

Original Article

Clinical outcome of phacoemulsification combined with intraocular lens implantation for primary angle closure/glaucoma (PAC/PACG) with cataract

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Abstract: Objective: To evaluate the efficacy of phacoemulsification (Phaco) combined with intraocular lens implantation for treatment of primary angle-closure glaucoma (PACG) patients with cataract. Methods: A total of 62 patients treated in our hospital meeting the inclusion criteria were included, including 62 eyes (26 PAC eyes and 36 PACG eyes). PACG patients were divided into early, middle, and advanced stages based on the HPA visual field staging system. The subjects were also grouped according to the extent of peripheral anterior synechia (PAS). Patients received topical medical treatment preoperatively and Phaco performed by the same surgeon. The visual acuity, intraocular pressure (IOP), anterior chamber depth (ACD), medication used, visual field and retinal nerve fiber layer (RNFL) were observed before and 6-24 months after surgery. Results: The mean age of the patients was 68 ± 8.91 years old, and postoperative follow-up was 13.1 ± 5.5 months. Postoperative visual acuity was improved in all patients ($P < 0.001$). Postoperatively, the IOP decreased significantly ($P < 0.001$), the number of medications was reduced ($P < 0.001$), and the ACD was deeper than that before operation ($P < 0.001$). There was no significant difference in visual field ($P = 0.973$) or RNFL ($P = 0.268$) after surgery during the follow-up. There was no statistical difference in postoperative changes of various indexes between PAC and PACG patients. The decrease of IOP in patients with early stage PACG was significantly higher than that in patients in the middle and advanced stages ($F = 3.519$, $P = 0.041$), and the number of medications used in early-stage PACG patients was also significantly lower than that of advanced patients ($P = 0.020$). There was no significant difference in postoperative visual acuity ($X^2 = 0.139$, $P = 0.987$) or IOP decline ($F = 0.260$, $P = 0.854$) among patients with different extents of preoperative PAS, nor was there any correlation between postoperative IOP control and preoperative PAS. No serious complications were observed in any subject. Conclusion: In PAC/PACG patients, Phaco can significantly control IOP, and prevent visual field defect and progressive loss of RNFL, indicating that the procedure has a protective effect on the optic nerve. Phaco is more effective in the treatment of early stage PACG than in middle or advanced stage, and can be used in PAC/PACG patients with different extents of PAS, but close follow-up is necessary.

Keywords: Phacoemulsification, primary angle-closure glaucoma, cataract, intraocular pressure, optic nerve

Introduction

Glaucoma is the major cause of irreversible blindness in the world. Women, the elderly, and patients with hyperopia have a predilection for primary angle-closure glaucoma (PACG), which is a disease most prevalent in Asia, accounting for about 76.7% of the world's total [1, 2]. In 2010, approximately 6.3 million patients were blinded or visually impaired by glaucoma [3]. According to statistics, the number of glauco-

ma patients in China reached 21 million in 2020, and the number blinded was 5.67 million [4].

PACG refers to a disease in which the peripheral iris is blocked or permanently adhered to the trabecular meshwork followed by the blocked outflow of aqueous humor, thus causing increased intraocular pressure (IOP). In the Preferred Practice Patterns (PPP) published by the American Academy of Ophthalmology (AAA)

in 2016 [5], the natural disease progression of whole primary angle closure disease was divided into the following three stages according to the standards proposed by the International Society of Geographical and Epidemiological Ophthalmology (ISGEO): Primary angle-closure suspect (PACS, Eyes in which the iris trabecular contact (ITC) is greater than 180 degrees, with normal IOP and no peripheral anterior synechia (PAS)); Primary angle closure (PAC, Eyes with ITC greater than 180 degrees and elevated IOP or PAS); and Primary angle-closure glaucoma (PACG, PAC with optic nerve lesions). Furthermore, glaucoma is classified into early, middle and advanced stages according to the severity of the visual field defects based on the Hodapp-Parrish-Anderson (HPA) visual field staging system [6].

