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Efficacy of Combined Phacoemulsification and Goniosynechialysis in the Treatment of Patients with Primary Angle Closure Disease and Concomitant Cataract at Preah Ang Duong Hospital in Cambodia

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Abstract

Background: Goniosynechialysis is a surgical procedure that has been shown to slow the progression of glaucoma in oriental eyes with chronic angle closure glaucoma. This procedure was successful in 80% of cases, and the peripheral anterior syenchiae did not exist until one year later. Nonetheless, there is little evidence of its efficacy in our context. Our study aims to investigate the efficacy of goniosynechialysis during phacoemulsification in patients with primary angle closure disease and concomitant cataract. **Methods:** This was an observational, prospective study. The intra-ocular pressure, need for anti-glaucoma drugs, visual acuity, the extent of synechiae, anterior chamber depth, surgical success rate, and other indicators were monitored for at least three months following surgery. **Results:** This study included 114 patients (118 eyes), 61 with chronic angle closure glaucoma (51.69%), 33 with primary angle closure (27.97%), and 24 with acute attack angle closure (20.34%), who were surgically treated with phacoemulsification and goniosynechialysis (Phaco-GSL). The mean intra-ocular pressure had significantly decreased three months after surgery (pre- vs post-op: 22.04 ± 10.86 vs 15.41 ± 6.06 mmHg, p-value < 0.00001). The anti-glaucoma drugs also decreased (median, 2 vs none, p-value < 0.05). The median visual acuity increased (0.50 vs 0.40 logMAR, p-value < 0.05). The extent of synechiae reduced (135.00 ± 89.68 vs 72.80 ± 61.64 degrees, p-value < 0.00001). Furthermore, the anterior chamber depth increased from 1.47 ± 0.40 to 2.79 ± 0.50 mm, p-value <

0.00001. Despite fibrins and hyphema in the early period, no remarkable complications were found in long-term follow-up. **Conclusion:** Regardless of the type of glaucoma, combined phacoemulsification-goniosynechialysis is effective in lowering pressure, restoring vision, reducing the need for anti-glaucoma drugs, and preventing the synechial recurrence. Success was higher in eyes with less extensive synechiae. Phaco-GSL is safe and effective in the treatment of primary angle closure diseases with co-existing cataract.

Keywords

Efficacy, Phacoemulsification, Goniosynechialysis, Primary Angle-Closure Disease, Chronic Angle-Closure Glaucoma, Gonioscopy, Intra-Ocular Pressure, Peripheral Anterior Synechiae, Anti-Glaucoma Drugs, Anterior Chamber Depth

1. Introduction

The World Health Organization (WHO) released a global estimate in 2010 that showed 39 million people living with blindness and 285 million living with visual impairment worldwide [1]. Similarly, overall blindness decreased by 15.40% in December 2020, but the number of cases with visual impairment and avoidable blindness increased significantly by 31.50% and 10.80%, respectively [2]. Furthermore, according to the International Agency for the Prevention of Blindness (IAPB), glaucoma is the fourth leading cause of irreversible blindness in 2015 [3], there are 3 million people worldwide who are blind due to glaucoma alone. Also in 2010, glaucoma stands out as the 2nd leading cause of blindness worldwide [1] and is also responsible for 8.30% of avoidable blindness in Cambodia [Rapid Assessment of Avoidable Blindness (RAAB) 2019].

Glaucoma is a group of diseases characterized by deterioration and atrophy of the optic nerve head as a result of increased intraocular pressure (IOP), resulting in visual field defects and, ultimately, visual impairment [4]. Glaucoma is classified into several types, most notably open and closed angle glaucomas. In particular, a shallow anterior chamber and an extended range of permanent peripheral anterior synechiae (PAS) are common causes of angle-closure glaucoma, resulting in blocked or obscured outflow of aqueous humour and a subsequent increase in pressure [5].

Primary angle-closure glaucoma (PACG) is a major cause of blindness worldwide, comprising of a disease of ocular anatomy associated with the pupillary block and angle crowding or a combination of both. Cataract, on the other hand, a disease of the elderly, is often concurrent with PACG in patients of old age. The thickened and more anterior-positioned lens plays a crucial role in the development of angle-closure glaucoma. When getting older, the lens progressively increases in both size and thickness and gradually approaches the pupil margin, resulting in a pupillary block. This causes a continuous increase in posterior

chamber pressure and further compression of the peripheral iris, leading to anterior chamber angle stenosis or even closure [6]. Thus, cataract removal has been used to deepen the anterior chamber and open the irido-corneal angle, and subsequently reducing the intra-ocular pressure [7]-[9]. More specifically, in chronic angle-closure glaucoma (CACG), portions of the anterior chamber angle are permanently closed by PAS [10]. The amount of damage to the trabecular meshwork, which may or may not correlate with the extent of PAS, determines intraocular pressure (IOP) control after appositional closure removal. When PAS closes greater than 180˚ (degrees) of the angle, intra-ocular pressure is usually elevated. Medical therapy is usually ineffective when more than 270˚ of the angle is closed, and filtering surgery becomes increasingly necessary [10] [11].

In adult Asians, the overall pooled prevalence of primary angle-closure glaucoma (PACG) was 0.75%. Pooled prevalence estimates by ethnicity were 0.97% in the Middle East group, 0.66% in the Southeast Asian group, 0.46% in India, 1.10% in China, and 1.19% in Japan, respectively [12]. Oriental eyes are thought to be predisposed to angle-closure and angle-closure glaucomas, particularly creeping angle-closure glaucoma with peripheral anterior synechiae formation [13].

To the best of our knowledge, phacoemulsification and intra-ocular lens (IOL) implantation can significantly reduce IOL in patients with PACG and co-existing cataracts. However, in patients with chronic angle-closure glaucoma or extensive gonio-synechial closure, the angle may remain firmly closed by the peripheral anterior synechiae even after lens extraction and replacement with a much better artificial IOL [14]. Also, further surgery aimed to maintain pressure control was need; combined phacoemulsification and trabeculectomy have been proposed for the treatment of chronic angle-closure glaucoma, as well.

To date, combined phacoemulsification, IOL implantation, and goniosynechialysis (Phaco-GSL) has been used in the treatment of PACG and cataracts, and it is quite safe and effective for intraocular pressure control in PACG with more than 180 degrees of peripheral anterior synechiae. This procedure is said to have theoretically provided high-quality visual rehabilitation, IOP spike prevention, angle widening after crystalline lens removal, and a decrease in bleb-less complications post-operatively [10].

Goniosynechialysis (GSL) is quite effective in lowering IOP in oriental eyes with chronic angle-closure glaucoma and PAS [15]. GSL is a method of deepening the anterior chamber angle in cataract surgery using a mechanical or viscoelastic agent, or both [10] [16]. The procedure is not only difficult, but complications are reported less frequently than in trabeculectomy or phaco-trabeculectomy. Some researchers discovered that phacoemulsification with goniosynechialysis (Phaco-GSL) had better pressure control than phacoemulsification alone [17] [18]. GSL is a surgical procedure designed to strip PAS from the angle and restore trabecular function in eyes with chronic angle-closure glaucoma. The procedure is successful in approximately 80% of eyes if the PAS has been present for less than 1 year [11]. Although GSL has not become widely popular in the

United States, it has in Japan, where promising results have been both phakic and pseudophakic eyes [15]. It can be effective in angle-closure glaucoma (ACG) when performed by itself, in conjunction with other surgical procedures [15] [19], and after failed filtration surgery [20].

However, whether combined phacoemulsification with goniosynechialysis for the treatment of patients with narrowed chamber angles and cataract(s) remains a contentious and hotly debated issue around the world, and particularly in our region, according to a meta-analysis of the study on combined phacoemulsification with GSL in the Chinese population with angle-closure glaucoma and cataract, and his study has shown a good result concerning better pressure control and an end to the reformation of PAS [21].

This study aims to examine the efficacy of combined phacoemulsification with intraocular lens implantation, and "goniosynechialysis" in patients with primary angle-closure disease and visually disabling cataract. Aside from the effect of lowering pressure and reducing anti-glaucoma drugs required post-operatively, and we hope to provide more reliable clinical data for the treatment of these patient groups. Last but not least, we investigate the frequency, timing, and extent of post-operative reformation of peripheral anterior synechiae (re-PAS) as well as recurrent complications.

2. Methodology

2.1. Study Design

A prospective, observational study was conducted from 1st December 2021 to 30th September 2022 (Duration: 10 months) at Preah Ang Duong Hospital. For the first three months following surgery, the intraocular pressure (IOP), the need for anti-glaucoma drugs, visual acuity, the extent of peripheral anterior synechiae (PAS), including the occurrence of PAS (re-PAS), surgical success rate, subsequent complications, and other indicators were monitored. The success cut-off point was set at three months, and the follow-up ended on the sixth month.

2.2. Study Site

Department of Ophthalmology, Preah Ang Duong Hospital (PADH), was chosen as the study site. Preah Ang Duong Hospital is one of the prestigious public hospitals and training centers. Preah Ang Duong Hospital is located in lots N˚118, Corner Kramuon Sar Street (St. 114) and Preah Norodom Blvd (St. 41), Sangkat Phsar Thmey I, Khan Daun Penh, Phnom Penh, Cambodia 12208.

2.3. Study Population

Eligibility Criteria:

This study included patients diagnosed with "primary angle-closure" or "primary angle-closure glaucoma" and cataract(s) by glaucoma specialists, who would then undergo surgical therapy and met the eligibility criteria with "informed consent" from 1st December 2021 to 30th September 2022 at Preah Ang Duong Hos-

pital. Patients must have existing cataracts, have best-corrected visual acuity less than 0.5 LogMAR (6/18 Snellen chart), and/or be complaining about visual obscuration, and/or having acute episode in the fellow eye or in the operated eye previously, and may require cataract extraction surgery to improve vision.

