Review Article 

# Efficacy of ultrasound cyclo-plasty in treatment of glaucoma in Asian population

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## Abstract

• As a non-invasive surgical procedure ultrasound cycloplasty (UCP) has gained attention among ophthalmologists in recent years. Derived from the application of highintensity focused ultrasound, it has been utilized for the treatment of various types of glaucoma, demonstrating notable efficacy and safety. This review focuses on the efficacy and safety of UCP in treating glaucoma among Asian populations. By summarizing and analyzing existing literature on indications, therapeutic outcomes, and safety profiles, this review further highlights the unique advantages of UCP in glaucoma treatment compared to traditional surgical approaches. These advantages include broader indications, non-invasive nature, quantifiable treatment, excellent intraocular pressure-lowering effects, fewer adverse reactions, and high safety. Additionally, by introducing the underlying mechanism of action, this review explores the factors influencing its therapeutic efficacy, providing theoretical insights for clinical practice and demonstrating UCP's potential in glaucoma management.

• **KEYWORDS:** ultrasound cyclo-plasty; high-intensity focused ultrasound; glaucoma; Asia populations; ciliary body surgery

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### INTRODUCTION

s the world's leading irreversible cause of blindness, **1** glaucoma, the only proven effective treatment is lowering intraocular pressure (IOP)<sup>[1]</sup>. Drug, laser, and surgery are the main methods to lower IOP<sup>[1]</sup>. However, drug therapy highly relies on patient compliance and may lead to local or systemic adverse reactions; laser therapy has limited effectiveness in reducing IOP and long-term results are suboptimal. Surgical intervention, with its direct and significant effect on IOP reduction, has become an important approach in clinical management of patients with glaucoma<sup>[1]</sup>. Commonly used surgical procedures include filtration surgeries to enhance aqueous humor outflow and ciliary body destructive surgeries such as ciliary body photocoagulation and ciliary body cryotherapy to reduce aqueous humor production<sup>[2]</sup>. Nevertheless, trabeculectomy often results in local tissue scarring, leading to unsatisfactory long-term outcomes. Ciliary body destructive surgery is limited in clinical application due to their poor repeatability and safety.

Ultrasound cyclo-plasty (UCP) is a non-invasive surgical procedure developed based on high-intensity focused ultrasound, offering advantages such as no incision, quantifiability, and precise focusing<sup>[3]</sup>. The ultrasound glaucoma treatment device (EyeOP1) had been first used in clinical practice in Europe and was later introduced in Asia. It had obtained market approval in China in 2017 and had been used in clinical practice<sup>[3]</sup>.

Several studies have reported the efficacy and safety of UCP in treating various types of glaucoma. However, due to the delayed clinical application of UCP in the Asian population compared to Europe, there is a scarcity of comprehensive review on the efficacy of UCP in Asian individuals with glaucoma. This review systematically searched relevant literature, including recent clinical studies, retrospective research, and randomized controlled trials. The paper compiled clinical data on UCP for treating glaucoma in the Asian population, encompassing criteria for surgical success, number and types of cases treated, baseline IOP, follow-up duration, surgical success rates, incidence of complications, and other relevant indicators. This review will provide an overview of the indications, effectiveness, and safety of UCP based on the literature. To ensure a comprehensive and in-depth analysis of the application of UCP in Asian glaucoma patients, this study collected data from 1095 eyes across 26 studies from 14 centers in 4 countries, encompassing 5 subtypes of glaucoma.

**UCP Procedure** Prior to the surgery, a comprehensive ophthalmological examination is conducted, encompassing but not limited to best-corrected visual acuity (both distant and near), gonioscopy with a slit lamp to observe the anterior chamber angle, fundus evaluation using an anterior segment lens, IOP measurement, as well as precise determination of corneal diameter (white-to-white) and axial length. These data are typically forwarded to EyeOP1 engineers for specialized calculations to select the appropriate probe size.

During the surgical procedure, the patient adopts a supine position with a slight backward tilt of the head to ensure the operative eye remains in a natural horizontal state. The anesthesia method is flexibly chosen based on the patient's specific conditions, with either peribulbar or retrobulbar anesthesia administered to achieve optimal surgical cooperation and comfort. Once the EyeOP1 device is activated, the patient's information is accurately entered into the system, and the number of treatment sectors is set according to preoperative planning.

In the treatment preparation phase, the therapeutic probe is precisely positioned within a positioning ring filled with room-temperature saline, ensuring precise alignment with the center of the eyeball and a snug fit against the ocular surface. Additionally, a minimum of 2 mm of sclera exposure is maintained between the limbus and the edge of the positioning ring to guarantee a clear surgical field of view and a safe margin. Subsequently, the negative pressure system is activated and undergoes a self-check procedure, laying a solid foundation for the smooth progression of the treatment process.

