Oftalmologi: Jurnal Kesehatan Mata Indonesia 2025, Volume 7, Number 3.
P-ISSN. 2723-6935, E-ISSN. 2541-4283
Received: 16 November 2025; Revised: 11 December 2025; Accepted: 15 December 2025

Impact of Ultrasound Cycloplasty on Intraocular Pressure and Clinical Outcomes in Angle-Closure Glaucoma: A Systematic Review and Meta Analysis

Hisyam Hartaman Putra[1], Rahmadina Djumain[1], Dafi Irsan Satria[1], Aan Tri Lutfi Muhammad[1], Brian Arditya Mahendra[2]
[1] *Medical Doctor Program, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia*
[2] *Department of Ophthalmology, Dr. Soeroto General Hospital, Ngawi, Jawa Timur, Indonesia*
**Correspondence: Hisyam Hartaman Putra, 24712135@students.uii.ac.id*

How to Cite:
Putra, H. H., Djumain, R., Satria, D. I., Muhammad, A. T. L., & Mahendra, B. A. (2025). Impact of Ultrasound Cycloplasty on Intraocular Pressure and Clinical Outcomes in Angle-Closure Glaucoma: A Systematic Review and Meta Analysis. *Oftalmologi: Jurnal Kesehatan Mata Indonesia*, *7*(3), 118–128. https://doi.org/10.11594/ojkmi.v7i3.95

ABSTRACT

Introduction: Angle-closure glaucoma (ACG) is a leading cause of permanent blindness, especially in Asia. Conventional therapies often fail to provide long-term intraocular pressure (IOP) control. Ultrasound Cycloplasty (UCP), a high-intensity focused ultrasound (HIFU) technology, lowers IOP through selective coagulation of the ciliary processes. This review aimed to evaluate the effectiveness and safety of UCP in patients with ACG.
Methods: A literature search was conducted in PubMed, Scopus, and Wiley until October 2025. Inclusion studies included ACG patients undergoing UCP with reported IOP outcomes, antiglaucoma medication use, and complications. Meta-analysis used a random-effects model and sensitivity analysis with a fixed-effects model.
Results: Four studies involving 142 eyes were analyzed. UCP reduced IOP by 18.12 mmHg, though not statistically significant (95% CI –1.27 to 37.51) with very high heterogeneity (I^2 = 99%). Antiglaucoma medication use decreased significantly (MD 1.79; p = 0.02). Early/mild complications were more common than late/severe complications. Sensitivity analysis showed stable results with reduced heterogeneity.
Conclusion: UCP is potentially effective in reducing IOP and antiglaucoma medication use in ACG patients, with an acceptable safety profile. However, considerable inter-study variability suggests that prospective studies are needed.
Keywords: Angle-closure glaucoma, Complications, Intra Ocular Pressure, Ultrasound Cycloplasty

ABSTRAK

Latar Belakang: Angle-closure glaucoma (ACG) merupakan penyebab kebutaan signifikan, terutama di Asia, dan terapi konvensional sering gagal memberikan kontrol tekanan intraokular (TIO) jangka panjang. Ultrasound Cycloplasty (UCP), teknologi high-intensity focused ultrasound (HIFU), menawarkan penurunan TIO melalui koagulasi selektif prosesus siliaris. Tinjauan ini bertujuan mengevaluasi efektivitas dan keamanan UCP pada pasien ACG.
Metode: Pencarian dilakukan pada PubMed, Scopus, dan Wiley hingga Oktober 2025. Studi yang melaporkan perubahan TIO, penggunaan obat antiglaukoma, dan komplikasi pasca-UCP diikutsertakan. Analisis dilakukan menggunakan random-effects model dan sensitivity analysis dengan fixed-effect model.
Hasil: Empat studi melibatkan total 142 mata. Meta-analisis menunjukkan penurunan TIO (MD 18.12 mmHg), namun tidak signifikan secara statistik dengan heterogenitas sangat tinggi (I^2 = 99%). Penggunaan obat antiglaukoma menurun signifikan (MD 1.79; p = 0.02). Komplikasi early/mild lebih sering dibandingkan komplikasi late/severe. Sensitivity analysis menunjukkan hasil yang stabil dengan penurunan heterogenitas.
Kesimpulan: UCP berpotensi menurunkan TIO dan kebutuhan obat pada ACG dengan profil keamanan yang dapat diterima. Namun, variabilitas antar studi membatasi kepastian bukti sehingga penelitian prospektif dengan protokol lebih seragam dan follow-up jangka panjang masih diperlukan.
Kata Kunci: Glaukoma sudut tertutup, Komplikasi, Tekanan Intraokular, Ultrasound Cyclo Plasty