Effective early intervention is necessary for glaucoma. The initial treatment for PACG is laser peripheral iridotomy (LPI) with topical eye drops, which can open the drainage channel and alleviate pupillary block to reduce IOP [7, 8]. Surgery is indicated when the condition is out of control. Trabeculectomy is widely used to control the IOP in glaucoma patients, which however, is associated with various postoperative complications such as cataract progression, hypotony, shallowing of the anterior chamber, malignant glaucoma, choroidal detachment, bleb leakage and blebitis [9-12]. In recent years, many studies have focused on the clinical efficacy of phacoemulsification (Phaco) combined with intraocular lens (IOL) implantation in the treatment of PACG. Phaco combined with IOL implantation has gradually become a conservative alternative method for the current treatment of PACG [13]. Angmo suggested that Phaco and Phaco combined with goniosynechialysis significantly reduced IOP and ameliorated anterior chamber angle parameters. Both procedures successfully reduced the requirement for glaucoma medications applied in PACG patients. For patients with PACG, there is no additional benefit from combined goniosynechialysis compared to Phaco alone [14]. Phaco has been shown to be more effective than laser peripheral iridotomy (LPI) and can avoid the complications associated with filtration surgery [13, 15-17]. Phaco, combined with trabeculectomy and LPI, is more effective and economical, and should be used as the preferred treatment for patients with PAC or PACG [13]. The study of Thomas et al.

showed that for PACG patients who cannot control IOP with anti-glaucoma medications, Phaco has a 50% chance of reducing IOP by more than 5 mmHg [18]. Phaco combined with IOL also can effectively deepen anterior chamber depth (ACD), reduce pupil block, reduce IOP, and improve visual acuity in PACG patients with fewer complications [19, 20].

In this study, cases were divided into PAC and PACG according to ISGEO. PACG patients were further grouped into early, middle, and advanced groups according to HPA visual field staging. Subjects were also grouped preoperatively according to the extent of PAS. To our knowledge, there are few studies comparing the effect of Phaco between PAC and PACG patients, and there was also no comparative study on the postoperative efficacy of PACG patients with different visual field staging. Moreover, there are also different opinions about postoperative efficacy of Phaco for patients with different extents of PAS. In particular, for patients with middle and advanced PACG, it needs to be determined whether the efficiency of reducing IOP obtained by Phaco alone can effectively prevent further reduction of retinal nerve fiber layer (RNFL) thickness and the advanced visual field defect. Therefore, the innovative point of our study lies in the analysis of IOP from the perspectives of RNFL and visual field in PACG patients undergoing Phaco, and the grouping of patients according into different types, stages, and PAS extents, so as to provide a reliable basis for relevant clinical research in China to guide clinical treatment.

Materials and methods

Patients

Patients with PAC or PACG coexisting with cataract were scheduled for Phaco with IOL implantation. They were recruited from the Second Affiliated Hospital of Xi'an Medical University from December 2018 to January 2021. Written informed consent was obtained from all patients before the surgical procedure. This study was approved by the Ethics Committee of hospital (X2Y202009). This was a retrospective study.

Inclusion criteria: 1) PAC or PACG patients with cataract. 2) the diagnostic criteria of PAC and PACG were in line with the Preferred Practice

Patterns (PPP) in 2016 [21]. 3) the affected eye was graded according to the Lens Opacities Classification System III (LOCS III) [22] with nuclear color (NC)/nuclear opalescence (NO) for grade 2 or above. 4) the IOP can be reduced to below 21 mmHg using 5 medications.

Exclusion criteria: 1) trauma or previous anti-glaucoma surgery. 2) preoperatively diagnosed with other types of glaucoma, such as: POAG, secondary glaucoma, or neovascular glaucoma. 3) complicated by other ocular diseases, such as retinopathy, uveitis, endophthalmitis and optic nerve disease. 4) contraindications to surgery or severe systemic diseases. 5) incomplete medical records or inadequate follow-up.

Preoperative indicators of patients

Data collected preoperatively included patient age, gender, telephone, subtype of glaucoma, the extent of PAS, date of surgery and the number of anti-glaucoma medications used. Each patient underwent complete ophthalmic examination, including slit lamp biomicroscopy, best-corrected visual acuity (BCVA) measured using the Snellen chart, intraocular pressure (IOP) measured by Goldmann applanation tonometry, gonioscopy, anterior-segment imaging by AS-OCT, fundoscopy, keratometry, ACD measured by A-scan, axial length (AL), vitreous body and retina examined by B-scan, visual field by HFA, lens thickness, corneal endothelial cell density (ECD) by non-contact specular microscope, and RNFL thickness. BCVA, IOP, visual field, and RNFL thickness were recorded at 1 day, and 1, 2, and 3 weeks, as well as 1, 2, 3, 6, 12, and 24 months postoperatively.

Measurement of anterior segment parameters: The related parameters were detected using a Pentacam anterior segment analyzer (Oculus, Germany) in the darkroom and the results were recorded. During the examination, the patient was seated with his/her lower jaw resting on the mandibular pad and the eyes fixed on the fixation target-the blue light band in the machine, for about 2 s. The operator moved the lever to aim and focus according to the prompts on the instrument screen. Finally, the detection result with "OK" imaging quality was selected, and the average value was obtained for several measurements.