The study enrolled patients who met the following baseline criteria: 1) Patients of Asian ethnicity; 2) Age of 25 years or older; 3) Need for a combined cataract procedure; 4) Patients with primary angle closures or medically uncontrolled primary angle-closure glaucoma; 5) Patients with high intraocular pressure (IOP) of 21 mmHg or above while on at least one anti-glaucoma drug or despite maximal tolerated anti-glaucoma drugs; 6) Patients with extensive peripheral anterior synechiae exceeding 180 degrees or involving 2 quadrants (of clock-hours); and, 7) Patients showing unstable progression, such as rapid progression of glaucomatous damage as evidenced by ocular computed tomography of the optic disc and/or peri-metric visual field status.

Exclusion criteria were as follows: 1) Patients with a history of uveitis or trauma or severe systemic diseases; 2) Patients who had undergone prior intra-ocular intervention or surgery (e.g. laser iridoplasty, laser peripheral iridotomy, and anterior chamber paracentesis); 3) Patients with an ocular disease known to affect anterior segment anatomy (e.g. ciliary body or iris cysts), or on long-term use of topical or systemic drugs (e.g. Steroids) affecting iris configuration; and, 4) Unwilling to participate in the study.

Sample Size and Sampling Method:

Data collection lasted for six months, starting from 01st December 2021 to 01st June 2022. In total, **114 patients** (*n* = **118 eyes**) were conveniently selected for the study. Besides, 24 patients (31 eyes) were excluded from the study because the eligibility criteria were missed out.

2.4. Data Collection Tools

A structured checklist was created and modified by the investigator based on previous literature [10] [19] [22]-[27]. The checklist was divided into two sections: Section 1 contains socio-demographic information such as age, gender, occupation, and place of residence. Section 2 includes clinical and therapeutic data such as the laterality of the affected eye, and associated ocular and general conditions, type of glaucoma, best-corrected visual acuity, ocular biometric data (mainly focusing on anterior chamber depth in milimeters), intra-ocular pressure (mmHg), the extent of peripheral anterior synechiae (in clock-hours, or degrees), visual field defects by perimetry (Oculus® twin-field 2 static perimetry), examination of the retinal gangion cells and retinal nerve fiber layers, and optic nerve head by ocular computed tomography (Zeiss® CIRRUS 500 OCT), number of anti-glaucoma drugs, and subsequent complications (See **Table 3**).

The intraocular pressure (IOP) from baseline and in each follow-up was measured using the air-puff tonometer (Tomey®). The IOP value was read off the scale and recorded in the medical records. At least, the mean of two meas-

urements with a time interval of five minutes was taken.

2.5. Data Collection Process

The data was gathered by the principal investigator (KCR), with assistance from a team of five glaucoma surgeons (CKS, SBS, SSO, KCD, and LSV) (See Abbreviations). Before surgery, all patients underwent a comprehensive ophthalmologic examination, and the following variables were recorded to determine the outcome of the procedure. The baseline examination before surgery would be done thoroughly. Follow-up visits were at 1 day, 1 week, 1 month (3 - 4 weeks), 3 months (12 weeks), and 6 months after the operation, and then, if possibly, every 3 months post-operatively (in 9- and 12-months post-op).

Furthermore, routine ophthalmic examinations were done and repeated at each post-surgical follow-up visit. The follow-up visits and the number of examination procedures were increased when deemed necessary. A complete ocular examination was performed each time, including best-corrected visual acuity (BCVA) by Snellen Chart (3 meters converted), slit-lamp exam, and fundus exam except the following: 1) IOP was measured by non-contact tonometers (iCare TA01i hand-held tonometer or Air-puff tonometer Tomey®) on the 1st day and 1st month after the operation, while Goldmann tonometer was used to measure intra-ocular pressure at the other follow-ups onwards; 2) gonioscopy (4-mirror Gss Volk® Indentation Gonio-lens) was performed at every follow-up visit beginning at the month 1 post-op exam; and 3) ocular biometry (Zeiss® IOL Master 500) was checked at every visit starting at month 3 post-operatively.

Criteria of Success:

The criteria used to define "surgical success" are as follows:

1) "Complete success" is achieved if the intraocular pressure (IOP) is less than 21 mmHg without requiring any additional treatment.

2) "Qualified success" is achieved if the IOP is 21 mmHg or less with the use of at least one eye pressure-lowering medication or the need for further surgery to manage the pressure.

3) "Failure" is indicated by an elevated IOP of more than 21 mmHg, including a measurement of 25 mmHg using the Goldmann applanation tonometer, or at least two measurements exceeding 21 mmHg (excluding measurements affected by residual visco-elastic agents or steroids). Additionally, failure is also indicated by a significant increase in peripheral anterior synechiae (PAS) beyond half a degree from 2:00 to 10:00 clock hours before surgery, or when the extent of PAS is equal to or exceeds 180˚ overall.

2.6. Data Management and Analysis

The collected data was double-checked for accuracy before being entered into Microsoft Excel® 2016 for Windows 8. STATA® Version 14.2 was used to analyse the results (StataCorp LP, College Station, TX).

For normally distributed data, the parametric test (Student's paired *t*-test, or

single-factor ANOVA) was used, while Wilcoxon's signed rank test was used for highly skewed data.

Univariate linear regression was used to examine variables being hypothesized to be associated with a reduction in IOP, a reduction in the number of anti-glaucoma drugs, a reduction in PAS, or an increase in ACD. Potential predictor variables include age, sex, laterality of the affected eye, glaucoma type or severity, visual acuity, baseline IOP, number of anti-glaucoma medications taken at baseline, and extent of PAS in degrees or clock-hours. A p-value of 0.05 or less was considered statistically significant.

2.7. Ethical Approval

The study was approved by the National Ethics Committee for Health Research, Ministry of Health, Cambodia on October 25th, 2021 (N˚258/2021 NECHR) and was carried out in accordance with the tenets of the Helsinki Declaration (See Annexes). All study participants provided written informed consent after the purposes and aims of the study were clearly explained beforehand.

2.8. Funding and Supports

This study was financially supported by a research grant in ophthalmology and ophthalmic cares from the Fred Hollows Foundations (FHF), as well as the Faculty of Medicine at the University of Health Sciences (UHS) and professors and mentors in the Ophthalmology Residency Training (ORT) program. The Cambodian Ophthalmological Society (COS) provided technical support for this study, which was later implemented at the Department of Ophthalmology, Preah Ang Duong Hospital (PADH), and coordinated and facilitated by the National Program for Eye Health (NPEH), Ministry of Health (MoH).

The study's funder(s) had no involvement in the study's design, data collection, data analysis, data interpretation, or report writing. The principal investigator (KCR) had full access to all study data. And, the principal investigator, both supervisor and co-supervisor are ultimately responsible for the decision to submit the manuscript for publication.

2.9. Surgical Procedure

Phacoemulsification combined with goniosynechialysis: The surgery was performed under local anesthesia by a glaucoma specialist(s) (CKS, SBS, KCR, SSO, KCD, and LSV), and may have assembled surgical steps as following (23): 1) Clear corneal incision phacoemulsification will be performed with an IOL implantation within the capsular bag; 2) Visco-elastic then was injected in the anterior chamber, especially into the anterior angles, to substantially deepen the peripheral anterior chamber; 3) Goniolens (Swan-Jacobs® surgical gonioprism lens) was placed on the cornea with coupling visco-elastic devices to visualize the angle; 4) Visible peripheral anterior synechiae (PAS) was gently broken under direct visualization by pushing down on the peripheral iris with a flat spatula

through the main wound or side-port incision (See Image 1). The end-point of the procedure was the visibility of the scleral spur. At a minimum, 240˚ (2:00~10:00 clock-hours) of angle could be seen and treated in this manner. The superior section was the most technically difficult to see and often was treated without the guidance of a gonio-lens; and 5) At the end of this procedure, the visco-elastic agent would be washed out and replaced with a balanced salt solution (BSS), air-exchange anterior chamber tamponade was in place to prevent any obvious bleeding from the angles, and the incision is hydrostatically sealed. To be noted, goniosyenchialysis can be done by two different methods or both combined: mechanical goniosynechialysis (MGSL) and visco-goniosynechialysis (VGSL) [23].

Image 1. The spatula is inserted through side-port wound and then used to manipulate the anterior chamber angle by gently breaking the synechiae after injecting viscoelastic agent and forming the anterior chamber, with assistance of Swan-Jacob gonioprism. (Photo courtesy of Sea Bunseng, MD)

All patients in post-operative care received topical steroids as well as topical antibiotics for 4 to 5 weeks, depending on clinical need. Anti-glaucoma medications will be stopped after surgery and restarted if necessary and as directed by a glaucoma specialist(s).

3. Results

This study included 138 patients (149 eyes) in total. Among those, 24 patients (31 eyes) were excluded from the study, including 1 patient (2 eyes) with chronic uveitis, 2 patients (2 eyes) who had already had prophylactic laser peripheral iridotomy, 1 patient (2 eyes) who had long-term use of systemic steroid (Methylprednisolone: Medixon®), 3 patients (3 eyes) who had severe ocular trauma history with/without angle recession, and 4 patients (8 eyes) who had peripheral anterior synechiae (PAS) less than 1 quadrant or cumulative PAS less than 90 degrees, and other 13 patients (14 eyes) had no complete documents.

This study examined 118 eyes from 114 patients, with a mean age of 54.22 ± 10.78 (range, 32 to 80) years old, and women made up three quarters of the total number of patients (75.44%, n = 86 patients) (women, 86 vs. men, 28). The median best-correct visual acuity (BCVA) at baseline was 0.50 logMAR (range 0.20

to 3.00). The mean intraocular pressure (IOP) at baseline was 22.04 ± 10.86 mmHg. The median number of anti-glaucoma drugs required prior to surgery was one (range, none to 4 drugs). At baseline, the average extent of peripheral anterior synechiae (PAS) was 135.00 ± 89.68 degrees. In terms of ocular biometrics, the mean anterior chamber depth (ACD) was 1.52 ± 0.34 mm. Although some reported complications from "direct" angle procedures, such as mild to severe iris or trabeculum haemorrhage, choroidal detachment, and shallow anterior chamber, our study found far too few.

