Phacoemulsification versus Trabeculectomy in Medically Uncontrolled Chronic Angle-Closure Glaucoma without Cataract

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Objective: To compare phacoemulsification versus trabeculectomy with adjunctive mitomycin C in medically uncontrolled chronic angle-closure glaucoma (CACG) without cataract.

Design: Prospective, randomized clinical trial.

Participants: Fifty medically uncontrolled CACG eyes without cataract of 50 patients.

Intervention: Patients were randomized into undergoing either phacoemulsification or trabeculectomy with adjunctive mitomycin C. After surgery, patients were followed up every 3 months for 2 years.

Main Outcome Measures: Intraocular pressure (IOP) and requirement for glaucoma drugs.

Results: Twenty-six CACG eyes were randomized to receive phacoemulsification, and 24 eyes underwent trabeculectomy with mitomycin C. Phacoemulsification and trabeculectomy resulted in significant and comparable IOP reduction at 24 months after surgery (reduction of 8.4 mmHg or 34% for phacoemulsification vs. 8.9 mmHg or 36% for trabeculectomy; \( P = 0.76 \)). Over first 24 months, trabeculectomy-treated eyes required on average 1.1 fewer drugs than phacoemulsification-treated eyes (\( P < 0.001 \)). However, trabeculectomy was associated with significantly more surgical complications than phacoemulsification (46% vs. 4%; \( P = 0.001 \)). Eight (33%) of 24 trabeculectomy eyes demonstrated cataract during follow-up.

Conclusions: Both phacoemulsification and trabeculectomy are effective in reducing IOP in medically uncontrolled CACG eyes without cataract. Trabeculectomy is more effective than phacoemulsification in reducing dependence on glaucoma drugs, but is associated with more complications.

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At least 180° of angle closure obliterating pigmented part of trabecular meshwork, whether synechial or appositional, segmented or continuous, in the presence of a patent peripheral iridotomy

- Requiring IOP-lowering medications, or IOP of more than 21 mmHg without IOP-lowering medications

- Visual field loss compatible with glaucoma,* glaucomatous optic disc changes, or both

- Definition of medically uncontrolled: IOP of more than 21 mmHg despite maximally tolerated medications or requiring more than 3 topical drugs for IOP control (combination drugs counted as 2 drugs)

- Best-corrected visual acuity of 20/40 or better and not affecting activities of daily living

- Eyes with medically uncontrolled CACG and no cataract as defined above

- Patient able and willing to give informed consent to phacoemulsification or trabeculectomy before randomization

- Single functional eye

- Patient declining either lens extraction or trabeculectomy

- Previous intraocular surgery, with the exception of laser peripheral iridotomy and laser peripheral iridoplasty

CACG = chronic angle-closure glaucoma; IOP = intraocular pressure.

*Minimal criteria for glaucomatous visual field defect as per published standard: glaucoma hemifield test results outside normal limits, pattern standard deviation with a $P$ value of less than 0.05, or a cluster of 3 points or more in the pattern deviation plot in a single hemifield (superior or inferior) with $P$ value of less than 0.05, one of which must have a $P$ value of less than 0.01. Any one of the preceding criteria, if repeatable, was considered sufficient evidence of a glaucomatous visual field defect.

Table 1. Recruitment Criteria

<table>
<thead>
<tr>
<th>Diagnostic criteria for medically uncontrolled CACG</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>At least 180° of angle closure obliterating pigmented part of trabecular meshwork, whether synechial or appositional, segmented or continuous, in the presence of a patent peripheral iridotomy</td>
<td>Age 50 years or older</td>
<td>Single functional eye</td>
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<tr>
<td>Requiring IOP-lowering medications, or IOP of more than 21 mmHg without IOP-lowering medications</td>
<td>Eyes with medically uncontrolled CACG and no cataract as defined above</td>
<td>Patient declining either lens extraction or trabeculectomy</td>
</tr>
<tr>
<td>Visual field loss compatible with glaucoma,* glaucomatous optic disc changes, or both</td>
<td>Patient able and willing to give informed consent to phacoemulsification or trabeculectomy before randomization</td>
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Clinical trial registration. Informed consent was obtained from all patients before recruitment.

Patients fulfilling the recruitment criteria in Table 1 were recruited. Only 1 eye from each patient could be recruited. If both eyes of 1 patient had medically uncontrolled CACG and no cataract, the eye with the worse IOP control was included in the study.