Gonioscopy: the patient was informed of the inspection precautions and the affected eye was subjected to local surface anesthesia in

the dark room. Transparent antibiotic eye ointment was smeared on the ophthalmoscope. The patient was instructed to pull the lower eyelid with the index finger of one hand, place the lower edge of the ophthalmoscope at the lower fornix with the thumb and index finger of the other hand, and quickly raise the upper eyelid to send the upper edge of the ophthalmoscope to the upper fornix. The patient was asked to look forward and observe the four quadrants in a static state. In addition, they were instructed to keep the first glance position, without tilting the ophthalmoscope or pressing the lens. The Scheie classification method was used. Wide angle (W): all the structures of room angle can be seen; Narrow 1 (N1): visible part of ciliary body zone, no iris root; Narrow angle 2 (N2): no ciliary body band, only scleral process; Narrow angle 3 (N3): no rear trabecular net seen; Narrow angle 4 (N4): only Schwalbe line. Dynamic angle examination was performed if there was no posterior trabecular meshwork. The anterior chamber angle would be open if there was a posterior trabecular meshwork, otherwise there would be an adhesion. Finally, the ophthalmoscope corner mirror was removed, and the affected eye was washed and disinfected.

Surgical technique

The procedure consisted of standard phaco-emulsification and IOL implantation. All the recruited patients were treated by the same surgeon. The patient was anaesthetized with proparacaine hydrochloride. A 1.5 mm corneal incision, which was an auxiliary incision, was created 1 mm from the limbus at the 2:30 o'clock position to enter into the anterior chamber. Then 0.2 mL sodium hyaluronate was injected into the anterior chamber, and a 3.2 mm tunnel corneal incision at the 10:30 o'clock position was made, followed by continuous curvilinear capsulorhexis and hydrodissection. The nucleus and cortex aspiration were performed by Phaco. After polishing the posterior capsule, the IOL was implanted in the capsular bag, and viscoelastic material was then removed from the anterior chamber.

Statistical analysis

Statistical analyses were performed to compare the results between the PAC and PACG groups before and after surgery. Postoperative outcomes of different field groups of patients with PACG were also statistically analyzed. Data

Primary angle-closure/glaucoma with cataract

Table 1. Baseline characteristics

Demographics and Ocular characteristics	PAC (n=26)	PACG (n=36)	Total (n=62)	P Value
Gender (female/male)	21/5	27/9	48/14	0.592
Age (years)	65±8.53	70±8.83	68±8.91	0.056
Maximum IOP (mmHg)	39.96±19.33	42.86±19.57	41.65±19.36	0.565
Antiglaucoma medications	3.12±1.53	3.16±1.12	3.14±1.29	0.889
Preoperative IOP (mmHg)	14.92±5.05	14.69±4.44	14.79±4.67	0.846
PACG (eyes)				
Early stage, MD≤6 dB	/	7	7	/
Middle stage, 6<MD<12	/	8	8	/
Advanced stage, MD≥12 dB	/	21	21	/
BCVA (LogMar)	0.89±0.72	1.72±0.86*	1.36±0.90	<0.001
Average RNFL (mm)	92.50±6.31	62.55±9.37*	76.81±17.23	<0.001
ACD (mm)	1.69±0.43	1.72±0.34	1.71±0.38	0.772
ECC (cells/mm ²)	2555.45±404.52	2469.16±521.36	2508.08±469.74	0.519
AL (mm)	22.04±0.78	22.47±0.89	22.29±0.87	0.057

Data are presented as mean ± standard deviation, *VS. PAC, P<0.001.

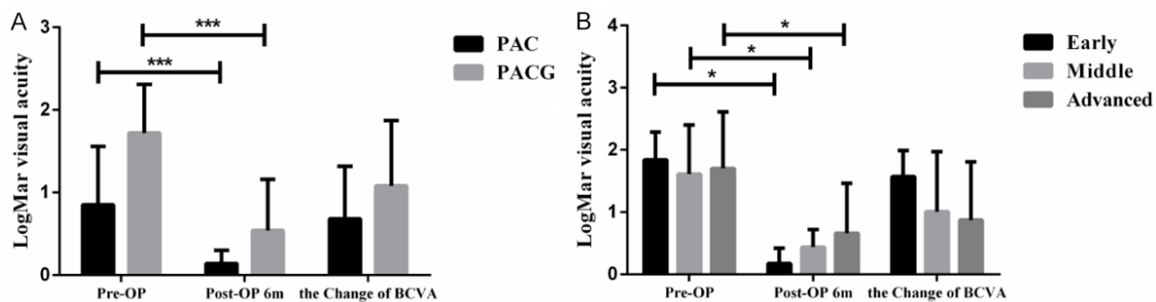


Figure 1. Bar graph showing BCVA before and after phacoemulsification. A. The BCVA in the PAC and PACG groups improved significantly at 6 months after surgery. B. Comparison of visual acuity difference among 3 PACG groups before and after surgery. *P<0.05, ***P<0.001.

