Accuracy of intraocular lens calculation formulas for eyes with insufficient capsular support

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Background: There is no consensus on which intraocular lens (IOL) power calculation formula provides the best refractive prediction in patients with inadequate capsular support whose anterior ocular anatomic structure differs from that of normal subjects. Therefore, the purpose of this study was to analyze the accuracy and performance of IOL calculation formulas (SRK/T, Holladay 1, Hoffer Q, Haigis, and Barrett Universal II) in predicting postoperative refractive prediction error (PE) for this subgroup of patients.

Methods: A total of 110 eyes from 110 patients with insufficient capsular support who underwent scleral fixation of an IOL at the Zhongshan Ophthalmic Center from July 1, 2016 to November 30, 2019 were enrolled in this retrospective study. Preoperative optical biometrics were measured with the IOL Master 500 (Carl Zeiss, Oberkochen, Germany). The performance of each formula in predicting PE was compared, and the effect of keratometry and axial length (AL) on PE was evaluated for each formula using univariate and multivariate linear regression analysis.

Results: The mean age of the included participants was 12.54±9.66 years. The Sanders, Retzlaff, and Manus/theoretical (SRK/T) (−0.25 D) and Holladay 1 (−0.28 D) formulas tended to have minimal postoperative PE compared to the Hoffer Q (−0.62 D), Haigis (−0.67 D), and Barrett Universal II (−0.62 D) formulas (P=0.005). All formulas individually resulted in <70% of eyes within ±1.00 D of the PE. Nevertheless, after constants were optimized, these formulas led to 7.3% to 13.6% of increase within ±1.00 D of the PE. Keratometry and AL were significantly associated with PE for each formula, but the relationship was weakest for SRK/T.

Conclusions: In eyes with insufficient capsular support, postoperative PE was minimal for the SRK/T formula, which suggested SRK/T to be the best choice, especially when the keratometry and AL of patients are extremely large or small.

Keywords: Insufficient capsular support; sclera-sutured intraocular lens (sclera-sutured IOL); intraocular lens calculation (IOL calculation); accuracy; prediction refraction error

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Introduction

The capsule of the crystalline lens is usually the assumed position for the intraocular lens (IOL) after implantation. However, some ocular comorbidities, such as ocular trauma (1), lens dislocation (2-4), and congenital or secondary weakness of zonules can result in inadequate capsular support and even cause severe visual impairment. For patients with such conditions, transscleral-fixated IOL implantation is one of the commonly used management strategies (5-7). Accurate intended surgical refractive prediction error (PE) is crucial for patients with inadequate capsular support, especially for young children who require good visual acuity (VA) to prevent amblyopia but whose compliance with spectacles is poor.

Preoperative estimation of postoperative IOL position, postoperative refraction determination, and preoperative axial length (AL) have been identified as the main factors contributing to PE (8). The Sanders, Retzlaff, and Manus/theoretical (SRK/T), Holladay 1, Hoffer Q, Haigis, and Barrett Universal II (Barrett II) formulas are five theoretical vergence formulas that are commonly built in optical biometers and are easily accessible online. They are based on Gaussian optics and depend on AL, keratometry, or other variables to estimate effective lens position and calculate IOL power. These IOL calculation formulas are commonly determined or optimized based on biometry parameters from common cataract-affected eyes with routine in-the-bag implantation of IOL, and have demonstrated excellent predictability with similar accuracy for eyes with an AL between 22–26 mm (9). However, prediction for eyes with inadequate capsular support is still challenging.

Compared to normal eyes, patients with inadequate capsular support due to conditions such as congenital ectopia lentis often have a longer AL (10), flatter cornea (4,11), and a larger variation of anterior chamber depth (ACD) measurement, all of which may present difficulties for IOL calculation. Therefore, application of the optimized IOL constants available on the User Group for Laser Interference Biometry (ULIB, http://ocusoft.de/ulib/) for preoperative IOL calculation may be not suitable for patients with inadequate capsular support. However, to our knowledge, no study to date has evaluated the accuracy of IOL calculation formulas or optimized their IOL constants for this subgroup of patients.