INTRODUCTION

Glaucoma is a leading cause of irreversible blindness globally. Reduced visual function due to optic nerve and visual field impairment has a profound impact on the clinical burden of glaucoma.[1] Glaucoma also has a large societal impact, as measured in disability-adjusted life years (DALYs).[2] Compared with open-angle glaucoma, angle-closure glaucoma (ACG) tends to carry a greater risk of blindness. This is due to more acute episodes of intraocular pressure (IOP) spikes, rapid progression of optic nerve damage, and angle closure that may occur before diagnosis, making management of the disease particularly challenging.[3] A population meta-analysis including 37 studies reported a global prevalence of PACG of approximately 0.6% (95% CI 0.5–0.8%), and a geographic analysis found that Asia has the highest proportion of PACG cases.[3,4]

Medication, laser peripheral iridotomy (LPI), iridoplasty, and filtration surgery are the most common treatments for ACG. However, these treatments frequently fail to provide consistent long-term IOP control.[4] One of the primary causes of failure is anatomical alterations in the anterior angle, such as residual angle closure, peripheral anterior synechiae, and structural changes in the ciliary body that interfere with aqueous humor generation and outflow.[5] These anatomical characteristics are frequently the cause of long-term pressure control failure since therapy only targets the angle and does not address the malfunctioning of the ciliary structures.[6]

The limitations of conventional therapies, primarily due to anatomical changes in the anterior angle, highlight the need for novel therapeutic approaches that target not only angle widening or opening, but also other intraocular structures involved in intraocular pressure regulation, specifically the ciliary body.[7,8] In response to this demand, Ultrasound Cyclo-Plasty (UCP) has arisen as a novel method that uses high-intensity focused ultrasound (HIFU) to selectively coagulate ciliary processes.[9–12] This method inhibits aqueous humor production, induces local scleral thinning, and enhances uveoscleral outflow, resulting in a decrease in intraocular pressure with minimal injury to surrounding tissues.[11,12] With its precise working profile and low risk of complications, UCP offers significant potential as a more adaptive therapeutic solution to the anatomical challenges of angle-closure glaucoma.[13–16]

Several previous reviews have addressed the utility of Ultrasound Cycloplasty (UCP) in the general glaucoma population.[11,12,17,18] However, based on the authors' assessment, no systematic review with meta-analysis has specifically evaluated the efficacy of UCP in patients with angle-closure glaucoma (ACG), despite the distinct morphological and pathophysiological characteristics that influence treatment response in this group. To date, no meta-analysis has focused exclusively on UCP in ACG, even though the effectiveness of cyclodestructive procedures is strongly affected by factors such as anterior chamber angle configuration, the extent of peripheral anterior synechiae, and the structural profile of the ciliary body, all of which differ substantially from those observed in open-angle glaucoma.

Consequently, findings derived from studies conducted in general glaucoma populations cannot be directly applied to ACG. This study provides the first meta-analytic evidence indicating that UCP outcomes in ACG vary considerably because of anatomical heterogeneity unique to this condition, an aspect that has not been captured in previous meta-analyses on UCP in broader glaucoma cohorts. As a result, this review was conducted to comprehensively evaluate the effects of UCP on intraocular pressure and other clinical outcomes in patients with angle-closure glaucoma.

METHODS

Eligibility Criteria

This systematic review was written based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 guidelines. Includes studies involving patient populations with angle-closure glaucoma, including primary or secondary angle-closure glaucoma and chronic angle-closure glaucoma (CACG). Secondary angle-closure glaucoma cases were considered only if their outcomes were reported separately. There are no age and gender restrictions included. The intervention reviewed is Ultrasound Cycloplasty (UCP) either pre-post study without or with control. The primary outcome assessed is the reduction percentage in IOP one month after UCP with secondary outcomes being the use of antiglaucoma medication and complications arising after UCP. Complications are divided into two based on the degree of clinical severity and their impact on visual function, as well as whether the complications are transient or have long-term consequences. Included study types can be randomized controlled trials or observational studies.