Preoperative IOP, number of IOP-lowering drugs, best-corrected visual acuity (BCVA) by Snellen chart and converted to logarithm of the minimum angle of resolution (logMAR) visual acuity, angle grading by darkroom indentation gonioscopy, vertical cup-to-disc ratio (VCDR), and optic nerve head assessment by an expert observer at the slit lamp using a 90-diopter (D) hand-held lens, and visual field static automated white-on-white threshold perimetry (program 24–2. Swedish interactive threshold algorithm-standard, model 750; Humphrey Instruments, Dublin, CA) were documented for the study eye.

Two IOP measurements by Goldmann applanation were obtained at the recruitment visit, but if the readings differed by more than 2 mmHg, a third measurement was obtained. The IOP was defined as the mean of 2 IOP measurements or the median of 3 measurements. All IOP measurements and the number of glaucoma drugs were recorded before stopping pilocarpine, if any, in the phacoemulsification group. The VCDR was taken to be the longest vertical cup diameter divided by the longest vertical disc diameter.

The study eye then was randomized into 1 of 2 treatment groups, using a random number table: lens extraction by phacoemulsification or trabeculectomy with adjunctive mitomycin C chemotherapy. The surgical interventions in the 2 treatment groups are summarized in Table 2. In both treatment groups, all surgical procedures were performed by a single experienced glaucoma surgeon (CCVT) under topical anesthesia in 2 ophthalmic centers (Hong Kong Eye Hospital and Prince of Wales Hospital).

After surgery, study visits were scheduled at 1 day, 1 week, 1 month, 3 months, and then every 3 months for 2 years, with documentation of IOP, number of IOP-lowering drugs required, logMAR BCVA, angle status by darkroom indentation gonioscopy, VCDR, complications, and additional interventions required to maintain filtration or to address complications. Visual field by Humphrey automated perimetry was repeated at 1 and then 2 years after surgery. Additional clinic visits and investigations were to be scheduled as and when required. All these were recorded in the data sheet.

Outcome Measures

The primary outcome measures were IOP and the number of IOP-lowering drugs. Secondary outcome measures included logMAR BCVA, surgical complications, and need for additional surgical interventions.

Indications for Additional Surgical Intervention in the Postoperative Period

In the phacoemulsification group, subsequent trabeculectomy with adjunctive mitomycin C chemotherapy was indicated if IOP increased to more than 21 mmHg despite maximally tolerated medications or if more than 3 topical drugs were required for IOP control (combination drugs counted as 2 drugs) at more than 1 follow-up visit.

In the phacoemulsification group, yttrium–aluminum–garnet laser posterior capsulotomy was indicated if there was significant posterior capsular opacification, and the BCVA deteriorated to worse than 20/40 and began to affect activities of daily living. In the trabeculectomy group, subsequent phacoemulsification was indicated if nucleus sclerosis, cortical cataract, subcapsular cataract, or a combination thereof were present clinically and the BCVA deteriorated to worse than 20/40 and began to affect activities of daily living.

In the trabeculectomy group, suturing for conjunctival wound leak was performed if the leak did not stop after aqueous suppression and eye patching for 3 days. Laser suture lysis was indicated if the IOP increased to more than 21 mmHg from 1 week to 1 month after surgery without IOP-lowering drugs, whereas subconjunctival 5-fluorouracil injection (5 mg once daily for 3 to 5 consecutive days, depending on clinical response) was indicated if there was significant and persistent conjunctival congestion despite maximal topical steroid treatment in the postoperative period. Intervention for overdrainage was indicated if hypotony (IOP <6
After surgery, any glaucoma eye drops were tailed down if the mean IOPs at 2 consecutive visits were 21 mmHg or less; glaucoma drugs were tailed down in the following order: adrenergic agonists first, followed by pilocarpine, carbonic anhydrase inhibitors, prostaglandin analogs, and finally β-blockers. IOP = intraocular pressure.

### Statistical Methods

The clinical outcomes reported for postoperative time points were based on the initial randomization (intent-to-treat analysis), regardless of complications or further surgical interventions. Statistics were calculated using Microsoft Office Excel 2007 (Microsoft, Inc, Redmond, WA) and PASW statistics 18 version 18.0.0 (SPSS, Inc, Chicago, IL). Continuous data were expressed in mean ± standard deviation with the range of values and were compared using Student t test or the Mann–Whitney U test as appropriate. Categorical data were expressed in percentages and were compared using the chi-square test. A P value of <0.05 was considered statistically significant.

