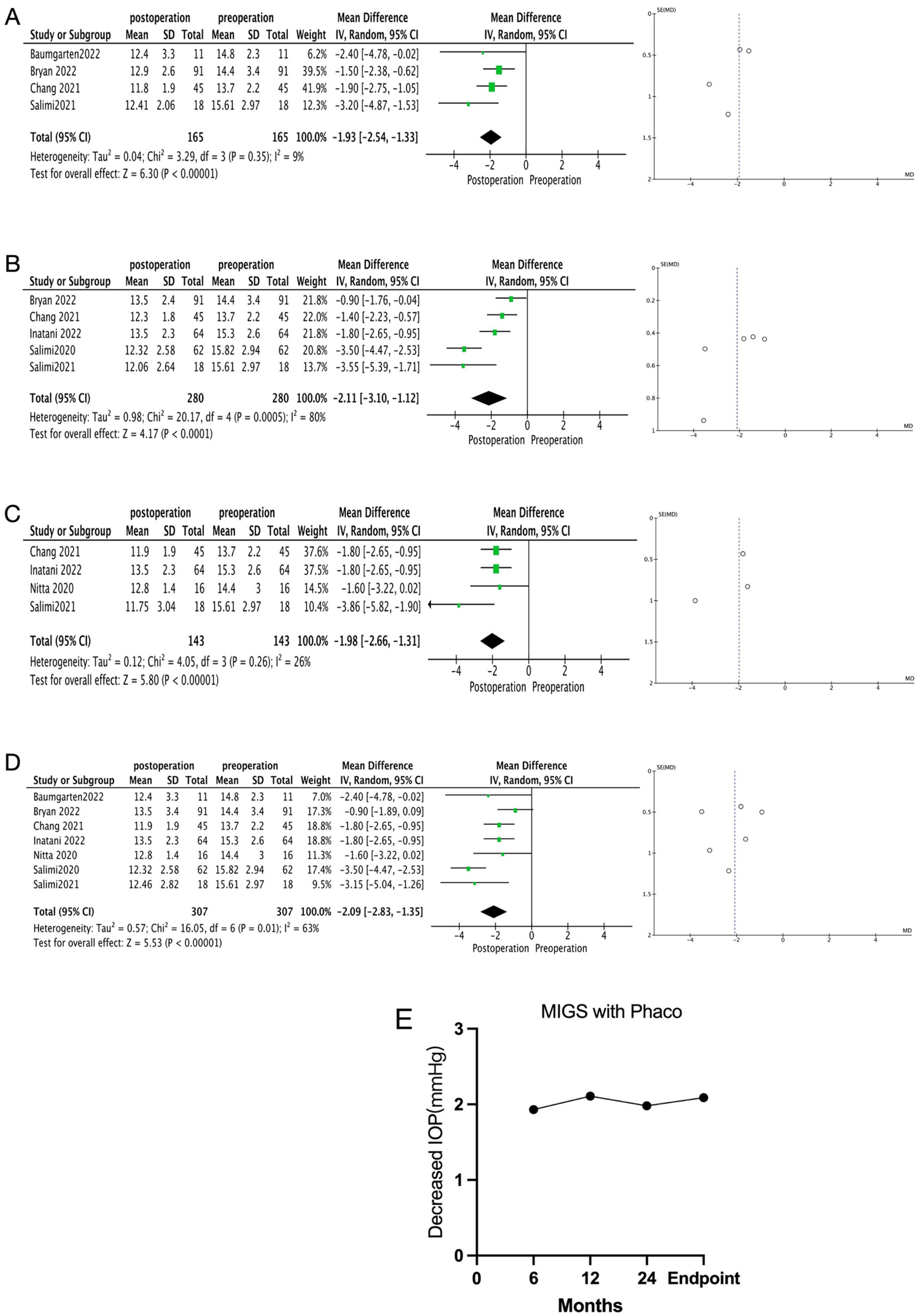

Fig. 4 Forest plots, funnel plots, the median changes (**E**) of microinvasive glaucoma surgery (MIGS) combined with phacoemulsification surgery showing postoperative and preoperative patients' IOP at 6 (**A**), 12 (**B**), 24 (**C**), and endpoints (**D**). CI = confidence interval; IV = inverse variance; SD = standard deviation