We conducted this study to assess and compare the accuracy of five commonly used IOL calculation formulas (SRK/T, Holladay 1, Hoffer Q, Haigis, and Barrett II) for the evaluation of postoperative PE with optimized IOL constants in patients with insufficient capsular support who underwent transscleral-fixated IOL implantation. The extent of bias within each formula for different biometric dimensions of the eye (AL and corneal curvature) was also investigated. We present the following article in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting checklist (available at http://dx.doi.org/10.21037/atm-20-3290).

Methods

This was a retrospective study of patients with insufficient capsular support who underwent lens extraction and transscleral IOL fixation at the Zhongshan Ophthalmic Center in Guangzhou, China between July 1, 2016 and November 30, 2019. All study participants had unilateral or bilateral surgery performed by the same surgeon (Dr. D Zheng). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethical committee of Zhongshan Ophthalmic Center (NO.: 2019KYPJ184) and individual consent for this retrospective analysis was waived.

Our selection criteria were summarized as follows: (I) eyes with insufficient capsule support and accepted transscleral-fixated IOL implantation; (II) biometrics measured using the IOL Master 500 (Carl Zeiss, Oberkochen, Germany); (III) keratometric cylinder <4.0 D; and (IV) manifest refraction within the 3 to 5 weeks postoperatively. Patients with any of the following were excluded: (I) a history of corneal or fundus disease; (II) severe postoperative complications, such as uveitis or glaucoma; (III) ≤6/20 best corrected vision post operation or invalid biometry. If both eyes of one participant met the inclusion criteria, only the first eye to receive surgery was included in this study.

The surgical procedures were as follows: after the conjunctiva was cut, limbal-based partial thickness scleral flaps were performed at the 4 and 10 o’clock positions, with the posterior edge located 3 mm behind the limbus. The capsular bag was completely removed in each eye, and an IOL was transscularly fixated at the 4 and 10 o’clock positions under the scleral flaps with 10-0 Prolene sutures (Ethicon Inc., Cornelia, Georgia, USA). Each IOL was sutured at approximately 2 mm posterior to the limbus. Rayner 970C and 920H IOL models (Rayner Intraocular Lenses Ltd., Worthing, West Sussex, UK) were implanted; both models share a similar aspherical design and the same...
manufacturer’s constant but have different diopter ranges.

Data of patient demographics, operative eye, preoperative optical biometrics measured with the IOL Master 500, postoperative refraction, and best corrected visual acuity (BCVA) were collected. All data mentioned above were entered in an electronic medical record by doctors and/or biometry technicians, and the authors of this study collected the data retrospectively.

Constants for the IOL formulas that we adopted postoperatively were the optimized values on the ULIB website, which were the default values of the IOL Master. We then adjusted the lens constants to reduce the mean error to zero for the SRK/T, Holladay 1, and Hoffer Q formulas using their mathematical formulas, as described in previous studies by using Microsoft Excel (Office 2019, Microsoft Corp., Redmond, WA, USA) (12-14). Lens constants for Haigis (http://www.eyecalcs.com/WEBCALCS/IOLcalc2/IOL2.html) and Barrett II formulas (www.apacrs.org/BARRETT_UNIVERSAL2/) were optimized online.

## Statistical analysis

All statistical analyses were performed using SPSS Version 16.0 (SPSS 16.0, Inc., Chicago, IL, USA). The Shapiro-Wilk test was performed to determine whether variables followed a normal distribution. All values are presented as mean ± standard deviation, except if their distribution was non-normal. The postoperative PE between the five formulas was compared using one-way analysis of variance (ANOVA), with post-hoc testing on indication and correction for multiple comparisons. Comparisons between absolute errors (AEs) were performed using repeated measure ANOVA (the Friedman test with Wilcoxon signed-rank post-hoc analyses and Bonferroni correction). Univariable and multivariable linear regression analyses were used to identify the association of the postoperative PE with AL and keratometry. A two-tailed P value of <0.05 was considered to be statistically significant.