were expressed as mean ± standard deviation (S.D.). Paired t test was performed for the comparison of BCVA, IOP, visual field, and RNFL at baseline and postoperatively within groups. Comparisons among groups were performed by one-way analysis of variance (ANOVA). Bonferroni's correction was used for post-hoc multiple comparisons. For nonparametric data, Mann-Whitney test was used. Pearson correlation analysis was used to examine the relationship between preoperative PAS and postoperative IOP. Statistical analyses were conducted using SPSS software version 20.0 (SPSS, Chicago, IL). P<0.05 was considered significant.

Results

Baseline characteristics

A total of 62 subjects were recruited for the study, including 26 PAC patients with 26 eyes

and 36 PACG patients with 36 eyes. There was no significant difference in gender ratio and age between the two groups (P>0.05). The BCVA was better and the average RNFL was shorter in PACG patients compared to PAC patients, with significant differences (P<0.05) (Table 1).

BCVA

The visual acuity (LogMar) in the PAC and PACG groups improved significantly at 6 months after surgery (Figure 1A). There was no significant difference in BCVA changes between the two groups (P>0.05).

As shown in Figure 1B, postoperative visual acuity was improved in early, middle, and advanced stages of PACG patients (P<0.05). There was no significant difference in the

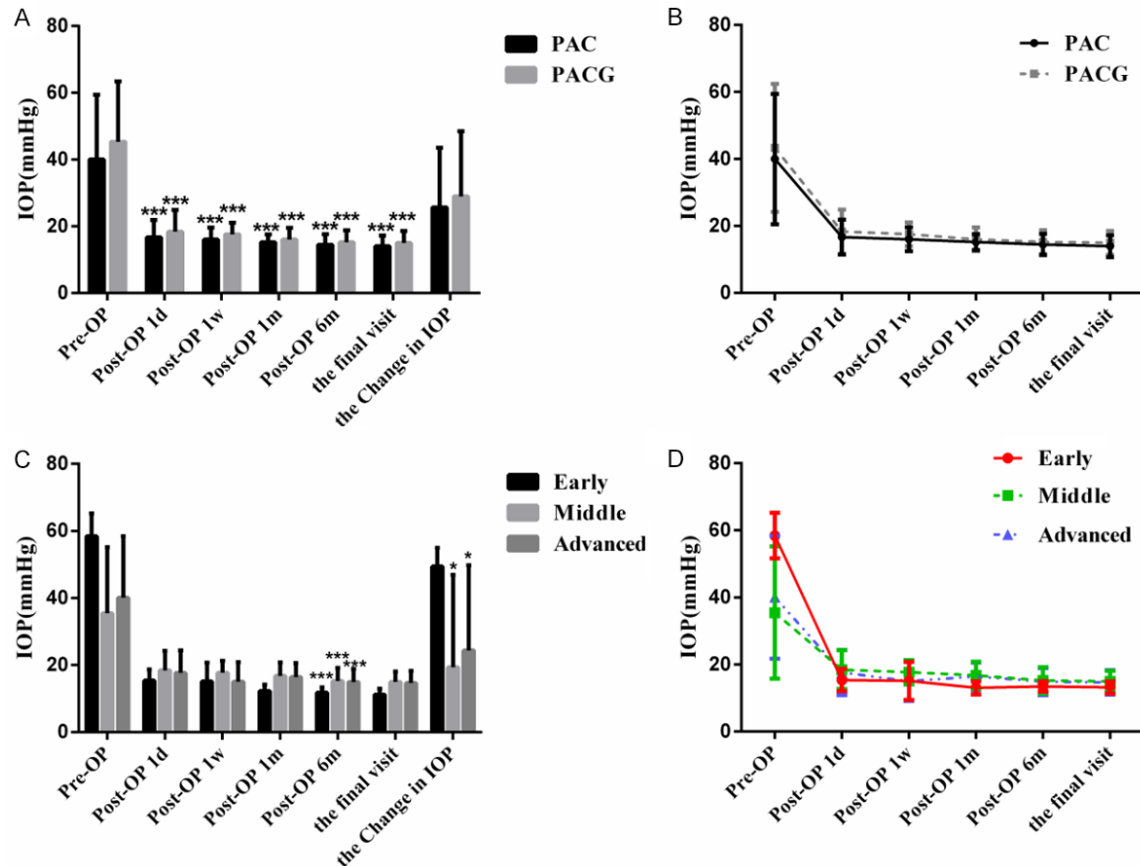


Figure 2. IOP changes during 6-month follow-up for each studied patient. A, B. This figure summarizes the mean IOP in PAC and PACG groups at various follow-ups. C, D. Comparison of postoperative IOP decrease among 3 PACG groups. Compared to pre-op in the same group, * $P < 0.05$, *** $P < 0.001$.

change of BCVA among patients with early, middle and advanced stage PACG ($P > 0.05$).

