Determinants of Long-term Intraocular Pressure After Phacoemulsification in Primary Angle-closure Glaucoma

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Aims: To determine the preoperative factors associated with long-term intraocular pressure (IOP) after cataract surgery in primary angle-closure glaucoma (PACG).

Methods: The data of 56 PACG patients who had undergone phacoemulsification consecutively were analyzed after detailed chart review. The associations between postoperative IOP and various preoperative factors were determined by multivariate linear regression analyses.

Results: The mean postoperative follow-up was of 33.0 ± 13.6 months. The postoperative IOP decreased ($P < 0.05$ at each visit) from the preoperative level over the years, with a mean percent reduction of 20%. Glaucoma medication number also reduced significantly, except at month 30 ($P = 0.088$), 36 ($P = 0.585$), and 48 ($P = 0.104$). Preoperative factors of higher IOP ($P < 0.001$) and deeper anterior chamber depth (ACD) ($P = 0.006$) were associated with higher postoperative IOP over the years. The multiplication product IOP × ACD accounted for 49% of the IOP variations 1 year after surgery, and eyes with this index less than or equal to 35 were more likely to achieve postoperative IOP readings of less than or equal to 12 mm Hg (odds ratio, 9.2, $P = 0.001$) than those with an index more than 35.

Conclusions: Long-term IOP after phacoemulsification in PACG is positively associated with preoperative IOP and preoperative ACD.

Key Words: anterior chamber depth, determinants, intraocular pressure, phacoemulsification, primary angle closure glaucoma

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Primary angle-closure glaucoma (PACG) is characterized by glaucomatous optic neuropathy (GON) and narrow anterior chamber angle with various extent of peripheral anterior synechia (PAS).[1] Population studies have shown that most PACG patients are asymptomatic and experience a chronic clinical course.[2,3] Sometimes chronic PACG may develop after the resolution or precede the occurrence of an acute attack of angle closure.

Laser peripheral iridotomy (LI) is the first-line treatment for PACG, but it alone fails to reduce intraocular pressure (IOP) in many patients once extensive PAS and/or GON have developed,[4,5] probably because of residual angle closure or compromised trabecular outflow.[6,7] Recently, the role played by thickened and anteriorly positioned lens in angle closure is being increasingly comprehended. The studies have shown a substantial reduction of mean IOP in PACG after cataract extraction and intraocular lens (IOL) implantation,[8–14] so the ophthalmologists may carry out cataract surgery alone for PACG patients who have suboptimal IOP control with medications. However, the surgical outcome regarding IOP control is unsatisfactory in some patients who may even require subsequent filtering surgery.[9,10,13,14] We have shown that the preoperative IOP and anterior chamber depth (ACD) help predict IOP level 3 months after clear cornea phacoemulsification (PHCE) and IOL implantation in PACG.[11]

In light of limited data regarding long-term IOP control after PHCE and IOL implantation in PACG, we conducted this study to identify preoperative variables that influence long-term IOP control. The resultant information is useful in preoperative patient counseling and in clinician's decision making regarding the need of combining a glaucoma procedure in PACG with coexistent cataract.

PATIENTS AND METHODS

All the PACG patients who underwent clear cornea PHCE and IOL implantation conducted by 1 surgeon (CJL) between July 2003 and December 2007 were identified from the hospital files and their charts were carefully reviewed. The study was approved by the institutional review board for conducting human research at the hospital.

The diagnosis of PACG was based on an occludable anterior chamber angle, elevated untreated IOP of more than 20 mm Hg, and characteristic glaucomatous optic neuropathy. An angle was deemed to be occludable if the posterior trabecular meshwork was visible for < 90 degree of the angle circumference as gonioscopy was conducted in the primary position in a dark room. All the patients had patent LI that was conducted 3 months or earlier before cataract surgery. The patients with angle closure secondary to other ocular abnormalities were not included. The eyes with earlier incisional ocular surgery, corneal abnormalities that might influence IOP measurement, concurrent retinal disease, or optic neuropathy other than glaucoma were excluded. Also excluded were the patients with post-operative follow-up of less than 6 months. If both eyes of 1 patient fulfilled all the criteria, the eye first operated on

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was selected for data analyses. Although not specifically designed for this study, it is our practice not to conduct cataract surgery alone for PACG patients requiring lens extraction if there is 360 degree PAS up to Schwalbe line, substantial visual field defect (mean deviation worse than −30 dB), or if the IOP is poorly controlled (> 30 mm Hg) with multiple medications.