## Results

A total of 110 eyes from 110 patients (44 females, 62 males) with implantation of Rayner 970C/920H models were included in this study. The mean age of the study participants was 12.54±9.66 years. Demographic characteristics of all participants are summarized in Table 1.

Systematic biases in refractive prediction were found in all of the formulas investigated. The mean PE for the SRK/T, Holladay 1, Hoffer Q, Haigis, and Barrett II formulas exhibited a myopic shift from the target refraction (Figure 1). The result of one-way ANOVA showed that the mean PE was relatively higher with Hoffer Q, Haigis, and Barrett II than with SRK/T and Holladay 1 (P=0.005). Distribution around the median AE is shown in Figure 2. The Friedman test demonstrated significant differences in median AE (P=0.002) between the five formulas, and according to the results of post-hoc analysis, SRK/T had a lower median AE than Hoffer Q, Haigis, and Barrett II (all P<0.05).

Optimized lens constants are shown in Table 2. The optimized lens constants in this study were slightly smaller than the values reported on the ULIB website. The median AE and median PE for the ULIB constants, before and

| Parameters | Value |
|------------|-------|
| Patients   | 110   |
| Female (%) | 44 (40.0) |
| Age, mean ± SD (years) | 12.54±9.66 |
| Eyes: right/left | 62/48 |
| Axial length, mean ± SD (mm) | 25.84±2.75 |
| Average keratometry, mean ± SD (D) | 41.04±1.77 |
| Flat keratometry | 40.10±1.72 |
| Steep keratometry | 41.99±1.94 |
| ACD ± SD (mm) | 3.46±0.69 |
| Intraocular lens power, mean ± SD (D) | 17.64±6.25 |

D, diopter; ACD, anterior chamber depth; SD, standard deviation.

Figure 1 Comparison of PEs (in diopter) for the five formulas. Note that myopic prediction errors are indicated by negative values. PEs, prediction errors.
after optimization, are summarized in Table 3. There was no significant difference in median AE between the five formulas after the lens constants were optimized (P=0.565). Before optimization, percentage of eyes within ±1.00 D of the PE of SRK/T, Holladay1, Hoffer Q, Haigis and Barrett II were 69.9%, 65.5%, 57.3%, 54.5% and 65.5%, respectively. After optimization, as a contrast, percentage of eyes within ±1.00 D of the PE increase to 79.1%, 72.7%, 68.2%, 68.2%, 74.5% respectively.

The results of univariate and multivariate linear regression analyses of the relationship of postoperative PE with AL and keratometry are summarized in Table 4. In the univariate linear regression analyses, AL was found to be positively associated with postoperative PE for each formula, but the association appeared to be weaker for SRK/T and Barrett II than for the other formulas. Keratometry was also significantly associated with postoperative PE for each formula, but the association was weakest for SRK/T. Additionally, in the multivariate linear regression analysis, the association between AL and postoperative PE was still significant for each formula after adjustment for the keratometry, and a significant association between keratometry and postoperative PE was observed for each formula after adjustment for the AL.

**Discussion**

In this study, we found that postoperative PE for scleral-sutured IOL positioned 2 mm posterior to the limbus showed a myopic shift from the target refraction with all estimated formulas using the constants from the ULIB website. The SRK/T and Holladay 1 formulas had better outcomes than the Hoffer Q, Haigis, and Barrett formulas in terms of accuracy of postoperative PE. Additionally, the performance of SRK/T was better than that of Hoffer Q, Haigis, and Barrett based on the value of the median AE. Nevertheless, no significant difference in median AE was observed between any of the estimated formulas after optimization of the constants. This study, to our knowledge, is the first to analyze the accuracy and performance of formulas to predict postoperative refraction outcomes in patients with insufficient capsular support after lens extraction and primary transscleral fixation of an IOL.