The treatment process is automatically initiated by pressing the device's foot pedal, during which the patient must remain stationary to ensure the unhindered progress of the treatment. Upon completion, the saline within the positioning ring is collected, the negative pressure is released, and the surgical equipment is gently removed. The operative eye is then administered with antibiotic and glucocorticoid eye drops for infection prevention and to facilitate postoperative recovery, followed by dressing.

**Indications** Numerous domestic and international studies have confirmed that UCP can be widely applied in the treatment of various types of glaucoma. Multiple clinical trials have evaluated various types of glaucoma, confirming the efficacy of UCP. Zhongshan Ophthalmic Center<sup>[4]</sup>, the First Affiliated Hospital of Zhengzhou University<sup>[5]</sup>, Ophthalmology

Department of Qingdao University Affiliated Hospital<sup>[6]</sup>, King Saud University College of Medicine<sup>[7-8]</sup>, Mansoura University School of Medicine<sup>[9]</sup>, the Qingdao Eye Hospital of Shandong First Medical University<sup>[10]</sup>, Foshan Hospital of Southern Medical University<sup>[11]</sup>, Win Vision Eye Hospital in India<sup>[12]</sup> have all confirmed the significant effects of UCP in the treatment of angle-closure glaucoma. Similarly, research conducted at Zhongshan Ophthalmic Center<sup>[4]</sup>, King Saud University College of Medicine<sup>[7-8,13]</sup>, the First Affiliated Hospital of Anhui Medical University<sup>[14]</sup>, Mansoura University School of Medicine<sup>[9]</sup>, the Qingdao Eye Hospital of Shandong First Medical University<sup>[10]</sup>, and Foshan Hospital of Southern Medical University<sup>[11]</sup> has demonstrated the specific efficacy of UCP in the treatment of open-angle glaucoma.

In addition to primary angle-closure and primary openangle glaucoma, UCP has also shown reliable efficacy in secondary and refractory glaucoma. Chinese Glaucoma Guidelines (2020) lists UCP as one of the surgical options for neovascular glaucoma<sup>[15]</sup>. Studies conducted at Zhongshan Ophthalmic Center<sup>[4]</sup>, the Ophthalmology Department of Foshan Hospital of Southern Medical University<sup>[16]</sup> Ningxia Hui Autonomous Region People's Hospital Ophthalmology Hospital<sup>[17]</sup>, Lianyungang Eye Hospital<sup>[18]</sup>, the First Affiliated Hospital of Zhengzhou University Ophthalmology<sup>[19]</sup>, the First Affiliated Hospital of Bengbu Medical College<sup>[16,20]</sup>, King Saud University College of Medicine<sup>[7-8]</sup>, Mansoura University School of Medicine<sup>[9,21]</sup>, the Qingdao Eye Hospital of Shandong First Medical University<sup>[10]</sup>, and Foshan Hospital of Southern Medical University<sup>[11]</sup> have collected cases of neovascular glaucoma, performed UCP surgery and followed up postoperatively, verifying the effectiveness of UCP. Additionally, in refractory glaucoma<sup>[6,22-25]</sup>. There was no significant response to conventional treatment strategies, *i.e.*, maximum tolerated dose of medicine, laser therapy, or routine trabeculectomy (with or without medicine), and IOP never dropped to the normal range or decreased after treatment but quickly rebounded to baseline, uncontrolled IOP following glaucoma surgery<sup>[17,26-27]</sup>, and other secondary glaucoma<sup>[4,6-11]</sup>. The reliable efficacy of UCP has been confirmed by various scholars. Although UCP is currently more commonly used for the treatment of advanced glaucoma in China, some scholars have also studied UCP in early and moderate glaucoma and found that the effects are significant with a good safety profile<sup>[28]</sup>. Therefore, these research results indicated that UCP, as a treatment method, had broad prospects for application in different types of glaucoma. Most of the clinical studies involved in this article are statistics of average IOP reduction rate and success rate. However, some literature reports that UCP has the best therapeutic effect in primary angle-closure glaucoma<sup>[4,29-30]</sup>. The possible reason is related to the fact that

