·Clinical Research·

Comparison of phacotrabeculectomy and sequential surgery in the treatment of chronic angle-closure glaucoma coexisted with cataract

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Abstract

• AIM: To compare the safety and effectiveness of phacotrabeculectomy versus sequential surgery in chronic angle-closure glaucoma (CACG) with coexisting cataract.

• METHODS: One hundred and sixty-two CACG patients (162 eyes) were retrospectively analyzed. Of them, 87 patients (87 eyes) in group A had underwent phacotrabeculectomy with intraocular lens (IOL) implantation, and 75 patients (75 eyes) in group B had underwent sequential surgery with IOL implanted. Best-corrected visual acuity (BCVA), intraocular pressure (IOP), complications and anterior chamber angle (ACA) were measured.

• RESULTS: Demographic characteristics of the two groups were similar. A mean follow-up period was 15±6mo (range 13 to 24mo), a mean IOP of 12.14±5.32 mm Hg in group A and 11.38±4.06 mm Hg in group B (P=0.84) at the last follow up. The Kaplan-Meier analysis revealed that the cumulative probability of success in both groups was similar (P=0.61). Anterior uveitis and hypotony were the most common complications in group A, whereas group B experienced shallow anterior chamber with trabeculectomy. With the exception of anterior uveitis, no complications occurred to 11 trabeculectomized eyes. All postoperative measurements of anterior chamber showed statistically significant differences in each group according to the preoperative data (P<0.05). However, fewer changes occurred in group B than in group A.

• CONCLUSION: Phacotrabeculectomy and sequential surgery exhibit similar IOP reduction, visual recovery, and complications when treating CACG patients with cataract. However, for a wider ACA, phacotrabeculectomy has demonstrated higher effectiveness than sequential surgery.

• **KEYWORDS:** chronic angle-closure glaucoma; phacotrabeculectomy; sequential surgery; anterior chamber angle
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INTRODUCTION

The chronic angle-closure glaucoma (CACG) and cataract frequently coexist in the same eye, and both are the two major causes of blindness among Chinese elderly. Documents indicate that a proportionately large lens plays a crucial role in the pathogenesis of primary angle-closure disease (related to pupillary-block and angle-crowding mechanisms of filtration angle-closure), especially when the lens becomes opaque [1-2]. When the posterior pigmented trabecular meshwork is not visible on gonioscopy of more than 180°, maximal medical therapy and/or laser iridotomy is usually ineffective in controlling intraocular pressure. This condition in turn may lead to surgical intervention [3]. Trabeculectomy is the classical surgical approach for the treatment of this condition, and there is also a rapid progression of lens opacities into visually-significant cataracts that require cataract surgery [4-6]. Treatment for patients experiencing concurrent cataract and glaucoma includes both phacotrabeculectomy and sequential surgery [an initial trabeculectomy was performed independently, and cataract extractions were further performed on the trabeculectomized eyes with intraocular lens (IOL) implantation]. There is a lack of consensus on the best approach to surgical management of such cases. Recent evidence indicates that lens should be extracted to widen the anterior chamber angle (ACA) in order to reduce the risk of recurrence of acute attacks [7-8]. Furthermore, the efficacy and safety of phacotrabeculectomy were also observed among primary open angle glaucoma patients [9-12]. However, longer-term data of phacotrabeculectomy and sequential surgery concerning CACG is still insufficient. Therefore, a retrospective analysis was conducted on the outcomes of these two surgical methods in the study.

SUBJECTS AND METHODS

A retrospective review was carried out of patients with CACG and coexisting cataract who underwent phacotrabeculectomy or sequential surgery with IOL implantation at the Department of Ophthalmology, Daping Hospital, the Third Mlitary Medical University, Chongqing, China, between June 2012 and December 2014. Informed consent was obtained from each patient and no participants receive a stipend. The study was approved by the local Ethics Committee and conformed to the tenets of the Declaration of Helsinki.

Inclusion and Exclusion Criteria CACG was diagnosed with typical glaucomatous cupping of the optic disc, visual field changes, or both, combined with trabecular meshwork invisible for more than 180°, confirmed by gonioscopy and an intraocular pressure (IOP) ⩾21 mm Hg. Eyes with visually-significant cataract according to the Lens Opacities Classification System, version Ⅲ (LOCS Ⅲ)[13]. No previous surgical or argon laser peripheral iridotomy were included.