One of the main factors influencing postoperative PE is the position of the IOL, which has varied in patients with scleral-fixated IOL implantation in previous studies (15-21). The most common choice of suture location in the sclera is 1.5–2 mm posterior to the limbus. In the current study, all scleral-fixated IOL were placed 2 mm posterior to the limbus, and no significant postoperative complications, such as anterior chamber cells and flare, corneal edema, elevated intraocular pressure, or wound leak, were reported in participants’ follow-up medical records. For adults, a scleral-fixated IOL positioned 3 mm behind the limbus was assumed to be the “in-the-bag” IOL position due to the slight difference in postoperative PE from the target refraction.
refraction (−0.19±0.72D) (15); however, little is known about the relationship between the position of scleral-fixated IOL and the “in-the-bag” IOL position in children with insufficient capsular support. It is difficult to determine the anatomic lens position by suture location in the sclera for scleral-fixated IOL; thus, the postoperative refraction following implantation of scleral-fixated IOL can vary. Our results showed that the postoperative PE was myopic for all formulas when the IOL power for a desired postoperative refraction was determined by assuming that the IOL was positioned in the capsular bag, suggesting that the location of IOL plane was in front of the “in-the-bag” position for patients with scleral-fixated IOL positioned 2 mm posterior to the limbus. Determining the relationship between the effective lens position and the actual position of a scleral-fixated IOL will help to improve and refine the IOL calculation formulas for children with insufficient capsular support in the future.

Only two variables (AL and keratometry) are used to predict the postoperative IOL position in the third-generation formulas which do not require measurement of ACD (12,13,22). Consistent with previous studies, patients with inadequate capsular support, due to conditions such as congenital ectopia lentis, often have a flatter cornea (4,11) and longer AL (10) than normal eyes; thus, using the lens constants from the ULIB website, which were acquired based on normal populations, will naturally reduce the accuracy of the third-generation formulas. In contrast, a preoperative ACD is required in the onward formulas including Barrett II and Haigis (23,24). As reported in a previous study (25), it is not surprising that formulas that use more than two variables can help to acquire good outcomes for routine cataract surgery. However, compared to normal eyes, the measurement of ACD is usually inaccurate or is not applicable for eyes with severely dislocated lenses; therefore, using the value of ACD may reduce the accuracy of the corresponding formulas.

In this study, all formulas individually resulted in <70% of eyes within ±1.00 D of the PE. These predicted outcomes using the five different formulas in our study were poorer than those in previous studies of common cataract populations that underwent routine cataract surgery, which suggested >90% of patients should achieve postoperative spherical equivalents within ±1.00 D of the target refraction (26-29). Also, the accuracy of IOL calculation formulas in determining the postoperative refraction in our study was

| Table 3 | The median AE and mean PE after and before optimization |
|---------|--------------------------------------------------------|
| **Formula** | Median AE (IQR) in diopter | Mean PE (SD) in diopter |
| Optimized | ULIB | Optimized | ULIB |
| SRK/T | 0.50 (0.27, 0.87) | 0.56 (0.22, 1.09) | −0.01 (0.94) | −0.31 (0.97) |
| Holladay 1 | 0.62 (0.23, 1.14) | 0.65 (0.29, 1.33) | 0.00 (1.04) | −0.36 (1.11) |
| Hoffer Q | 0.59 (0.25, 1.13) | 0.73 (0.47, 1.59) | 0.00 (1.10) | −0.64 (1.21) |
| Haigis | 0.62 (0.29, 1.18) | 0.88 (0.46, 1.71) | 0.00 (1.12) | −0.80 (1.27) |
| Barrett II | 0.54 (0.27, 1.03) | 0.80 (0.46, 1.29) | −0.01 (0.98) | −0.66 (1.03) |

AE, absolute error; PE, prediction error; ULIB, User Group for Laser Interference Biometry; IQR, interquartile range; SD, standard deviation.

| Table 4 | Results of univariable and multivariate analyses to evaluate the relationship of postoperative PE with AL and keratometry |
|---------|--------------------------------------------------------|
| **Formulas** | AL | Keratometry |
| | Univariable (standard β) | Multivariate (standard β) | Univariable (standard β) | Multivariate (standard β) |
| SRK/T | 0.32** | 0.32** | 0.19* | 0.20* |
| Holladay 1 | 0.53** | 0.54** | 0.28** | 0.30** |
| Hoffer Q | 0.52** | 0.53** | 0.41** | 0.43** |
| Haigis | 0.52** | 0.54** | 0.36** | 0.38** |
| Barrett II | 0.26** | 0.34** | 0.33** | 0.27** |