#### Table 1 Comparison of success criteria of UCP in each center

Institutions	Success criteria
Zhongshan Ophthalmic Center <sup>[4]</sup>	IOP reduced by ≥20% but still ≥5 mm Hg despite the presence of ocular hypotensive agent
the First Affiliated Hospital of Zhengzhou University $^{\scriptscriptstyle{[5]}}$	Complete success: IOP $\leq$ 21 mm Hg without medication; Partial success: IOP $\leq$ 21 mm Hg with less than pre-op medications, or >21 mm Hg without medications but $\geq$ 20% and $\geq$ 5 mm Hg decrease from preoperative
Qingdao University Affiliated Hospital <sup>[6]</sup>	IOP<21 mm Hg or $\geq\!30\%$ decrease at 3mo after surgery without medication or with one medication
King Saud University College of Medicine <sup>[7-8]</sup>	Complete success: $6 \le 10P \le 21$ mm Hg without extra treatment; Qualified success: the same as above but need extra medications
Mansoura University School of Medicine <sup>[9]</sup>	IOP reduction $\geq$ 30%, and IOP>5 mm Hg
The Qingdao Eye Hospital of Shandong First Medical University $^{\scriptscriptstyle \rm [10]}$	IOP reduction ≥30%, and IOP>5 mm Hg
Foshan Hospital of Southern Medical University <sup>[11]</sup>	IOP reduction $\geq$ 20%, and IOP>5 mm Hg without medication
Win Vision Eye Hospital in India <sup>[12]</sup>	IOP reduction >20%, and IOP>5 mm Hg without medication
King Saud University College of Medicine <sup>[13]</sup>	IOP reduction ≥20%, and IOP>5 mm Hg
The First Affiliated Hospital of Anhui Medical University $^{\left[ 14 ight] }$	$5{\le}IOP{\le}21$ mm Hg, or baseline IOP reduction>20% and >5 mm Hg postoperatively, with no severe complications and no need to increase medications
Lianyungang Eye Hospital <sup>[18]</sup>	10 <iop<21 hg<="" mm="" td=""></iop<21>
the First Affiliated Hospital of Zhengzhou University Ophthalmology $^{\!\scriptscriptstyle [19]}$	IOP reduction ≥20%, and IOP>5 mm Hg
the First Affiliated Hospital of Bengbu Medical $College^{^{[20]}}$	10<10P<21 mm Hg, or postoperative IOP decreased by >30% without medication or only 1-2 medications
Pidu District Hospital of Traditional Chinese Medicine <sup>[22]</sup>	IOP: 6-21 mm Hg
Qingdao Eye Hospital of Shandong First Medical University Shandong Eye Institute $^{\left[ 24\right] }$	IOP<21 mm Hg
King Abdul Aziz University Hospital <sup>[27]</sup>	IOP reduction of $\geq$ 20% from baseline and IOP between 6 and 21 mm Hg with or without medications, no loss of vision due to glaucoma progression, no complications and no need for further procedure
Affiliated Eye Hospital of Wenzhou Medical University <sup>[28]</sup>	IOP reduction of more than or equal to 20% compared with the baseline value and an IOP of more than 5 mm Hg at the last follow-up visit, without adding new medication
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University $^{\!$	Complete success: IOP decreased by $\geq$ 20% from the baseline, 5 <iop </iop  ≤21 mm Hg; Qualified success: IOP decreased by $\geq$ 20% from the baseline, IOP >5 mm Hg

UCP: Ultrasound cyclo-plasty; IOP: Intraocular pressure.

UCP treatment can lead to the thinning of the sclera and open the aqueous humor channel<sup>[31]</sup>. In addition, it is also related to the preoperative baseline IOP, sector selection, and the exposure time of ultrasound<sup>[4,12,30,32]</sup>.

#### **Preoperative Efficacy Evaluation**

Criteria for successful UCP The postoperative IOP reduction rate is often considered as a crucial indicator for evaluating the success rate of glaucoma surgery in both domestic and international research. The comparison of criteria for successful UCP in each study was summarized in Table 1<sup>[4-14,18-20,22,24,27-28,33]</sup>. Success more frequently defined as IOP<21 and  $\geq$ 5 mm Hg, and/or and IOP decrease >20% compare to baseline. However, some researchers have further refined the criteria for surgical success. Zhang *et al*<sup>[5]</sup> categorized the pre- and post-operative use of antihypertensive medications as follows: complete success: no medication usage, IOP≤21 mm Hg; partial success: usage of fewer medications than preoperatively, with IOP≤21 mm Hg, or in the absence of antihypertensive medication usage, IOP>21 mm Hg but reduced by ≥20% and  $\geq$ 5 mm Hg compared to preoperative levels; failure: requiring reoperation, or unable to reduce IOP to  $\leq 21 \text{ mm Hg even}$ with the same amount of preoperative medications. In fact, such classification is more applicable, as to achieve a steady reduction in IOP, patients after UCP are typically gradually weaned off antihypertensive medications within three months

to achieve a steady reduction in pressure in clinical practice. In addition, different from moderate glaucoma with good vision, for some advanced patients with low or no vision, the main objective is not to obtain an IOP<21 mm Hg, but is to reduce/stop ocular pain<sup>[14,23]</sup>. This helps in comprehensively understanding patients' postoperative pain experiences and reflects the attention given to patients' quality of life and comfort in medical research and clinical practice. These detailed evaluation criteria provide important references for a comprehensive assessment of the effectiveness of UCP surgery. Preoperative baseline IOP The articles retrieved on the efficacy of UCP treatment for Asian glaucoma patients can be roughly categorized into the following four groups based on the baseline IOP. The comparison of preoperative baseline IOP in each study was summarized in Table 2<sup>[4-14,16-20,22-28,33]</sup>. We compare their success rates based on the magnitude of IOP reduction mentioned in each article.