The patients received a detailed ophthalmic examination before cataract surgery, including automated refraction, best corrected visual acuity (BCVA), slitlamp biomicroscopy, fundoscopy, Goldmann applanation tonometry, ultrasound ocular biometrical measurement, gonioscopy, and automated perimetry if data within 6 months were unavailable. The surgical procedure consisted of a clear cornea incision, manual continuous curvilinear capsulorrhexis, and hydrodissection. The 2-handed method for PHCE was adopted to remove the nucleus. After cortical aspiration, an acrylic foldable IOL (AcrySof MA60BM or AcrySof SA60AT, Alcon Loboratories, Inc. Huston, TX) was placed in the capsular bag. Pilocarpine was discontinued 2 weeks before surgery, and prostaglandin analogue was replaced with oral acetazolamide after surgery, if necessary, for 3 weeks. Other glaucoma medications were initially maintained but then adjusted based on the clinical judgment of the surgeon. Topical prednisolone acetate 1% eyedrops were given postoperatively and tapered over 4 to 6 weeks.

Preoperative data including sex, age at surgery, operated eye, BCVA, IOP, number of glaucoma medication, ocular biometrics, gonioscopy findings, cup-to-disc ratio, and visual field global indices were collected. The history of acute angle-closure attack or earlier ocular laser procedures were recorded. Fixed combination glaucoma medications, such as Cosopt (Merck Sharp and Dohme Pty. Limited, South Granville, Australia) were regarded as 2 medications. Postoperative data of IOP and the number of glaucoma medication were recorded at month 3, month 6, and then at 6-month intervals. The complications or further interventions were also recorded. Data of patients who underwent further glaucoma procedure that required a return to the operating room were no longer included for statistical analyses once they underwent subsequent interventions.

Statistical Analyses

The statistical analyses were done by using Stata statistical software (StataCorp, College Station, TX). Generalized estimating equations (GEE) with robust variance estimates under an independence working correlation matrix were used to assess repeated measures of postoperative IOP and number of glaucoma medication.[15] This approach accounts for the correlation of IOP readings from the same eyes over time and for potential missing data. Multivariate linear regression analysis with a backward stepwise selection procedure was conducted to determine the associations between postoperative IOP levels during the follow-up period and various preoperative factors, including demographic (age and sex), clinical (IOP, number of glaucoma medication, history of acute attack, gonioscopy findings, vertical cup-to-disc ratio and global indices of Humphrey Field Analyzer SITA-standard 24-2 strategy), and biometrical factors (central corneal thickness, ACD, lens thickness, and axial length). Considering the effect of glaucoma medication on postoperative IOP readings, we also included the number of glaucoma medication at each postoperative visit as a covariate in the regression models. The final model adopted was the most parsimonious one that was believed to adequately explain the data. In all analyses, $P < 0.05$ was considered as statistically significant.

TABLE 1. Preoperative Characteristics of the Patients (n=56)

Character	Mean±SD
Age (y)	73.4 ± 8.0
Sex, female no (%)*	30 (53.6%)
Best corrected visual acuity (LogMAR)	0.48 ± 0.20
Intraocular pressure (mm Hg)	16.4 ± 4.0
Number of glaucoma medication	1.8 ± 1.0
Vertical cup-to-disc ratio	0.8 ± 0.1
Visual field mean deviation (decibel)	−14.74 ± 7.62
Visual field pattern standard deviation (decibel)	7.44 ± 3.30
Central corneal thickness (μm)	538 ± 33
Anterior chamber depth (mm)	2.35 ± 0.24
Lens thickness (mm)	5.08 ± 0.41
Axial length (mm)	22.71 ± 0.84
Average chamber angle grading after indentation†	2.00 ± 0.88
Clock hour of visible posterior TM after indentation	7.65 ± 3.80

*Expressed as number (%); LogMAR: logarithm of the minimum angle of resolution that was converted from the decimal visual acuity.

