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## Effect of intraoperative factors on IOP reduction after phacoemulsification

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### Abstract

The purpose of the study was to determine the independent predictors of long-term intraocular pressure (IOP) reduction after cataract surgery with phacoemulsification. This is a retrospective review of uncomplicated cataract surgeries from 2006 to 2008 at the Baltimore VA Medical Center with longitudinal follow-up. Demographic, clinical, biometric, and intraoperative variables including phacoemulsification parameters were recorded. Univariate and multivariate linear regression were used to analyze the relationship between these variables and postoperative IOP, which was the outcome variable. Analysis was performed in 115 eyes of 115 patients who underwent uncomplicated phacoemulsification during the study period. There was an average postoperative IOP reduction through 12, 24, and 36 months of  $-1.7 \pm 3.1$ ,  $-1.5 \pm 3.8$ , and  $-1.3 \pm 2.6$  mmHg, respectively. Higher preoperative IOP ( $P < 0.001$ ), a more anterior relative lens position ( $P < 0.05$ ), and longer phaco time ( $P < 0.05$ ) were significantly associated with greater postoperative decrease in IOP using univariate analysis. Using multivariate analysis, preoperative IOP ( $P < 0.001$ ), and phaco time ( $P = 0.038$ ) were associated with greater postoperative IOP reduction through 24 months. Phaco time is independently associated with IOP reduction after adjusting for age and preoperative IOP. Higher preoperative IOP is associated with a greater IOP-lowering effect after phacoemulsification.

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#### Author contribution

Dr. DeVience takes full responsibility for the integrity of the data.

#### Compliance with ethical standards

#### Conflict of Interest

The authors declare that they have no conflict of interest.

#### Informed consent

Informed consent was obtained from all individual participants included in the study.

## Keywords

Phacoemulsification cataract surgery; IOP; Glaucoma; Phaco time

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## Introduction

A large body of evidence has emerged suggesting that cataract surgery with phacoemulsification (phaco) lowers intraocular pressure (IOP) in the long term [1–9]. The mechanism by which IOP is lowered is not well understood, though several hypotheses have been proposed: hyposecretion of aqueous humor due to production of free radicals or irritation [4]; improved trabecular outflow due to deepening of the anterior chamber [10]; or phacoemulsification-induced stress remodeling from the ultrasonic vibrations, an effect similar to that of laser trabeculoplasty [11–13].

Accurate identification of which patients will experience an IOP-lowering response could influence surgical decision-making, for instance determining when a cataract surgery alone would lower IOP adequately, or whether a concurrent glaucoma procedure is indicated [2, 14, 15]. Eyes with highest preoperative IOP have the greatest reduction in IOP in the long term [11]. Whereas multiple studies have evaluated the effect of biometric properties on IOP reduction following phacoemulsification surgery [1–8, 16], few have evaluated the role of modifiable intraoperative factors [2, 17, 18], such as the influence of phacoemulsification energy, on the long-term reduction of IOP.

To further examine these questions in a veteran population, we conducted a retrospective study of intraoperative, biometric, and other clinical predictors of IOP. Detailed information and long-term follow-up were possible as patients received all their follow-up visits in the VA system, and clinical and surgical information was recorded in the VA computerized patient record system (CPRS). The aim of our study was to evaluate various clinical, biometric, and intraoperative predictors of IOP response.

## Materials and methods

This study was a retrospective chart review of 115 eyes from 115 patients undergoing cataract surgery who had uncomplicated phacoemulsification with Posterior Chamber Intraocular Lens (PCIOL) implantation between January 2006 and August 2008 at the Baltimore Veterans Administration Medical Center. These surgical cases were performed by multiple surgeons. The institutional review board at University of Maryland, Baltimore and the Research Committee at the Baltimore VA approved this study. One eye per patient was enrolled in the study (or the first operated eye if both eyes underwent cataract surgery). Only patients with uncomplicated phacoemulsification cataract surgery were included. Patients with incomplete records were excluded, such as those who did not have three preoperative IOP values prior to. Patients with a history of prior intraocular surgery or who underwent phacoemulsification combined with another ocular surgery were excluded. Data were collected from 157 eligible charts. Of these, 37 patients were treated with IOP-lowering medications pre- or postoperatively and were omitted from analysis due to potential confounding factors that the medications may have had on IOP. Two patients with implanted

sulcus lenses and three with pressures that were not recorded with a Goldmann Applanation Tonometer were also omitted. Analysis was performed in the remaining 115 subjects. All surgeries were performed at the Baltimore VA hospital with an Accurus system (Alcon, Fort Worth, Texas).