The 23-30 mm Hg group includes 5 articles, with an average last follow-up success rate of  $55.46\%^{[7-8,12-13,27]}$ , 31-40 mm Hg group includes 3 articles, with an average last follow-up success rate of  $66.7\%^{[9-10,28]}$ , 41-50 mm Hg group includes 5 articles, with an average last follow-up success rate of  $70.86\%^{[4-5,18-19,22]}$ , and 51-60 mm Hg group includes 3 articles, with an average last follow-up success rate of  $69.74\%^{[14,20,24]}$ . Among these, 41-50 mm Hg group has the highest surgical

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#### Table 2 Comparison of follow-up data of UCP in each center

Institution	Baseline IOP (mm Hg)	Types (cases)	IOP reduction (follow-up timepoints)	
Zhongshan Ophthalmic Center <sup>[4]</sup>	41.11±10.7	POAG (10), PACG (18), NVG (29), traumatic (10)	29.2% (1d), 43.2% (1wk) <sup>a</sup> , 34.8% (1mo), 23.1% (3mo)	
The First Affiliated Hospital of Zhengzhou University <sup>[5]</sup>	41.78±81.7	PACG (32)	23.2% (1d), 37.6% (1wk), 43.9% (2wk), 47.8% (1mo), 48.1% (3mo), 50.5% (6mo)	
The Ophthalmology Department of	54.73±5.44	PACG (11)	25.9% (1d), 42.17% (1wk), 51.7% (1mo), 52.0% (2mo), 64.1% (3mo) <sup>a</sup>	
Qingdao University Affiliated Hospital <sup>16</sup>	55.00±10.74	NVG (9)	36.0% (1d), 45.7% (1wk), 45.9% (1mo), 50.0% (2mo), 51.8% (3mo) <sup>a</sup>	
King Saud University College of Medicine <sup>[7]</sup>	23.46±6.30	POAG (69), PACG (66), NVG (19), other (28)	33.0% (1d), 31.7% (2wk), 28.1% (1mo), 24.2% (3mo), 27.8% (6mo), 32.1% (9mo), 26.1% (12mo), 31.5% (18mo), 30.8% (24mo), 36.0% (36mo), 37.4% (48mo) <sup>a</sup>	
King Saud University College of Medicine <sup>[8]</sup>	23.16±6.4	POAG (37), PACG (38), NVG (13), other (10)	34.5% (1d) <sup>3</sup> , 25.9% (1mo), 20.6% (3mo), 29.0% (6mo), 33.0% (9mo), 28.5% (12mo), 32.3% (18mo), 30.1% (24mo)	
Mansoura University School of Medicine <sup>[9]</sup>	35.2±8.3	POAG (13), PACG (10), SG (26), other (13)	67.4% (1d) <sup>3</sup> , 64.5% (1wk), 61.5% (1mo), 44.2% (3mo), 48.2% (6mo), 42.3% (12mo)	
The Qingdao Eye Hospital of Shandong First Medical University <sup>[10]</sup>	39.7±6.1	POAG (1), PACG (6), NVG (12), SG (6)	19.9% (1d), 52.8% (1wk) <sup>a</sup> , 43.7% (1mo), 42.0% (3mo), 25.0% (6mo), 29.6% (12mo)	
Foshan Hospital of Southern Medical University <sup>[11]</sup>	38.3±3.6	POAG (7), SG (35), PACG (17)	39.1% (1d), 60.0% (1wk), 60.1% (1mo) <sup>a</sup> , 53.7% (3mo), 33.5% (6mo), 30.6% (12mo), 31.9% (18mo)	
Win Vision Eye Hospital in India <sup>[12]</sup>	23.5±3.0	POAG (65), others (8)	82.0% (1d), 93.0% (1wk) <sup>a</sup> , 85.0% (1mo), 76.0% (2mo), 81.0% (3mo), 78.0% (6mo), 78.0% (12mo)	
King Saud University College of Medicine <sup>[13]</sup>	23.02±6.1	POAG (66)	34.8% (1d), 28.8% (1mo), 32.3% (3mo), 41.0% (6mo), 42.0% (9mo) <sup>3</sup> , 35.5% (12mo)	
The First Affiliated Hospital of Anhui Medical University <sup>[14]</sup>	53.61±12.4	POAG (2), PACG (2), NVG (24), other (8)	29.7% (1d), 44.9% (1wk) <sup>a</sup> , 39.5% (1mo), 44.0% (2mo), 41.8% (3mo), 43.0% (6mo)	
