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Original Article

Effectiveness, Sensitivity, and Specificity of Intraocular Lens Power Calculation Formulas for Short Eyes

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Abstract

Objectives: To compare intraocular lens (IOL) power calculation formulas in terms of absolute error (AE) and receiver operating characteristic curves in eyes with axial length (AL) shorter than 22.0 mm.

Materials and Methods: The data of hyperopic patients who underwent uneventful phacoemulsification with IOL implantation in MW-med Eye Centre, Cracow, Poland between October 2015 and June 2019 were retrospectively reviewed. IOL power was calculated using Holladay1, SRK/T, Hoffer Q, Holladay2, Haigis, and Barrett Universal II formulas. The power of the implanted lens was based on Hoffer Q. Three months after phacoemulsification, refraction was measured and AE was calculated. The percentage of patients with full visual acuity without any correction and the percentage of hyperopic patients was determined for each formula. Receiver operating characteristic curves with cut-off points for AL were drawn for each formula and the area under the curve was evaluated.

Results: Fifty-six patients (62 eyes) whose ocular AL ranged between 20.58 mm and 21.97 mm were included in the study. Hoffer Q formula yielded the lowest mean AE (0.09±0.08 D), the highest percentage of patients with full visual acuity without correction (75.8%), and the lowest rate of postoperative hyperopia (8.1%). However, the SRK/T formula had the largest area under the curve (0.667).

Conclusion: The Hoffer Q formula gave the lowest level of AE in the study and seems to be recommendable for IOL power calculation for hyperopic eyes. Further studies are needed on the use of receiver operating characteristic curves in assessing the effectiveness of IOL power calculation formulas.

Keywords: Phacoemulsification, hyperopia, intraocular lenses, ROC curve

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Introduction

Accurate intraocular lens (IOL) power calculation is a very important aspect of cataract surgery because patients' expectations for perfect vision after surgery are still increasing.[1] Therefore, new IOL power calculation formulas based on more parameters are still being developed. Historically, first-generation formulas like the Binkhorst or SRK (Sanders-Retzlaff-Kraff) were based on axial length (AL), corneal power (K), and lens constant (A) only. In second-generation formulas like the SRK II, A was modified based on AL. Third-generation formulas (Holladay 1, SRK/T, Hoffer Q) incorporated more variables such as anterior chamber depth (ACD).[2] Later came fourth-generation formulas like the Haigis (which uses three constants [a0, a1, a2] that are analogous to surgeon factor [SF], ACD, and AL, respectively) and the Holladay 2, which added further parameters like lens thickness and corneal white-to-white, leading to the fifth-generation formulas (Olsen, Barrett Universal II, Hill-Radial Basis Function).[3] While the Barrett Universal II and the Olsen formulas are based on Holladay 2-like globe parameters, the Hill-RBF formula is a mathematical algorithm developed to select IOL power independent of an effective lens position estimation.[4]

It is well known that most IOL power calculation formulas perform well for eyes with AL between 22.0 and 25.0 mm.[5] The accuracy of IOL power calculation formulas for eyes shorter than 22.0 mm or longer than 25.0 mm is still questionable.[6,7] There have been many studies conducted on this. Most often the research methodology is based on calculation of absolute error (AE) using an absolute value of the difference between postoperative and predicted spherical equivalences of refractive error.[6,7,8,9,10,11,12] Only some studies have considered other aspects of the accuracy of IOL power calculation formulas, such as the percentage of patients with full visual acuity (VA) without any correction and the percentage of patients with postoperative hyperopia.[2,3,13,14,15] Although the receiver operating characteristic (ROC) curve method is widely used in medicine to assess the sensitivity and specificity of certain tests, the concept of using it to compare the accuracy of IOL power calculation formulas is new.[16]

This study aimed to compare IOL power calculation formulas in eyes shorter than 22.0 mm in terms of AE, the percentage of patients with full VA without any correction, and the percentage of hyperopic patients after phacoemulsification. Additionally, the study attempted to demonstrate the accuracy of IOL power calculation formulas using ROC curves, which is a novel approach.