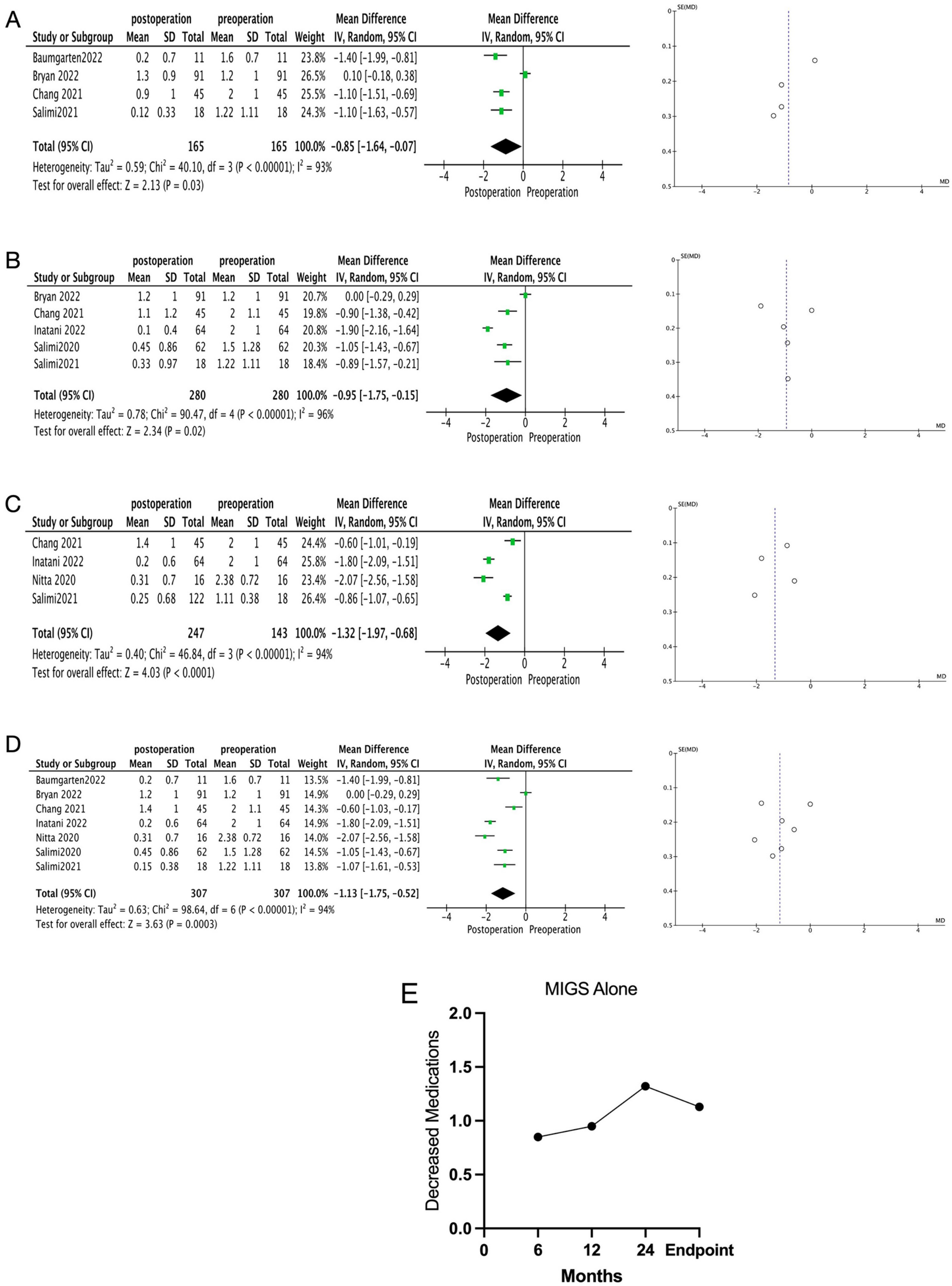

Fig. 5 Forest plots, funnel plots, the median changes (**E**) of microinvasive glaucoma surgery (MIGS) combined with phacoemulsification surgery showing postoperative and preoperative patients' medications at 6 (**A**), 12 (**B**), 24 (**C**), and endpoints(b). CI = confidence interval; IV = inverse variance; SD = standard deviation