IOP

Figure 2A shows the preoperative IOP and postoperative IOP of PAC patients and PACG patients over time. There was a marked reduction in IOP in all subjects. Before surgery, IOP-lowering medication was given to control all subjects' IOP under 21 mmHg. As shown in **Figure 2B**, IOP at all postoperative timepoints in both groups decreased significantly compared to that before surgery.

The IOP of PACG patients in the early, middle, and advanced stages also decreased significantly after surgery (**Figure 2C** and **2D**). There was a significant difference in IOP reduction in 3 PACG groups before surgery and 6 months after surgery ($P < 0.05$). The IOP of patients with early, middle, and advanced PACG decreased by 80.24%, 61.77% and 67.38% respectively in

the 6 months after surgery. The IOP decrease in early PACG patients was the most significant ($P < 0.05$).

Medications in PACG patients

All patients used antiglaucoma medications to control IOP below 21 mmHg before surgery. The number of medications used in the PAC group and PACG group were 3.12 ± 1.53 and 3.16 ± 1.12 respectively (**Figure 3**). In this study, tafluprost or carteolol hydrochloride was given to reduce the IOP if the postoperative IOP was still greater than 21 mmHg. There was a significant reduction in the number of IOP-lowering medications postoperatively ($P < 0.001$).

ACD

As shown in **Figure 4A**, the preoperative ACDs of the PAC group and the PACG group was 1.75 ± 0.33 mm and 1.66 ± 0.32 mm, respectively. The ACD in the PAC group and the PACG

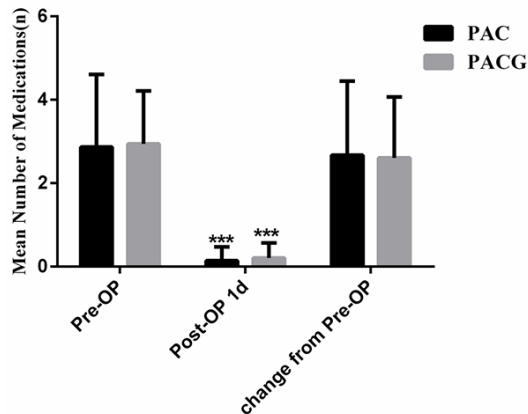


Figure 3. Bar graph showing the number of medications before and after phacoemulsification in all patients. Compared to Pre-op in the same group, * $P < 0.05$, *** $P < 0.001$.

group were deeper than the preoperative level in both groups ($P < 0.001$). There was no significant difference in the change of ACD between the two groups ($P > 0.05$).

The preoperative ACDs of patients with early, middle, and advanced PACG were 1.67 ± 0.14 mm, 1.70 ± 0.58 mm, and 1.60 ± 0.05 mm respectively (**Figure 4B**). ACD was significantly increased in the early, middle, and advanced stages groups respectively after surgery ($P < 0.05$). However, there was no significant difference among the three groups in ACD increase ($P > 0.05$).

RNFL

There was a significant difference between the early and advanced stage patients in the average RNFL before surgery. At 6 months postoperatively, compared to early stage PACG patients, there were significant decreases in RNFL in both middle and advanced stage PACG patients ($P < 0.05$). Nevertheless, the average postoperative RNFL of the three groups was not significantly reduced compared with that before the operation (**Figure 5A**, $P > 0.05$). There was no significant difference in the change of the average RNFL before and after the operation in the 3 groups of PACG patients ($P > 0.05$).

The temporal RNFL of PACG patients was not significantly decreased compared to the preoperative ones (**Figure 5B**, $P > 0.05$). There was no difference of the change in temporal RNFL before and after surgery in the 3 PACG groups ($P > 0.05$).