Materials and Methods

Hyperopic patients (i.e., axial length of 22.0 mm or less) with Wisconsin grade 3 or 4 cataracts who underwent uneventful sutureless phacoemulsification with monofocal IOL implantation through a 2.4-mm clear corneal incision in MW-med Eye Centre, Cracow, Poland between October 2015 and June 2019 were included in the study.

The exclusion criteria were: corneal astigmatism greater than 2.0 diopters (D) or a history of other ophthalmic procedures such as vitrectomy, limbal relaxing incisions, and corneal refractive surgery.

The study was conducted adhering to the tenets of Declaration of Helsinki. Each patient signed an informed consent for a routine cataract surgery.

Preoperatively, all patients underwent a full ophthalmological examination including the evaluation of best corrected Snellen VA, intraocular pressure measurement, anterior biomicroscopy, and fundoscopy. Preoperative keratometry and ocular biometry were performed using a Zeiss IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany) with partial coherence interferometry to measure K and AL. IOL power was calculated with six different formulas (Holladay 1, SRK/T, Hoffer Q, Haigis, Holladay 2, Barrett Universal II) but the Hoffer Q formula was chosen to predict the definite IOL power. All phacoemulsification (phaco) procedures were performed by the same eye surgeon who used a similar accumulated energy complex parameter (actual phaco power multiplied by time). Monofocal, single-piece, hydrophobic, acrylic foldable IOLs (AcrySof SA60AT, Alcon Laboratories, Fort Worth, TX, USA) were implanted during the surgery. Postoperative refraction was measured 3 months after the surgery using an autorefractor keratometer (Nidek ARK-1, Nidek Co Ltd, Tokyo, Japan) and at least three K measurements were taken for each patient.

Numerical error (NE) was defined as the difference between the real postoperative refractive outcome expressed as spherical equivalent (sum of spherical power and half of cylindrical power) and the refraction predicted by each formula. A positive value indicated a hyperopic error and a negative value referred to myopic error, while the absolute value is AE. Therefore, the mean AE for each formula was calculated as the average of the absolute value of the deviation from predicted postoperative refractive outcome for all cases. AE values were used to determine the percentage of patients with full VA without any correction (AE between 0 and 0.12 D), with correction up to ±0.25 D (AE between 0.13 D and 0.37 D), and with correction up to ±0.5 D (AE >0.37 D). Additionally, the percentage of hyperopic patients (NE ≥0.13) was calculated for each formula (patients with AE ≤ 0.12 were regarded as full VA without any correction, while NE ≤-0.13 corresponded to myopia).

Finally, ROC curves were drawn for each formula and cut-off points for AL (the highest true positive rate and the lowest false negative rate) were identified. To develop an ROC curve, the sensitivities and specificities for different values of a continuous test measure were first tabulated. Then, the graphical ROC curve was drawn by plotting sensitivity (true positive rate) on the y-axis against 1-specificity (false positive rate) on the x-axis for the various values tabulated. This allowed the area under the curve (AUC), which ranges from 0 to 1, to be calculated for each formula.

Statistical analysis was performed using the Statistica 13.1 package. P value <0.05 was considered statistically significant unless it was necessary to apply Bonferroni corrections for multiple comparisons, which reduced the significance level to 0.003. Normality of data distributions was checked using the Shapiro-Wilk test. The non-parametric Kruskal-Wallis test was used to check for statistically significant differences between groups. The Mann-Whitey U test (for quantitative variables) and chi-square or Fisher exact test (for qualitative variables) were used for pairwise formula comparisons.

Results

The study included 62 eyes of 56 patients (30 women and 26 men) with a mean age of 71.2 years (range: 55-92). AL varied between 20.58 and 21.97 mm (median: 21.49 mm).

The Hoffer Q formula provided the lowest mean AE of 0.09±0.08 D. Detailed results of the AE calculated for each formula are listed in Table 1.

Considering the AE, which indicates the expected correction after cataract surgery, the studied group was divided into three subgroups. The first subgroup had expected emmetropia (AE ≤0.12 D), the second had expected correction of ±0.25 D (AE 0.13-0.37 D), and the third group had expected correction of ±0.5 D or more (AE >0.37 D). The percentage distribution of the subgroups is presented in Figure 1.