Studies were excluded if they did not provide extractable data on intraocular pressure or other relevant clinical outcomes, or if the postoperative follow-up duration was less than one month, as periods shorter than this are insufficient to assess the early effectiveness and stabilization of ultrasound cycloplasty. Single case studies, case series, narrative reviews, editorials, and commentaries are also not included. Studies are limited to full-text articles in English.

Information Sources and Search Strategy

The literature search used in this meta-analysis was conducted through 3 databases, namely PubMed, Scopus, and Wiley Online Library. The search included all studies published until October 2025. The keywords used were ("ultrasound cycloplasty" OR "ultrasound cyclo-plasty" OR "high-intensity focused ultrasound cycloplasty" OR "HIFU cycloplasty") AND ("angle-closure glaucoma" OR "primary angle closure glaucoma" OR "angle closure glaucoma" OR PACG).

Data Collection Process

The Rayyan QCRI website was used to collect, screen, and delete duplicates from the searched literature. The identified material was filtered based on the title and abstract. Following that, every literature that met the inclusion criteria or contained incomplete information underwent a full-text examination. If the necessary data was missing, the literature was removed from the analysis.

Data Items

Characteristic data extracted from the articles included authors, study design, location, number of participants, preoperative and postoperative intraocular pressure, complications, and key conclusions. Data collection was performed by two independent reviewers. Disagreements between the reviewers were resolved through discussion with a third party until consensus was reached.

Study Risk of Bias Assessment

Risk of bias assessment for each included study was performed using Review Manager version 5.4 from The Cochrane Collaboration. Each domain was classified as low risk, unclear risk, or high risk of bias, and the assessment results were visualized as a risk of bias summary and a risk of bias graph using RevMan 5.4.

Effect Measures

The effect sizes used in the meta-analysis were adjusted according to the type of data available in each study. For continuous outcomes, such as changes in intraocular pressure (IOP) and the number of antiglaucoma medications, data were combined using the mean difference (MD) or standardized mean difference (SMD) if the units of measurement differed between studies. For dichotomous outcomes, such as the incidence of complications, odds ratios (ORs) and 95% confidence intervals (CIs) were used. All analyses were conducted using a random-effects model to account for inter-study variation, while a fixed-effects model was used in sensitivity analyses to assess the consistency of the results.

Synthesis Method

Data from each study were quantitatively synthesized using meta-analysis. For the outcomes of intraocular pressure (IOP) change and number of antiglaucoma medications, the mean difference (MD) was used with the inverse variance (IV) method. Meanwhile, the outcome of complication incidence was analyzed using the odds ratio (OR).

Due to the high clinical and methodological variation between studies, the primary model used was a random-effects model to obtain a more conservative effect estimate. Heterogeneity was evaluated using the I^2 statistic, with an I^2 value >75% considered to indicate high heterogeneity. We conducted a subgroup analysis comparing prospective and retrospective studies to assess whether study design influenced the treatment effect. To assess the effect's stability, a sensitivity analysis was conducted by removing potential outlier research. All analyses were performed using Review Manager (RevMan) software version 5.4. Publication bias assessment was not performed due to insufficient number of studies.

RESULT

Study Selection

The literature search returned 243 initial publications across all databases. After deleting 101 duplicates, 142 papers were screened for title and abstract evaluation, with 109 articles being eliminated because they did not fulfill the requirements. A total of 33 papers underwent full-text review, with 29 articles eliminated due to inappropriate clinical data, review articles, editorials, and articles not written in English. Finally, four publications matched the inclusion criteria, and all were used in the narrative synthesis and meta-analysis. The search results are shown in Figure 1.