The Ophthalmology Department of Foshan Hospital of Southern Medical University <sup>[16]</sup>	34.1±9.7	NVG (36)	22.9% (1d), 35.1% (1wk), 50.4% (1mo), 24.3% (6mo), 43.7% (10mo)	
Ningxia Hui Autonomous Region People's Hospital <sup>[17]</sup>	47.53±11.28		53.6% (1d), 60.9% (1wk), 65.2% (1mo), 66.0% (3mo) <sup>a</sup> , 64.7% (6mo)	
Lianyungang Eye Hospital <sup>[18]</sup>	43.9	NVG (10)	36.9% (1d)ª, 28.5% (1wk), 23.8% (1mo), 21.7% (3mo)	
The First Affiliated Hospital of Zhengzhou University Ophthalmology <sup>[19]</sup>	44.19±13.72	NVG (30)	57.3% (1d) <sup>3</sup> , 56.5% (3d), 56.8% (1wk), 55.6% (1mo), 52.4% (2mo), 50.2% (3mo), 49.2% (6mo)	
The First Affiliated Hospital of Bengbu Medical College <sup>[20]</sup>	50.37±8.49	NVG (15)	29.7% (1d), 49.9% (1wk), 52.9% (1mo) <sup>a</sup> , 44.6% (3mo), 42.2% (6mo), 36.0% (10mo)	
Pidu District Hospital of Traditional Chinese Medicine <sup>[22]</sup>	43.81±5.64	NVG (16), traumatic (10), SG (15)	21.5% (1d), 23.8% (1wk), 27.6% (1mo), 29.8% (3mo) <sup>a</sup>	
The Second Affiliated Hospital of Anhui Medical University <sup>[23]</sup>	43.97±10.39	NVG (13), other (9), postoperative IOP out of control (8)	14.7% (1d), 20.1% (1wk), 18.7% (1mo), 20.3% (3mo)	
The Second Affiliated Hospital of Nanjing Medical University in Wuxi <sup>[24]</sup>	51.86±9.75	POAG (1), PACG (7), NVG (5)	33.1% (1d)ª, 47.4% (1wk), 63.6% (1mo), 64.1% (2mo)	
The Second Affiliated Hospital of Anhui Medical University <sup>[25]</sup>	45.12±8.26	Refractory (55)	18.2% (1d), 22.7% (1wk), 24.8% (1mo), 25.8% (3mo) <sup>a</sup>	
The First Affiliated Hospital of Zhengzhou University <sup>[26]</sup>	45.82±8.81	NVG (12), POAG (7), PACG (4), SCG (5)	12.9% (1d), 20.0% (1wk), 21.3% (2wk), 21.8% (1mo) $^{\rm a},$ 21.5% (3mo)	
King Abdul Aziz University Hospital <sup>[27]</sup>	23.91±6.3	POAG (26), PACG (21), NVG (6), SG (16), congenital (1), POAG (26)	29.3% (1d), 28.5% (1mo), 26.9% (3mo), 23.6% (6mo) <sup>a</sup> , 25.2% (12mo), 30.2% (18mo), 29.9% (24mo)	
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University <sup>[26,33]</sup>	34.9±4.9	Moderate POAG (32)	25.9% (1d) <sup>3</sup> , 36.7% (1wk), 34.7% (1mo), 32.3% (3mo), 33.3% (6mo), 31.0% (12mo), 32.6% (18mo)	
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University <sup>[33]</sup>	36.4±9.5	SG (16), NVG (6)	27.0% (1d), 40.0% (1wk), 46.0% (1mo) <sup>a</sup> , 42.0% (3mo), 41.0% (6mo), 32.0% (12mo)	

UCP: Ultrasound cyclo-plasty; IOP: Intraocular pressure; PACG: Primary angle-closure glaucoma; POAG: Primary open angle glaucoma; SG: Secondary glaucoma; NVG: Neovascular glaucoma. <sup>a</sup>The most significant time point for lowering IOP.

success rate, but more research is needed to confirm the relationship between baseline IOP and surgical success rate, especially after controlling for variables such as glaucoma type.