†The anterior chamber angle was evaluated with a Posner 4-mirror goniolens. The average width was calculated by adding the grade in each quadrant and dividing the sum by 4. Grade 4 represents an open angle with the ciliary band visible; 3 represents an angle with the scleral spur visible; 2 represents an angle with the posterior TM visible; and 1 represents an angle in which only the Schwalbe's line is visible.

TM indicates trabecular meshwork.

RESULTS

After excluding 1 patient who experienced intraoperative vitreous presentation, a total of 56 patients were included for data analyses, all of Sino-Mongoloid ethnicity. Their preoperative data are listed in Table 1. Six patients (11%) had suffered from acute angle-closure 1 year or earlier before undergoing cataract surgery in the study eye. Four other patients (7.1%) had received argon laser gonioplasty in addition to LI. The mean postoperative follow-up time was 33.0 ± 13.6 months. Postoperatively, 9 patients (16.1%) underwent further glaucoma procedures that required a return to the operating room. None have developed corneal decompensation as of the last visit.

The final postoperative BCVA improved in all except 3 (5.4%) patients. The BCVA dropped 2 or more Snellen lines in 1 patient (1.8%) owing to progressive GON. The postoperative IOP reduced significantly ($P < 0.05$ at each follow-up visit) from the preoperative level during the 48-month follow-up period (Fig. 1). The mean percentage reduction in IOP ranged from 16.6% (month 42) to 24.1% (month 24) over the years. The number of glaucoma medication also decreased ($P < 0.05$) postoperatively, except at month 30 ($P = 0.088$), month 36 ($P = 0.585$), and month 48 ($P = 0.104$) (Fig. 2).

Multivariate linear regression analysis showed that the preoperative factors of IOP ($P < 0.001$) and ACD ($P = 0.006$) were positively associated with postoperative IOP levels throughout the follow-up period (Table 2). The patient's age at surgery ($P = 0.043$) was inversely associated with postoperative IOP levels, but the effect was small (Table 2). One year after surgery, the multiplication product of preoperative IOP and ACD (IOP × ACD) accounted for 49% of the variations in IOP (Fig. 3), and

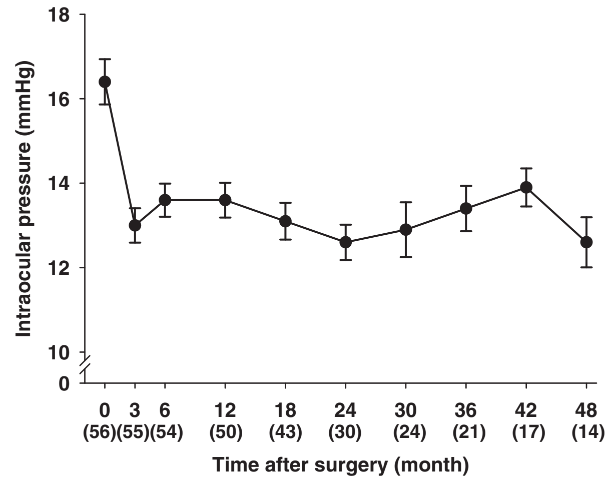

FIGURE 1. Postoperative changes in intraocular pressure (mean±SE) throughout the follow-up period as compared with the preoperative level (month 0). The number in parenthesis at bottom indicates number of eyes remaining at the corresponding follow-up time.

TABLE 2. Final Multivariate Lineal Regression Model Assessing the Association Between the Postoperative IOP Over the Follow-Up Period and the Preoperative Variables*

Preoperative Variables	Coefficient	95% Confidence Interval	*P*
Age (y)	−0.05	(−0.10, −0.02)	0.043
Preoperative IOP (mm Hg)	0.33	(0.21, 0.45)	< 0.001
Anterior chamber depth (mm)	2.39	(0.68, 4.09)	0.006

*Adjusted for number of glaucoma medications.
IOP indicates intraocular pressure.

patients with the index less than or equal to 35 were 9.2-fold (95% confidence interval, 2.4 to 35.3, $P = 0.001$) more likely to achieve IOP readings less than equal to 12 mm Hg than those with the index more than 35. Meanwhile, the number of glaucoma medication used was comparable ($P = 0.536$) between the patients with the index less than or equal to 35 (0.92 ± 0.83) and those with the index more than 35 (1.08 ± 0.98).