Glaucoma secondary to inflammation, trauma, iridocorneal endothelial syndrome and neovascularization *etc*., and eyes with a history of ocular surgery, vitreoretinal disorders and non-glaucomatous optic neuropathy (GON), advanced glaucomatous visual field defects threatening central vision, and less than one year of follow-up postoperative duration had been excluded.

All patients underwent a comprehensive ophthalmologic evaluation by qualified glaucoma doctors, including: slit-lamp biomicroscopy, best-corrected visual acuity (BCVA), measured with the logarithm of minimum angle of resolution (logMAR) notations; and IOP, measured with a calibrated Goldmann applanation tonometry. Parameters of anterior chamber were assessed by slit lamp-adapted optical coherence tomography (SL-OCT, Heidelberg Engineering, Heidelberg, Germany). ACA (°), anterior chamber distance (ACD, mm) angle opening distance (AOD, mm), and trabecular-iris space area (TISA, mm^2) were measured automatically using a software program supplied with this device. The cross-sectional OCT image with the best quality was further analyzed with the Zhongshan Angle Assessment Program (ZAAP, Guangzhou, Guangdong Province, China)[14].

Surgical Procedure Trabeculectomy was performed under peribulbar or topical anaesthesia. A superiorly located, fornix-based conjunctival flap was prepared. A mixture of 4×3 mm rectangular partial-thickness scleral flap and a sponge soaked in 0.04% mitomycin C was applied onto the subconjunctival pocket and under the scleral flap for one to three minutes, and rinsed with approximately 50 mL of balanced saline solution. Phacoemulsification of cataract through a temporal clear cornea incision was performed and combined with acrylic IOL implantation. A 2×2 mm section of corneoscleral tissue was excised, and a peripheral iridectomy was performed. Scleral flap was closed with 10-0 nylon sutures, whereas the Tenon capsule and conjunctiva were closed with 8-0 vicryl sutures.

Table 1 Demographic and preoperative characteristics of subjects between both groups

Characteristics	Group A	Group B	^1P
Patients, *n* (%)	87 (53.7%)	75 (46.3%)	-
Eye (right/left)	42/45	41/34	0.09
Mean age (SD, a)	58.4±16.3	62.6±10.4	0.78
Gender (male/female)	35/52	37/38	0.06
BCVA (logMAR)	0.65±0.64	0.53±0.46	0.17
IOP (mm Hg)	31.50±4.71	30.27±5.00	0.76
MD (dB)	17.4±6.3	15.3±7.4	0.16

BCVA: Best-corrected visual acuity; LogMAR: Log of the minimum angle of resolution; MD: Mean deviation of the visual field. ^1P measured with the Chi-squared test or Student's *t*-test as appropriate.

Patients in group A underwent trabeculectomy combined with phacomusification, while patients in group B initially underwent trabeculectomy, followed by phacomusification on the trabeculectomized eye. All of the surgeries were carried out by qualified glaucoma doctors. After surgery, topical corticosteroid and antibiotics were administered for one week. Cycloplegics were used only on the day after surgery and were continued only if the anterior chamber was shallow.

Patient reviews were conducted approximately 1d, 1wk, 1, 3mo after surgery. Subsequent reviews were conducted every 6mo. The surgical results were assessed in terms of IOP, visual acuity, complications, and anteriro chamber as measured by SL-OCT. Complete IOP control success was defined as 6 to 21 mm Hg without any application of glaucoma medications. Qualified success was applied to the same IOP levels mentioned above, using two medications or less. Failure was defined as IOP >21 mm Hg, and/or the event of an eye with a lower IOP requiring more than two medications [12].

Statistical Analysis SPSS software version 19.0 (IBM Corp., New York, NY, USA) was used for statistical analysis. The differences between the two groups were examined using Student's *t*-test for independent samples with normal distribution. Fisher's exact test was used to compare the complication; One-way ANOVA for repeated IOP; the Kaplan-Meier survival analysis to assess the cumulative probability of surgery; and the log-rank test to compare survival curves between the groups' success. Parameters of AC by SL-OCT between baseline and the last follow-up with two-sample *t*-test, *P* values of 0.05 or less were considered to be statistically significant.