Due to non-normal data distribution, the non-parametric Kruskal-Wallis test was used to determine differences in AE values between formulas. As the achieved probability value was $p<0.001$, post-hoc analysis with chi-square test (or Fisher exact test in special cases) was performed to compare AE distribution between pairs of formulas. Due to multiple comparisons, Bonferroni correction was applied, thereby lowering the assumed level of significance to $\alpha = 0.05/15 = 0.003$. Statistically significant differences were found in the following pairs of variables: Hoffer Q versus all other formulas, Haigis versus Holladay 1, Haigis versus Holladay 2, and Barrett Universal II versus Holladay 1 (Table 2).

To calculate the expected hyperopia after cataract surgery, two additional groups of patients were formed. The first group had expected emmetropia or myopia (NE ≤0.12 D) and the second group had expected hyperopia (NE >0.12 D). The percentage distribution of these groups is presented in Figure 2.

Similarly, due to non-normal data distribution, Kruskal-Wallis test followed by post-hoc chi-square or Fisher exact test with Bonferroni correction was performed to compare percentage distribution of NE between pairs. Statistically significant differences were found in the following pairs of variables: Hoffer Q versus Barrett Universal II, Hoffer Q versus Holladay 1, and Hoffer Q versus SRK/T (Table 2).

Additionally, ROC curves were drawn for each formula and cut-off points for AL were determined as decision thresholds. The AUC value was also calculated for each formula, with higher AUC values reflecting better formula performance. The calculation results are presented in Table 3 and ROC curves with cut-off points are illustrated graphically in Figure 3.

Discussion

The exact prediction of IOL power for hyperopic eyes is still a problem in daily practice for a cataract surgeon. There are many studies investigating this problem[2-15,17] and assessing the accuracy of selected formulas basing on different variables, most frequently AE.[6-12] Only a few authors have proposed other criteria for assessing the effectiveness of IOL power calculation formulas, such as percentage of patients with ±0.25 D, ±0.5 D, ±0.75 D, and ±1.0 D refraction after phacoemulsification.[3,4,14,15] Such parameters are useful, but results can vary widely. For example, postoperative refraction up to ±0.5 D in short eyes using the Hoffer Q formula was reported in 42.5% of patients in a study by Doshi et al.,[1] 71% in a study by Aristodemou et al.,[13] and 84.9% of patients in a study by Gökce et al.[4] Even greater differences were obtained using the Haigis formula, with rates of 17.5% reported by Doshi et al.,[1] 62.8% by Gokce et al.,[4] and 72.0% by Moschos et al.[3] In the present study, postoperative refraction up to ±0.5 D ranged from 82.3% (Haigis) to 100%

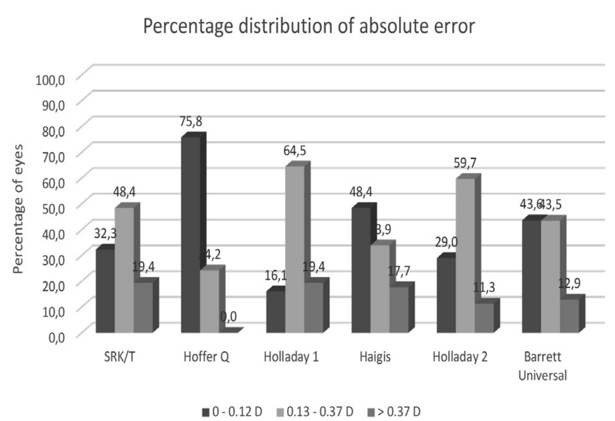

Figure 1. Percentage distribution of absolute error (AE) for all formulas. There was a significant difference among the groups (p<0.001, Kruskal-Wallis)

Table 1. Descriptive statistics of absolute error

	Absolute error (D)					
	SRK/T	**Hoffer Q**	**Holladay 1**	**Haigis**	**Holladay 2**	**Barrett Universal**
Mean ± SD	0.23±0.17	0.09±0.08	0.26±0.17	0.21±0.22	0.20±0.13	0.19±0.16
Median	0.20	0.06	0.23	0.13	0.19	0.14
Range	0.01-0.63	0.00-0.34	0.01-0.73	0.00-0.91	0.00-0.54	0.00-0.71