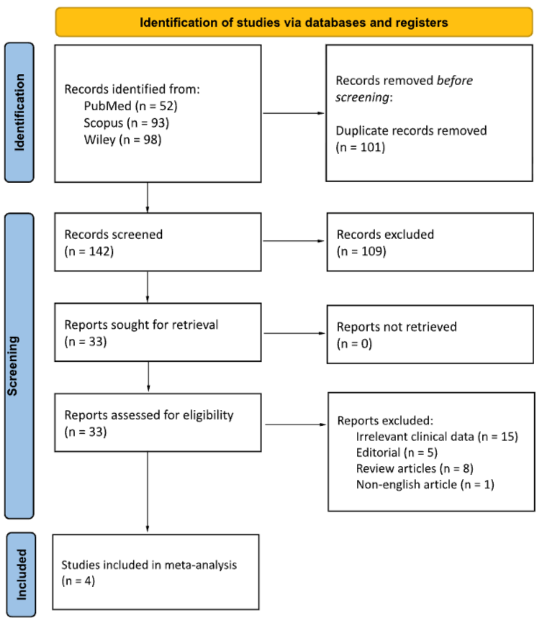

Figure 1. Study Flow Diagram

Study Characteristics

Included studies were published between 2017 and 2025 and consisted of two prospective and two retrospective studies. A total of 142 eyes diagnosed with angle-closure glaucoma (ACG) were included, including primary angle-closure glaucoma (PACG), secondary angle-closure glaucoma (SACG), and chronic angle-closure glaucoma (CACG). The mean age of participants ranged from 57 to 67 years. All studies evaluated the effects of ultrasound cycloplasty (UCP) using a HIFU device, varying in the number of sectors, energy levels, and application protocols. Follow-up duration ranged from 1 week to 6 months, with the majority of studies reporting outcomes at day 1, week 1, month 1, month 3, and month 6. Only one study reported long-term outcomes after 2 years. Primary outcomes included changes in intraocular pressure (IOP), number of antiglaucoma medications, and the incidence of complications. The characteristics of the included studies are shown in Table 1. The details of postoperative complications are shown in Table 2.

Table 1. Characteristics of Included Studies

Study (Year)	Design	Sample Size	Age	Glaucoma Type	IOP (mmHg)			Antiglaucoma medication	
					Preop	Postop	Percentage of Reduction (%)	Preop	Postop
Almobarak 2023[19]	Retrospective cohort study	62	59.00 ± 14.7	PACG	23.03 ± 6.4	15.32 ± 6.3	33.5	3.42 ± 0.9	1.91 ± 1.5
Liu 2025[14]	Prospective clinical study	56	58.93 ± 15.97	Primary and secondary ACG	39.08 ± 14.75	19.63 ± 8.68	49.8	2.37 ± 0.97	0.94 ± 1.03
Wang 2025[20]	Retrospective study	16	67.0 ± 7.0	AACG	52.31 ± 4.21	11.06 ± 1.57	78.9	3.875 ± 0.34	0.25 ± 0.577
Graber 2017[21]	Prospective single center study	8	57.5 ± 8.6	CACG	18.4 ± 3.5	14.4 ± 3.6	21.7	3.4 ± 1.1	3.3 ± 0.7

*PACG: Primary Angle-Closure Glaucoma, AACG: Acute Angle-Closure Glaucoma, CACG: Chronic Angle-Closure Glaucoma

Table 2. Details of Postoperative Complications

	Long-term								Short-term			
	Cataract	Rebound AC reaction	Hypotony	Phthisis bulbi	Macular edema	Aqueous problem	Uncon trolled IOP	IOP spike	Conjunctival congestion	Aniso coria	SCH	Ciliary body detach ment
Almobarak 2023	19	5	2	2	2	1	-	1	-	-	-	-
Liu 2025	-	-	-	-	-	-	-	-	8	3	-	-
Wang 2025	-	-	-	-	-	-	-	-	16	-	14	8
Graber 2017	-	-	-	-	-	-	2	-	-	-	-	-

*AC: Anterior Chamber, SCH: Subconjungtival Hemorrhage

Risk of Bias in Studies

The methodological quality of the included studies ranged from low to high risk across multiple dimensions. The majority of research posed a significant risk in terms of random sequence generation, allocation concealment, and blinding. Because the majority of studies offered complete outcome data, the domain with incomplete outcome data was rated low risk. There was no clear indication of skewed reporting. The other sources of bias domain had a low risk across all investigations. Figure 2 shows the risk of bias evaluation.

