Accuracy of different lens power calculation formulas in patients with phacomorphic glaucoma

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Abstract:
PURPOSE: The purpose of the study was to determine the most accurate formula for intraocular lens (IOL) power calculation among five currently used formulas in eyes with phacomorphic glaucoma (PG) undergoing cataract extraction surgery.

MATERIALS AND METHODS: In this prospective interventional case series Patients diagnosed with PG were undergone uneventful phacoemulsification and IOL implantation. After 3 months, the refractive outcome for each formula was evaluated with mean prediction error (PE), mean absolute error (MAE), and the percentages of eyes within 0.25 D and 0.5 D of predicted error.

RESULTS: Twenty-three patients completed the study. PEs were significantly different among the 5 formulas \((P = 0.019)\), and Holladay I had the least error \((-0.02 \pm 1.11)\). Haigis formula had the highest hyperopic shift \((0.37 \pm 1.22)\), highest MAE \((0.99 \pm 0.78)\) and the lowest percentages of desired PEs, while the SRK II produced the greatest percentages. The overall differences in MAE between the 5 formulas were statistically insignificant \((P = 0.547)\).

CONCLUSION: In some extreme situations like patients with PG, lower generation of IOL power calculation formulas may still produce more acceptable refractive outcomes.

Keywords:
Angle closure, IOL Calculation, IOL power, lens induced glaucoma, phacomorphic glaucoma, shallow AC

Introduction
Phacomorphic glaucoma (PG) or lens-induced glaucoma, a secondary type of angle closure glaucoma (ACG), is defined as a pupillary block due to the compressing effect of a mature, swollen cataract compromising the aqueous drainage normally resulting in an angle closure and subsequent increase in intraocular pressure (IOP). It is mostly associated with aging and inadequate access to medical and surgical care services and delay in cataract extraction especially in developing countries with 3.91% prevalence.\(^1\,2\)

The acute IOP rising in PG leads to optic nerve damage and consequent irreversible visual impairment. Cataract extraction after initial IOP control is the definitive treatment, however, the prognosis of visual recovery depends on the early diagnosis and prompt treatment. In the cases of prolonged IOP rising, the postoperative visual prognosis is guarded.\(^1\,3\)

Biometry studies in patients with PG pointed to the prominent anterior displacement of the intumescent lens, crowding of the anterior chamber and narrow angles. These predisposing factors change the configuration of the anterior chamber to be at risk of PG, however the anteriorly-displaced swollen cataract is the main pathology and

\(^{1}\) Tabatabaei SA, Samadi M, Soleimani M, Fonoodi H, Ghods S, Inanloo B. Accuracy of different lens power calculation formulas in patients with phacomorphic glaucoma. Taiwan J Ophthalmol 2022;12:164-9.
deep anterior chambers may also be affected.\[4,10\] After cataract extraction as a definitive treatment, deepening of the anterior chamber is occurred and consequent postoperative declining IOP leads to a decrease in axial length.\[4,10\] Moreover, corneal edema and mature intumescent cataract in PG prohibit the use of optical biometry in IOL power calculation. The postoperative anatomic changes in ACG patients, especially PG as well as the suboptimal measurement techniques, influence the preoperative IOL power calculation. Hence, precise investigation is required to find out the accurate formula for IOL power prediction to prevent postoperative refractive surprise.\[9,11\]

Gökce et al. suggested to use multiple variable vergence formulas (Holladay II, Haigis, Barret universal II), which include the preoperative ACD, for IOL calculation in eyes with shallow ACs,\[12\] whereas some other studies believe that the unpredictable ACD after cataract extraction in eyes with PG was a source of estimation error in formulas taking into account the preoperative ACD.\[9,11,13,14\] They suggested that 2-variable vergence formulas resulted in more accurate refractive outcome in shallow ACDs.\[11,15\]

These conflicting results mainly pointed to the fact that shallow ACs in PG were lens-induced and cataract extraction resulted in biometric changes different from true shallow anterior chambers. Thus, these variability must be noted and appropriately managed in IOL power calculation to be accurately fit such patients. In this study, we aim to determine the most accurate formula for IOL power calculation with the least postoperative prediction error (PE) among currently used formulas (SRK II, SRK/T, Hoffer Q, Holladay I, and Haigis) in eyes with PG undergoing cataract extraction surgery.