### Results

#### Patient Demographics and Preoperative Clinical Status

During the study recruitment period from April 2005 through April 2009, 50 medically uncontrolled CAGC eyes without cataract of 50 patients were recruited. Of these 50 eyes, 26 were randomized into the phacoemulsification group, whereas 24 eyes were randomized into the trabeculectomy group. Table 3 (available at http://aaojournal.org) summarizes the patient demographics and the preoperative clinical status of the 2 treatment groups. There was no statistically significant difference (P > 0.05) between the 2 treatment groups in all key patient demographics and preoperative clinical parameters.

### Surgical Procedures and Follow-up

In the trabeculectomy group, 3 CAGC eyes underwent mitomycin C application for 2 minutes, whereas 21 eyes underwent mitomycin C application for 3 minutes, in accordance with criteria in Table 2. All 50 patients completed 24 months of follow-up.

### Primary Outcome Measures

#### Intraocular Pressure

Figure 1 compares the IOP profiles of the 2 groups of patients. Phacoemulsification alone reduced the mean IOP from a preoperative level of 24.1 ± 4.1 mmHg (range, 20.0–34.0 mmHg) to 15.9 ± 3.9 mmHg (range, 9.0–22.0 mmHg) at 24 months after surgery, that is, a 34% reduction (P < 0.001, paired t test). Trabeculectomy with adjunctive mitomycin C chemotherapy reduced the mean IOP from a preoperative level of 24.8 ± 3.4 mmHg (range, 20.0–32.0 mmHg) to 15.8 ± 2.3 mmHg (range, 8.0–21.0 mmHg) at 24 months after surgery, that is, a 36% reduction (P < 0.001, paired t test). Within both treatment groups, the mean postoperative IOPs at all postoperative time points up to 24 months were statistically significantly lower (P < 0.001, paired t test) than the mean preoperative IOP. Table 4 (available at http://aaojournal.org) summarizes the IOP reductions at various follow-up visits, as compared with the preoperative IOP level, in the 2 treatment groups. There were no statistically significant differences (P > 0.05) in mean IOP.
Glaucoma Drugs. None of the study patients required systemic IOP-lowering drugs to control IOP either before or after surgery. Figures 2 and 3 summarize the drug profiles before and at 24 months after surgery in the 2 treatment groups, respectively.

In the phacoemulsification group, the median number of glaucoma drugs before surgery was 4 (range, 2–5). At 24 months after surgery, the median number of glaucoma drugs was reduced to 1 (range, 0–4). In the trabeculectomy group, the median number of glaucoma drugs before surgery was 3.5 (range, 2–5). At 24 months after surgery, the median number of glaucoma drugs was reduced to 0 (range, 0–2). In both treatment groups, the mean postoperative number of glaucoma drugs at all postoperative time points was statistically significantly lower (P≤0.001) than the mean preoperative number of glaucoma drugs.

At the study follow-up time points during the first 24 months, phacoemulsification-treated eyes required on average 1.5 topical IOP-lowering drugs, compared with 0.4 drugs in the trabeculectomy-treated group, that is, the trabeculectomy group required on average 1.1 fewer IOP-lowering drugs than the phacoemulsification group during 24 months of follow-up (P<0.001).

Over 24 months, trabeculectomy-treated patients seemed to have a lower dependence on glaucoma drugs than phacoemulsification-treated patients. By 24 months after surgery, 7 (27%) of the 26 eyes in the lens extraction group did not require IOP-lowering drugs or further surgery to maintain an IOP of less than 21 mmHg. By 24 months after surgery, 11 (46%) of the 24 eyes in the trabeculectomy group did not require IOP-lowering drugs or further surgery to maintain an IOP of less than 21 mmHg. This difference between the 2 groups at 24 months, however, was not statistically significant (P = 0.16, Pearson chi-square test).

Secondary Outcome Measures

Logarithm of the Minimum Angle of Resolution Best-Corrected Visual Acuity. Table 5 (available at http://aaojournal.org) summarizes the mean logMAR BCVA, VCDR, and the mean deviation and pattern standard deviation in Humphrey automated perimetry of the 2 treatment groups during follow-up. In both treatment groups, there were no statistically significant differences in mean LogMAR BCVA at both 12 and 24 months compared with before surgery (P≥0.05). There were no statistically significant differences in mean logMAR BCVA between the 2 groups before surgery and at 12 and 24 months after surgery (P≥0.05).