Patient charts were reviewed to specifically include demographic factors such as age, sex, and race, clinical information including prior ocular history (e.g., diagnosis of glaucoma, macular degeneration, or ocular surgeries), ocular medications (including number and type of IOP-lowering medications), history of systemic disease, and systemic medications including use of Tamsulosin. All patients underwent a preoperative evaluation including Snellen visual acuity, refraction, slit lamp examination, and dilated funduscopy examinations. To achieve an accurate representation of preoperative baseline IOP, the three most recent separate IOP measurements within 1 year preceding phacoemulsification surgery were averaged together. Biometric information including keratometry, axial length (AL), anterior chamber depth (ACD), and lens thickness (LT) were obtained, the latter three using an immersion A-scan system (Quantel Medical Cedx, France). Relative lens position was calculated as  $RLP = (0.5 \times \text{lens thickness} + \text{ACD})/AL$  [1], where RLP is the lens position relative to the axial length, with smaller RLP values representing more anterior lens positions. Intraoperative variables were recorded in a prospective fashion for each case. These variables included phaco time, percent phacoemulsification, duration of surgery, number of viscoelastic cannulas used, attending surgeon, and number of bottles of balanced salt solution. Finally, each patient's eye exams were reviewed for 5 years postoperatively and visual acuity, IOP measurements, slit lamp examination (including presence of persistent cell), IOP medications, and mortality were recorded. Due to the large number of deaths and loss to follow-up at 5 years, only data up to 3 years postoperatively were included in the analysis.

### Statistical analysis

Statistical analysis was performed using the mean preoperative IOP from three separate IOP measurements. The mean postoperative IOP for each patient was determined from 1 month through 12, 24, and 36 months postoperatively. The absolute change in postoperative IOP from mean preoperative IOP is defined as

Absolute change in postoperative IOP from mean preoperative IOP (in mmHg) = Postoperative IOP – mean preoperative IOP.

To examine the relative change in IOP as a fraction of the baseline IOP, we also calculated the percent change in postoperative IOP as:

$$\begin{aligned} \text{Percent change in postoperative IOP } (\Delta\% \text{IOP}) \\ = (\text{Postoperative IOP} - \text{Mean preoperative IOP}) / \\ \times (\text{Mean preoperative IOP}) \times 100\%. \end{aligned}$$

IOP lowering was assessed as both a continuous and categorical variable. As a categorical variable, IOP lowering was dichotomized to IOP lowering of greater than 20 % or IOP

lowering of 20 % or less for each time period. Continuous demographic (e.g., age), clinical, biometric, and intraoperative predictors of %IOP were determined by univariate linear regression analysis. Categorical predictors (e.g., sex, race, inter-surgeon differences) were compared using Student's *t* test. Multivariate models adjusting for age were constructed using significant univariate variables by regression analysis. Two multivariate models were used, one using IOP as a continuous variable and the other using IOP as a dichotomized variable (IOP lowering greater than 20 %). Predictors of greater phaco time were also determined using univariate analysis. Statistical software (version 21, SPSS, Inc., Chicago, IL) was used to calculate  $r^2$  and statistical significance (*P* value). A *P* value less than 0.05 was considered statistically significant.

To determine whether preoperative IOP has an effect on the postoperative course, patients were divided into upper and lower 50 percentiles of mean preoperative IOPs and the differences in their postoperative IOP were analyzed.

## Results

The analysis included 115 eyes of 115 patients. 110 patients (95.7 %) were male, 62 (53.9 %) were white, and the mean age was  $70.4 \pm 11$  years. Table 1 shows the baseline demographic, clinical, biometric, and intraoperative characteristics of the subjects. The mean postoperative IOP (in mmHg) was lower than the mean preoperative IOP for all postoperative follow-up intervals ( $P < 0.01$ ). Figure 1 shows the percent change in mean postoperative IOP through 36 months, indicating that the reduction in IOP (both as percentage change and absolute value in mmHg) persisted over time. IOP reduction was defined as a postoperative IOP measurement less than mean pre-operative IOP.