Table 1 Summary of findings

Author and Year		Patients/NTG patients	Glaucoma type	Operational Styles		Assessed Points
Emil Nasyrov, 2024		23/23	NTG	XEN-45 gel stent implantation		IOP, Meds, C/O
Ali Salimi, 2021		124/NA	All types	iStent injection + P/I		IOP, Meds
Ali Salimi, 2020		62/62	NTG	iStent injection + P/I		IOP, Meds
Koji Nitta, 2020		73/16	NTG	iStent injection + P/I		IOP, Meds
Kyoko Ishida, 2017		63/15	POAG(NTG)	EXPRESS filter device		IOP
Masaru Inatani, 2022		232/64	POAG(NTG)	iStent injection + P/I		IOP, Meds, C/O
Colin Clement, 2020		340/20	POAG(NTG)	iStent injection + P/I		IOP
Enchi Kristina Chang, 2021		45/45	NTG	iStent injection/KDB/ECP+P/I		IOP, Meds
Sabine Baumgarten, 2022		55/11	HTG(NTG)	SBG+ P/I		IOP, Meds
Bryan Chin Hou Ang, 2022		30/30	NTG	iStent injection+ P/I		IOP, Meds
Makoto Aihara,2019		37/37	NTG	EXPRESS filter device +/- P/I		IOP, C/O
Preoperation IOP(mmHg)	**Postoperation IOP(mmHg)**	**Reduction rate/ amount of reduction**	**Preoperation Medications**	**Postoperation Medications**	**Reduction rate/ amount of reduction**	**Follow-up time**
19.3 ± 2.0	12.7 ± 2.5	34%	2.3 ± 1.3	1.5 ± 1.5	35%	5 Year
16.90±3.85	13.17±2.83	22%	2.38±1.29	0.16 ± 1.22	51%	3 Year
15.82±2.94	12.32±2.58	22%	1.50±1.28	0.45 ± 0.86	70%	1 Year
14.4±3.0	12.8±1.4	18%	2.38 ±0.72	0.31±0.70	87%	2 Year
17.7±4.3	11.2±3.6	34%	3.5 ± 0.7	0.4 ± 0.8	89%	1 Year
15.3±2.6	13.5±2.3	12%	2.0±1.0	0.1±0.04	95%	2 Year
16.4±4.7	13.7±3.1	16%	1.49±1.20	0.49±0.95	67%	2 Year
13.7± 2.2	11.9 ± 1.9	13%	2.0 ± 1.1	1.1±1.1	45%	24.1 Month
14.0 ± 2.3	12.4±2.3	11%	1.6 ± 0.7	0.3 ± 0.7	81%	2-6 Month
14.4 ± 3.4	13.5 ± 3.4	6%	1.3 ± 0.7	1.2 ± 1.0	8%	12 Month
14.8 ± 2.3	10.0 ± 3.1	32%	3.3 ± 1.0	0.1 ± 0.4	97%	12 Month

NTG: Normal tension glaucoma. POAG: Primary open-angle glaucoma. P/I: Phacoemualsification and Intraocular lens implantation. KDB: Kahook Dual Blade. ECP: Endoscopic cyclophotocoagulation. SBG: Single-use dual blade goniotomy. Meds: IOP-lowering medications, C/O| complications