3.1. Socio-Demographic Characteristics

Our patients were divided into five age groups based on their age. There were 9 patients (7.89%) between the ages of 31 and 40, 36 patients (31.58%) between the ages of 41 and 50, 41 patients (35.96%) between the ages of 51 and 60, 20 patients (17.54%) between the ages of 61 and 70, and 8 patients (7.02%) between the ages of 71 and 80. Most importantly, in our study, the age group 51 - 60 years old is the largest. Furthermore, the mean age of treated participants was 54.22 ± 10.78 years (range, 32 to 80).

Table 1. Socio-demographic profiles.

Variables		
Age, y: **54.22 ± 10.78** (Range 32 - 80)		
Gender (n of patients, total)	**114**	Proportion
Women	86	75.44%
Men	28	24.56%
Residence (n of patients, total)	**114**	
Phnom Penh	61	53.51%
Kandal	10	8.77%
Takeo	9	7.89%
Kampong Chhnang	8	7.02%
Kampong Cham	7	6.14%
Battambang	6	5.26%
Siem Reap	5	4.39%
Sihanoukville	4	3.51%
Prey Veng	4	3.51%
Diagnosis (n of eyes, total)	**118**	
Chronic angle closure glaucoma	61	51.69%
Acute attack angle closure	24	20.34%
Primary angle closure	33	27.97%
Laterality (n of eyes, total)	**118**	
Right Eye	86	72.88%
Left Eye	32	27.12%

The majority of the 114 patients (75.44%, n = 86) were women, with the remainder being men (24.56%, n = 28). Table 1 summarizes the full demographics. The majority of the participants, 53.51% (n = 61), lived in Phnom Penh or in some suburban areas of the town or city.

In terms of diagnosis distribution, chronic angle closure glaucoma was the most common (n = 61 eyes, 51.69%), followed by primary angle closure glaucoma (n = 33 eyes, 27.97%) and acute attack angle closure glaucoma (n = 24 eyes, 20.34%). Three-quarters of the affected eyes in this study (72.88%) were right eyes, with the remaining quarter (27.12%) being left eyes.

3.2. Visual Acuity

The baseline best-corrected visual acuity (BCVA) ranged from 0.20 logMAR (6/9.5 on Snellen Chart 3 meters) to 3.00 logMAR (Snellen, Hand Motion). The median best-corrected visual acuity (BCVA) at baseline was 0.50 (Snellen, 6/19), which improved over time to 0.50 logMAR (range, 0.00 - 3.00; Snellen 6/6 to HM), 0.45 logMAR (range, 0.00 - 3.00; Snellen 6/6 to HM), and 0.40 logMAR (range, 0.00 - 3.00; Snellen 6/6 to HM) at day 1, week 1, month 1, and month 3 (p-value < 0.00001).

As a baseline, the mean BCVA is 0.72 ± 0.55 logMAR. The post-op visual acuity was 0.61 ± 0.57 logMAR, 0.61 ± 0.58 logMAR, 0.57 ± 0.53 logMAR, and 0.47 ± 0.50 logMAR at day 1, week 1, month 1, and month 3, respectively (Figure 1). At the final follow-up visit, none of the patients' visual acuity had deteriorated.

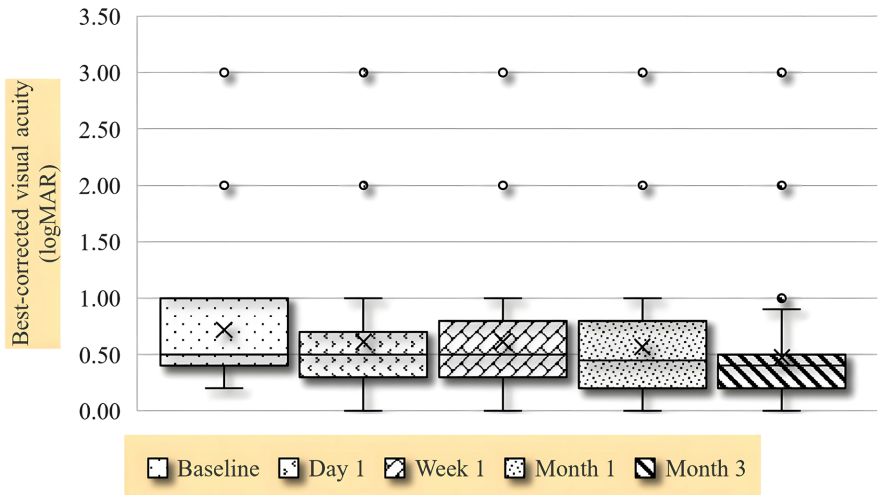

Figure 1. Box-plot of best-corrected visual acuity.

3.3. Intra-Ocular Pressure

Mean intra-ocular pressure was reduced in all eyes from 22.04 ± 10.86 mmHg pre-operatively to 17.30 ± 5.56 mmHg, 15.92 ± 4.72 mmHg, 17.49 ± 10.39 mmHg, and 15.41 ± 6.06 mmHg at day 1, week 1, month 1, and month 3, respectively. Figure 2 summarized the trend of intraocular pressure changes at various follow-up visits. When compared to pre-treatment pressures, all time points showed a significant reduction in pressure. The mean pressure at different time points and

three months after surgery was significantly lower than the baseline pressures (p-value < 0.00001).

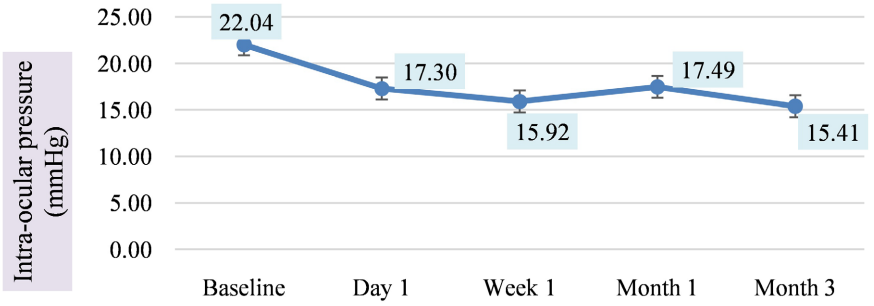

Figure 2. Intra-ocular pressure changed over time. Comments: Mean IOP (±SD) progression curve in mmHg over the consecutive follow-up periods. The X-axis represents the different follow-up periods, and the Y-axis represents mean IOP (± SD).

3.4. Number of Anti-Glaucoma Drugs Required

Only 10 (8.47%) of all participants (n = 114) did not use any drugs to lower intra-ocular pressure via topically or systemically. The median number of anti-glaucoma drugs required pre-operatively or used as needed to lower the pressure was one (range, none to four) (See Table 2). At week 1, month 1, and month 3, the median number of anti-glaucoma drugs used was none (range, 0 to 3), none (range, 0 to 2), and none (range, 0 to 2) (p-value < 0.00001) (Figure 3 & Figure 4).

Table 2. Clinical and therapeutic profiles.

Variables		Baseline	Day 1	Week 1	Month 1	Month 3
Best Corrected Visual Acuity (logMAR):		0.72 ± 0.55	0.61 ± 0.57	0.61 ± 0.58	0.57 ± 0.53	0.47 ± 0.50
Mean ± SD		0.50	0.50	0.50	0.45	0.40
Median, Range		(0.20 - 3.00)	(0.00 - 3.00)	(0.00 - 3.00)	(0.00 - 3.00)	(0.00 - 3.00)
	p-value*					<0.00001
Intra-ocular Pressure (mmHg): *Mean ± SD*		22.04 ± 10.86	17.30 ± 5.56	15.92 ± 4.72	17.49 ± 10.39	15.41 ± 6.06
	p-value*					<0.00001
Number of Drugs Required:		1.72 ± 1.09	---	0.49 ± 0.76	0.36 ± 0.56	0.27 ± 0.50
Mean ± SD		1		0	0	0
Median, Range		(0 - 4)		(0 - 3)	(0 - 2)	(0 - 2)
	p-value*					<0.00001
Extent of PAS (degrees): *Mean ± SD*		135.00 ± 89.68	---	---	83.14 ± 63.11	72.80 ± 61.64
	p-value*					<0.00001
Anterior Chamber Depth (mm): *Mean ± SD*		1.52 ± 0.34	---	---	---	3.00 ± 0.62
	p-value**					<0.00001

SD: Standard deviation; *Single factor ANOVA test, **Student's paired t test.

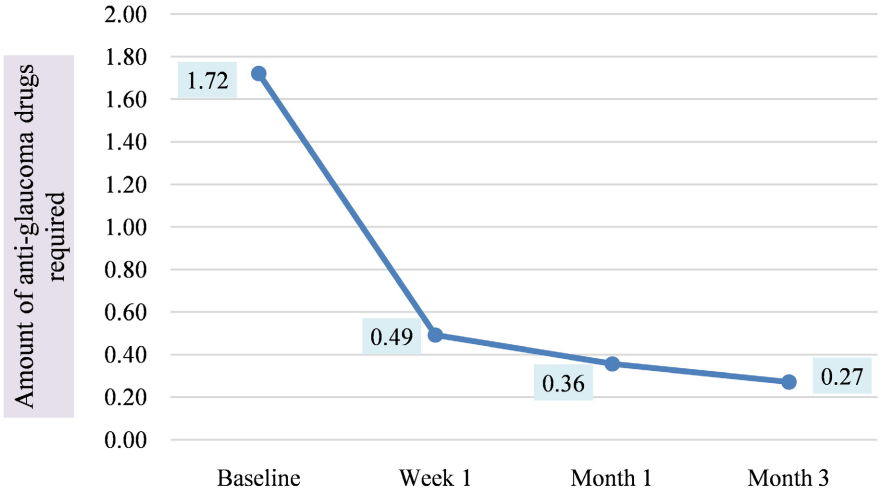

Figure 3. Amount of anti-glaucoma drugs required to lower pressure before and after surgery.