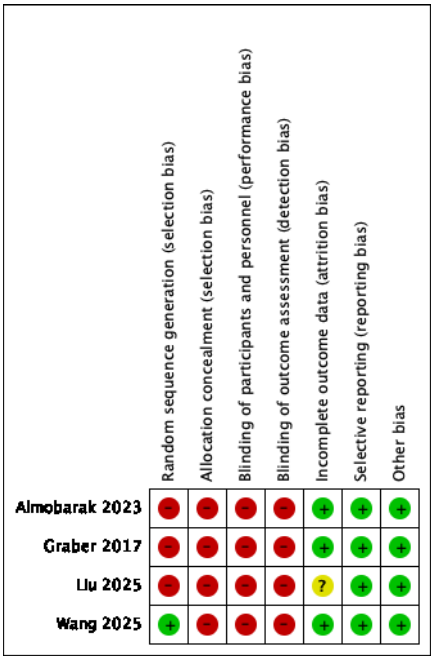

Figure 2. Risk of Bias Summary

Results of Individual Studies

Each of the included studies reported changes in intraocular pressure (IOP) after Ultrasound Cycloplasty (UCP) in angle-closure glaucoma patients with varied follow-up periods. Overall, all studies showed a drop in IOP from baseline, however the degree differed between research. Almobarak et al. (2023) conducted a retrospective analysis on 62 PACG eyes and found that IOP decreased from 23.03 ± 6.4 mmHg to 15.32 ± 6.3 mmHg at follow-up. Additionally, medication needs decreased from 3.42 to 1.91. This trial found that UCP was helpful for up to two years, however problems such as anterior chamber flare and progressive cataracts persisted.[19]

In a study of 56 eyes with primary and secondary ACG, Liu et al. (2025) found that IOP decreased significantly from 39.08 ± 14.75 mmHg to 19.63 ± 8.68 mmHg. Medication requirements also decreased, from 2.37 to 0.94. These findings were supported by an assessment of structural alterations that suggested enhanced uveoscleral outflow as an additional mechanism of the UCP impact.[14] Wang et al. (2025) found that 16 eyes with AACG attacks had a significant drop in IOP, from 52.31 ± 4.21 mmHg to 11.06 ± 1.57 mmHg. This study also found that UCP resulted in partial closure of the nonadhesive angle. The most prevalent problems were conjunctival congestion and an initial increase in IOP, but no significant issues were discovered.[20]

In a short prospective study of eight CACG eyes, Graber et al. (2017) found that IOP decreased from 18.4 ± 3.5 to 14.4 ± 3.6 mmHg with minor changes in medication use. This study underscored the safety of UCP in individuals at high risk for malignant glaucoma and recommended it as a safe alternative to filtration.[21]

Intraocular Pressure (IOP) Reduction Percentage

Four studies involving patients with angle-closure glaucoma treated with ultrasound cycloplasty (UCP) were included in the meta-analysis. The pooled analysis using a random-effects model demonstrated a significant reduction in intraocular pressure (IOP) following UCP, with a mean percentage decrease of 49.67% (95% CI 14.68 - 84.65; $p = 0.005$). Although all studies showed a consistent direction of effect favoring IOP reduction, the magnitude of reduction varied substantially across studies. Heterogeneity was high ($I^2 = 70\%$, $p = 0.02$), indicating considerable variability in treatment effect, likely attributable to differences in baseline IOP, disease severity, UCP parameters, and follow-up duration. Despite this heterogeneity, the overall evidence supports a clinically meaningful IOP-lowering effect of UCP in angle-closure glaucoma.