### Univariate predictors of postoperative IOP reduction

Table 2 shows results from a univariate analysis comparing clinical, demographic, biometric, and intraoperative variables associated with percent change in mean postoperative IOP through 24 and 36 months. In terms of clinical predictors, high preoperative IOP is significantly correlated with postoperative IOP reduction (Pearson correlation coefficient  $r = -0.59$  with  $r^2 = 0.37$  through 36 months). Patients in the lower 50th percentile of mean preoperative IOP (57 patients, average of 12.7 mmHg) had an average postoperative IOP reduction of 0.1 mmHg, whereas those in the upper 50 % of preoperative IOP (58 patients, average of 17.1 mmHg) had an average postoperative IOP reduction of 2.6 mmHg through 36 months. In other words, patients with a higher baseline IOP experience greater IOP reduction than those with a lower baseline IOP.

Increased phaco time is also significantly correlated with greater IOP reduction through 12, 24, and 36 months (Pearson correlation coefficient  $r = -0.20$ ,  $P < 0.05$  at 36 months). A more anterior relative lens position is also correlated with greater postoperative percent IOP reduction through 24 months (Pearson correlation coefficient  $r = 0.23$ ,  $P < 0.05$  at 24 months) though not at 36 months.

### Preoperative IOP and phaco time as significant variables associated with postoperative IOP reduction in multivariate analysis

After multivariate analysis adjusting for age and other significant univariate predictors (RLP and preoperative IOP) through 12 and 24 months postoperatively, phaco time was found to be significantly associated with percentage change in postoperative IOP reduction ( $P = 0.038$  at 24 months). This association becomes insignificant through 36 months ( $P = 0.090$  at 36 months). No association was found for RLP ( $P = 0.14$  at 36 months). In a separate multivariate analysis, using IOP as a dichotomized variable, preoperative IOP was associated with IOP reduction greater than 20 % through 36 months ( $P < 0.01$  at 36 months), while phaco time was only significant through 24 but not 36 months ( $P = 0.041$  at 24 months and  $P = 0.12$  at 36 months, respectively), and no association was found for RLP ( $P = 0.17$  at 36 months) (Table 3).

Phaco time itself was found to be significantly higher for patients with denser cataracts (defined as nuclear sclerosis grade 3+ or greater,  $P = 0.028$ ), greater age ( $P = 0.047$ ), as well as greater phacoemulsification percentage ( $P = 0.008$ ), and longer surgery duration ( $P < 0.001$ ). However, no significant association was found between phaco time and lens characteristics such as AL ( $P = 0.46$ ) and RLP ( $P = 0.65$ ).

### Discussion

Multiple studies have examined the effect of phacoemulsification cataract surgery on IOP, ACD, and angle opening [1–8, 17], but few have studied the effects of clinical and intraoperative phacoemulsification variables [2, 17, 18]. A unique finding of this work is that phaco time is an independent intraoperative variable associated with postoperative IOP reduction.

Prior research assessing the impact of phaco parameters on IOP has yielded conflicting results. Lee et al. found no association between the amount of CDE and postoperative IOP up to 3 months after surgery [17]. The differences in our findings may be due to the different racial makeup of the patient populations, with the majority of patients in Lee's study being Asian (89 out of 161), while a substantial fraction of our patients are African American. Pradhan et al. also did not find a statistically significant relationship between phaco time and long-term IOP [2]. Our study had a longer follow-up time than the studies of Lee and Pradhan. Damji et al. found associations between irrigation volume and IOP lowering after cataract surgery in patients with pseudoexfoliation, with a trend toward higher mean phaco time and IOP lowering [18]. While pseudoexfoliation patients may have a different response to phaco than normals, this is consistent with our findings.