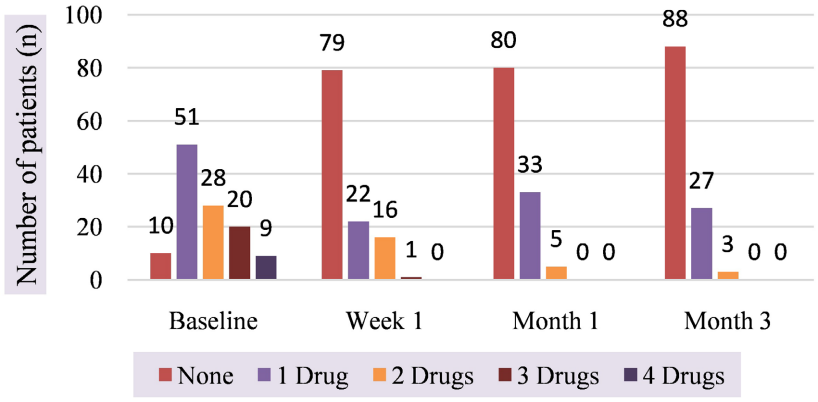

Figure 4. Number of patients using anti-glaucoma drugs stratified over follow-up period.

The average number of anti-glaucoma drugs taken at baseline was 1.72 ± 1.09, but after surgery, the number of drugs taken was reduced to 0.49 ± 0.76 at week 1, 0.36 ± 0.56 at week 3, and 0.27 ± 0.50 at month 3. Almost half of them (n = 51, 43.22%) used at least one anti-glaucoma drug, whether instilled through eye drops or taken orally. However, this trend has shifted over time, with the majority of them switching to none or no anti-glaucoma drugs at all. In the first post-operative week, 79 patients (66.95%) did not use any anti-glaucoma medications.

Furthermore, at first month post-operatively, 80 patients (67.80%) did not use any drugs, and at the final visits, 88 patients out of 114 (74.58%), or roughly three quarters of them, did not use any anti-glaucoma drugs in the long-term period to optimize intra-ocular pressure and thus prevent progression of the glaucoma.

3.5. Extent of Synechiae

Only 86 of the 118 eyes in this study had gonioscopic examinations, and the

mean extent of peripheral anterior synechia was 135.00 ± 89.68 degrees (simply ranging from 2 to 3.5 quadrants), and this amount decreases significantly after surgery (p-value < 0.00001) (See Table 2). This extent of synechiae was reduced to approximately 83.14 ± 63.11 degrees on average at month 1 post-operatively. Finally, by month 3, these values had dropped to around 72.80 ± 61.64 degrees (Figure 5) (Table 3).

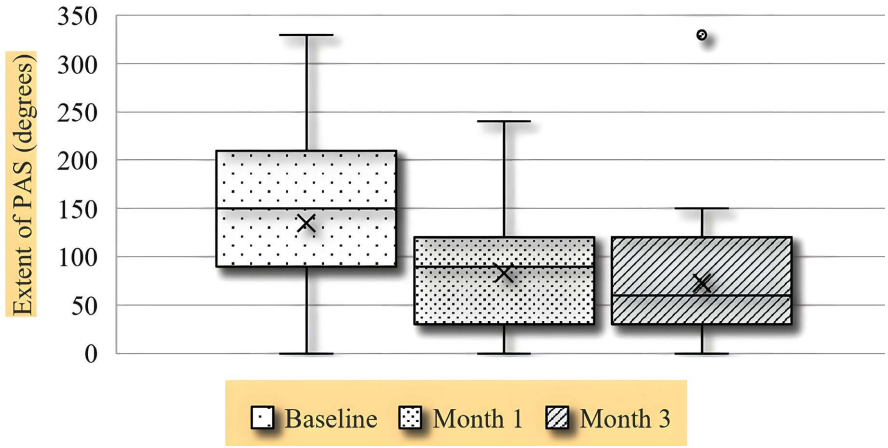

Figure 5. Extent of peripheral anterior synechiae over time.

Table 3. Distribution of anti-glaucoma required (frequency, proportion) over time.

	Baseline		Week 1		Month 1		Month 3	
Anti-glaucoma drugs used	*n*	*proportion*	*n*	*proportion*	*n*	*proportion*	*n*	*proportion*
None	10	8.47%	79	66.95%	80	67.80%	88	74.58%
1 Drug	51	43.22%	22	18.64%	33	27.97%	27	22.88%
2 Drugs	28	23.73%	16	13.56%	5	4.24%	3	2.54%
3 Drugs	20	16.95%	1	0.85%	0	0.00%	0	0.00%
4 Drugs	9	7.63%	0	0.00%	0	0.00%	0	0.00%
Total	118		118		118		118	

In terms of PAS recurrence, almost all of the eyes assessed (n = 52 eyes) have good PAS reduction from baseline. While 24 eyes had poor PAS reduction (n = 24 eyes), PAS recurred in 10 eyes more than pre-operatively. Aside from these, 24 eyes (20.34%, all with acute attack angle closure) were not properly assessed, and the remaining 8 eyes (6.78%) had few synechiae or hardly no PAS at baseline and hardly had any post-operatively at the final visit (See Table 4(a)).

Aside from that, among patients who were gonioscopically examined both pre- and post-operatively, 60.47% (n = 52 eyes) had good PAS reduction, 27.91% (n = 24 eyes) had poor PAS reduction, and 11.63% (n = 10 eyes) had more PAS than baseline (See Table 4(b)).

Table 4. (a) Status of PAS reduction. (b) Status of PAS reduction among gonioscopically examined patients.

(a)		
Status of PAS Reduction	Frequency	Proportion
Unknown	8	6.78%
Not Assessed	24	20.34%
Good PAS Reduction (*90 degrees or above*)	52	44.07%
Poor PAS Reduction (*<90 degrees*)	24	20.34%
PAS Recurrence (*>Baseline*)	10	8.47%
Total	118	
(b)		
Status of PAS Reduction (among gonioscopically examined patients)	Frequency	Proportion
Good PAS Reduction (*90 degrees or above*)	52	60.47%
Poor PAS Reduction (*<90 degrees*)	24	27.91%
PAS Recurrence (*>Baseline*)	10	11.63%
Total	86	

3.6. Anterior Chamber Depth

In terms of ocular biometric data, the average anterior chamber depth (ACD) at baseline was 1.52 ± 0.34 mm, which is considered relatively narrow in the Asian population in general (See **Table 2**). This depth was increased to approximately 3.00 ± 0.62 mm (p-value < 0.00001) at month 3 post-operatively, which may have been deepened after removing the natural cystralline lens and due to manually manipulating both combined mechanical and visco-elastic synechial breaking (**Figure 6**).

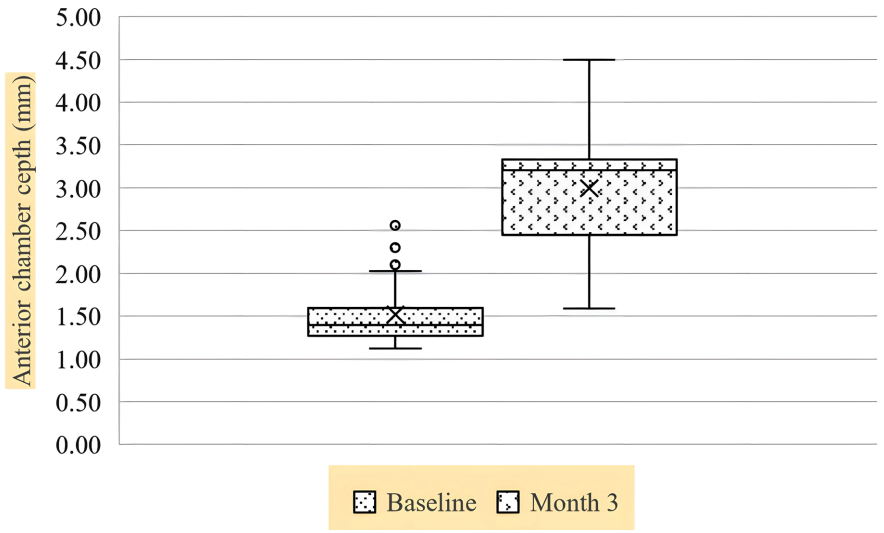

Figure 6. Distribution of anterior chamber depth.

3.7. Success Rate

According to the criteria of success mentioned above, 98 eyes (83.05%) were classified as "successful", while the remaining 20 eyes (16.95%) were classified as "failed" to surgery (See Table 5).

Table 5. Profile of success [3].

Criteria of Success	*n*	Proportion
Complete Success	75	63.56%
Qualified Success	23	19.49%
IOP ≤ 21 mmHg with 1 drug	20 eyes (16.95%)	
IOP ≤ 21 mmHg with 2 drugs	3 eyes (2.54%)	
Failure	20	16.95%
Recurrence of PAS ≥ 180 degrees	8 eyes (6.78%)	
IOP > 21 mmHg	12 eyes (10.17%)	
Total	118 eyes	100%

There were no significant complications associated with this procedure, both immediately and after 3 to 6 months of follow-up.

3.7.1. Level of Success

Among the 88 successful eyes, 70 (63.56%) were classified as "*complete success*", which means that the pressure in those eyes was 21 mmHg or lower after surgery at the final visit (month 3). Indeed, of the 23 (19.49%) "*qualified success*", 20 eyes (16.95%) used one drug only, while the remaining 3 (2.54%) required two drugs to achieve a pressure less than 21 mmHg post-operatively, or slowing progress of the glaucoma. Indeed, 8 eyes were considered as "*failed*" surgery due to the presence of re-occurrence of the extensive PAS cumulatively (more than 2 quadrants, or 180 degrees) after surgery at the final visit, while the other 12 eyes consistently had intra-ocular pressure greater than 21 mmHg over time.

3.7.2. Factors Associated with Success

Using bivariate logistic regression, all independent variables were tested for a crude association with the level of success (of the surgery). Multiple logistic analyses revealed that variables such as the laterality of the affected eye, the extent of PAS at baseline, and gender were significantly associated with success.

