Pre-operative intraocular pressure as a predictor of post-operative intraocular pressure after phacoemulsification in non-glaucomatous patients

Titiek Ernawati1,2,*, Kevin Anggakusuma Hendrawan1, Wilson Christiano Khudrati1, and Kevin Samsudin1

ABSTRACT

BACKGROUND
Cataract has been known to cause high intraocular pressure which may lead to secondary glaucoma. Some anatomical changes in cataract patients are assumed to be factors contributing to increased intraocular pressure (IOP). The changes in IOP after cataract surgery tend to help surgeons to predict clinical outcomes. Therefore, IOP control is very important in these patients. This study aimed to determine the ocular biometric parameters and pressure-to-depth (PD) ratio associated with IOP in non-glaucomatous patients who undergo cataract surgery.

METHODS
A prospective study using secondary clinical data collected from 81 non-glaucomatous patients. Data were collected by examining each subject pre- and post-operatively. The changes in ocular biometry parameters and IOP were measured one week before surgery and 8 weeks after the surgery. Univariate and multivariate linear regression were performed to analyze the data.

RESULTS
The mean anterior chamber depth (ACD) change was 0.73 ± 0.16 mm, mean PD ratio was 5.04 ± 1.16, and the mean pre-operative IOP was 16.07 ± 2.92 mmHg, decreasing by 2.35 mmHg (14.6%) to 13.72 ± 3.42 mmHg at 8 weeks postoperatively. Univariate linear regression results showed a significant correlation between PD ratio and post-operative IOP (p=0.000), but no significant association was observed between PD ratio and post-operative IOP in multiple linear regression (p=0.126). However, pre-operative IOP was significantly associated with post-operative IOP (Beta=1.244; p=0.004)

CONCLUSIONS
Our data demonstrated that pre-operative IOP was the most influential risk factor of IOP reduction after phacoemulsification in non-glaucomatous patients.

Keywords: Biometry, intraocular pressure, phacoemulsification, pressure to depth ratio, non-glaucomatous patients
INTRODUCTION
Rapid assessment of avoidable blindness data shows that the frequency of blindness in people aged >50 years in Indonesia in the year 2018 was 3%, with cataract as the leading cause of blindness in Indonesia. Cataract causes visual impairment which can be prevented and treated through cataract extraction surgery.\(^1\)

Cataract surgery has become one of the most frequently performed surgical procedure in the world. The high cataract prevalence increases the need for cataract surgery to reduce the cataract backlog.\(^2\) Biometric measurements are important in cataract surgery to achieve the targeted post-operative refraction.\(^3,4\)

Unaddressed cataract can lead to further complications, one of them being the increase in intraocular pressure (IOP) which can cause glaucoma. Phacoemulsification is one of the cataract surgery techniques that has been proposed as a potential procedure to lower IOP.\(^5\) The specific ocular parameters which can be used to predict the IOP lowering effect following phacoemulsification, remain unclear.\(^6\)

The pressure-to-depth (PD) ratio is the ratio of the pre-operative intraocular pressure to pre-operative anterior chamber depth. It has been shown that PD ratio is a useful predictor of changes in the IOP post-surgery.\(^7\) The PD ratio is a simple indicator to check because ACD and IOP are standard pre-operative examinations that must be performed in all cataract patients. If the PD ratio can be used as a predictor of IOP reduction, it would be great if it can be applied in clinical practice. The study of Hsu et al.\(^8\) reported a diurnal fluctuation in IOP, which makes other predictors, such as pre-operative IOP and PD ratio, become less reliable. Furthermore, the study of Markic et al.\(^9\) showed that the predictability of the PD ratio parameter was low in post-operative IOP changes. On the other hand, Ramakrishnan et al.\(^10\) demonstrated that the PD ratio is a valuable prognostic indicator to predict postoperative IOP outcome. Dhamankar et al.\(^11\) also found that pre-operative PD ratio was consistently associated with changes in the IOP among glaucomatous eyes undergoing cataract surgery.

The contradictory results reported by previous studies provided us the opportunity for further research. The difference between present study and the previous ones are that our study employed only non-glaucomatous patients. The objective of this study was to determine the ocular biometric parameters and pressure-to-depth (PD) ratio associated with IOP in non-glaucomatous patients undergoing cataract surgery.