The exact mechanism of IOP reduction after phacoemulsification remains unclear. One possible explanation is that lens extraction opens up the angle, thereby improving the aqueous outflow facility, especially in eyes with low ACD or occludable angles [1]. Our study did find that a more anterior RLP was associated with greater IOP reduction in univariate analysis, which may also support this hypothesis, although this was not significant in multivariate analysis and none of the patients studied had occludable angles. Our study lends support to another potential mechanism for IOP lowering after cataract surgery: a laser

trabeculoplasty-like effect on the trabecular meshwork related to ultrasound energy. The theoretical explanation for such an effect is that a longer phacoemulsification delivers more ultrasound energy, activating the cytokine pathway in trabecular meshwork, thereby increasing outflow and decreasing IOP. This explanation is supported by in vitro experiments on human trabecular meshwork by Wang et al. [12]. Similar to laser trabeculoplasty, this effect wears off over time [19]. This proposed mechanism is further supported by the observation that phacoemulsification may provide more optimal long-term IOP control than extracapsular surgery [12, 20]. Phaco time may thus be a modifiable risk factor for IOP lowering after cataract surgery. While increased phaco time is also linked to loss of corneal endothelial cells [21], the patients in this study required phaco times well within the typical range [2, 21]. For most patients, modern phacoemulsification surgery is well within the range considered safe for the cornea [22].

The strongest factor associated with IOP lowering after cataract surgery is high preoperative IOP, which is consistent with the findings in our study [2, 4, 8, 11]. While regression to the mean may explain this finding [23], the ocular hypertension treatment study (OHTS) showed that the proportional IOP response held true even after instituting measures to prevent regression to the mean, including multiple IOP measurements and testing according to strict guidelines [8].

This study has certain limitations inherent to a retrospective chart review such as missing or incomplete data. In our study, phacoemulsification was performed with the Accurus system, which could not directly calculate the cumulative dissipated energy (CDE) for each surgery. However, our analysis showed that increased phaco time was correlated with a denser cataract, in which one would expect greater CDE. Irrigation volume was also not recorded at the time of cataract surgery and is thus missing from this analysis.

The setting of the study in the VA system also allowed for certain strengths and limitations. Many veterans generally seek all their optometry, general ophthalmology, and subspecialty care in the VA system, and hence these data were readily available for use in this study, decreasing the potential for selection or referral bias. Although the VA population is biased toward males, numerous studies on cataract surgery performed in the VA system [2, 5] have been conducted and considered applicable to the general population. Furthermore, there is no known effect of gender on IOP lowering after cataract surgery. We are currently conducting a prospective study to examine the relationships between CDE, phaco time, and postoperative IOP.

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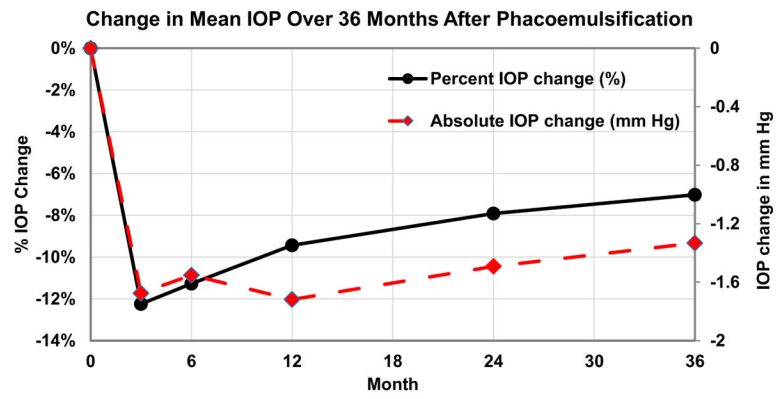
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**Fig. 1.** Change in mean IOP over 36 months after phacoemulsification. The IOP reduction [expressed as both percentage change (%) and absolute change (mm Hg)] persisted through 36 months in subjects without the use of IOP-lowering medications ( $N=115$ )