RESULTS

A total of 162 eyes in 162 patients were included. Eighty-seven patients underwent phacotrabeculectomy and IOL implantation (group A), while 75 patients underwent sequential surgery with IOL implanted (group B). All patients were followed with a mean of 15±6mo, with a follow-up period ranging from 13 to 24mo. Patients' characteristics were summarized in Table 1. No significant

Table 2 Preoperative and postoperative characteristics at the last follow up for both groups

Characteristics	Group A			Group B			P^2
	Preoperative	Postoperative	P^1	Preoperative	Postoperative	P^1	
BCVA (logMAR)	1.06±0.48	0.65 ± 0.64	0.03	1.05±0.64	0.53±0.46	0.04	0.33
IOP (mm Hg)	31.50±4.71	16.61±6.43	<0.01	30.27±5.0	15.80±5.35	<0.01	0.84
MD (dB)	17.4±6.3	8.13±1.12	0.04	15.3±7.4	7.41±0.43	0.03	0.11
ACA (°)	15.64±4.19	32.35±5.28	<0.01	16.32±4.23	22.35±4.73	0.07	0.001
ACD (mm)	2.01±0.32	2.5±0.28	<0.01	2.05±0.33	2.46±0.25	<0.01	0.121
AOD500 (mm)	0.206±0.106	0.226±0.126	<0.01	0.213±0.128	0.212±0.125	0.004	0.006
AOD750 (mm)	0.410±0.101	1.12±0.67	<0.01	0.311±0.31	1.15±0.54	<0.01	0.226
TISA500 (mm^2)	0.134±0.119	0.213±0.120	<0.01	0.126±0.20	0.173±0.231	<0.01	0.003
TISA750 (mm^2)	0.235±0.137	0.401±0.165	<0.01	0.242±0.181	0.385±0.236	<0.01	0.104

BCVA: Best-corrected visual acuity; LogMAR: Log of the minimum angle of resolution; IOP: Intraocular pressure; MD: Mean deviation; ACA: Anterior chamber angle; ACD: Anterior chamber depth; AOD: Angle open distance; TISA: Trabecular-iris space area. [1]Comparison of postoperative and preoperative; [2]Comparison of group A and group B postoperatively.

differences between the two groups were found for preoperative IOP, age, gender, and BCVA. Table 2 lists the mean IOP, BCVA, ACA, central ACD, AOD500, AOD750, TISA500, TISA750, and mean deviation (MD) of the visual field at the last follow-up after surgery.

Intraocular Pressure At the last follow-up, the mean IOP in group A was decreased from 31.50±4.71 mm Hg to 16.61±6.43 mm Hg (P<0.01). Postoperative values in group B were similar, with a decrease from 30.27±5.0 mm Hg to 15.80±5.35 mm Hg (P<0.01), when compared to values obtained preoperatively. However, there were no significant differences in mean IOP between these groups at the last follow-up (P=0.84). Figure 1 shows the distribution of IOP of both groups at baseline and the follow up. Overall, of the 87 eyes that received the phacotrabeculectomy in group A, 62 (71.26%) were considered successes, 11 (12.64%) qualified success, and 14 (16.09%) failures, while in the sequent surgery group, there were 56 (74.67%) successes, 7 (9.33%) qualified successes, and 12 (16.0%) failures (Table 3). Figure 2 illustrates the Kaplan-Meier survival analysis for all subjects. There was no significant difference in cumulative probability of success between the two groups (P=0.61, log-rank test).

Visual Acuity Visual acuity outcomes are summarized in Table 2. The logMAR BCVA in group A improved from 1.06±0.48 preoperatively to 0.65±0.64 at the last follow-up (P =0.03), and can be associated with a total of 79.31% patients' who experienced improved visual acuity. Similar improvement was observed in group B from 1.05±0.64 to 0.53 ±0.46 (P =0.04), with 82.67% of subjects having improved visual acuity. However, there were no significant differences in BCVA between these groups at the last follow-up (P=0.33).

In group A, visual acuity maintained in 16 eyes (18.39%), while two patients (2.30%) experienced deteriorated vision. In group B, 12 (16.0%) maintained, and 1 (1.33%) experienced loss of more than one line at the last follow up (Table 3).