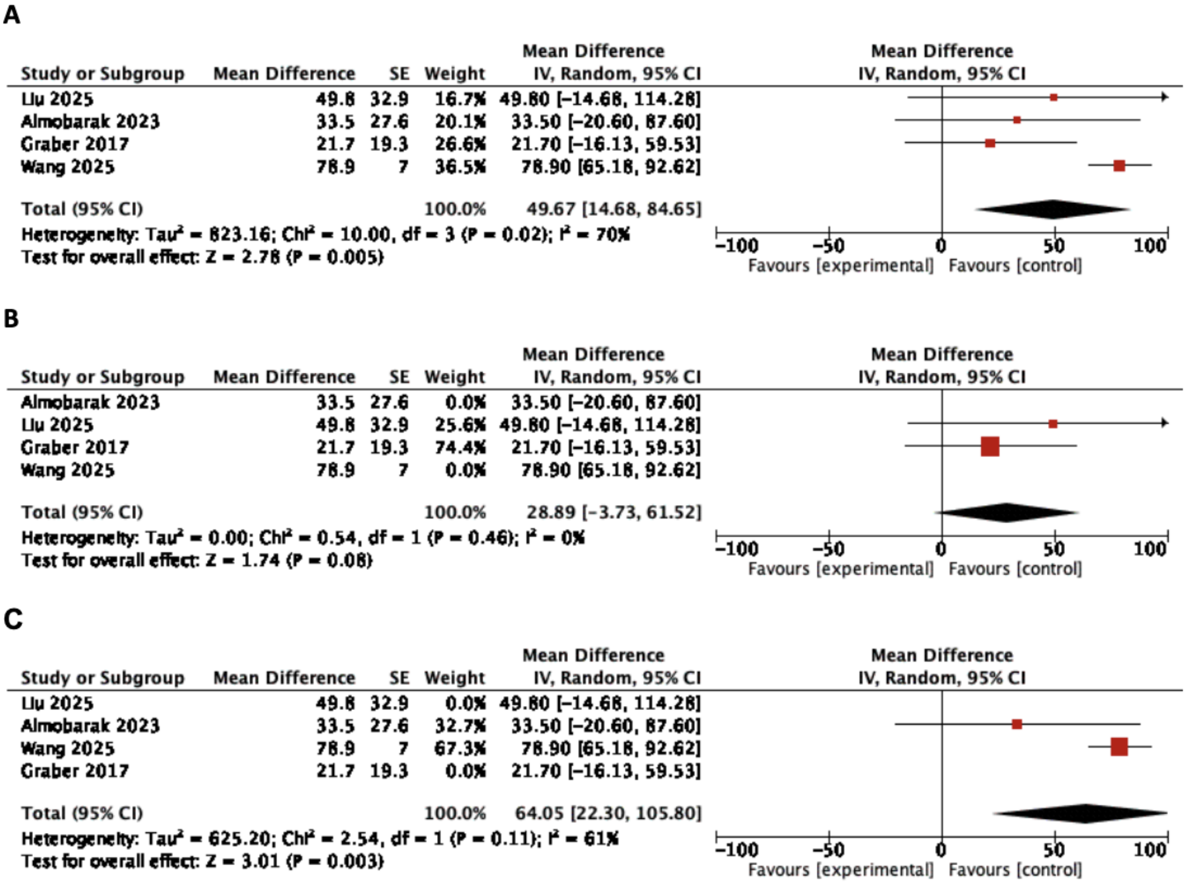

Figure 3. Forest plots of the primary outcomes: IOP reduction percentage (A), subgroup analysis: prospective study (B) and retrospective study (C)

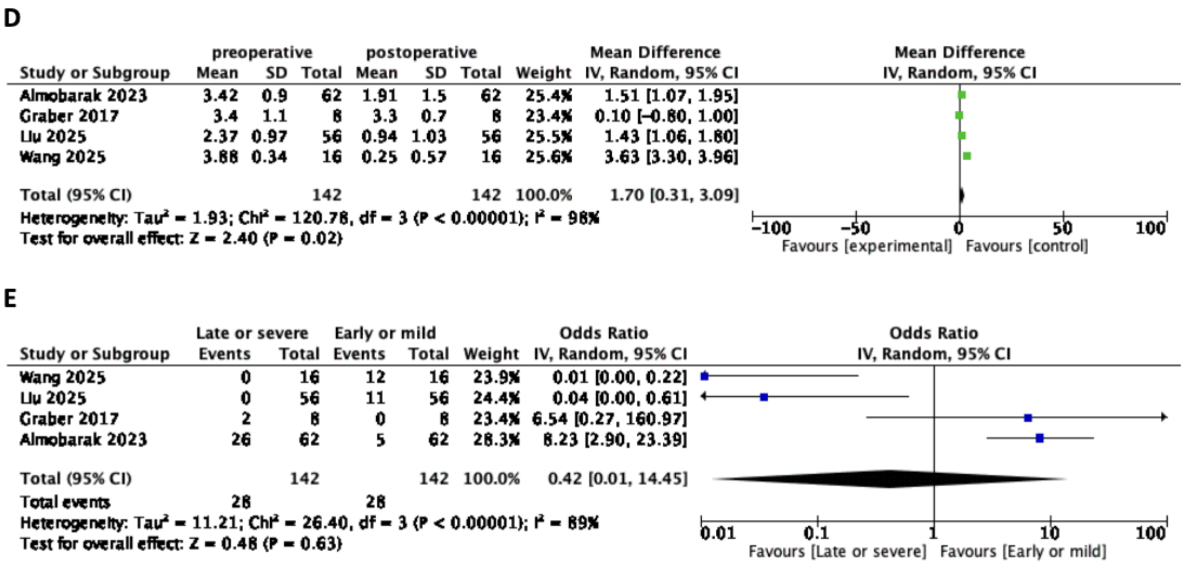

Figure 4. Forest plots of the secondary outcomes: antiglaucoma medications usage (B), and Post UCP Complications (C)