Visual field

The preoperative visual field defects of patients with early, middle, and advanced stage PACG were 3.14 ± 2.73 dB, 8.07 ± 0.65 dB and 19.74 ± 10.29 dB respectively, showing a significant difference between patients with early stage and advanced stage. At 6 months after the operation, the visual field of the advanced stage group was elevated compared to the early and middle stage groups, but there was no significant loss of visual field before and after the operation in the 3 groups (**Figure 6**, $P > 0.05$). Moreover, there was no significant difference in visual field changes before and after the operation among the 3 groups ($P > 0.05$).

Extent of PAS

BCVA: As **Figure 7A** shows, there was no difference in the changes in preoperative and postoperative BCVA in 4 different PAS extent groups ($P > 0.05$).

The IOP decreased significantly in the 6 months after Phaco in the 4 groups (**Figure 7B**, $P < 0.05$). However, there was no significant IOP change after surgery between the 4 groups with different PAS extents ($P > 0.05$). Pearson correlation analysis showed that there was no significant correlation between the decrease in postoperative IOP decrease and preoperative PAS extent (**Figure 7C**, $P > 0.05$).

Complications

There were no serious intraoperative complications such as rupture of the capsule and explosive choroidal hemorrhage in all cases. A few cases developed mild conjunctival hyperemia and corneal edema after surgery, which recovered after conservative treatment with hypertonic agents for 2-5 days. There were no postoperative complications such as endophthalmitis, malignant glaucoma, corneal endothelial decompensation, cystoid macular edema, or retinal detachment.

Discussion

Glaucoma is a common ocular disease characterized by increased (intermittent or persistent) intraocular pressure that can damage various tissues in the eye [23]. Patients with angle closure glaucoma have a complex eye anatomic structure. Due to the constantly increased IOP

Primary angle-closure/glaucoma with cataract

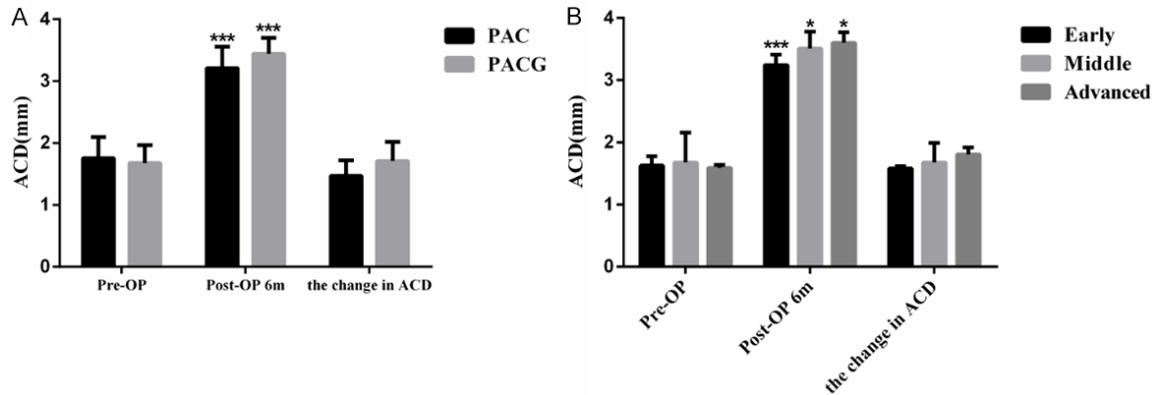


Figure 4. Comparison of ACD before and after surgery. (A) Increase in postoperative ACD of PAC and PACG patients. (B) Comparison of ACD between PACG patients before and after surgery. Compared to pre-op in the same group, *P<0.05, ***P<0.001.

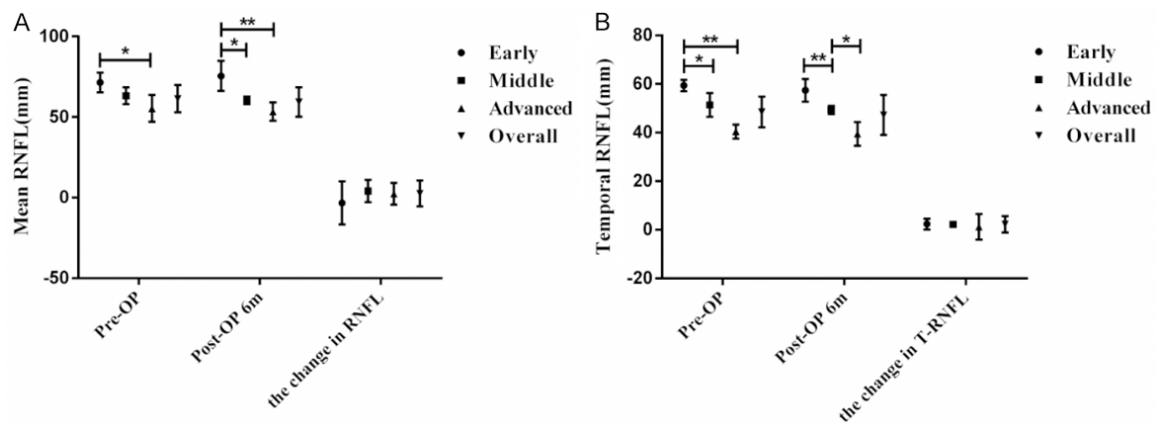


Figure 5. A. Mean RNFL between PACG patients before and after surgery. B. Temporal RNFL between PACG patients before and after surgery. *P<0.05, **P<0.01.