**Methods**

This prospective interventional case series study included 38 eyes of 38 patients presented with acute pain and blurred vision and diagnosed as PG at the Farabi Eye Hospital emergency clinic at the time of the study (study no: 38184). The patients were scheduled for cataract extraction surgery after IOP control in a time period between July 2017 and December 2018. The local ethical committee of the institutional review board of the Tehran University of medical sciences approved the study, and the principles in the Declaration of Helsinki were followed. We informed all the patients about the goal of the study, and a written informed consent was obtained prior to their inclusion.

We included the patients with the diagnosis of PG with normal axial length of 22–25 mm measured by ultrasound (US) biometry. Patients with any ocular pathology other than PG, corneal pathology like dystrophy, scarring or ectasia and history of previous surgical procedures such as corneal refractive surgery or any intraocular surgery were excluded. Intraoperative complications such as vitreous loss, the need for corneal sutures and zonular rupture which prohibited the “in-the-bag” IOL implantation securely were also considered as exclusion criteria.

We diagnosed PG based on the following criteria: an IOP, elevated above 21 mmHg in the presence of an anteriorly displaced mature intumescent cataract and consequent signs of shallow anterior chamber, corneal edema, conjunctival injection, and mid-dilated nonreactive pupil. Moreover, we differentiated PG and acute attack in ACG based on the following: in PG, we identify an intumescent cataractous lens compressing the anterior chamber, while acute ACG attack is expected to develop due to anterior chamber and angle configuration, without the compressing effect of the swollen lens. In PG the contralateral anterior chamber is not shallow, and it may be even deep with open angle; however, in ACG, the contralateral eye is also shallow with closable angle.\[16-18\]

All patients were managed uniformly to lower the IOP at presentation with a combination of topical glaucoma eye drops and systemic acetazolamide. If the IOP was not controlled, intravenous mannitol infusion was also used.

Age, sex, presenting IOP (with Goldmann applanation tonometry), and preoperative visual acuity (VA) were recorded to determine the demographic representation of PG. After lowering the IOP and corneal clarity improvement, complete slit lamp examination and automated keratometry were done. Gonioscopy was performed with 4-mirror gonioscopic Zeiss lens (OPDSG model; Ocular Instruments, Inc., Bellevue, USA) to address angle closure in each quadrant, in both the affected and the fellow eyes. US biometry was also carried out to measure the anterior chamber depth, axial length, and the lens thickness. Ocular US biometry was performed using 11-MHz contact A-scan probe (US-800; Nidek Co, Ltd, Tokyo, Japan) applanated on the surface of the anesthetized eye with minimal pressure and the mean values of ten measurements were documented. One experienced examiner performed all of the measurements. Automated keratometry was separately performed by an auto keratorefractometer (Topcon KR-8100) to measure the corneal power by calculating the mean of three measurements for each eye. Data were transferred into the biometry software program to calculate the IOL power using the SRK II, SRK/T, Holladay I, Hoffer Q, and Haigis formulas, and the predicted spherical equivalents (SE) using each formula were documented. We chose the reference power the ones that provided the final postoperative refractive error closest to emmetropia.
All patients underwent phacoemulsification by a single surgeon under local anesthesia. A 3.2 mm temporal self-sealing clear corneal incision was made, and all of the operations were performed using an Infiniti Vision System phacoemulsification machine (Alcon, Fort Worth, TX, USA) with Ozil torsional handpiece. Following routine uncomplicated phacoemulsification, a foldable acrylic IOL was securely implanted in the capsular bag.