SD: Standard deviation

(Hoffer Q). In other studies, the percentage of patients with full VA without correction was also estimated.[2]

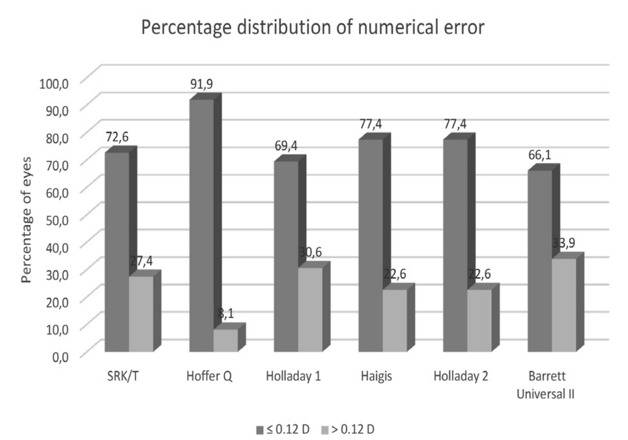

Figure 2. Percentage distribution of numerical error (NE) for all formulas. There was a significant difference among the groups (p<0.001, Kruskal-Wallis)

This study demonstrated that the Hoffer Q formula provided the lowest AE, the highest percentage of patients with full VA without correction, and the lowest percentage of hyperopic patients when used for IOL power calculation in eyes with AL smaller than 22.0 mm.

Consistent with the results of this study, the Hoffer Q is considered by many the most accurate formula for IOL power prediction in hyperopic eyes.[2,4,8,9,11,13] According to the literature, the second best in terms of accuracy would be the Haigis formula.[3,6,8,11,12] However, a 2018 meta-analysis based on 11 observational studies involving 1161 eyes demonstrated superiority of Haigis over Hoffer Q, whereas Holladay 2 gave the smallest mean AE but without a statistically significant difference.[6] The Holladay 2 formula was also shown to be the most accurate in IOL power prediction for short eyes in a few studies.[4,11] Single studies indicated the Holladay 1 formula,[13] Hill-RBF,[14] Barrett Universal II,[15] or Kane formula[17] as the most exact for IOL power calculation in hyperopic eyes. Hoffer and Savini's[11] analysis of studies published in the past 50 years revealed that the Hoffer Q, Haigis, and Holladay 2 formulas were the best options for IOL power prediction in short eyes.

Table 2. Results of pairwise comparisons of percentage distribution of absolute error (AE) and percentage distribution of numerical error (NE)

Chi-square test results	p (AE)	p (NE)
SRK/T vs. Hoffer Q.	<0.001	<0.001
SRK/T vs. Holladay 1	0.021	0.618
SRK/T vs. Haigis	0.054	0.433
SRK/T vs. Holladay 2	0.174	0.433
SRK/T vs. Barrett Universal II	0.199	0.319
Hoffer Q vs. Holladay 1	<0.001	<0.001
Hoffer Q vs. Haigis	<0.001	0.004
Hoffer Q vs. Holladay 2	<0.001	0.004
Hoffer Q vs. Barrett Universal II	<0.001	<0.001
Holladay 1 vs. Haigis	<0.001	0.200
Holladay 1 vs. Holladay 2	0.049	0.200
Holladay 1 vs. Barrett Universal II	<0.001	0.618
Haigis vs. Holladay 2	0.001	1
Haigis vs. Barrett Universal II	0.332	0.076
Holladay 2 vs. Barrett Universal II	0.062	0.076

Table 3. Area under the curve (AUC) values with two-sided confidence level

Formula	AUC	SE	95% lower confidence level	95% upper confidence level	p
SRK/T	0.667	0.076	0.518	0.815	0.028
Hoffer Q	0.645	0.096	0.458	0.833	0.129
Holladay 1	0.649	0.089	0.475	0.823	0.093
Haigis	0.493	0.075	0.347	0.639	0.928
Holladay 2	0.615	0.074	0.47	0.759	0.119
Barrett Univ. II	0.564	0.073	0.421	0.707	0.380