DISCUSSION

We show that the mean IOP remains lower than the preoperative level during the 4-year follow-up period after PHCE and IOL implantation in postiridotomy PACG eyes. The postoperative glaucoma medication number also reduces, but it tends to increase as follow-up extends. Moreover, we found the preoperative variables of IOP and ACD are determinants that positively associate with postoperative IOP over the years.

Our findings are similar to the results of Hayashi's study that has shown a persistently lower postoperative IOP after PHCE and IOL implantation in glaucoma patients with a minimum follow-up of 12 months.[10] They also found the percentage reduction in IOP after surgery is greater in PACG patients than that in POAG patients. Direct comparisons between their results and ours are infeasible because 41 (55.4%) PACG patients in their study had no earlier iridotomy. In another study of 21 postiridotomy PACG eyes with a mean follow-up of 20.7 months, Lai et al[12] have shown that mean IOP reduces by 21% at final follow-up after PHCE and IOL implantation, which is similar to our finding of 20% mean IOP reduction over the years.

Long-term postoperative IOP probably depends on the openness of the drainage angle and the facility of the trabecular outflow. Considering the role the lens plays in angle closure and the fact that cataract extraction yields a greater IOP reduction in PACG than in POAG,[10] it is likely that widening of the drainage angle contributes to the reduction in postoperative IOP. Studies on PACG using ultrasound biomicroscopy or Scheimpflug have shown an increase in the width and depth of the drainage angle after cataract extraction with complete dissolution of lens

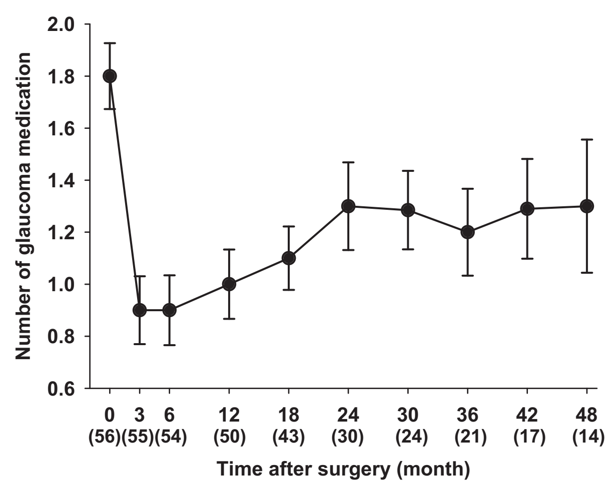

FIGURE 2. Postoperative changes in the number of glaucoma medications (mean±SE) throughout the follow-up period as compared with the preoperative level (month 0).

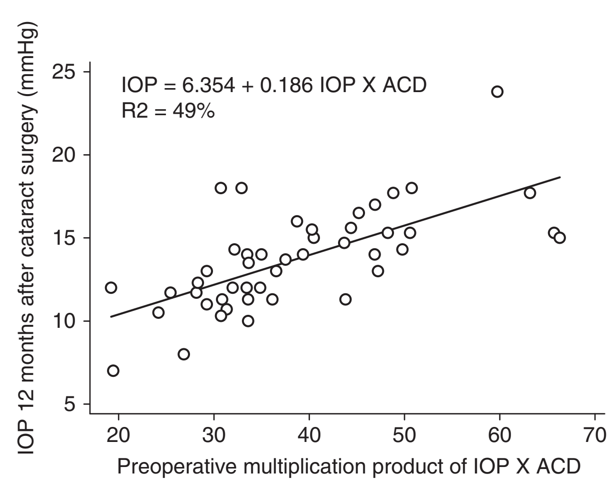

FIGURE 3. The scatter plot of intraocular pressure (IOP) 12 months after phacoemulsification and intraocular lens implantation versus the preoperative multiplication product of IOP and anterior chamber depth (IOP × ACD).

volume and pupillary block.[16,17] Even for the eyes with plateau iris syndrome, cataract surgery results in slit opening in the drainage angle.[17,18] Furthermore, studies have shown a negative correlation between preoperative ACD and postoperative widening of the drainage angle.[11,19] This indicates that the lens in eyes with a shallower preoperative anterior chamber play a more predominant role in causing angle closure, so lens removal in such eyes will end up with lower postoperative IOP.