Three months after cataract surgery, refractive outcome was evaluated in a stable refraction state. The SE was measured by an autorefractometer (Topcon Auto-Refractometer, Tokyo, Japan). The mean PE was calculated by subtracting each of the predicted SE of the tested formulas from the actual postoperative SE. Negative PE value indicated tendency for more myopic refractive outcome than predicted. The mean absolute error (MAE) was the absolute value of the PE, representing its magnitude regardless of the sign. For each formula, we also calculated the percentages of refractive outcomes with the absolute errors <0.25 D and 0.5 diopter (D).

For statistical data analysis we used Microsoft Excel and SPSS software ver. 22.0 (IBM, Armonk, New York, USA). For descriptive parameters without normal distribution, we used Mann–Whitney U-test and continuous data were described as mean ± standard deviation. We also used Friedman test with Bonferroni correction to determine the significance of the PE and MAE differences between 5 IOL power calculation formulas, and the percentages of refractive outcomes with the absolute errors <0.25 D and 0.5 D for each formula were assessed by Cochrane Q test with a Bonferroni correction. The level of significance was set at $P < 0.05$.

**Results**

Among the 38 cases of PG presented between July 2018 and December 2019, five patients were not eligible for inclusion due to out-of-range axial length (<22 mm or more than 25 mm) and ten patients were excluded due to postoperative lost-to-follow up. Twenty-three patients were ultimately completed the study. The baseline preoperative clinical data as well as postoperative changes are summarized in Table 1. The mean presenting age was 70 ± 11 years old with male-to-female ratio of 1:1. The mean presenting IOP in PG patients was 37.5 ± 15.3. The mean preoperative keratometry readings in flat and steep meridians were 43.9 ± 2.5 D and 45.3 ± 1.7 D, respectively. The mean preoperative axial length and ACD were 23.36 ± 0.69 mm (range, 22.15–24.42 mm), and 2.52 ± 0.23 mm (range, 1.9–2.96 mm), respectively.

After phacoemulsification and intrabagal implantation of a monofocal IOL, the mean postoperative IOP decreased significantly to 17.22 ± 8.0 ($P < 0.001$); the mean ACD and the mean axial length changed significantly to 3.90 ± 0.52 mm and 22.11 ± 0.61, respectively ($P < 0.001$). The mean keratometry readings remained without significant changes. The postoperative clinical data were summarized in Table 1.

Table 2 shows the PE and MAE of each biometric formula. There were statistically significant differences in PEs between the five IOL power formulas ($P = 0.019$). Holladay 1 had the least error from the predicted refraction ($-0.02 ± 1.11$), while the Haigis and SRK II formulas had the highest hyperopic shift ($0.37 ± 1.22$) and postoperative myopic shift ($-0.31 ± 1.04$), respectively. The second column of the Table 2 represented the MAE of each formula. The SRK/T and Haigis formulas, respectively had the lowest ($0.72 ± 0.73$) and the highest ($0.99 ± 0.78$) MAE; however, the overall differences in MAE between the 5 formulas were statistically insignificant ($P = 0.547$).

Table 3 shows the percentages of eyes within the dioptric ranges of ± 0.25 D and ± 0.5 D of predicted refraction. The SRK II formula, in comparison with the others, produced a greater percentage of refractive outcomes within ± 0.25 D and ± 0.5 D of error and Holladay I was the second-best performing formula. However, in multiple comparisons, no significant differences were achieved between formulas in percentages of eyes within ± 0.25 D and ± 0.5 D of predicted error ($P = 0.546$ and $P = 0.059$, respectively).