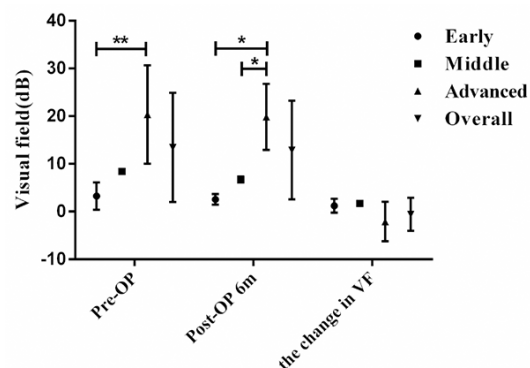


Figure 6. Pre- and post-operative visual field defects in PACG patients. *P<0.05, **P<0.01.

as a result of pupil block and atrial angle stenosis, the atrial angle structure changes, which in turn leads to the shallowing of the anterior chamber and the expansion and gradual thick-

ening of the lens, resulting in expansion of the iris and eventual glaucoma [24]. Angle closure glaucoma is often associated with cataract. With the aging of the population, the incidence of PACG associated with cataract has increased significantly. Currently, surgical treatment is preferred clinically [25]. Thanks to the continuous development of ultrasound and microscopy, patients can be treated by cataract Phaco and IOL implantation, which can well control the intraocular pressure, thus improving the vision level of patients. The objective of this study was to observe the efficacy of Phaco combined with IOL implantation in the treatment of PAC and PACG combined with cataract.

The results showed that Phaco combined with IOL implantation could improve the visual acuity in PAC and PACG patients and effectively