*, P<0.05; **, P<0.01. PE, prediction error; AL, axial length.
consistent with the results of a previous study on secondary scleral-fixated IOL implantation, which showed that Haigis generally underperformed compared to Holladay 1 and SRK/T (15). However, our results differed from those of studies of routine cataract surgery that reported Haigis and Barrett II to have a worse predicted outcome than the third-generation formulas (23-27). Nevertheless, after constants were optimized, five formulas resulted in >68% (with an increase of 7.3% to 13.6%) within ±1.00 D of the PE. Our results suggested that surgeons may be able to reduce the postoperative PE for this subgroup of patients by optimizing the constant for each formula based on their previous clinical data.

Both AL and mean keratometry have been reported to have significant associations with postoperative PE for the third-generation and Haigis formulas in routine cataract surgery (26,27,30-32). These associations lie in that a longer AL resulted in a hyperopic refraction with SRK/T, Holladay, Hoffer Q, and Haigis, while a flatter keratometry (K) reading tended to result in a myopic PE with Haigis and Hoffer Q and a hyperopic PE with SRK/T. In this study, both univariate and multivariate linear regression analyses showed that postoperative PE was significantly associated with AL and keratometry for each formula. In other words, a trend toward hyperopic PE was found in eyes with a longer AL, and a myopic prediction could be accounted for by a flatter mean keratometry for each formula. Nevertheless, the associations of postoperative PE with AL and keratometry were weakest for SRK/T than for the other formulas. Additionally, our result differed from that of a previous study which reported PE to have no significant association with AL or keratometry for Barrett II in neither univariate nor multivariate linear regression analysis (27).

Based on these results of our study, both AL and keratometry could have a significant effect on postoperative PE in patients with insufficient capsular support when the SRK/T, Holladay 1, Hoffer Q, Haigis, and Barrett II formulas are used; thus, the potential effects of AL and keratometry on PE should be considered together when using these formulas. The weakest association between postoperative PE with AL and keratometry when using SRK/T may account for it having the smallest mean and median AE, which represents a better performance. SRK/T has been suggested as the best choice for eyes with a flatter keratometry or a longer AL. However, definitive conclusions must be carefully drawn due to the relatively small sample size of this study.

In addition to biometric measurements, the accuracy of IOL calculation formulas can also be lens-related and dependant on the surgeon; thus, each surgeon should optimize lens constants for IOL calculation based on the biometric measurements, type of lens, and IOL position from the limbus to achieve better results in the future.

Our study has several limitations. Firstly, patients with insufficient capsular support are not encountered very often in our clinical practice, and the sample size may not reflect the overall population of this subgroup. Nevertheless, the results of post-calculated statistical power showed that the sample size of 110 involved in our study could achieve high enough power to detect the smallest difference of predictive error among different groups. Secondly, tilt and decentration of sclera-sutured IOL was another concern compared to “in-the-bag” IOL implantation (33). Although none of the participants were reported to have significant IOL tilt using the slit lamp or ultrasound biomicroscopy (UBM) examination, detailed tilt and decentration degree could not be assessed in this study due to its retrospective nature. For these reasons, our conclusion may not be generalizable, and further research including larger sample sizes and better designs is required. However, our results suggest that the characteristics and performance of IOL calculation are significantly different from common populations undergoing routine cataract surgery.

Conclusions

In conclusion, the use of the constants from the ULIB website tended to result in a myopic PE in patients with sclera-sutured IOL positioned 2 mm posterior to the limbus. In general, the SRK/T and Holladay 1 formulas were superior to the other formulas, including Haigis and Barrett II, for the prediction of postoperative refraction in eyes with insufficient capsular support. The accuracy of these formulas could be improved by using optimized constants; however, the performances of the scleral fixation of an IOL using these formulas are still poorer than the outcomes of routine cataract surgery. Further studies to optimize these formulas or to develop better formulas to address this challenge are still urgently required.

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