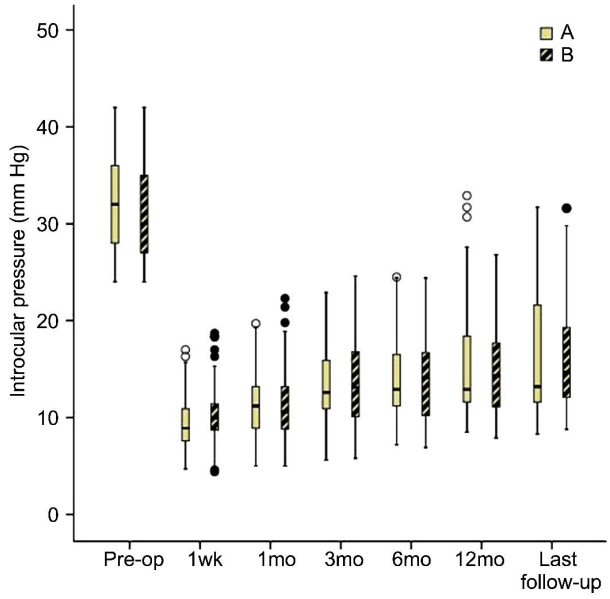

Figure 1 The distribution of IOP of both groups at baseline and the follow up IOP distribution preoperatively and during follow-up at 1wk, 1, 3, 6, 12mo and last visit for subjects. Box extend to 25th and 75th percentiles (interquartile range) and also show median value. There were no statistically significant differences between both groups at the last follow up.

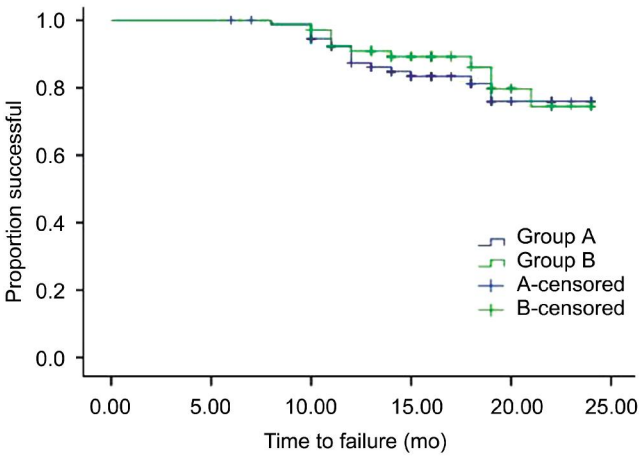

Figure 2 The Kaplan-Meier survival analysis for all subjects There was no significant difference in cumulative probability of success between the two groups (P=0.61, log-rank test).

Table 3 Overall IOP and visual outcome of both groups *n* (%)

Groups	Overall IOP outcome			*P*	Overall visual outcome			*P*
	Success	Qualified success	Failure		Improved	Maintained	Loss of more than one line	
Group A	62 (71.26)	11 (12.64)	14 (16.09)	0.19	69 (79.31)	16 (18.39)	2 (2.30)	0.15
Group B	56 (74.67)	7 (9.33)	12 (16.0)		62 (82.67)	12 (16.0)	1 (1.33)	

Complete IOP control success was defined as IOP of 6 to 21 mm Hg without any glaucoma medications. Qualified success was applied to the same IOP levels mentioned above, using two medications or less. Failure was defined as IOP >21 mm Hg. The Chi-squared test was used between two groups.

Surgical Complications Postoperative complications are listed in Table 4. No patient had an intra-operative complication. Overall, 40 eyes (45.9%) in group A and 29 eyes (38.7%) in group B experienced postoperative complications (P=0.07). Anterior uveitis (36.7%) and hypotony (19.5%) were the most common complications in group A, whereas shallow anterior chamber (25.3%) and hypotony (22.6%) mostly affected group B (with trabeculectomy alone). Except for anterior uveitis, no complications occurred to 11 trabeculectomized eyes (14.6%) that underwent phacomusificaiton. Complications in both groups were resolved using medication, with the exception of three cases in group B (which had malignant glaucoma and were resolved by lens extraction). No serious complications, such as corneal decompensation, suprachoroidal hemorrhage and endophthalmitis occurred in the two groups.