The odds of success in women's eyes were 0.15 times higher than in men's eyes (AOR = 0.15: 95% CI, 0.01 - 0.84), or simply put, men undergoing surgery are 6.67 times more likely to have a successful outcome than women. The odds of success in the left eye undergoing surgery are 0.16 times higher than in the right eye (AOR = 0.16: 95% CI, 0.02 - 0.92), implying that the right eye is 6.25 times more likely to produce satisfactory results than the left eye. Eyes with acute attack angle closure is 1.19 times (AOR = 1.19: 95% CI 0.12 - 11.83), and eyes with primary angle closure is 1.51 times (AOR = 1.51: 95% CI 0.39 - 5.88) more

likely to be successful compared to chronic angle closure glaucoma; however, these findings were not found to be statistically significant. When compared to those with lower pressure (21 mmHg), those with higher pressure are 1.15 times more likely to have a successful outcome after this procedure (AOR = 1.15: 95% CI 0.28 - 4.69). In terms of PAS extent at baseline, the odds of success of eyes with PAS extent of 91 - 180 degrees and extensive PAS (>180 degrees) are 0.07 times (AOR = 0.07: 95% CI, 0.00 - 0.76) and 0.03 times (AOR = 0.03: 95% CI, 0.00 - 0.37) more as compared to those with little PAS status or PAS less than 180 degrees. As a result, eyes with lower PAS are less likely to fail surgery. In terms of the anti-glaucoma drugs required at baseline, the odds of success were found to be 0.88 times higher in participants who had used one drug compared to participants who had none (AOR = 0.88: 95% CI 0.11 - 6.59).

3.8. Complication(s)

None of the cases experienced serious complications as a result of the procedures or the GSL. Endophthalmitis or posterior capsular rupture with vitreous loss occurred in none of the patients. There were no reports of prolonged uveitic episodes, significant iris trauma or tears, or unusual bleeding following surgery. Furthermore, only 14 patients experienced hyphema during surgery, which was quickly resolved by visco-tamponade and air filling. Then, only four eyes developed mild to moderate fibrin reactions on day one after surgery, but those resolved almost completely by week one.

4. Discussion

Angle closure diseases are a group of ocular anatomy disorders characterized by appositional or syenchial approximation of the iris against the trabecular meshwork, obstructing its access to aqueous humor [28] [29]. Because of the secondary impairment of asqueous humor outflow from the eye and the development of glaucomatous optic neuropathy, the final common result of either acute or chronic angle closure is IOP elevation. When the angle is closed more than 180 degrees due to PAS, intra-ocular pressure elevation usually occurs. If the angle is closed more than 270 degrees (3 quadrants), surgery is required to relieve pressure [29]-[32].

Several mechanisms for pressure reduction following cataract surgery have been proposed [27]: 1) the lens bulk is removed, so the pupillary block, which is the main mechanism of acute closure glaucoma, is resolved; 2) lens extraction moves the ciliary processes posteriorly and widens the angle [33]; and 3) it has also been suggested that capsular bag contraction following cataract surgery causes the ciliary body processes to produce less aqueous humor, which may play an additional role [34]. Furthermore, goniosynechialysis may add to this benefit by lysing synechiae and preventing its reformation and may serve as definitive treatment option in angle closure diseases.

The goal of this study was to evaluate the efficacy of combined phacoemulsi-

fication and goniosynechialysis in patients with primary angle-closure disease and visually disabling cataract. Our study provided evidence-based and reliable data for lowering pressure, reducing post-operative anti-glaucoma drugs, decreasing the extent of the PAS, and thus preventing further PAS reformation.

We discovered that performing Phaco-GSL in patients with synechial angle closure diseases and concomitant cataract resulted in a significant reduction in intraocular pressure, the number of anti-glaucoma drugs used, and the extent of PAS three months after surgery when compared to baseline. Furthermore, in our study, the success of GSL is significantly predicated by the extent of the synechiae at baseline (See **Image 2**).

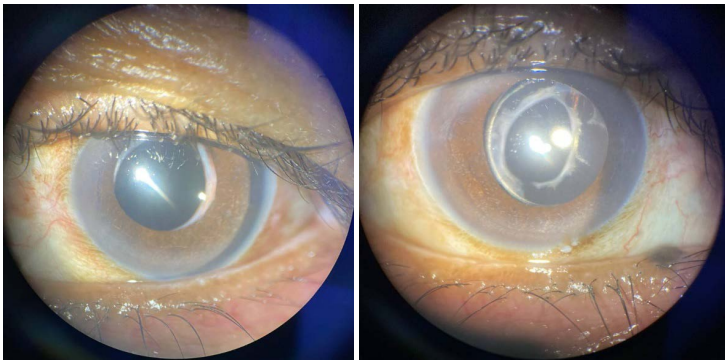

Image 2. Stereoscopic photograph (via slitlamp) of both eyes in patients with chronic angle closure glaucoma several months after phaco-GSL. The anterior chamber is deeper post-operatively. As seen here, the pupil is semi-dilated and with formation of the anterior phimosis contraction of the remaining of anterior capsule. The pressure of this patient is well controlled, and no further progression was detected. (Photo courtesy of Kith Channdarith, MD)

4.1. Demographic Analysis

4.1.1. Age

Regarding the individual age group, our participant was 54.22 ± 10.78 (range, 32 to 80) years old, which was similar to other recent studies as shown below (See **Table 1**). Consistent with our study, Teekhasaenee *et al.* [35] and Fakhraie *et al.* [27], the mean age of the participants was 59.60 ± 10.60 years (range, 38 - 91) and 56.04 ± 9.53 years (range, 39 - 77).

In other studies, however, the average age of the patients was higher. Moghimi *et al.* [36], Razeghinejad *et al.* [22], Tun *et al.* [18], Hiep *et al.* [37], Rodrigues *et al.* [38], Husain *et al.* [39], and Zhao *et al.* [40] were 61.60 ± 8.30 years (range, 48 - 79), 64.30 ± 7.60 years, 66.75 ± 6.53 years, 67.82 ± 15.50 years (range, 54 - 90), 67.20 ± 8.40. Nonetheless, the mean age of the participants was found to be the highest in Varma *et al.* [41] and Shao *et al.* [28]: 72.40 ± 8.90 years and 73.61 ± 8.44 years, respectively.

4.1.2. Sex

Women (75.44%, n = 86) made up the majority of our study, while men made up only a quarter of the participants (24.56%, n = 28). Similarly, the majority of

respondents in recent studies were women. Moghimi *et al.* [36] had 26 women and 19 men in their study. Husain *et al.* [39] had 25 women to just 13 men. Tun *et al.* [18] conducted the study with 8 women and 3 men. Zhao *et al.* [40] included 21 women versus only 12 men, whereas Rodrigues *et al.* [38] included 9 women versus 5 men.

However, Lee *et al.* [25] included 11 men in their study versus only 4 women. Indeed, Fakhraie *et al.* [27] and Razeghinejad *et al.* [22] had comparable numbers of participants in terms of sex (male:female) ratios of 11:13 and 10:11, respectively, in their other two studies.

In terms of diagnosis distribution, chronic angle closure glaucoma was the most common (n = 61 eyes, 51.69%), followed by acute attack angle closure glaucoma (n = 24 eyes, 20.34%) and primary angle closure glaucoma (n = 33 eyes, 27.97%). Three-quarters of the affected eyes in this study (72.88%) were right eyes, with the remaining quarter (27.12%) being left eyes.

4.1.3. Sample Size

Our study includes the most sample sizes for analysis to date. The total number of eyes included was 118 (n = 114 patients), whereas the maximum number of eyes included in recently published data by Lee *et al.* [25] in 2015 was only 66. The study with the fewest participants was also published in 2015 by Tun *et al.* [18], who used only 11 eyes for the analysis.

4.1.4. Nature of Disease

In our study, chronic angle closure glaucoma forms the majority of diagnosis in the eyes included for surgery (n = 61 eyes, 51.69%), while other 24 eyes (20.34%) were acute attack angle closure glaucoma. Only our study included the eye with primary angle closure and cataract consisting of 33 eyes (27.97%).

By contrast, the study by Lee *et al.* [25] in 2015 included only chronic angle closure glaucoma with 66 eyes. Indeed, Fakhraie *et al.* [27] included only eyes in acute state of 24 eyes. Furthermore, Zhao *et al.* [40] included 21 acute versus 12 chronic angle closure glaucomas. And, Tian *et al.* [23] included similar number of eyes in terms of diagnosis 13 acute versus 14 chronic. No other studies had disclosed clearly about the diagnosis and severity.

4.2. Clinical and Therapeutic Data Analysis

4.2.1. Effects on Intra-Ocular Pressure

In our study, the mean intraocular pressure (IOP) at the final visit (3 months post-operatively) was 15.41 ± 6.06 mmHg, compared to 22.04 ± 10.86 mmHg at baseline. Recent studies have similar baseline pressures, and all of those data have significantly lower pressure at month 3 post-op compared to the baselines. These results were consistent with other studies.

Fakhraie *et al.* [27], Rodrigues *et al.* [38], Xu *et al.* [42], Teekhasaenee *et al.* [35], and Zhao *et al.* [40] reported pressures of 16.83 ± 3.81 mmHg, 16.10 ± 4.00 mmHg, 15.14 ± 2.63 mmHg, 14.10 ± 3.51 mmHg, and 13.95 ± 3.75 mmHg, respectively, at 3 months post-op. And, after a 12-month follow-up, the majority

of them still had pressures below 21 mmHg. Table 6 summarizes all relevant peer-review studies from previous years.

Table 6. Logistic regression of success of the surgery [4].