**Table 1: Demographic and preoperative and postoperative clinical measurements in participants**

| Formula       | Mean±SD | P   |
|---------------|---------|-----|
| Age (years)   | 70±11   |     |
| Gender (% male) | 47.8    |     |
| IOP (mmHg)   | 37.5±15.3 | 0.001 |
| AL (mm)      | 23.36±0.69 | 0.001 |
| ACD (mm)     | 2.52±0.23 | 0.001 |
| Flat K (D)   | 43.9±2.5  |     |
| Steep K (D)  | 43.9±2.5  |     |
| K1 Keratometry | 40.6±2.5 | 0.001 |
| K2 Keratometry | 40.6±2.5 | 0.001 |
| IOP Postoperative | 17.22±8.0 | 0.001 |
| AL Postoperative | 22.11±0.61 | 0.001 |
| ACD Postoperative | 2.52±0.23 | 0.001 |
| Flat K Postoperative | 43.9±2.5  |     |
| Steep K Postoperative | 43.9±2.5  |     |
| K1 Keratometry Postoperative | 40.6±2.5 | 0.001 |
| K2 Keratometry Postoperative | 40.6±2.5 | 0.001 |

**Table 2: The Target power, mean prediction error and mean absolute error with five formulas**

| Formula       | Target power | Mean PE±SD | MAE±SD |
|---------------|--------------|------------|--------|
| HofferQ       | 20.69±4.09   | -0.11±1.23 | 0.82±0.90 |
| Haigis        | 19.62±4.1    | 0.37±1.22  | 0.99±0.78 |
| Holladay 1    | 20.86±3.99   | -0.02±1.11 | 0.78±0.78 |
| SRK II        | 20.78±3.1    | -0.31±1.04 | 0.76±0.77 |
| SRKT          | 20.92±3.58   | -0.23±1.22 | 0.72±0.73 |

PE=Prediction error, MAE=Mean absolute error, SD: Standard deviation, SRK: Sanders, Retzlaff and Kraff, SRKT: Sanders, Retzlaff and Kraff Theoretical
Furthermore, we found that the cataract AC deepening. IOP reducing effect of cataract extraction and secondary studies have shown this correlation and attributed the IOP and consequent reduction in axial length. humor inflow and outflow and lead to the decrease in prominent chamber deepening facilitates aqueous compared to preoperative values. It seems that such anterior chamber and a decrease in axial length with PG follow cataract extraction and IOL implantation. A number of studies have similarly demonstrated the IOP-reducing effect of cataract surgery in both glaucomatous and nonglaucomatous eyes.\(^{[15,20]}\) Furthermore, we found that the cataract extraction resulted in a significant deepening of the anterior chamber and a decrease in axial length compared to preoperative values. It seems that such prominent chamber deepening facilitates aqueous humor inflow and outflow and lead to the decrease in IOP and consequent reduction in axial length.\(^{[10,21]}\) Several studies have shown this correlation and attributed the postoperative axial length change in eyes with ACG to IOP reducing effect of cataract extraction and secondary AC deepening.\(^{[22‑25]}\)

**Table 3: Percentage of eyes with refractive prediction error within±0.25 D and±0.50 D**

| Formula   | ±0.25 (%) | ±0.5 D (%) |
|-----------|-----------|------------|
| HofferQ   | 25        | 45.8       |
| Haigis    | 12.5      | 25         |
| Holladay 1| 29.2      | 45.8       |
| SRK II    | 33.3      | 45.8       |
| SRKT      | 25        | 37.5       |
| P         | 0.546     | 0.059      |

SRK=Sanders, Retzlaff and Kraft, SRKT=Sanders, Retzlaff and Kraft Theoretical

In summary, the following significant results were found: (1) The mean postoperative IOP decreased significantly after cataract extraction and IOL implantation and (2) among the postoperative biometric parameters, the AL and ACD changed significantly and (3) the Haigis formula produced the highest hyperopic shift and the SRK II had the highest myopic shift from the preoperative predicted refraction.

**Discussion**

PG is still a worthwhile study topic due to its relatively high prevalence among developing countries and interestingly in some well-developed districts despite accessible and affordable healthcare systems. This irreversible sight threatening condition presents acutely in aged people with medical comorbidities whose mature cataracts have been ignored to be timely extracted.\(^{[12]}\) Emergent preoperative IOL power calculation is almost always challenging due to inadequate view to perform optical biometry, elevated IOP and consequent corneal edema and anteriorly displaced hypermature lens shallowing the anterior chamber and altering its anatomic relationships.\(^{[1‑3]}\) In the present study we compare various IOL power formulas to investigate the accuracy of IOL power calculation and to predict the refractive outcomes in eyes with PG.