Primary angle-closure/glaucoma with cataract

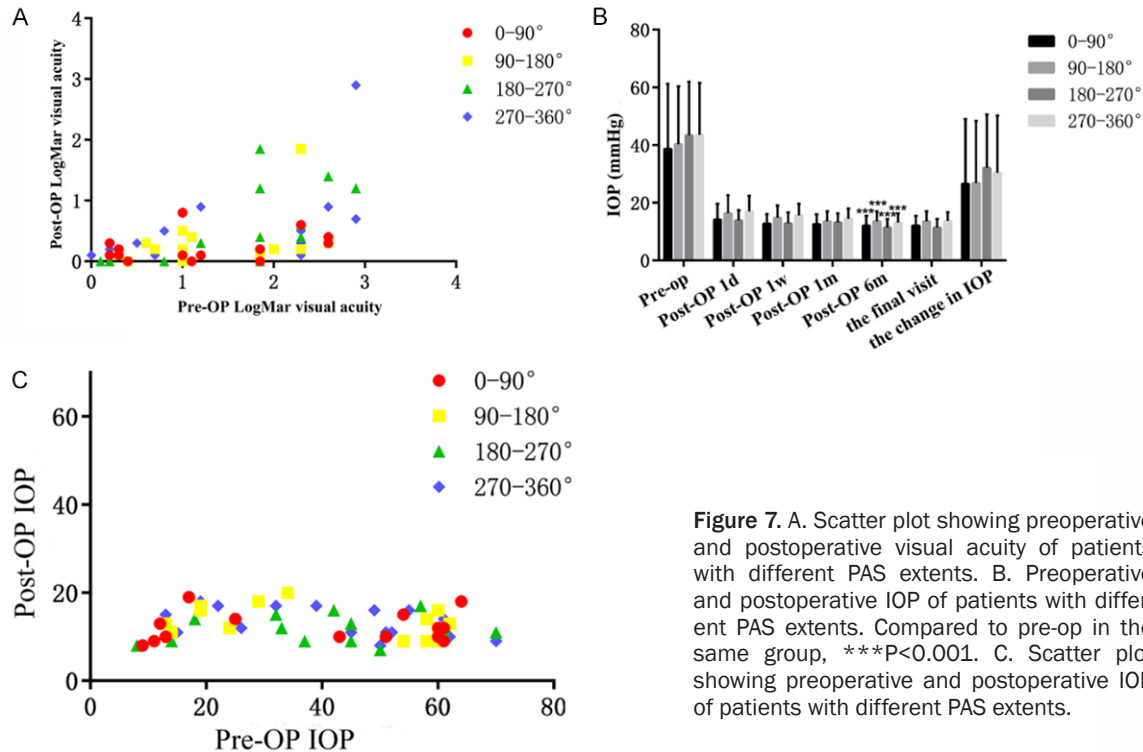


Figure 7. A. Scatter plot showing preoperative and postoperative visual acuity of patients with different PAS extents. B. Preoperative and postoperative IOP of patients with different PAS extents. Compared to pre-op in the same group, ***P<0.001. C. Scatter plot showing preoperative and postoperative IOP of patients with different PAS extents.

control IOP, with similar IOP reduction between the two groups, which was similar to the study of Romkens [26]. The main reason is that IOL implantation after lens resection can deepen the central anterior chamber, eliminate pupil obstruction, and effectively ameliorate the narrowing of the anterior chamber angle due to the thickness and anterior position of the lens. In the absence of adhesions, the intraocular pressure level can be effectively controlled by opening and closing the anterior chamber angle [27]. Phaco has a small incision and quick wound healing; moreover, the intraoperative angle reopening or adhesion caused by the impact of the pressure of the anterior chamber perfusion on the angle is reduced [15]. Moreover, Phaco combined with IOL implantation can improve the visual acuity and reduce the blood pressure at the same time, avoiding the need for a secondary surgery. In addition to this, the use of anti-glaucoma medications in the PAC group and PACG group was also significantly reduced at 1 month after surgery. None of the subjects used anti-glaucoma medications 1 month after surgery, and the ACD of patients was deeper than that before surgery. These results suggest that Phaco has a preferable tensile strength and closure, which can

promote the opening of the atrial angle, thus improving the anterior depth.

Since glaucoma can be divided into early, middle, and late stages according to the severity of the visual field defect, treatment outcomes can be vary in patients with different stages. Target IOP was defined [28] as “the IOP that prevents further progression of glaucomatous visual field loss, without compromising a patient’s quality of life”. Only by setting the target IOP for PACG patients at each stage can IOP be actively controlled and further optic nerve damage can be effectively prevented. Therefore, individualized treatment plan and target IOP should be developed according to the disease characteristics of different individuals. In our study, all the PACG patients in the early and middle stages achieved their target IOP postoperatively, while patients with advanced stage PACG did not reach the reference target IOP. Even so, vision was improved in advanced stage patients and the ACD was increased in early, middle, and advanced PACG patients as well. Thus, it can be seen that Phaco combined with IOL implantation in the treatment of PACG at different stages can have an effective therapeutic effect.

The efficacy of Phaco in PAC/PACG patients with varying extents of PAS is controversial. Zhuo, et al. [29] showed that Phaco for patients with PACG and PAS >180 degrees could effectively control IOP in the 6 months after surgery. Latifi, et al. [30] believed that for PACG eyes with PAS greater than or less than 180 degrees, Phaco can open the atrial angle and reduce the extent of postoperative PAS. Sham et al. [31], showed that PAC/PACG patients with PAS greater than 180 degrees had a more significant postoperative reduction in IOP than those with a smaller PAS. In our study, visual acuity in the 4 groups was significantly improved, and IOP was also significantly decreased after surgery. However, there were no significant differences in visual acuity improvement and IOP changes among the groups. In addition, the results of our study preliminarily showed that there was no correlation between IOP controls and the extent of PAS.

In conclusion, we propose that Phaco combined with IOL implantation can be used as the preferred treatment for patients with PAC and early PACG patients. It can achieve good clinical efficacy for patients in the middle and advanced stages, and effectively prevent further reduction in RNFL thickness and an advanced visual field defect in such patients. However, Phaco can be implemented only after careful evaluation according to individual differences among patients. To make the analysis more convincing and reliable, further observation and analysis of clinical cases with multi-center and large sample size should be performed, which can provide therapeutic direction and guidance, that have clinical significance and value.

Disclosure of conflict of interest

None.

Abbreviations

Phaco, Phacoemulsification; PACG, Primary angle-closure glaucoma; PAC, Primary angle closure; PACS, Primary angle-closure suspect; IOP, Intraocular pressure; HPA, Hodapp-Parrish-Anderson; LPI, Laser peripheral iridotomy; BCVA, Best-corrected visual acuity; ACD, Anterior chamber depth; AL, Axial length; ECD, Endothelial cell density; RNFL, Retinal nerve fiber layer.

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