## Postoperative Efficacy Evaluation Effectiveness

1) Postoperative follow-up duration In all the articles describing the efficacy of UCP for Asian glaucoma patients, the clinical studies conducted by different centers had varying follow-up durations, ranging from 2 to 48mo postoperatively. The comparison of postoperative follow-up duration in each study was summarized in Table 2. Most

scholars chose to observe the UCP treatment effect within 3mo postoperatively<sup>[4,6,18,22-23,25-26]</sup>. However, Almobarak *et al*<sup>[7]</sup> conducted a longer-term clinical study to assess the sustained hypotensive effect of UCP. Their findings revealed a remarkable 37.38% reduction in IOP and an impressive surgical success rate of 88.9% at the 48-month postoperatively. This is the longest follow-up study on the efficacy of UCP treatment for Asian glaucoma patients to date, which indicates that UCP may potentially offer sustained hypotensive effects for glaucoma patients in Asia. In addition, Almobarak *et al*<sup>[7]</sup> also summarized the reduction in IOP of patients at different follow-up time points postoperatively. At 48mo postoperatively, the

Table 3 Comparison of	surgical success	rates and recomme	ndation levels acros	s institutions
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Institutions	Success rate (%, last follow-up)	Recommendation level
Zhongshan Ophthalmic Center <sup>[4]</sup>	50.0	Recommended
The First Affiliated Hospital of Zhengzhou University <sup>[5]</sup>	90.6	Highly recommended
The Ophthalmology Department of Qingdao University Affiliated Hospital <sup>[6]</sup>	-	Highly recommended
King Saud University College of Medicine <sup>[7]</sup>	88.9	Recommended
King Saud University College of Medicine <sup>[8]</sup>	42.9	Recommended
Mansoura University School of Medicine <sup>[9]</sup>	77.4	Recommended
The Qingdao Eye Hospital of Shandong First Medical University <sup>[10]</sup>	41.7	Highly recommended
Foshan Hospital of Southern Medical University <sup>[11]</sup>	60.0	Recommended
Win Vision Eye Hospital in India <sup>[12]</sup>	56.0	Highly recommended
King Saud University College of Medicine <sup>[13]</sup>	-	Recommended
The First Affiliated Hospital of Anhui Medical University <sup>[14]</sup>	77.8	Recommended
Ophthalmology Department of Foshan Hospital of Southern Medical University <sup>[16]</sup>	-	Highly recommended
Ningxia Hui Autonomous Region People's Hospital Ophthalmology Hospital <sup>[17]</sup>	-	Highly recommended
Lianyungang Eye Hospital <sup>(18)</sup>	60.0	Recommended
The First Affiliated Hospital of Zhengzhou University Ophthalmology $^{[19]}$	58.0	Highly recommended
The First Affiliated Hospital of Bengbu Medical College <sup>[20]</sup>	90.0	Recommended
Pidu District Hospital of Traditional Chinese Medicine <sup>[22]</sup>	60.0	Highly recommended
The Second Affiliated Hospital of Anhui Medical University <sup>[23]</sup>	-	Highly recommended
The Second Affiliated Hospital of Nanjing Medical University in Wuxi <sup>[24]</sup>	71.4	Highly recommended
The Second Affiliated Hospital of Anhui Medical University <sup>[25]</sup>	-	Highly recommended
The First Affiliated Hospital of Zhengzhou University <sup>[26]</sup>	-	Highly recommended
King Abdul Aziz University Hospital <sup>[27]</sup>	48.6	Recommended
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University <sup>[28,33]</sup>	81.0	Highly recommended
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University <sup>[33]</sup>	54.0	Highly recommended

study found that the most significant reduction in IOP occurred. In other similar studies, it has been noted that the reduction in IOP does not consistently increase over time. For instance, in some studies, the maximum reduction in IOP occurred on the first day postoperatively<sup>[8-9,18,20,24,28]</sup>. This could be attributed to the immediate effect following surgery, but over time, the IOP may gradually stabilize and reach its maximum reduction. Additional long-term observations and research are necessary to fully understand the evolving trend in postoperative reduction of IOP. Furthermore, some scholars have proposed that the hypotensive effect of UCP was most pronounced at 3mo postoperatively<sup>[6,17,22-23,25]</sup>. Nevertheless, a more extensive sample size is imperative to elucidate the evolving trajectory of UCP's hypotensive impact. Such an endeavor would significantly enhance the all-encompassing assessment of the surgical procedure's enduring effectiveness and furnish more dependable evidence for clinical interventions.

**2)** The success rate of the last follow-up after surgery Current research on the efficacy of UCP treatment for glaucoma in Asian populations has predominantly concentrated on shortterm follow-ups, typically spanning a 12-month duration. The comparison of success rates at the final follow-up post-surgery in each study is outlined in Table 2. We compared the surgical

success rates at the final follow-up of various studies and found that the majority of studies reported a success rate of over 60% at the last follow-up. The specific surgical success rates and recommendation levels for each institution was presented in Table 3<sup>[4-14,16-20,22-28,33]</sup>. Specifically, the average surgical success rate during short-term follow-ups was 66.63%, while the average surgical success rate during long-term follow-ups was 60.38%. This suggested that UCP may pose certain challenges in terms of long-term effectiveness, necessitating further research to explore the durability and long-term efficacy of the procedure. It is noteworthy that the surgical success rate in short-term follow-ups tends to be marginally higher than that observed in long-term follow-ups. This observation suggests that the reduction in IOP is more pronounced in the immediate postoperative period; however, over time, there may be a tendency for IOP to rebound, potentially resulting in a slightly lower surgical success rate during long-term followups. Hence, clinicians are urged to incorporate long-term follow-up data and integrate them with other pertinent clinical indicators to conduct a thorough evaluation of the efficacy of UCP surgery. Moreover, larger-scale, multicenter, randomized controlled trials are essential to substantiate the surgical success rate and postoperative complications associated with