Interestingly, we found the preoperative gonioscopic finding was not a determinant of long-term postoperative IOP. Other studies also show little correlation between the degree of preoperative PAS and IOP control after cataract extraction in PACG.[8–11] Possible explanations include: (1) It is difficult to ascertain the extent of PAS in eyes with a large lens and shallow anterior chamber[9,10]; (2) Surgical manipulation, such as viscoelastic agent injection and positive flushing pressure may resolve PAS that is of weak adherence[20]; (3) Gonioscopic findings may not truly reflect the extent of damage in the trabecular outflow pathway as there is loss of trabecular cells and irregular architecture of the trabeculum in areas away from visible PAS.[7]

Another possible mechanism that contributes to IOP-lowering after cataract surgery is that PHCE ultrasound induces an IOP-lowering stress response in trabecular cells with an increased secretion of interleukin 1α, which in turn increases the synthesis of matrix metalloproteinases and facilitates trabecular outflow facililty.[21,22] High preoperative IOP despite laser therapy and glaucoma medications may denote eyes having few trabecular cells with much compromised trabecular outflow, in which the PHCE ultrasound induces little IOP-lowering stress response and results in a more modest IOP reduction than those with more viable trabecular cells. It is noteworthy that although eyes with preoperative IOP >30 mm Hg are excluded from this study, the preoperative IOP still distinguishes itself as an important determinant of postoperative IOP.

We found the IOP $\times$ ACD product accounts for 49% of the IOP variations 1 year after surgery and the eyes with an index less than or equal to 35 are more likely to achieve postoperative IOP readings of less than or equal to 12 mm Hg than those with the index of more than 35. This agrees with our earlier short-term prospective study and supports the notion that this preoperative index is useful in estimating IOP control long-term after PHCE and IOL implantation in PACG. Recently, several studies have indicated that target pressure of low teens may be required for eyes with advanced PACG to prevent glaucoma progression.[23,24] It is likely that phacotrabeculectomy is a better option than PHCE alone for patients with advanced PACG who have a preoperative IOPXACD product greater than 35 while on multiple medications.

To our disappointment, none of the preoperative factors are found to be significantly associated with surgical failure as defined by the need to return to the operating room for further glaucoma procedures (data not shown). One possible reason is that the number of cases that need further glaucoma procedure is small, which makes it hard to detect factors with statistical significance. More importantly, the decision to conduct further glaucoma procedure is a complex process that takes factors other than the IOP level itself into consideration, such as the target pressure required, the compliance of the patients, and adverse effects of glaucoma medications.

We acknowledge several limitations in this retrospective study. The patients with very high preoperative IOP, complete PAS, or advanced field defects were not included, which limit the generalization of our findings. In a clinical trial of chronic PACG patients who were recruited from 18 centers in 7 Asian countries, an angle with more than 8 clock hours of PAS was identified in only 15% of the eyes and most eyes had untreated IOP less than equal to 30 mm Hg.[25,26] It is likely that most PACG patients in Asia do not have very high IOP and not have drainage angles extensively closed with PAS, thus our study results are applicable in most clinical settings. Second, a potential sampling bias cannot be dismissed because the sample size is small, the patients are of one ethnicity, and the study setting is one tertiary referral center. Third, the patients were gradually lost to follow-up over the years owing to a variety of reasons, including living far away, being institutionalized, and death. In addition, all the study patients had some degree of lens opacity, so it is unknown whether the findings can be extrapolated to PACG patients with clear lens. Despite all the limitations, we provide information useful in preoperative patient counseling that help decide whether it is preferable to combine a glaucoma procedure while conducting cataract surgery in PACG. The postoperative IOP control may be difficult in PACG eyes with high preoperative IOP $\times$ ACD while on multiple glaucoma medications if PHCE alone is conducted. In contrast, the risk of postoperative hypotony after phacotrabeculectomy may be high for PACG eyes that only need lens extraction but not a glaucoma procedure.[13]

In conclusion, for PACG eyes with preoperative IOP controlled at or below 30 mm Hg, the mean IOP after PHCE and IOL implantation remains significantly reduced for several years. The preoperative variables of IOP and ACD are 2 determinants of long-term IOP control.

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