METHODS
Research design
A longitudinal analysis using secondary clinical data was performed at Primasatya Husada Citra Hospital Surabaya, from December 2019 until March 2020.

Study subjects
A total of 81 non-glaucomatous subjects were enrolled in this study. Patients were monitored until 2 months after the cataract surgery to evaluate the post-operative biometry parameter changes and post-operative IOP. The inclusion criteria in this study were: 1) non-glaucomatous patients; 2) age more than 40 years old; 3) male and female; 4) IOP of less than 21 mmHg; 5) no history of ocular intervention or trauma; 6) undergoing cataract extraction surgery using phacoemulsification and willing to participate in the study. The exclusion criteria were: patients who were absent on the scheduled biometry and intraocular pressure examinations, patients with co-morbidities, except cataract, patients who were absent on the scheduled follow-up and patients with complications during and after the surgery.

Sample size determination
\[
n = \frac{(Z_\alpha + Z_\beta)^2}{0.5 \ln \left(\frac{1 + \tau}{1 - \tau}\right)} + 3 = \frac{(1.960 + 1.282)^2}{0.5 \ln \left(\frac{1 + 0.56}{1 - 0.56}\right)} + 3 = 47 \text{ subjects}
\]
Notes:
n: minimum number of subjects
Zα: 1.96 with α = 0.05
Zβ: 1.282 with β = 0.2
r: correlation coefficient, the reference r=0.56 from Ramezani et al. (7) that shows the correlation between pre-operative IOP and post-operative IOP. The anticipated drop-out was 15% and the optimal sample size was 54.

Surgical technique
Phacoemulsification was conducted under topical anesthesia by a skilled surgeon. Eyes were prepared for surgery by instilling tropicamide 0.5 % and phenylephrine 10 % for pupil dilation. After making a 2.75 mm incision in the temporal cornea, viscoelastic injection was performed, then continuous curvilinear capsulorrhexis, that creates access to the cataract, followed by phacoemulsification and intraocular lens implantation.

Study assessment
Pressure-to-depth (PD) ratio, anterior chamber depth, lens thickness, and ocular axial length were measured with Alcon OcuScan RxP ophthalmic ultrasound; IOP was measured using a Canon TX-20P full auto non-contact tonometer. Pre-operative biometry and IOP measurements were performed one week prior to the surgery while the post-operative measurements were determined 8 weeks after the surgery.

Statistical analysis
We analyzed the data using univariate regression analyses, in which the associations between independent variables and the post-operative IOP change were evaluated; these variables included gender, age, pre-operative IOP, underlying disease, PD ratio, anterior chamber depth, lens thickness, and axial length. All variables showing a significant association in the univariate analysis at p<0.25 were entered into a multivariate linear regression model of risk factors associated with the post-operative IOP. A value of p<0.05 was considered statistically significant.

Ethical clearance
The ethical clearance protocol of this study was approved by the Health Research Ethics Committee of the Medical Faculty, Widya Mandala Surabaya Catholic University, under No. 070/WM12/KEPK/DOSEN/T/2019 in accordance with the WHO-CIOMS International Ethical Guidelines for Health Related Research.

RESULTS
Eighty-one patients were enrolled into the study. In Table 1, the baseline characteristics show that most of the patients suffered from diabetes mellitus as co-morbidity. Sex and history of hypertension did not exhibit any significant differences in the number of patients. All subjects were non-glaucomatous.

<table>
<thead>
<tr>
<th>Table 1. Baseline demographics and clinical features of non-glaucomatous subjects (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Characteristic</strong></td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>History of DM</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>History of HT</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>ACD (mm)</td>
</tr>
<tr>
<td>Pre-operative</td>
</tr>
<tr>
<td>Post-operative</td>
</tr>
<tr>
<td>AL (mm)</td>
</tr>
<tr>
<td>Pre-operative</td>
</tr>
<tr>
<td>Post-operative</td>
</tr>
<tr>
<td>LT (mm)</td>
</tr>
<tr>
<td>Pre-operative</td>
</tr>
<tr>
<td>IOP (mmHg)</td>
</tr>
<tr>
<td>Pre-operative</td>
</tr>
<tr>
<td>Post-operative</td>
</tr>
<tr>
<td>Pressure to depth ratio</td>
</tr>
</tbody>
</table>