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Table 4 Complications after UCP in each center

Institutions	Complications (cases)
Zhongshan Ophthalmic Center <sup>[4]</sup>	Anterior chamber reaction (22), conjunctival hyperemia (15), keratic precipitates (15), chemosis (14), intraoperative pain (13), subconjunctival hemorrhage (13), scleral thinning (12)
The First Affiliated Hospital of Zhengzhou University <sup>[5]</sup>	Corneal edema (10), conjunctival hyperemia (24), transient high IOP (2)
The Ophthalmology Department of Qingdao University Affiliated Hospital <sup>[6]</sup>	Conjunctival hyperemia (17)
King Saud University College of Medicine <sup>[7]</sup>	Early stage (within 1mo): anterior chamber reaction (44), IOP spike (39), corneal defect (2), corneal edema (2); Late stage: cataract development (34), prolonged/rebound anterior chamber, reaction (13), macular edema (5), choroidal detachment (3), phthisis bulbi (3), hypotony (2), posterior synechia (1), aqueous misdirection (1), scleritis (1), progression of visual field defect (1)
King Saud University College of Medicine <sup>(8)</sup>	Early stage (within 1mo): anterior chamber reaction (19), corneal defect (2), IOP spike (2), corneal edema (1); Late stage: cataract development (17), anterior chamber reaction (9), macular edema development (4), phthisis bulbi (1)
Mansoura University School of Medicine <sup>[9]</sup>	Anterior chamber reaction (62), punctate keratitis (6), macular edema (3), mydriasis (2)
The Qingdao Eye Hospital of Shandong First Medical University <sup>10]</sup>	Conjunctival hyperemia (13), anterior chamber reaction (10), scleral ring congestion (3), scleral impression (3)
Foshan Hospital of Southern Medical University <sup>[11]</sup>	Conjunctival hyperemia (61), scleral impression (2), hypotony (3), choroidal detachment (1)
Win Vision Eye Hospital in India <sup>[12]</sup>	Subconjunctival hemorrhage (4), anterior chamber reaction (67), superficial punctate keratitis (4), conjunctival hyperemia (67), corneal defect (3)
King Saud University College of Medicine <sup>[13]</sup>	Cataract development (8), prolonged anterior chamber reaction (7)
The First Affiliated Hospital of Anhui Medical University <sup>[14]</sup>	Eye pain (6), conjunctival hyperemia (24)
The Ophthalmology Department of Foshan Hospital of Southern Medical University <sup>[16]</sup>	Conjunctival hyperemia (24)
Ningxia Hui Autonomous Region People's Hospital Ophthalmology Hospital <sup>[17]</sup>	Conjunctival hyperemia (4)
Lianyungang Eye Hospital <sup>[18]</sup>	Eye pain (3)
The First Affiliated Hospital of Zhengzhou University Ophthalmology <sup>[19]</sup>	Conjunctival hyperemia (22)
The First Affiliated Hospital of Bengbu Medical College <sup>[20]</sup>	Conjunctival hyperemia (4), corneal edema (1)
Pidu District Hospital of Traditional Chinese Medicine <sup>[22]</sup>	Conjunctival hyperemia (11), corneal edema (5), anterior chamber reaction (4)
The Second Affiliated Hospital of Anhui Medical University <sup>[23]</sup>	Conjunctival hyperemia (4)
The Second Affiliated Hospital of Nanjing Medical University in Wuxi <sup>[24]</sup>	Eye soreness (1)
The Second Affiliated Hospital of Anhui Medical University <sup>[25]</sup>	Conjunctival hyperemia (23), superficial punctate keratitis (2), postoperative IOP out of control (1)
The First Affiliated Hospital of Zhengzhou University <sup>[26]</sup>	Pain (10), anterior chamber reaction (6), conjunctival edema (19)
King Abdul Aziz University Hospital <sup>[27]</sup>	Anterior chamber reaction (17), cataract development (13), choroidal detachment (3)
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University <sup>[28]</sup>	Pain (4), loss of visual acuity >2 lines (1), induced astigmatism >1 D (1), conjunctival hyperemia (3)
The Affiliated Xuzhou Municipal Hospital of Xuzhou Medical University <sup>[33]</sup>	Scleral marks (6), ocular pain (4), loss of vision >2 lines at last follow-up (1), conjunctival hyperemia (3)

IOP: Intraocular pressure; UCP: Ultrasound cyclo-plasty.