Responses		***Successful***		***Failed***		**Crude Odds Ratio**			**Adjusted Odds Ratio**		
Age	*Sub-Total*	*n*	*proportion*	*n*	*proportion*		95% CI	*p*-value		95% CI	*p*-value
31 - 40 years	9	9	9.18%	0	0.00%	1*					
41 - 50 years	36	29	29.59%	9	45.00%	0.5028	(0.0745 - 3.3918)	0.480			
51 - 60 years	41	34	34.69%	9	45.00%	0.415	(0.0656 - 2.6264)	0.350			
61 - 70 years	20	18	18.37%	2	10.00%	--					
71 - 80 years	8	8	8.16%	0	0.00%	--					
		98		20							
Sex											
Male	29	27	27.55%	2	10.00%	1*			1*		
Female	89	71	72.45%	18	90.00%	0.1538	(0.0268 - 0.8810)	0.036	0.1159	(0.0159 - 0.8460)	0.034
		98		20							
Diagnosis											
Chronic angle closure glaucoma	61	50	51.02%	11	55.00%	1*			1*		
Acute attack angle closure	24	22	22.45%	2	10.00%	0.876	(0.0947 - 8.1009)	0.907	1.1942	(0.1205 - 11.8315)	0.879
Primary angle closure	33	26	26.53%	7	35.00%	1.3138	(0.3632 - 4.7521)	0.677	1.5165	(0.3907 - 5.8867)	0.547
		98		20							
Laterality											
Left Eye	32	14	14.29%	18	90.00%	1*			1*		
Right Eye	86	84	85.71%	2	10.00%	0.1682	(0.0337 - 0.8382)	0.030	0.1645	(0.0293 - 0.9235)	0.040
		98		20							
Pressure at Baseline											
IOP ≤ 21 mmHg	79	65	66.33%	14	70.00%	1*			1*		
IOP > 21 mmHg	39	33	33.67%	6	30.00%	1.5622	(0.4152 - 5.8772)	0.509	1.1539	(0.2838 - 4.6914)	0.841
		98		20							
PAS Extent at Baseline											
Little PAS or PAS extent ≤ 90 degrees	46	44	44.90%	2	10.00%	1*			1*		
PAS extent: 91 - 180 degrees	38	30	30.61%	8	40.00%	0.0928	(0.0098 - 0.8756)	0.038	0.0714	(0.0066 - 0.7679)	0.029
Extensive PAS: PAS > 180 degrees	34	24	24.49%	10	50.00%	0.0442	(0.0052 - 0.3754)	0.004	0.0359	(0.0034 - 0.3792)	0.006
		98		20							
Drugs Required at Baseline											
None	10	8	8.16%	2	10.00%	1*			1*		
1 Drug	51	43	43.88%	8	40.00%	0.9027	(0.1264 - 6.4456)	0.919	0.8893	(0.1199 - 6.5952)	0.909

Continued

2 Drugs	28	22	22.45%	6	30.00%	0.4399	(0.0561 - 3.4487)	0.434	0.3240	(0.0381 - 2.7520)	0.302
3 Drugs	20	17	17.35%	3	15.00%	0.2178	(0.0180 - 2.6217)	0.230	0.1939	(0.0141 - 2.6612)	0.220
4 Drugs	9	8	8.16%	1	5.00%	0.4452	(0.2075 - 9.5525)	0.605	0.1365	(0.0051 - 3.6023)	0.233
		98		20							

**Reference*

4.2.2. Effects on Anti-Glaucoma Drug Reduction

The average amount of anti-glaucoma drugs taken at baseline was 1.72 ± 1.09, which decreased to 0.27 ± 0.50 at month 3 post-operatively. In recently published data, the baseline amount of anti-glaucoma drugs used varied. Angmo *et al.* [43] reported the most drugs taken at 4.03 ± 0.41 on average at baseline, while Rodrigues *et al.* [38] reported the least at 0.92 ± 0.86 at baseline, as well as 0.41 ± 0.67 at month 3 post-operatively.

Four studies reported the amount of anti-glaucoma medication required at 12 months post-operatively. Zhao *et al.* [40], Husain *et al.* [39], and Moghimi *et al.* [36] discovered that the amount of drugs consumed at the final visit was 0.64 ± 1.41, 0.60 ± 1.20, 0.40 ± 0.80. The most recent report in by Tun *et al.* [18] in 2015 revealed that the drugs were 0.09 ± 0.30, implying that almost all of the participants were free of anti-glaucoma drugs.

4.2.3. Effects on Visual Acuity

The mean visual acuity at the final visit (3 months post-op) improved significantly in our study, from 0.72 ± 0.55 logMAR at baseline to 0.47 ± 0.50 logMAR at the final visit.

Our patients' final visual acuity (VA) was not as good as in other studies. At 3 months, Shao *et al.* [28] found that visual acuity was 0.28 ± 0.29 logMAR (vs. 0.93 ± 0.65 at baseline), while Rodrigues *et al.* [38] found that it was 0.19 ± 0.17 logMAR (vs. 0.29 ± 0.32). These two studies also had better visual acuity at the final visit (6 months post-op): Shao *et al.* [28] had 0.23 ± 0.28 logMAR and Rodrigues *et al.* [38] had 0.19 ± 0.16 logMAR, respectively.

Lee *et al.* [25] discovered satisfying visual acuity at 6 months post-operatively as 0.16 ± 0.44 logMAR (vs. 0.25 ± 0.22 at baseline). Moghimi *et al.* [36] had the longest follow-up of 12 months and had visual acuity of 0.28 ± 0.23 logMAR at the final visit (vs. 0.49 ± 0.35). Zhao *et al.* [40], on the other hand, had 30 eyes with improved visual acuity after 12 months but did not mention the quantitative analysis.

Even if the final visual acuity was better than the baseline, it did not meet expectations; this could be due to the inclusion of more severe conditions in the study (3/4 are primary angle closure glaucoma) and the severity of the glaucoma condition was not properly assessed. As a result, we are unable to investigate the relationship between visual outcome and the severity of glaucoma to the Phaco-GSL. On the other hands, the lens opacity in each patient was not properly and rigorously documented. So, data was missing in lens opacity grading in the

study.

4.2.4. Effects on PAS and Its Reformation

Due to poor corneal transparency or poor patient or missing documentation, a quarter of the patients (n = 36 eyes) were partly missed out in gonioscopic examination. In our study, the mean extent of peripheral anterior synechiae (PAS) at baseline was 135.00 ± 89.68 degrees, which decreased to approximately 72.80 ± 61.64 degrees after surgery at month 3.

In comparison to other recent data, our study has the least amount of PAS. Rodrigues *et al.* [38], Moghimi *et al.* [36], Husain *et al.* [39], and Lee *et al.* [25] reported mean baseline extents of PAS of 249.20 ± 83.40 degrees, 245.70 ± 91.30 degrees, 234.00 ± 72.00 degrees, and 209.00 ± 114.30 degrees, respectively. A similar result of PAS reduction was reported by Rodrigues *et al.* [38] as 121.20 ± 79.50 degrees at month 3 post-op.

Tun *et al.* [18] discovered a similar PAS extent to ours, but at 12 months post-op: 76.50 ± 73.80 degrees. Husain *et al.* [39] also reported that the PAS extent was approximately 96.3 ± 106.8 degrees one year after surgery. Furthermore, at month 12 post-op, Rodrigues *et al.* [38] and Moghimi *et al.* [36] discovered that the PAS extent was 110.8 ± 53.9 degrees and 121.90 ± 88.30 degrees, respectively.

The described technique above [41], combined phacoemulsification with goniosynechialysiss, both mechanical and visco-goniosynechialysis (MGSL and VGSL), has an advantage over phacoemulsification alone and/or phaco combined with mechanical synechial breaking alone. After IOL implantation, visco-elastic agent was injected to gently break the angle, followed by pilocarpine injection if necessary. Hence, with viscogonioplasty (VGP), the angle is never touched, but rather gently and properly dissected open by the viscoelastic agent, followed by a spatula manipulation to break synechiae.

As a result, it is assumed that VGP is superior to surgical procedures on the angle and may cause less damage to the trabecular meshwork and should be performed before MGS. There is still a chance that a trabecular meshwork that has been occluded for some time will not resume full function, even if the angle is anatomically opened by this procedure. The fact that 8 of our patients still have a PAS extent of 180 degrees or greater at 3 months post-operatively (See **Table 4(a)**).

Furthermore, 24 of our patients continued to have poor PAS reduction (PAS reduction less than 90 degrees from baseline) because the PAS may be too sticky and more strictly adherent and difficult to successfully break, whereas the remaining 10 eyes had PAS recurrence greater than baseline at month 3 post-operatively (See **Table 4(b)**). Long-term research will shed more light on this.

Because normalization of IOP after surgery is dependent on the function of the trabecular meshwork, prolonged PAS and angle closure may result in irreversible trabeculum damage, including scarring and trabecular collapse, and

failure of pressure control, even if the angle is mechanically reopened [28]. If the PAS have been present for less than a year, the GSL is reported to be successful in approximately 80% of eyes [35]. As a result, GSL is preferable for eyes with recent-onset PAS rather than those with extensive and prolonged angle closure [44]-[46].

In our study, the duration of PAS existence was not clearly discussed; therefore, the duration and onset of angle closure would be discussed in future studies.

4.2.5. Effects on Anterior Chamber Depth

At the final visit (3 months post-operatively), the anterior chamber depth (ACD) is approximately 3.00 ± 0.62 mm, compared to only 1.52 ± 0.34 mm at the baseline. Our data showed a significant deepening of the anterior chamber when compared to other recent data, which were also found to be very consistent to ours.

Lee *et al.* [25] concluded in 2015 that the final ACD was 4.06 ± 0.48 mm (at baseline: 2.50 ± 0.28 mm). According to Zhao *et al.* [40] in 2013, the mean ACD at the final visit was 3.61 ± 0.27 mm (at baseline: 1.94 ± 0.22 mm). However, the other two studies showed less significant depth. Moghimi *et al.* [36] found the mean ACD at the final visit to be 2.35 ± 0.21 mm (range, 1.98 - 2.77 mm), while Teekhasaenee *et al.* [35] found it to be 2.33 ± 0.54 mm (range, 1.73 - 3.78 mm).

4.3. Strength and Limitations

To the best of our knowledge, this is the first study to look at the effects of Phaco-GSL on trabecular outflow facility. The use of previously validated tools for measuring variables included in the study from randomized controlled trial studies was the study's strength. Furthermore, the method and procedures for measuring intra-ocular pressure before and after surgery were clearly demonstrated using validated and highly calibrated automated tonometers. Second, none of our participants were missed for follow-up, and there was a good compliance to follow-up. Third, the subjects in our study had no prior experience with angle manipulation, surgeries, or laser. All of these can reduce selection and information biases. Last but not least, potential confounding factors were also identified and adjusted for multiple logistic regression in our study.