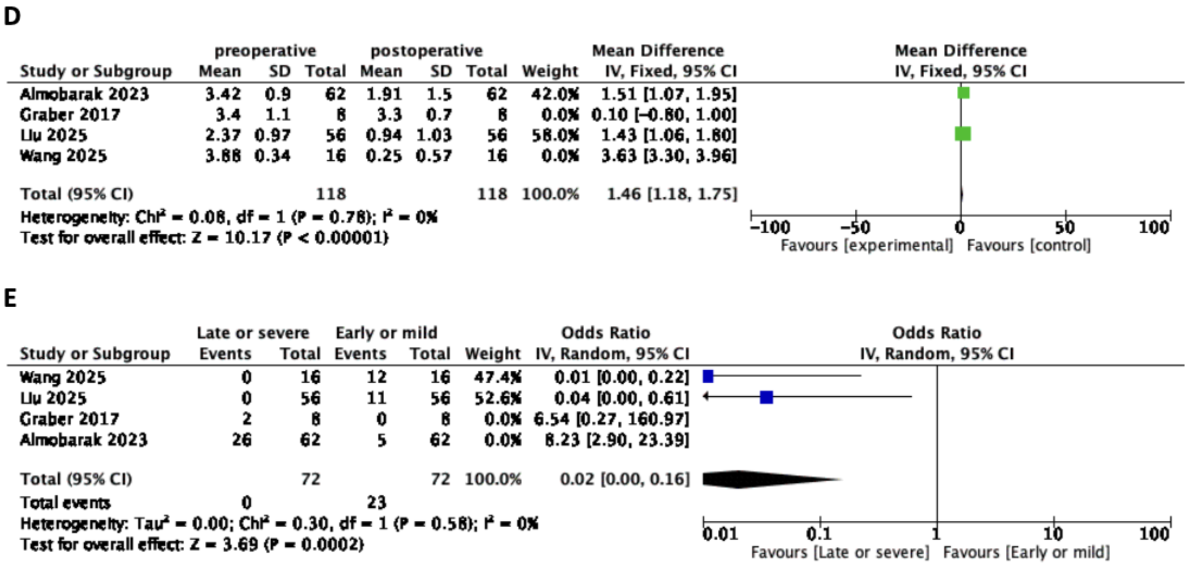

Figure 5. Sensitivity Analysis of the secondary outcomes: antiglaucoma medications usage (B), and Post UCP Complications (C)

Antiglaucoma Medications Usage

Secondary outcomes, such as preoperative and postoperative antiglaucoma medication use, revealed that all trials indicated a decrease in post-procedure antiglaucoma medication use, with a mean difference of 1.79 (95% CI [0.24 – 3.35], p = 0.02). The high heterogeneity value ($I^2 = 99\%$, $p < 0.00001$) also indicates clinical variation between studies that influences the results. Sensitivity analysis showed an MD value of 1.46 (95% CI: 1.18–1.75) with between-study heterogeneity ($I^2 = 0\%$), indicating that all studies included in the analysis produced uniform results in terms of both direction and magnitude of effect. This disappearance of heterogeneity indicates that the main meta-analysis findings are stable, and that the results remain significant even when changes in the analysis model or exclusion of studies with potential sources of instability are made.

Post UCP Complications

The secondary outcome of complications following UCP revealed no significant difference in risk between late/severe and early/mild difficulties (OR 0.42, 95% CI [0.01 - 14.45]; p = 0.63). High heterogeneity ($I^2 = 89\%$) suggests significant differences between trials. Sensitivity analysis results showed an OR of 0.02 (95% CI [0.00 – 0.16]; p = 0.0002) with study heterogeneity ($I^2 = 0\%$). This value indicates that late/severe complications are much less common than early/mild complications. Furthermore, the absence of heterogeneity indicates that the observed effect is stable and consistent across the remaining studies.