Note: data presented as Mean ± SD, except for sex, history of DM and history of HT; DM = diabetes mellitus; HT = hypertension; ACD = anterior chamber depth; AL = axial length; LT = lens thickness; IOP = intraocular pressure
Table 1 shows us some data about baseline demographics and clinical features of age, sex, history of diabetes mellitus, history of hypertension, ACD, axial length (AL), lens thickness (LT), and IOP. These data are descriptive pre-operative values in non-glaucomatous patients. The mean intraocular pressure reduction was 2.35 mmHg.

Table 2 shows analysis of univariate and multivariate linear regression of baseline demographics, pre-operative clinical features and post-operative IOP. The data show that the univariate linear regression analysis gave significant results except for history of hypertension ($p=0.729$), pre-operative ACD ($p=0.085$) and pre-operative AL ($p=0.561$). The multivariate linear regression analysis showed that the variables of sex ($p=0.014$), pre-operative AL ($p=0.036$) and pre-operative IOP ($p=0.004$) were significantly associated with post-operative IOP. Pre-operative IOP was the most influential predictive factor of post-operative IOP (Beta = 1.244; $p=0.004$)

**DISCUSSION**

This study showed that the mean value of post-operative IOP was 13.72 ± 3.42 mmHg. This is in agreement with the average post-operative IOP value (14.47 ± 2.39 mmHg), as reported by a study in Malaysia.$^{12}$ Another study conducted by Ramakrishnan et al.$^{10}$ reported the mean 3-month post-operative IOP to be 19.23 ± 2.2 mmHg. Our study showed that the post-operative ACD increased from 3.24 ± 0.44 mm to 3.97 ± 0.28 mm. This is similar to that of the study by Huang et al.$^{13}$ where mean ACD increased from 2.52 ± 0.43 mm before surgery to 3.84 ± 0.29 mm after surgery. Our study showed that there were no significant roles of ACD and LT in post-operative IOP after phacoemulsification. Many studies have been conducted in order to analyze the role of many parameters which can be used to predict post-operative IOP after phacoemulsification.$^{14-17}$ Most studies which have been carried out prior to our study used pre-operative parameters in predicting post-operative IOP. The results of our study are in agreement with a study performed in Malaysia, reporting that there was no significant correlation between post-operative IOP reduction and the parameters of ACD and LT.$^{12}$ On the contrary, Huang et al.$^{14}$ observed a significant role of ACD widening and lens vault in predicting the IOP reduction after phacoemulsification surgery.$^{14}$ Deepening of the ACD is postulated as the mechanism of IOP reduction. Although there was a significant change in ACD in our study, this was not significantly associated with IOP reduction. We assumed that this might be associated with other factors such

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate linear regression</th>
<th>Multivariate linear regression*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td>-0.418</td>
<td>-0.584, -0.221</td>
</tr>
<tr>
<td>Sex</td>
<td>0.217</td>
<td>0.008, 0.425</td>
</tr>
<tr>
<td>History of DM</td>
<td>0.263</td>
<td>0.055, 0.449</td>
</tr>
<tr>
<td>History of HT</td>
<td>-0.039</td>
<td>-0.269, 0.171</td>
</tr>
<tr>
<td>Pre-operative ACD</td>
<td>0.193</td>
<td>-0.049, 0.415</td>
</tr>
<tr>
<td>Pre-operative AL</td>
<td>-0.066</td>
<td>-0.288, 0.151</td>
</tr>
<tr>
<td>Pre-operative LT</td>
<td>-0.288</td>
<td>-0.491, -0.074</td>
</tr>
<tr>
<td>Pre-operative IOP</td>
<td>0.643</td>
<td>0.500, 0.741</td>
</tr>
<tr>
<td>Pre-operative PD ratio</td>
<td>0.431</td>
<td>0.203, 0.608</td>
</tr>
</tbody>
</table>

*Including age, sex and parameters with $p<0.25$ in univariate linear regression analysis
Note: $\beta$: regression coefficient; CI: confidence interval; DM: diabetes mellitus; HT: hypertension; ACD: anterior chamber depth; AL = axial length; LT = lens thickness; IOP = intraocular pressure; PD: pressure to depth
as angle configuration which was not being investigated and observed in our study. The differences might be caused by the different measurement methods involved in this study. A USG scan was utilized in measuring the biometry parameters in this study, whereas Huang et al. (14) used anterior segment ocular computed tomography (AS-OCT) as their modality.