Despite the fact that our study was conducted in the largest eye care tertiary care centre in the country, it may not probably encompass the full spectrum of patients with angle closure diseases and may not be representative of the entire population. Moreover, it is difficult of course to understand the true relative association of cataract extraction by phacoemulsification and goniosynechialysis in our study because our design is observational and have no comparative control, and the sample sizes were relatively not too large and then were conveniently selected without randomization. For this reason, a further study with randomized controlled trial design is recommended to investigate the treatment efficacy different between cataract extraction with and without GSL. Third, we did not sep-

arate or compare the manipulative details (MGSL vs. VGSL) in our study, and these two combined were used in our cases, which may lead to not quite validated reliabilities of the combined results rather than individual procedure. Furthermore, because our observational period of one year was allowed, our study has the final follow-up visit set at three months post-operatively; it is therefore unknown if the benefits of GSL that were demonstrated in the first 3 months after surgery are sustained long term. However, in order to assess the more reliable efficacy of long-term outcomes, we may need to follow patients up to 12 months after surgery. Given these limitations, multi-centered, larger sample size, randomized controlled trial study, with longer period of follow-up, and with more standardized criteria should be performed to further ensure its accuracy and precision in a wide spectrum of this angle closure diseases in Cambodia.

5. Conclusions and Recommendation

5.1. Conclusions

Goniosynechialysis is a less invasive and simple procedure that can be used in all eyes with angle closure diseases during phacoemulsification. Despite the fact that glaucoma is a progressive disease, GSL can significantly lower pressure and break synechiae. Because of its bleb-free nature, Phaco-GSL may be an optimal procedure for treating angle closure diseases with concomitant cataract, and its clinical and therapeutic benefits appear to be superior to phacoemulsification alone and comparable to phaco-trabeculectomy/trabeculectomy alone.

In fact, cataract extraction can reduce pressure in patients with primary angle closure diseases or narrow angles, and this must be considered when evaluating the efficacy of goniosyenchialysis (GSL). Our study has determined that Phaco-GSL provides additional options for lowering intra-ocular pressure compared to cataract extraction alone. This conclusion is based on a variety of factors: 1) The intra-ocular pressure reductions described in our study are far greater than previous reports in the literature for cataract surgery alone. 2) The decrease in the number of anti-glaucoma drugs was greater than in any recent studies. 3) In final follow-up visits, the recurrence of PAS was still less severe than the eyes at baseline. 4) There were no significant complications associated with the surgery reported in our study both in 3 or 6 months post-operatively.

Our findings strongly indicate that less extensive synechiae at baseline is significantly associated with surgical success. Even with cataract extraction, eyes with more and more extensive gonio-synechiae are likely to fail to control pressure post-operatively and this may need additional drugs or other filtering surgeries to control the pressure.

5.2. Recommendations

We strongly advise eye care professionals to consider and apply this Phaco-GSL as an initial and definitive treatment option for angle closure disease patients

who also have a visually disabling cataract. This procedure is much safer and has far fewer complications than other filtering surgeries, and it can be easily manipulated during phacoemulsification right after intra-ocular implantation. We encourage all ophthalmologists to perform this procedure during phacoemulsification.

We strongly encourage future researchers to conduct a larger randomized control trial in our Cambodian clinical setting to gather much more evidence of this procedure and improve the quality of care, or before other novel and alternative methods for treating patients with angle closure conditions could be discovered.

We express deep concern to policymakers about the burden of primary angle closure disease in Cambodia because the oriental eyes are prone to angle closure. Furthermore, this procedure and its benefits should be widely disseminated and practiced on a national scale.

In order to comply with the National Strategic Plan 2023-2030, The National Program for Eye Health, we recommend that all patients aged 40 and up come to screening for glaucoma and other relevant eye conditions. Far and above all, we encourage all ophthalmologists and residents-in-training to include gonioscopic assessment in elderly patients over the age of 40, or patients at risk of angle closure diseases, particularly aging women (e.g. Patients with history of ocular inflammation, or with shallow anterior chamber, or with an episode of acute attack in fellow eye, or having relatives diagnosed with glaucoma, etc.).

In short, because of its safety and potential benefits in terms of optimal pressure reduction, satisfying reduction in anti-glaucoma drugs used post-operatively, low frequency of PAS reformation, and a rare complication related to GSL, we recommend that all eyes with primary angle closure disease, whether primary angle closure and/or glaucoma and visually disabling cataract, with or without obvious PAS, should better undergo cataract extraction with goniosynechialysis.

Although this is the first study on Phaco-GSL, the findings strongly support the use of GSL in addition to standard cataract extraction, particularly phacoemulsification, as a safe and effective means of increasing aqueous outflow and, as a result, lowering intraocular pressure and anti-glaucoma medication use in patients with primary angle closure diseases. Yet, more research is needed to determine the long-term efficacy. Furthermore, it would be very beneficial to protect visual function if it was known whether controlled intra-ocular pressure could prevent the progression to primary angle closure diseases, as well as if the post-operative angle recurred to adhesions as well as closure during longer follow-up periods.

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Conflicts of Interest

The authors declare that this report discloses no commercial or financial relationships that could be constructed as a potential conflict of interest.

References

[1] Pascolini, D. and Mariotti, S.P. (2011) Global Estimates of Visual Impairment: 2010. *British Journal of Ophthalmology*, **96**, 614-618. https://doi.org/10.1136/bjophthalmol-2011-300539

[2] Adelson, J.D., Bourne, R.R.A., Briant, P.S., Flaxman, S.R., Taylor, H.R.B., Jonas, J.B., *et al.* (2020) Causes of Blindness and Vision Impairment in 2020 and Trends over 30 Years, and Prevalence of Avoidable Blindness in Relation to VISION 2020: The Right to Sight: An Analysis for the Global Burden of Disease Study. *The Lancet Global Health*, **9**, e144-e160.

[3] Nuzzi, R., Marolo, P. and Nuzzi, A. (2020) The Hub-And-Spoke Management of Glaucoma. *Frontiers in Neuroscience*, **14**, Article 180. https://doi.org/10.3389/fnins.2020.00180

[4] Kuper, H. and Foster, A. (2006) Impact of VISION 2020 on Global Blindness. *Canadian Journal of Ophthalmology*, **41**, 669-672. https://doi.org/10.3129/i06-080

[5] Man, X., Chan, N.C.Y., Baig, N., Kwong, Y.Y.Y., Leung, D.Y.L., Li, F.C.H., *et al.* (2015) Anatomical Effects of Clear Lens Extraction by Phacoemulsification versus Trabeculectomy on Anterior Chamber Drainage Angle in Primary Angle-Closure Glaucoma (PACG) Patients. *Graefe's Archive for Clinical and Experimental Ophthalmology*, **253**, 773-778. https://doi.org/10.1007/s00417-015-2936-z

[6] Friedman, D.S. (2003) Ultrasonographic Biomicroscopy, Scheimpflug Photography, and Novel Provocative Tests in Contralateral Eyes of Chinese Patients Initially Seen with Acute Angle Closure. *Archives of Ophthalmology*, **121**, 633-642. https://doi.org/10.1001/archopht.121.5.633

[7] Shin, H.C., Subrayan, V. and Tajunisah, I. (2010) Changes in Anterior Chamber

Depth and Intraocular Pressure after Phacoemulsification in Eyes with Occludable Angles. *Journal of Cataract and Refractive Surgery*, **36**, 1289-1295. https://doi.org/10.1016/j.jcrs.2010.02.024

[8] Tai, M., Chien, K., Lu, D. and Chen, J. (2010) Angle Changes before and after Cataract Surgery Assessed by Fourier-Domain Anterior Segment Optical Coherence Tomography. *Journal of Cataract and Refractive Surgery*, **36**, 1758-1762. https://doi.org/10.1016/j.jcrs.2010.05.011

[9] Huang, G., Gonzalez, E., Lee, R., Chen, Y., He, M. and Lin, S.C. (2012) Association of Biometric Factors with Anterior Chamber Angle Widening and Intraocular Pressure Reduction after Uneventful Phacoemulsification for Cataract. *Journal of Cataract and Refractive Surgery*, **38**, 108-116. https://doi.org/10.1016/j.jcrs.2011.06.037

[10] Teekhasaenee, C. (1999) Combined Phacoemulsification and Goniosynechialysis for Uncontrolled Chronic Angle-Closure Glaucoma after Acute Angle-Closure Glaucoma. *Ophthalmology*, **106**, 669-675. https://doi.org/10.1016/s0161-6420(99)90149-5

[11] Campbell, D.G. and Vela, A. (1984) Modern Goniosynechialysis for the Treatment of Synechial Angle-Closure Glaucoma. *Ophthalmology*, **91**, 1052-1060. https://doi.org/10.1016/s0161-6420(84)34195-1

[12] Cheng, J., Zong, Y., Zeng, Y. and Wei, R. (2014) The Prevalence of Primary Angle Closure Glaucoma in Adult Asians: A Systematic Review and Meta-Analysis. *PLOS ONE*, **9**, e103222. https://doi.org/10.1371/journal.pone.0103222

[13] Lowe, R.F. (1964) Primary Creeping Angle-Closure Glaucoma. *British Journal of Ophthalmology*, **48**, 544-550. https://doi.org/10.1136/bjo.48.10.544

[14] Eid, T.M. (2011) Primary Lens Extraction for Glaucoma Management: A Review Article. *Saudi Journal of Ophthalmology*, **25**, 337-345. https://doi.org/10.1016/j.sjopt.2011.07.004

[15] Tanihara, H., Nishiwaki, K. and Nagata, M. (1992) Surgical Results and Complications of Goniosynechialysis. *Graefe's Archive for Clinical and Experimental Ophthalmology*, **230**, 309-313. https://doi.org/10.1007/bf00165936

[16] Fraser, S., Adams Varma Phelan, P., Bunce, C. and Fraser, S. (2010) Viscogoniоplasty in Narrow Angle Glaucoma: A Randomized Controlled Trial. *Clinical Ophthalmology*, **4**, 1475-1479. https://doi.org/10.2147/opth.s15447

[17] Varma, D., Baylis, O., Wride, N., Phelan, P.S. and Fraser, S.G. (2006) Viscogoniоplasty: An Effective Procedure for Lowering Intraocular Pressure in Primary Angle Closure Glaucoma. *Eye*, **21**, 472-475. https://doi.org/10.1038/sj.eye.6702224