Parameters of Anterior Chamber The mean values of the anterior chamber parameters are summarized in Table 2. All subjects of both groups had small parameters of ACA before surgery, and there was no significant difference among the ACA, AOD750 and TISA500 between them. When parameters before and after surgery in each group were compared, all measurements showed statistically significant differences (P<0.05). At the last follow up, there were significant statistical differences in group A and group B among ACA (32.35°±5.28° in group A, 22.35°±4.73° in group B, P=0.001), AOD500 (0.226±0.126 mm in group A, 0.212±0.125 mm in group B, P=0.006), and TISA500 (0.213±0.120 mm^2 in group A, 0.173±0.231 mm^2 in group B, P=0.003); whereas there were no significant difference for AOD750 (1.12±0.67 mm in group A, 1.15 ±0.54 mm in group B, P =0.226) and TISA750 (0.401±0.165 mm^2 in group A, 0.385±0.236 mm^2 in group B, P=0.104).

Table 4 Postoperative complications between both groups *n* (%)

Complications	Group A[a]	Group B[a]	*P*
None	40 (45.9)	29 (38.7)	0.07
Hypotony	17 (19.5)	17 (22.6)	
Shallow anterior chamber	3 (3.4)	19 (25.3)	
Choroidal effusion	9 (10.3)	8 (10.6)	
Anterior uveitis	32 (36.7)	6 (8.0) & 11 (14.6)[b]	
Malignant glaucoma	0	3 (4.0)	

[a]One patient had two complications; [b]Complication occurred in trabeculectomized eyes receiving lens extraction only. Fisher's exact test was applied to them.

DISCUSSION

For medically-unresponsive CACG patient with established synechial angle closure and advanced GON, active management of the IOP is essential. Combined cataract extraction with trabeculectomy or sequential surgery has been suggested as a treatment option for glaucoma coexist cataract in the elderly population[10-11,15-17]. Appropriate surgical decisions for angle closure should be congruous with the patient's anatomic defects. However, limited studies have been completed to evaluate the effects of two different treatment options for patients with CACG.

In our clinical study, we compared results of phacotrabeculectomy and sequential surgery on eyes with CACG and cataract. We found that phacotrabeculectomy reduced the mean IOP from a preoperative level of 31.50±4.71 mm Hg to 16.61±6.43 mm Hg at the last follow up (P<0.01), which was similar to patients treated with sequential surgery from a preoperative level of 30.27±5.0 mm Hg to 15.80±5.35 mm Hg (P<0.01). However, there were no statistically significant differences between both groups, which is consistent with the reported literature [18]. The reduction in IOP in both groups was modest and sustained. This may be due to the angle width increasing the outflow of aqueous humor with the cataract extraction and/or a functional filtering bleb[17,19-20]. In terms of overall IOP control, 71.26% *vs* 74.67% of patients achieved IOP within 6 to 21 mm Hg without the use of anti-glaucoma medication; and 12.64% *vs* 9.33% achieved qualified success IOP using medications in two groups. Figure 2 illustrates the Kaplan-Meier survival analysis for all subjects. There was no significant difference in cumulative probability of success between the two groups(P=0.61). Fourteen patients in group A and twelve in group B failed to control the IOP in the end, despite the angle opening by SL-OCT; if the IOP is well controlled on a low dose of well-tolerated medication with mild glaucomatous damage, early cataract surgery alone may be a reasonable choice to deepen the anterior chamber. When the glaucoma is uncontrolled despite maximum tolerable medical therapy and laser trabeculoplasty, the eyes may require filtering surgery first that has the greatest chance of providing long-term IOP control, the cataract can be removed 4 to 6mo later, a modest sustained reduction of IOP should be dependent on a functional filtering bleb as the onset of permanent trabecular dysfunction. Bleb function will decrease spontaneously for its gradual vascularization, even

in a trabeculectomy alone. Furthermore, inflammatory mediators and cells released by lens extraction have been shown to aggravate bleb's vascularization. The risk of more vascularized blebs and less prominent IOP is increased if the time between trabeculectomy and cataract surgery is shorter[21-23].