We found significant IOP reduction in patients with PG following cataract extraction and IOL implantation. A number of studies have similarly demonstrated the IOP-reducing effect of cataract surgery in both glaucomatous and nonglaucomatous eyes.\(^{[15,20]}\) Furthermore, we found that the cataract extraction resulted in a significant deepening of the anterior chamber and a decrease in axial length compared to preoperative values. It seems that such prominent chamber deepening facilitates aqueous humor inflow and outflow and lead to the decrease in IOP and consequent reduction in axial length.\(^{[10,21]}\) Several studies have shown this correlation and attributed the postoperative axial length change in eyes with ACG to IOP reducing effect of cataract extraction and secondary AC deepening.\(^{[22‑25]}\)

It is known that ACD is an important index in predicting the postoperative effective lens position (ELP) and consequently determine the refractive outcome after cataract surgery in many IOL power calculation formulas.\(^{[12,14,20]}\) Cataract surgery in eyes with ACG and PG with preoperative shallow ACs contributes to larger postoperative deepening of the anterior chamber, occasionally resulting in a more posteriorly implantation of the IOL than preoperatively planned and a subsequent hyperopic shift with higher PEs.\(^{[9,11,13]}\) In another word, most patients with ACG/ PG have large capsular bags occupied by thick lenses and cataract extraction lead to more increase in ELP in comparison with true shallow ACs.\(^{[9,14]}\) Furthermore, patients with PG presented with variable degrees of PAS formation depending on the duration of Phacomorphic attack and cataractous lens displacement, reflected by more variability in postoperative ACDs.\(^{[9]}\) Such variability in biometric parameters leads to discrepancy in IOL power prediction in comparison to normal eyes; so, applying the IOL constants used for normal eyes induced inaccurate results in these patients.\(^{[9,11]}\) Utilizing the fellow eye ACD in IOL power calculation in such eyes was another source of error, as we have demonstrated in our previous study that fellow eye ACD in these patients had an inherent shallowness than other nonglaucomatous mature cataracts and could not reflect the postoperative ELP correctly.\(^{[15]}\) On the other hand, corneal edema and intumescent mature cataract made the optical biometry measurements difficult. The necessity to perform US biometry for IOL power calculation in addition to unpredictable postoperative biometric parameters are prohibiting factors to compare these eyes with idiopathic shallow ACs or patients with primary ACG. The ongoing debate about the accuracy of IOL power calculation formulas in such eyes with US biometry persists.\(^{[27,28]}\)

We evaluated the accuracy of second generation formula SRK II, the third generation formulas SRK/T, Hoffer Q and Holladay I and the fourth generation formula, Haigis, in predicting refractive outcomes. Previously it was demonstrated that the myopic PEs in 2-variable vergence formulas (Holladay I and Hoffer Q) were anticipated in shallow anterior chambers due to noninclusion of preoperative ACD in their algorithms.\(^{[12]}\) Göcke et al. concluded that multiple-variable vergence formulas (such as Haigis) performed more accurately than 2-variable vergence formulas (Hoffer Q and Holladay 1) in eyes with normal axial lengths and shallow ACDs.\(^{[12]}\) However, several studies showed that multiple variable formulas gave more inaccurate results in eyes with ACG probably due to unpredictable change in ACD and the inaccurate ACD simulation after cataract extraction. Thus, they suggested to apply Hoffer Q or SRK II formulas in such cases for IOL power calculation.\(^{[11,13]}\) Miraftab et al. believed that the anteriorly located IOL in shallow ACs in combination
with underestimation tendency of IOL power calculation with SRK II resulted in the most accurate refractive outcome postoperatively.\footnote{15}