that blood flow and vascular factors lead to vascular ischemia, insufficient perfusion pressure, and subsequent optic nerve damage. Others indicate that elevated plasma endothelin-1 (ET-1), a potent vasoconstrictor that regulates ocular blood flow, may play a role. Additionally, impaired autoregulation of ocular blood flow, increased vascular resistance, and nocturnal hypotension have been implicated. Mitochondrial dysfunction and oxidative stress may also contribute to retinal ganglion cell apoptosis. Furthermore, some researchers have proposed that abnormalities in cerebrospinal fluid pressure across the lamina cribrosa could lead to optic nerve damage. Collectively, these mechanisms highlight the complex and multifactorial nature of NTG pathogenesis [31]. On the one hand, MIGS can increase aqueous humor outflow by decreasing the resistance to outflow in the trabecular meshwork and Schlemm's canal pathways [32]. On the other hand, it can shunt aqueous humor to the suprachoroidal or subconjunctival space [33, 34]. In conclusion, because of the different mechanisms of blood pressure lowering by MIGS surgery, the specific MIGS procedure applicable to NTG needs to be studied in more detail. In addition, NTG's optic nerve damage mechanism also includes blood flow and vascular theory [35]. The pathogenesis of NTG is not yet fully understood, and some scholars believe that it is related to the blood flow theory. The mechanisms underlying the blood flow abnormalities in NTG patients are unknown, but oxidative stress, vasospasm, and endothelial dysfunction appear to be risk factors for glaucomatous optic neuropathy. Thus, lowering IOP alone for the treatment of glaucoma is not enough. Treatment strategies should also include optic nerve protection, of which improving ocular blood flow(OBF) is key [36]. Of course, some scholars believe that it is the cerebrospinal fluid dynamics theory.

European Glaucoma Society terminology and guidelines for glaucoma state that the target IOP reduction percentage (i.e., 20%, 30%, 40%) depends primarily on the VF defect at diagnosis and the rate of progression [37]. A Collaborative Normal Tension Glaucoma Study (CNTGS) shows that reducing IOP by 30% from baseline is a therapeutic goal [38]. So is the IOP-lowering effect of MIGS surgery still applicable to NTG patients? Some scholars believe that traditional trabeculectomy can achieve the effect of reducing NTG IOP, but the postoperative follow-up time is required to be at least 3 months, and postoperative complications need to be treated through massage and adjustment of adjustable sutures.

Table 2 Postoperative complications and interventions

Observed complication	Author and Year	Patients/NTG patients	Glaucoma type	Operational Styles
Hyphema	Emil Nasyrov, 2024	3/28(10.7%)	NTG	XEN-45 gel stent implantation
	Makoto Aihara,2019	4/37(10.8%)	NTG	EXPRESS filter device +/- P/I
Hypotony	Emil Nasyrov, 2024	3/28(10.7%)	NTG	XEN-45 gel stent implantation
	Makoto Aihara,2019	1/37(2.7%)	NTG	EXPRESS filter device +/- P/I
Elevated IOP	Emil Nasyrov, 2024	1/28(3.6%)	NTG	XEN-45 gel stent implantation
	Masaru Inatani, 2022	7/64(10.9%)	POAG(NTG)	iStent injection + P/I
PAS formation	Masaru Inatani, 2022	3/64(4.7%)	POAG(NTG)	iStent injection + P/I
Uveitis	Masaru Inatani, 2022	3/64(4.7%)	POAG(NTG)	iStent injection + P/I
Macular edema	Masaru Inatani, 2022	1/64(1.6%)	POAG(NTG)	iStent injection + P/I
	Makoto Aihara,2019	1/37(2.7%)	NTG	EXPRESS filter device +/- P/I
Capsule rupture	Masaru Inatani, 2022	1/64(1.6%)	POAG(NTG)	iStent injection + P/I
IOL dislocation	Masaru Inatani, 2022	1/64(1.6%)	POAG(NTG)	iStent injection + P/I
Secondary cataract	Masaru Inatani, 2022	1/64(1.6%)	POAG(NTG)	iStent injection + P/I
Vitreous loss	Masaru Inatani, 2022	1/64(1.6%)	POAG(NTG)	iStent injection + P/I
Device malposition	Makoto Aihara,2019	5/37(13.5%)	NTG	EXPRESS filter device +/- P/I
	Masaru Inatani, 2022	13/64(20.3%)	POAG(NTG)	iStent injection + P/I
Secondary glaucoma surgery	Masaru Inatani, 2022	6/64(6.3%)	POAG(NTG)	iStent injection + P/I
Choroidal detachment	Makoto Aihara,2019	5/37(13.5%)	NTG	EXPRESS filter device +/- P/I
Corneal epithelial defect	Makoto Aihara,2019	2/37(5.4%)	NTG	EXPRESS filter device +/- P/I
Epiretinal membrane	Makoto Aihara,2019	1/37(2.7%)	NTG	EXPRESS filter device +/- P/I
Blebitis	Makoto Aihara,2019	1/37(2.7%)	NTG	EXPRESS filter device +/- P/I
Optic disc hemorrhage	Makoto Aihara,2019	1/37(2.7%)	NTG	EXPRESS filter device +/- P/I
Contact with the iris and device	Makoto Aihara,2019	5/37(13.5%)	NTG	EXPRESS filter device +/- P/I