UCP. The implementation of such studies will enhance the thorough assessment of the effectiveness and safety of UCP surgery, yielding more dependable evidence for clinical practice.

**Safety** Existing research both domestically and internationally generally supports the notion that UCP is a non-invasive and relatively safe treatment method. The comparison of the complications after surgery in each study was summarized in Table 4<sup>[4-14,16-20,22-28,33]</sup>. Summarizing all the complications mentioned in the articles about the efficacy of UCP in Asian populations, the occurrence rates are as follows, sorted by frequency: conjunctival hyperemia 27.2%, cataract development 6.80%, IOP spike 5.29%, corneal edema 2.27%,

anterior chamber reaction 1.79%, punctate keratitis 1.42%, macular edema 1.42%, anterior uveitis 1.23%, corneal abrasion 1.23%, hyphemia 1.13%, scleral thinning 1.13%, transient hypotony 1.04%, choroidal detachment 0.94%, scleral imprint 0.76%, subconjunctival hemorrhage 0.47%, ocular deformity 0.38%, induced astigmatism 0.28%, mydriasis 0.28%, scleral ring congestion 0.28%, aqueous misdirection 0.19%, posterior synechia 0.09%, scleritis 0.09%, loss of vision because of high IOP 0.09%, postoperative uncontrolled IOP 0.09%, ocular discomfort 0.09%, phthisis bulbi 0.09%, loss of visual acuity (>2 lines) 0.09%. Among these, conjunctival congestion is the most common complication in Asian populations undergoing UCP, with the highest frequency of occurrence.

This is consistent with the data reported by other scholars<sup>[31,34]</sup>. However, conjunctival congestion is usually temporary and will resolve on its own within several days or weeks after the surgery. Non-steroidal anti-inflammatory drugs are typically needed to alleviate the symptoms after the surgery. Second, cataract progression ranks second<sup>[8,13,27]</sup>. The main reason for cataract progression is age evolution, considering preexisting cataract before UCP procedure. Another possible reason is related to the UCP mechanism: necrosis of the ciliary epithelium, further leading to the breakdown of the bloodaqueous barrier and the outflow of inflammatory mediators<sup>[35]</sup>. IOP spike can be observe in case of ocular inflammation, and sometimes due to the fact that patients stopped antiglaucoma medications after UCP procedure. Generally, most complications will resolve on their own or with treatment within 30d after the surgery. Wang *et al*<sup>[33]</sup> have compared the postoperative complications and surgical safety between UCP and endoscopic cyclophotocoagulation procedures, and they found that the UCP group had fewer postoperative complications than the endoscopic cyclophotocoagulation group (respectively 18 cases in the UCP group and 35 cases in the endoscopic cyclophotocoagulation group). In general, UCP is considered a safe, effective, and well-tolerated treatment modality<sup>[31]</sup>. Additionally, it is crucial for clinicians to have a comprehensive understanding of the potential complications that may arise from UCP procedures. The incidence rates and specific characteristics of these complications serve as valuable guidelines for clinicians, enabling them to conduct more precise risk-benefit assessments for patients undergoing the procedure.

Shortcomings and Prospects The limitations of this review stem from the constrained scope and limited volume of literature retrieval, as well as discrepancies in study quality. Future research endeavors should aim to expand the breadth of literature retrieval and augment the number of studies to provide a comprehensive evaluation of UCP efficacy. Additionally, considering the diverse subtypes and individual variations in glaucoma among Asian populations, the effectiveness of UCP may vary across different glaucoma types. Therefore, further investigation is warranted to explore the varying efficacy of UCP across distinct glaucoma types and to formulate more tailored treatment approaches for specific glaucoma subtypes. Moreover, there is a necessity for more rigorous and standardized success criteria for UCP and glaucoma surgeries in general. These criteria should encompass baseline IOP reduction, postoperative IOP levels, decrease in glaucoma medication usage, alterations in patient pain scores, and incidence of complications to accurately evaluate surgical outcomes. Future research should prioritize

targeted studies, particularly focusing on the impact of factors such as baseline IOP, selection of treatment zones, and duration of exposure of the ultrasound probe on surgical efficacy. In addition to the 48-month follow-up conducted by Almobarak *et al*<sup>[7]</sup>, there remains a significant lack of research on the long-term efficacy and safety of UCP treatment for glaucoma in Asian populations. The majority of researchers have only pursued postoperative follow-ups for three months. Hence, extensive research efforts are essential to comprehensively evaluate the long-term effectiveness and safety of UCP surgery in managing glaucoma among Asian populations.

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