We found that the Haigis formula resulted in positive mean PE values that were more hyperopic than predicted, whereas the other formulas resulted in myopic mean PEs, implying that the IOL located more anteriorly than predicted. It was inconsistent with previous studies that myopic surprise was more common than hyperopia in glaucomatous eyes with shallow ACs.\footnote{12,29} We also found that the SRK II formula produced significant negative PE which was in contrast with former studies which indicated that SRK II underestimated the IOL power and produced the highest hyperopic shift in shallow ACDs.\footnote{15,28} The difference possibly associated with erroneous shallowness in PG due to thick lenses rather than true shallow ACDs.

Although the MAEs in our study revealed no significant differences between the formulas, the Haigis formula produced the highest MAE and the lowest percentages of eyes within 0.25 D and 0.5 D PEs. Hence, it seems that the Haigis formula was the least accurate formula in our study to predict the refractive outcome in patients with PG. Holladay I was the formula with PE that was closest to emmetropia. It seems that if multivariable vergence formulas precisely predict the postoperative ACD, they produce more accurate refractive outcome than 2-variable vergence formulas, but if the postoperative ACD is unpredictable, like in eyes with PG/ACG, the 2-variable formulas have more improved predictive capacity.

In comparing different studies and their achievements, the method of biometry (US versus optical) should be noted which can affect the refractive results. In eyes with PG, the optical biometry application is almost impossible and conventional US biometry is the method of choice. Several studies compared the two methods and reported the better accuracy and greater reproducibility of optical biometric measurements than US biometric ones.\footnote{11,30-33} However, considering the different measuring points of the two methods, optimization of the formulas can improve the refraction results of US method significantly.\footnote{34} Ellakwa et al. similarly found insignificant difference between the two methods in IOL power calculation using SRK T formula and concluded that US biometry is adequate method if the optical biometry is not applicable.\footnote{35}

In this study, we found that SRK II and Holladay I formulas achieved the highest percentages of eyes within the dioptric ranges of ± 0.25 and ± 0.5 of the predicted refraction; conversely, Haigis formula with corresponding respective percentages of 12.5% and 25% was the worst performing formula. Thus, we concluded that lower generation of IOL power calculation formulas produced more acceptable refractive outcomes, possibly due to unpredictable postoperative ACD, and more predictive errors of multivariable vergence formulas like Haigis. It might be also related to the inborn calculation error in pseudophakic condition in which the postoperative IOL power is measured with shorter axial length and deeper ACD in the pseudophakic eye. So, the Haigis formula including the both variables reasonably yielded more estimation error than the third generation formulas which only include axial length in their IOL power calculation algorithms.\footnote{36}

The missing aspects of the study are the small sample size, not including best corrected VA, and high ratio of lost-to-follow up as well as the inability to include lens thickness due to the cataract density and the device limitations. Besides, we did not include eyes with long and short axial lengths so we couldn’t generalize the results to the entire AL ranges. The application of US biometry is inevitable however, it would be better to apply newly designed immersion shell US biometry with comparable results to optical methods.

Despite these limitations, we could demonstrate that the 2-variable vergence formulas may be still more accurate in some extreme situations like patients with PG. Further studies are required with a larger sample size, the comparison with modern biometric formulas, and the inclusion of all ranges of ALs.

Acknowledgments
No grant from funding agencies; no financial disclosures.

What was known
- Multiple-variable vergence formulas performed more accurately than 2-variable vergence formulas in eyes with normal axial lengths and shallow ACDs
- Patients with glaucoma were more likely at risk of refractive surprise and inaccurate IOL power calculation after phacoemulsification cataract surgery.

What this paper adds
- In eyes with PG, lower generation of IOL power calculation formulas produced more acceptable refractive outcomes in comparison with multiple-variable vergence formulas like Haigis.

Financial support and sponsorship
Nil.

Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

Taiwan J Ophthalmol - Volume 12, Issue 2, April-June 2022
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