The psychological and financial burdens on patients are heavy, so most patients prefer emerging MIGS surgeries with less invasive risks, shorter operation times, and less postoperative follow-up time [39]. Some scholars believe that each method should be provided for patients with different situations, different indications, and different clinical situations to obtain different results [39]. In contrast, traditional trabeculectomy is supported by a large amount of literature and data from ophthalmology colleagues, while MIGS, as a new technology, currently lacks a large amount of experience and long-term results. All in all, NTG patients tend to choose minimally invasive surgery, but some scholars are skeptical about the specific efficacy of MIGS for NTG patients.

However, many current studies have proven that MIGS is effective in controlling IOP and reducing medications in NTG patients. One study showed that NTG patients with a baseline mean IOP of 14.8 ± 2.3 mmHg who underwent combined EX-PRESS implantation and phacoemulsification had significantly lower IOPs at all postoperative time points compared with baseline ($P < 0.0001$) [22]. From the immediate postoperative period to 1 month postoperatively, the IOP was stable. From months 1 to 12, the mean IOP ranged from 9.4 to 10.0 mmHg; the mean falling IOP increased from 4.9 mmHg to 5.4 mmHg; and the percentage reduction in intraocular pressure decreased from 21.1 to 35.4%. At 12 months, mean IOP was 10.0 ± 3.1 mmHg, a decrease of 4.9 mmHg (31.1%) from baseline ($P < 0.0001$) [17]. And while achieving these IOP reductions, almost all NTG patients no longer need to take IOP-lowering medications [38]. Another prospective, single-center case series of all NTG Asian eyes undergoing combined iStent injection implantation and phacoemulsification showed significant and sustained reductions in IOP and glaucoma medications 12 months postoperatively [17]. And in a real clinical population with NTG, significant and sustained IOP stabilization and reduced or even no medication use were achieved 1–3 years after MIGS surgery, with a good safety profile [19, 20, 22, 24, 25]. Due to variations in baseline IOP and the number of IOP-lowering medications across studies, direct comparisons of outcomes at different follow-up time points may not be meaningful.

Potential bias may arise from the lack of detailed classification of MIGS procedures across studies, with some failing to distinguish between standalone MIGS and MIGS combined with phacoemulsification. Additionally, baseline differences in IOP and medication use, especially among NTG patients, could affect treatment outcomes. Variations in IOP measurement methods and devices also contribute to inter-study heterogeneity.

These factors may influence the overall effect estimates and should be considered when interpreting the results.

The results of this study show that MIGS combined with phacoemulsification can well reduce postoperative IOP in patients, which also contributes to the IOP-lowering medications of NTG patients. While MIGS combined with phacoemulsification reduces IOP, the incremental IOP-lowering effect attributable to phacoemulsification alone appears minimal. However, we cannot ignore the role of phacoemulsification surgery. Studies have shown that MIGS combined with phacoemulsification surgery can improve the VA and IOP of patients with glaucoma and cataract, and is definitely a better surgical option for eligible NTG patients [40]. MIGS combined with phacoemulsification surgery can also reduce the risk of secondary surgery for patients due to postoperative cataract aggravation [41]. Therefore, the choice of whether to combine phacoemulsification for NTG patients requires clinicians to make a careful decision based on the patient's condition. Several epidemiologic studies have shown that NTG accounts for the largest proportion of POAG in Asian populations, which is also consistent with the racial proportions of this study [42, 43]. Therefore, it is hoped that in the future, Asian countries will increase the number of studies related to surgery in NTG patients.