It is difficult to compare the incidence of hypotony-related complications between two groups, as they do not exist independently. Rather, they influence each other and experience reciprocal causation. Hypotony is often found in the early period after surgery; as the literature reports, this was mostly induced by a strong bleb filtering or choroidal detachment, and even by an inflammatory response that would inhibit aqueous secretion[4,21]. But this occurred to none of the patients who underwent lensectomy on trabeculctomized eyes, as it relies on an intact eyeball without blood ocular barrier damage and relative stability of the IOP. Additionally, previous studies have shown that trabeculectomy is associated with higher risk of postoperative complications, such as shallow anterior chamber [24]. In most of those eyes, the anterior deepens spontaneously with time and requires no special management beyond the usual postoperative care. These findings were comparable to our results, with the exception of a low incidence in group A (which may be due in part to intumescent lens extraction). Moreover, a higher incidence of anterior uveitis was observed in 36.7% of eyes with phacotrabecutomy, compared to 8.0% of eyes with trabeculectomy alone and 14.6% of phacomusificaiton on trabeculectomized eyes. This might be a disadvantage when compared with phacomusificaiton subsequent trabeculectomy, which in turn can be attributed to a combination of prolonged operation times and damaged blood ocular barrier. However, treatment is possible through corticosteroid eye drops. According to documents, malignant glaucoma is not a rare complication after trabeculatomy. Only 3 cases (4.0%) occurred after trabeculectomy alone in group B, which was treated by removing the lens- results which are similar to Wang *et al*'s work [25]. This can be explained by thick lens being one risk factor for malignant glaucoma in CACG. No other adverse complication such as corneal decompensation and endophthalmitis following implanted IOL were encountered in both groups.

It is well recognized that combined cataract extraction with implanted IOL can lead to visual rehabilitation. LogMAR BCVA improved in group A from 1.06±0.48 preoperatively to 0.65±0.64 at the last follow-up (P=0.03), and can be associated with a total of 79.31% patients' who experienced improved visual acuity. Similar improvement was observed in group B, from 1.05±0.64 to 0.53±0.46, with 82.67% of subjects having improved visual acuity and 16.0% of subjects having equal preoperational vision. However, no differences were confirmed in both groups at the last follow-up (P=0.15). Two patients in group A and one in group B lost more than one line; these occurences were mostly induced by advanced GON and other hypotony-related diseases. This result is similar to those found in reported literature[26].

In addition, several results indicated that extracting the thick lens and replacing it with a thinner IOL will result in a deepened anterior chamber. Such actions sustained a modest reduction in IOP, with the angle more open, and a lower IOP for primary angle closure glaucoma (PACG) as well as less risk factor of progressive glaucomatous damage[17,27-28]. Similar to previous studies, patients of CACG had significantly shallow anterior chamber, as assessed by SL-OCT [8,29-30]. Parameters of anterior chamber among, ACA, AOD500, TISA500 of both groups at the last follow up increased significantly after lens extraction. However, no differences in AOD 750 and TISA750 were found, and less widening occurred in group B. This may be due to cataract expansion and subsequent inflammation in the postoperative period, which resulted in permanent iris peripheral anterior synechiae (after independent trabeculectomy). Also, biometry and clinical examination of PACG patients identifies that anatomic risk factors for angle closure and lens can push the peripheral iris (angle crowding) against the trabecular meshwork. This allows for long-standing inflammatory peripheral anterior synechia agreement with literature that shows that lensectomy combined with goniosynechialysis precedes cataract surgery alone[27,31].

All of the data suggests that the shallowing of the anterior chamber occurs from intumescent cataract or plateau-iris syndrome , and combining lens extraction in CACG patients with established synechial angle-closure is essential not only for visual rehabilitation, but also for a wider ACA, however, phacotrabeculectomy has demonstrated higher effectiveness than sequential surgery. With respect to these results, phacotrabeculectomy and sequential surgery exhibit similar IOP reductions, success rates, and complications. But with regards to wider angle, we prefer phacotrabeculectomy when it comes to treating CACG patients with coexisting cataract.

However, there are some limitations in this study, as it was performed retrospectively with a small sample population. Furthermore, prospective randomized studies need to be completed in order to further explore the safety and effectiveness of phacotrabeculectomy versus sequential surgery.

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