In the phacoemulsification group, 4 (15%) of 26 eyes had worse logMAR BCVA at 24 months compared with before surgery. Deterioration in logMAR BCVA ranged from 0.10 to 0.12. Three of these 4 eyes had advanced glaucoma (VCDR ≥0.90, mean deviation in automated perimetry ≥−24.0 db, or both) at time of surgery. One of these 3 eyes with advanced glaucoma had confirmed glaucomatous progression by 24 months. Two of these 3 eyes with advanced glaucoma and visual deterioration demonstrated significant posterior capsular opacification by 24 months after surgery and subsequently were treated by yttrium–aluminum–garnet laser capsulotomy with good visual recovery. In the remaining 1 eye with worsened BCVA, the visual loss was attributable to corneal punctate epitheliotopathy from dry eye and long-term use of glaucoma eye drops. None of these 4 eyes with deteriorated logMAR visual acuity in the phacoemulsification group had significant surgical complications.

In the trabeculectomy group, 6 (25%) of 24 eyes had worse logMAR BCVA at 24 months compared with before surgery. Deterioration in logMAR BCVA ranged from 0.02 to 0.20. Five of these 6 eyes had advanced glaucoma (VCDR ≥0.90, mean deviation in automated perimetry ≤−24.0 db, or both) at time of surgery. Three of these 5 eyes had confirmed glaucomatous progression. One eye had poor postoperative IOP control, necessitating a needling revision of the trabeculectomy site with adjunctive 5-fluorouracil chemotherapy that eventually was performed at 25 months after initial surgery. In the remaining 3 eyes with no documentable progression of glaucoma, there was clinically observable development of cataract. Cataract extraction was not yet performed in these 3 eyes by 24 months because of patients’ preferences. None of these 6 eyes with deteriorated logMAR visual acuity in the trabeculectomy group...
had significant surgical complications. It should be noted that another 5 eyes (21%) in the trabeculectomy group also demonstrated cataract, but these eyes had the same or improved logMAR BCVA after phacoemulsification by the 24-month follow-up (see below), and so these eyes were not included among the 25% of eyes with worse logMAR BCVA at 24 months. There was no statistically significant difference between the 2 treatment groups in the proportion of eyes showing a deterioration in logMAR BCVA at 24 months compared with before surgery (P = 0.396).

Surgical Complications. One (4%) of the 26 eyes in the phacoemulsification group had 1 surgical complication: zonular dehiscence necessitating implantation of capsular tension ring for stabilization of the intraocular lens. Five (19%) of 26 eyes in the phacoemulsification group remained or became medically uncontrolled within 24 months, although only 3 of these 5 eyes underwent a subsequent trabeculectomy during the study period because of the patients’ preferences.

Eleven (46%) of the 24 eyes in the trabeculectomy group had a total of 13 surgical complications, including cataract (8 eyes), overdrainage with mild choroidal detachment that resolved with conservative measures (2 eyes), conjunctival wound leak that resolved with aqueous suppression and eye patching only (2 eyes), and overdrainage requiring anterior chamber reformation and subsequent revision of trabeculectomy (1 eye). Complications occurred in a significantly higher proportion of eyes in the trabeculectomy group than in the phacoemulsification group (P = 0.001).

Need for Additional Surgical Interventions. Three (12%) of the 26 eyes in the phacoemulsification group underwent subsequent trabeculectomy at 12, 15, and 23 months after the initial phacoemulsification. Another 2 eyes (8%) in the phacoemulsification group had medically uncontrolled IOP, but because of patients’ preferences, trabeculectomy had not been performed by the 24-month study visit.

Six (25%) of the 24 eyes in the trabeculectomy group required a total of 10 additional surgical interventions during the 24 months of follow-up. Five eyes (21%) in the trabeculectomy group underwent phacoemulsification for progressive lens opacity at 5, 10, 14, 20, and 22 months after initial trabeculectomy. Another 3 eyes (12%) in the trabeculectomy group demonstrated cataract, but because of patients’ preferences, phacoemulsification had not been performed by the 24-month study visit. Two eyes required 3 needling revisions of the trabeculectomy with adjunctive 5-fluorouracil chemotherapy. One eye had anterior chamber reformation and subsequent revision of trabeculectomy for significant overdrainage. With additional needling revisions, no eyes (0%) in the trabeculectomy group were medically uncontrolled by the 24-month follow-up. The difference in the proportion of eyes requiring additional surgical interventions between the 2 treatment groups was not statistically significant (P = 0.216).