At present, only postoperative IOP and medications indicators are included, and not all studies include detection data of optic nerve structure and function. Although reducing IOP is the most obvious and effective way to protect glaucoma optic nerve, it is not always possible in real clinical diagnosis and treatment. NTGs with well-controlled IOP (target IOP reduction of 20% or more) or low basic IOP may still experience decreased Retinal Nerve Fiber Layer (RNFL) and Visual Field Index (VFI) after MIGS. Therefore, it is recommended that follow-up studies pay more attention to the optic nerve and visual field, and comprehensively evaluate the RNLF thickness and VFI in the mid- and long-term follow-up of NTG patients after surgery. It is also recommended that follow-up studies further refine the surgical methods and indication groups, compare intraocular pressure control between high-tension glaucoma (HTG) and NTG patients, and examine patients at different glaucoma stages after different MIGS surgeries. Additionally, these studies should clarify the best indications for various MIGS procedures based on individualized factors such as disease stage and patient age. A multi-center, large-sample, prospective controlled study would be ideal to address these questions. MIGS is a relatively new surgical approach in glaucoma management, especially for NTG patients, where high-quality evidence remains limited. This study was initiated to address that gap. Previous meta-analyses confirmed IOP reduction with MIGS with Phaco in NTG but lacked subgroup analysis and evaluation of medication reduction.

One of the major limitations of this meta-analysis is the presence of substantial heterogeneity in several pooled estimates. This can be partially attributed to differences in baseline IOP values across studies, which directly affects the postoperative IOP reduction. Furthermore, variations in measurement methods, devices used, follow-up durations, and the number and type of preoperative glaucoma medications contribute to this heterogeneity. While subgroup and meta-regression analyses were performed to explore these sources, residual heterogeneity remained. Nonetheless, the overall direction of effect was consistent, suggesting a generally favorable efficacy profile for MIGS interventions in NTG patients.

Conclusion

The meta-analysis demonstrated that MIGS alone or combined with phacoemulsification effectively reduced the IOP and the requirement for IOP-lowering medications in postoperative patients with NTG. Whether MIGS combined with phacoemulsification can more effectively lower IOP and reduce the amount of IOP-lowering drugs required compared with MIGS alone requires further research. MIGS alone or combined with phacoemulsification reduced the IOP most at 12 months, and the lowest IOP-lowering medications at 24 months in postoperative patients with NTG.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12886-025-04104-w.

Supplementary Material 1: Supplemental Fig. 1. The cooperation network between the top productive countries (A) and institutions (B).

Supplementary Material 2: Supplemental Fig. 2. The timeline visualization of keywords.

Supplementary Material 3: Supplemental Table 1. The Newcastle-Ottawa Scale (NOS) quality assessment of included studies. The study quality score mainly includes three parts. The first part is "selection", that is, the representativeness of the selection of the exposed cohort and the non-exposed cohort. 1–4 represent the representativeness of the exposed cohort, the selection of the non-exposed cohort, the determination of exposure, and the fact that no study subjects have developed the disease studied at the beginning of the study. The second part is "comparability", which is evaluated based on the study design and analysis results and whether the confounding variables have been adjusted. 1 represents the selection and analysis of the control based on the most important factors, and 2 represents the selection and analysis of the control based on other important factors. The third part is "outcome", which is determined by independent blind evaluation, record contact or self-report based on the follow-up time and cohort retention. 1–3 represent the method of measuring the results, whether the disease studied and the follow-up time are long enough, and the completeness of the follow-up.

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Z.Y MF.W designed this project. YF.T, ZH.H, MM.Y and XH.P search the paper from 4 database. Z.Y, D.N and N.F writes the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

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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