**Table 1**Baseline patient characteristics in ( $N= 115$ )

Clinical parameters	Patient characteristics
Mean age (years)	70.4 ± 11.0
Sex	4.3 % (5/115) females
Race	53.9 % (62/115) white 35.6 % (41/115) African American 10.4 % (12/115) unknown
Medical history	
Diabetes	57.4 % (66/115)
Hypertension	67.8 % (78/115)
Ocular history	
Nuclear sclerosis grade 3+ or greater	56.2 % (41/73)
Biometric (preoperative)	
Anterior chamber depth (mm)	3.20 ± 0.47
Lens thickness (mm)	4.61 ± 0.57
Axial length (mm)	23.72 ± 0.94
Spherical equivalent (D)	-0.88 ± 2.89
Average keratometry (D)	43.36 ± 1.56
RLP	0.23 ± 0.02
Intraoperative	
Phaco time (seconds)	18.83 ± 23.28
Phaco percentage (%)	10.18 ± 6.3
Surgery duration (minutes)	43.44 ± 21.10
Lens power (D)	20.88 ± 2.56
Number of viscoelastic cannulas	
1	5.2 % (6/115)
2	87.8 % (101/115)
3	3.5 % (4/115)
Mean preoperative IOP, mm Hg*	14.9 ± 2.8
Change in postoperative IOP**	
1–12 months	-1.7 ± 3.1 (-9.4 ± 18.3 %)
1–24 months	-1.5 ± 3.8 (-8.0 ± 19.0 %)
1–36 months	-1.3 ± 2.6 (-7.0 ± 18.0 %)
Postoperative IOP reduction > 20 % of mean preoperative IOP	31 patients

\* Preoperative IOP was the mean IOP of 3 measurements within 1 year before the surgery date

\*\* The postoperative IOP for each patient was assessed from 1 month through 36 months postoperatively (e.g., 3, 6, 12, 24 months). Percent change in postoperative IOP from preoperative IOP is calculated as (postoperative IOP – preoperative IOP)/preoperative IOP × 100 %

**Table 2**

Univariate predictors of the percent change in mean postoperative IOP through 36 months ( %IOP), with clinical, biometric, and intraoperative parameters

Clinical, biometric, intraoperative predictors of %IOP, 1–36 months	$r^2$ (24 months)	$P$ value (24 months)	$r^2$ (36 months)	$P$ value (36 months)
Categorical variables				
Sex		0.62		0.54
Race		0.59		0.49
Diabetes		0.81		0.50
Hypertension		0.79		0.44
Nuclear sclerosis grade 3+ or greater		0.73		0.28
Number of viscoelastic cannulas		0.15		0.17
Inter-surgeon differences		0.56		0.38
Continuous variables				
Age	0.03	0.06	0.02	0.11
Mean preoperative IOP (mm Hg)	0.35	<0.001 **	0.37	<0.001 **
Anterior chamber depth (mm)	0.02	0.16	0.02	0.16
Lens thickness (mm)	< 0.01	0.79	< 0.01	0.57
Axial length (mm)	0.02	0.15	0.02	0.17
keratometry (D)	< 0.01	0.64	< 0.01	0.58
Relative lens position (RLP)	0.05	0.029 *	0.04	0.08
Mean preoperative spherical equivalent (D)	0.01	0.29	0.01	0.28
Phaco percentage (%)	< 0.01	0.99	< 0.01	0.86
Surgery duration (min)	0.02	0.13	0.01	0.32
Lens power (D)	0.01	0.25	0.01	0.23
Phaco time (s)	0.05	0.018 *	0.04	0.049 *

\*  $P$  value is significant at the 0.05 level

\*\*  $P$  value is significant at the 0.01 level

**Table 3**

Multivariate analysis of clinical predictors of postoperative IOP reduction

	<i>P</i> value		
	1 year	2 years	3 years
A. Predictors associated with postoperative IOP reduction (1–36 months) ( <i>N</i> = 115) (Model $r^2$ = 0.37)			
Age	0.63	0.66	0.62
Preoperative IOP	<0.01 **	<0.01 **	<0.01 **
Relative lens position (RLP)	0.084	0.054	0.14
Phaco time	0.043 *	0.038 *	0.090
B. Predictors associated with IOP reduction of 20 % or greater (1–36 months) ( <i>N</i> = 115) (Model $r^2$ = 0.22)			
Age	0.38	0.27	0.61
Preoperative IOP	<0.01 **	<0.01 **	<0.01 **
RLP	0.75	0.53	0.17
Phaco time	0.026 *	0.041 *	0.12

*RLP* relative lens position

\* Correlation is significant at the 0.05 level (2-tailed)

\*\* Correlation is significant at the 0.01 level (2-tailed)