[18] Tun, T.A., Baskaran, M., Perera, S.A., Htoon, H.M., Aung, T. and Husain, R. (2015) Swept-source Optical Coherence Tomography Assessment of Iris-Trabecular Contact after Phacoemulsification with or without Goniosynechialysis in Eyes with Primary Angle Closure Glaucoma. *British Journal of Ophthalmology*, **99**, 927-931. https://doi.org/10.1136/bjophthalmol-2014-306223

[19] Shingleton, B.J., Chang, M.A., Bellows, A.R. and Thomas, J.V. (1990) Surgical Goniosynechialysis for Angle-Closure Glaucoma. *Ophthalmology*, **97**, 551-556. https://doi.org/10.1016/s0161-6420(90)32542-3

[20] Yoshimura, N. and Iwaki, M. (1988) Goniosynechialysis for Secondary Angle-Closure Glaucoma after Previously Failed Filtering Procedures. *American Journal of Ophthalmology*, **106**, 493. https://doi.org/10.1016/0002-9394(88)90893-8

[21] Yu, J., Zhao, F. and Xiang, Y. (2021) Phacoemulsification with Goniosynechialysis

versus Phacoemulsification Alone in Angle-Closure Glaucoma: A Meta-Analysis of Randomized Controlled Trials. *Journal of Ophthalmology*, **2021**, Article ID: 8831479. https://doi.org/10.1155/2021/8831479

[22] Razeghinejad, M.R. and Rahat, F. (2010) Combined Phacoemulsification and Viscogoniosynechialysis in the Management of Patients with Chronic Angle Closure Glaucoma. *International Ophthalmology*, **30**, 353-359. https://doi.org/10.1007/s10792-010-9353-4

[23] Tian, T., Li, M., Pan, Y., Cai, Y. and Fang, Y. (2019) The Effect of Phacoemulsification Plus Goniosynechialysis in Acute and Chronic Angle Closure Patients with Extensive Goniosynechiae. *BMC Ophthalmology*, **19**, Article No. 65. https://doi.org/10.1186/s12886-019-1070-9

[24] White, A.J., Orros, J.M.A. and Healey, P.R. (2013) Outcomes of Combined Lens Extraction and Goniosynechialysis in Angle Closure. *Clinical & Experimental Ophthalmology*, **41**, 746-752. https://doi.org/10.1111/ceo.12121

[25] Lee, C., Rho, S.S., Sung, G.J., Kim, N.R., Yang, J.Y., Lee, N.E., *et al.* (2015) Effect of Goniosynechialysis during Phacoemulsification on IOP in Patients with Medically Well-Controlled Chronic Angle-Closure Glaucoma. *Journal of Glaucoma*, **24**, 405-409. https://doi.org/10.1097/ijg.0000000000000043

[26] Zhang, H., Tang, G. and Liu, J. (2016) Effects of Phacoemulsification Combined with Goniosynechialysis on Primary Angle-Closure Glaucoma. *Journal of Glaucoma*, **25**, e499-e503. https://doi.org/10.1097/ijg.0000000000000297

[27] Fakhraie, G., Vahedian, Z., Moghimi, S., Eslami, Y., Zarei, R. and Oskouee, J.F. (2012) Phacoemulsification and Goniosynechialysis for the Management of Refractory Acute Angle Closure. *European Journal of Ophthalmology*, **22**, 714-718. https://doi.org/10.5301/ejo.5000101

[28] Shao, T., Hong, J., Xu, J., Le, Q., Wang, J. and Qian, S. (2015) Anterior Chamber Angle Assessment by Anterior-Segment Optical Coherence Tomography after Phacoemulsification with or without Goniosynechialysis in Patients with Primary Angle Closure Glaucoma. *Journal of Glaucoma*, **24**, 647-655. https://doi.org/10.1097/ijg.0000000000000061

[29] Aung, T., Lim, M., Chan, Y., Rojanapongpun, P. and Chew, P. (2005) Configuration of the Drainage Angle, Intraocular Pressure, and Optic Disc Cupping in Subjects with Chronic Angle-Closure Glaucoma. *Ophthalmology*, **112**, 28-32. https://doi.org/10.1016/j.ophtha.2004.06.033

[30] Campa, C., Pierro, L., Bettin, P. and Bandello, F. (2011) Anterior Chamber Angle Assessment Techniques. In: Rumelt, S., Ed., *Glaucoma—Basic and Clinical Concepts*, InTech, 371-390. https://doi.org/10.5772/19617

[31] Hsiao, C., Hsu, C., Shen, S. and Chen, H.S.L. (2003) Mid-Term Follow-Up of Nd: YAG Laser Iridotomy in Asian Eyes. *Ophthalmic Surgery, Lasers and Imaging Retina*, **34**, 291-298. https://doi.org/10.3928/1542-8877-20030701-04

[32] Thomas, R. (2003) Five Year Risk of Progression of Primary Angle Closure Suspects to Primary Angle Closure: A Population Based Study. *British Journal of Ophthalmology*, **87**, 450-454. https://doi.org/10.1136/bjo.87.4.450

[33] Nonaka, A., Kondo, T., Kikuchi, M., Yamashiro, K., Fujihara, M., Iwawaki, T., *et al.* (2006) Angle Widening and Alteration of Ciliary Process Configuration after Cataract Surgery for Primary Angle Closure. *Ophthalmology*, **113**, 437-441. https://doi.org/10.1016/j.ophtha.2005.11.018

[34] Tipperman, R. (2006) A Novel Index for Predicting Intraocular Pressure Reduction Following Cataract Surgery. *Yearbook of Ophthalmology*, **2006**, 3-4.

https://doi.org/10.1016/s0084-392x(08)70217-x

[35] Teekhasaenee, C. (1999) Combined Phacoemulsification and Goniosynechialysis for Uncontrolled Chronic Angle-Closure Glaucoma after Acute Angle-Closure Glaucoma. *Ophthalmology*, **106**, 669-675. https://doi.org/10.1016/s0161-6420(99)90149-5

[36] Moghimi, S., Latifi, G., ZandVakil, N., Mohammadi, M., Khatibi, N., Soltani-Moghadam, R., *et al.* (2015) Phacoemulsification versus Combined Phacoemulsification and Viscogonioplasty in Primary Angle-Closure Glaucomaa: A Randomized Clinical Trial. *Journal of Glaucoma*, **24**, 575-582. https://doi.org/10.1097/ijg.0000000000000196

[37] Nguyen Xuan, H., Nguyen Dinh, N., Nguyen Thu, H., Nguyen Van, C., Aung, T., Loo, Y., *et al.* (2021) Comparing the Safety and Efficacy of Phacogoniosynechialysis with Phacotrabeculectomy in the Management of Refractory Acute Primary Closure Angle Glaucoma with Cataract: A Multicenter Randomized Trial. *Journal of Glaucoma*, **30**, 552-558. https://doi.org/10.1097/ijg.0000000000001868

[38] Rodrigues, I.A., Alaghband, P., Beltran Agullo, L., Galvis, E., Jones, S., Husain, R., *et al.* (2016) Aqueous Outflow Facility after Phacoemulsification with or without Goniosynechialysis in Primary Angle Closure: A Randomised Controlled Study. *British Journal of Ophthalmology*, **101**, 879-885. https://doi.org/10.1136/bjophthalmol-2016-309556

[39] Husain, R., Do, T., Lai, J., Kitnarong, N., Nongpiur, M.E., Perera, S.A., *et al.* (2019) Efficacy of Phacoemulsification Alone vs Phacoemulsification with Goniosynechialysis in Patients with Primary Angle-Closure Disease: A Randomized Clinical Trial. *JAMA Ophthalmology*, **137**, 1107-1113. https://doi.org/10.1001/jamaophthalmol.2019.2493

[40] Zhao, X., Yang, X., Fan, Y., Li, B. and Li, Q. (2013) Comparison of Combined Phacoemulsification, Intraocular Lens Implantation, and Goniosynechialysis with Phacotrabeculectomy in the Treatment of Primary Angle-Closure Glaucoma and Cataract. *Asia-Pacific Journal of Ophthalmology*, **2**, 286-290. https://doi.org/10.1097/apo.0b013e318299df62

[41] Varma, D. (2006) Viscogonioplasty in Patients with Chronic Narrow Angle Glaucoma. *British Journal of Ophthalmology*, **90**, 648-649. https://doi.org/10.1136/bjo.2005.087577

[42] Xu, X.S., Wan, X.H., Jiang, L.J. and Sun, D.C. (2017) Clinical Study of Phacoemulsification and Intraocular Lens Implantation Combined with Goniosynechialysis in the Treatment of Primary Chronic Angle Closure Glaucoma. *International Eye Science*, **17**, 2289-2291.

[43] Angmo, D., Shakrawal, J., Gupta, B., Yadav, S., Pandey, R.M. and Dada, T. (2019) Comparative Evaluation of Phacoemulsification Alone versus Phacoemulsification with Goniosynechialysis in Primary Angle-Closure Glaucoma: A Randomized Controlled Trial. *Ophthalmology Glaucoma*, **2**, 346-356. https://doi.org/10.1016/j.ogla.2019.05.004

[44] Liebmann, J.M. and Ritch, R. (2002) Laser Surgery for Angle Closure Glaucoma. *Seminars in Ophthalmology*, **17**, 84-91. https://doi.org/10.1076/soph.17.2.84.14720

[45] Wormald, R. and Shah, R. (n.d.) Acute and Chronic Angle Closure Glaucoma. In: *Evidence-Based Ophthalmology*, 205-209. https://doi.org/10.1002/9780470698709.ch30

[46] Liu, L. (2008) Anatomical Changes of the Anterior Chamber Angle with Anterior-Segment Optical Coherence Tomography. *Archives of Ophthalmology*, **126**, 1682-1686. https://doi.org/10.1001/archopht.126.12.1682

Note and Abbreviations

The glaucoma team consists of six surgeons, including: 1) Dr. Chukmol Kossama, MD (CKS), 2) Dr. Sea Bunseng, MD (SBS), 3) Dr. Kith Channdarith, MD, as Principal Investigator (KCR), 4) Dr. Samreth SereyOudam, MD (SSO), 5) Dr. Kim Chenda, MD (KCD), and 6) Dr. Leang Sereyvath, MD (LSV).