DISCUSSION

This meta-analysis found that Ultrasound Cycloplasty (UCP) reduces IOP in angle-closure glaucoma patients, although the impact was not statistically significant in the primary analysis because of substantial heterogeneity ($I^2 = 99\%$). The considerable range between studies is most likely due to a variety of factors, including changes in research design, wide variation in baseline IOP, type of ACG (acute, chronic, or mixed), and procedure differences. Furthermore, differing follow-up times may affect the stability of effect estimates, especially in cases where post-UCP anatomical alterations occur gradually. These findings provide important clinical implications, as variability in anatomical configuration and treatment timing may influence how clinicians stratify ACG patients who are most likely to benefit from UCP.

Sensitivity analysis helps to clarify the consistency of the findings. By altering the analysis approach or removing studies that contributed the most to variability, heterogeneity was significantly reduced while the results remained steady in terms of IOP reduction. This suggests that, notwithstanding the heterogeneity of the initial data, the effect of UCP on IOP reduction may be consistent in a more homogeneous population. The considerable reduction in antiglaucoma medication use also supports UCP's potential as an adjuvant or alternative therapy for those who have failed conventional therapy. In terms of safety, early/mild problems like conjunctival congestion and IOP spikes were more common, whereas late/severe issues were uncommon. Sensitivity analysis revealed that the findings remained stable, with few significant problems.

However, the findings of this meta-analysis must be interpreted in the context of variable patient characteristics. Patients with ACG exhibit varied angle anatomy, including degree of angle closure, synechiae, and ciliary body alterations caused by inflammation or repetitive ischemia.[11,12,22,23] These parameters may alter the efficacy of ultrasound energy on ciliary processes, resulting in varied IOP-lowering effects. Furthermore, very high baseline IOP in acute instances results in a higher IOP drop than in chronic patients with slower advancement. This variability is most likely responsible for the substantial heterogeneity of the study's findings.

The findings of this meta-analysis are consistent with the findings of Wu et al., 2023, who conducted efficacy testing on the general glaucoma population. UCP provides an effective and safe treatment for appropriate glaucoma.[24] UCP can effectively reduce TIO in glaucoma patients, reduce patient reliance on TIO aftercare, and have more complicated surgical procedures. however BCVA is not widely used.[25–28] A 6-month prospective study conducted by Luo (2022) found that the UCP method is an effective and well-tolerated treatment for lowering IOP in glaucoma patients in the Asian population, notably China.[29] Another study comparing ultrasonic cycloplasty to endoscopic cyclophotocoagulation found that UCP is more safe and tolerated by patients.[30] Patient age, history of previous glaucoma surgery, baseline white-to-white (corneal diameter), and the extent of UCP treatment all have an impact on the procedure's success rate.[9,29] Comparison with earlier reviews shows that while previous evidence focused largely on OAG or mixed glaucoma populations, this meta-analysis expands current understanding by specifically evaluating outcomes among ACG patients, who have substantially different anatomical and clinical profiles.

The effects of UCP may differ between OAG and ACG due to distinct disease mechanisms and anterior segment anatomy. In OAG, there is no mechanical obstruction of aqueous outflow, so reducing aqueous production with UCP leads to a more consistent and predictable IOP response. In contrast, ACG involves angle blockage and anatomical changes such as a narrow angle or anterior rotation of the ciliary body that can affect ultrasound energy delivery. ACG also tends to present with higher baseline IOP and structural or inflammatory changes in the ciliary body, making the tissue response to UCP more variable. These factors contribute to greater heterogeneity of UCP outcomes in ACG compared with OAG.

While these findings show that UCP has the potential to be used as a supplementary therapy for ACG patients, other factors, such as post-procedure angle stability, must also be considered. In other investigations, UCP has also been shown to cause local scleral thinning, which leads to greater uveoscleral outflow and may explain why some individuals have a stronger clinical reaction. This opens the door to examining combination therapy or earlier use of UCP in those at risk of fast development. Furthermore, combining UCP with other modalities, such as LPI or lensectomy, could be considered a multimodal approach to better address the anatomical and physiological elements of ACG.

Key limitations of the evidence include the small number of studies, the predominantly observational design, significant variation in treatment protocols, and the lack of long-term data. Limitations of the review process included the restriction to English-language studies and the possibility of publication bias. UCP may be investigated as a therapeutic alternative for individuals with ACG who are uncontrolled by current medication or are at high risk of filtration. To better understand the causes, future research should include randomized clinical trials with a standardized UCP procedure, as well as imaging examination of anterior chamber structural changes.

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