Discussion

This study aimed to compare the effect on IOP control of phacoemulsification versus trabeculectomy with mitomycin C in medically uncontrolled CACG with no significant cataract. This report also addressed secondary outcome measures such as visual acuity, surgical complications, and additional surgical interventions. Based on the results from the first 24 months of follow-up, it seems that both phacoemulsification and trabeculectomy each may have a role in the management of medically uncontrolled CACG without cataract, with specific benefits and drawbacks. These results confirmed that lens extraction by phacoemulsification alone was effective in reducing IOP and drug requirement, with a low rate of complication. By performing phacoemulsification alone, the potential complications of trabeculectomy and mitomycin C were avoided. This may be of greater significance in patients who are prone to, or do not wish to endure, such complications. Five (19%) of 26 eyes in the phacoemulsification group remained or became medically uncontrolled within 24 months. The subsequent trabeculectomies did not seem to be compromised by the prior phacoemulsification. With available evidence, it is not known whether the IOP control achieved by phacoemulsification will decay with time and whether an increasingly larger proportion of phacoemulsification eyes will require trabeculectomy with longer follow-up. After phacoemulsification alone, the dependence on glaucoma drugs remained significant: only 7 (27%) of the 26 eyes in the lens extraction group did not require IOP-lowering drugs or further surgery by 24 months after surgery. This may be an important consideration in patients with poor compliance with drugs or in those who have allergic reactions to drugs or their preservatives. This also may be important in situations where the regular refill of drugs is difficult or the cost of drugs is prohibitive.

In comparison, trabeculectomy with mitomycin C seemed more effective than phacoemulsification in reducing drug dependency. Using fewer glaucoma drugs may mean fewer adverse drug effects and more convenience for the patients, improved compliance with the remaining drugs, and also lower cost to patients and society. None of the trabeculectomy eyes were medically uncontrolled by 24 months, although 2 eyes (8%) required 3 needling revisions to retain IOP control. However, trabeculectomy was associated with significantly more surgical complications than phacoemulsification (46% vs. 4%; P = 0.001). Although these complications did not seem to result in worse visual outcomes in the involved individuals or overall in the trabeculectomy group, they doubt caused additional suffering, anxiety, and clinic visits and interventions.

It is known that trabeculectomy accelerated cataract progression, and 8 (33%) of the 24 trabeculectomy eyes actually did demonstrate visually significant cataract during the first 24 months. With long enough follow-up, a large proportion, if not all, of the trabeculectomy eyes may demonstrate cataract that will require phacoemulsification. Combined phacoemulsification and trabeculectomy is another possible surgical option to evaluate in the future, but its role in CACG with clear lens remains uncertain with currently available evidence.

This study has inherent limitations. All phacoemulsification and trabeculectomy procedures in this study were performed by 1 surgeon (CCYT). On the one hand, this eliminated variations in surgical techniques. On the other hand, the outcomes and complication rates may not accurately reflect those of surgeons whose patient population is not predominantly angle closure. This study was powered to study the differences in IOP control between the 2 treatment groups. This study may not have sufficient power (sample size) and follow-up duration to examine outcomes such as glaucomatous progression. The results from this study may...
not be applicable to those CACG cases with coexisting cataract, which was addressed in previous studies by the authors.\textsuperscript{18,19}

In summary, trabeculectomy with adjunctive mitomycin C is more effective than phacoemulsification in reducing dependence on glaucoma drugs in medically uncontrolled CACG eyes without cataract, but is associated with more complications. The authors believe that phacoemulsification alone may be a possible alternative to trabeculectomy as an initial surgical option in medically uncontrolled CACG eyes without cataract. Phacoemulsification may be even more favorable in patients who are prone to, or cannot accept, the complications of trabeculectomy and mitomycin C. However, in situations where drug reduction is a high priority, trabeculectomy may be more suitable. The surgical decision has to be based on individual circumstances and preferences of each patient. The role of combined phacoemulsification and trabeculectomy in CACG eyes without cataract remains to be evaluated.

References