In this study, we found that the pre-operative IOP value was the determinant factor in predicting the post-operative IOP and also the reduction in IOP. Similarly, Beato et al. (5) and Picoto et al. (18) found that a higher preoperative IOP is significantly associated with the reduction in IOP, measured 6 months after surgery.

Our study found that the PD ratio played an important role in determining both the post-operative IOP. Our results were also in agreement with the study by Ramakrishnan et al. (10) showing a significant correlation between reduction in IOP and PD ratio. Furthermore Yoo et al. (19) stated that the PD ratio was found to be a significant predictor of absolute IOP change following cataract surgery in patients with or at risk of primary open angle glaucoma (POAG). Additionally Dhamankar et al. (11) found that the pre-operative PD ratio was consistently associated with changes in IOP. However, our multivariate analysis of the PD ratio shows no significant relation with post-operative IOP. This finding can indirectly explain the importance of ACD in IOP reduction. Calculation of the PD ratio can help the clinician predict IOP reduction after cataract extraction surgery.

This study also shows that age and IOP reduction have a significant inverse correlation in univariate linear regression, thus supporting the findings of Zhao et al. (20) that age and IOP reduction in cataract surgery have inverse longitudinal and cross-sectional associations. Structural changes in the trabecular meshwork can explain the inverse association because an aging trabecular meshwork increases the resistance to aqueous humor outflow, resulting in increased IOP. (20)

Sex-related post-operative IOP reduction has been inconsistent across studies. In our study, men had lower IOP reduction than women. In contrast, the Kangbuk Samsung Health (20) and Gutenberg Health studies (21) found that women had lower IOP. They hypothesized that higher IOP in men could be due to a higher prevalence of cardiovascular risk factors. Also, estrogen may affect the inflow of aqueous humor; an Indian study (22) showed that the IOP was higher in postmenopausal than in premenopausal women and attributed this difference to higher levels of testosterone and decrease of estrogen and progesterone levels with onset of menopause. However, our study found that sex-related IOP reduction is significant in univariate and multivariate analysis. Further research is needed to understand the sex-related difference in intraocular pressure.

As the limitation of our study, the IOP measurement was done using non-contact tonometry instead of the Goldmann Applanation Tonometer which is the gold standard in measuring IOP value. The follow-up period in our study was also limited to two months only. A longer follow-up period needs to be used to further evaluate the IOP changes.

The clinical implication of this study is that the clinicians will know that phacoemulsification can decrease intraocular pressure. In non-glaucomatous patients the PD ratio is significantly associated with postoperative IOP in univariate analysis and non-significantly associated with IOP in multivariate analysis so that it has been shown that the PD ratio can be used independently as a predictive factor of IOP after phacoemulsification.

CONCLUSIONS

This study demonstrated that pre-operative IOP is an independent and good predictor of IOP reduction after phacoemulsification surgery in non-glaucomatous patients.
CONFLICT OF INTEREST

There is no conflict of interest in this study.

ACKNOWLEDGEMENT

We would like to acknowledge the support of Medical Faculty, Widya Mandala Surabaya Catholic University, for this study as an approved research proposal, and Primasatya Husada Citra Hospital for their support and assistance.

CONTRIBUTORS

ET and HKA contributed to study concept and design, provision of study material or patients. ET, HKA and KWC contributed to data analysis and interpretation. ET and KS contributed to administrative support and data collection and assembly. ET, HKA, KWC and KS contributed to manuscript writing and reviewing. All authors approved the final manuscript and will take public responsibility for the content of the manuscript submitted to Universa Medicina.

REFERENCES

17. Back SU, Kwon S, Park IW, Suh W. Effect of phacoemulsification on intraocular pressure in