SH: Sayısal hata

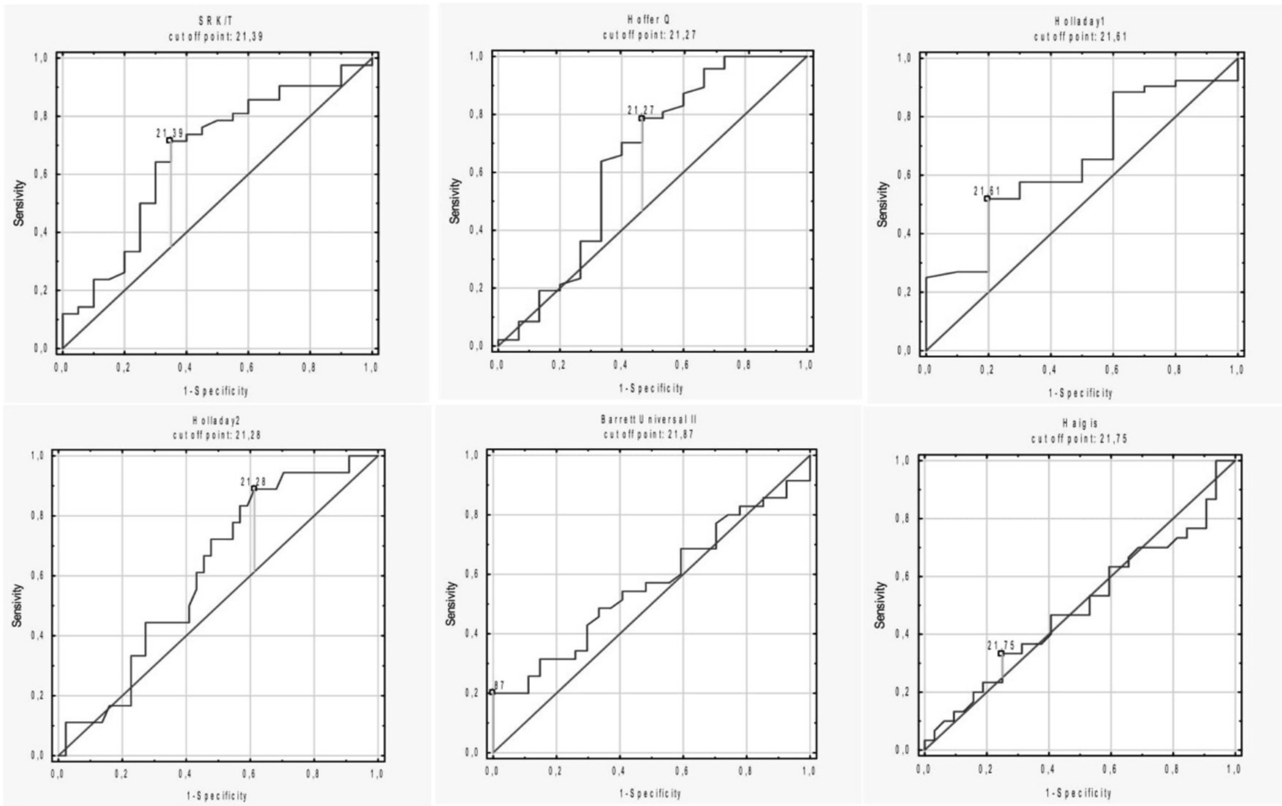

Figure 3. Receiver operating characteristic curves and cut off-points for each formula

Previous studies based on AE have shown the percentage of patients requiring both plus and minus correction after phacoemulsification. However, it is known that postoperative low myopia is less burdensome than hyperopia. Therefore, in this study I showed the percentage of hyperopic patients after cataract surgery based on NE, not only on AE. The Hoffer Q formula yielded the lowest outcomes in terms of postoperative hyperopia (8.1%). In a 2014 study of 69 patients, Moschos et al.[3]. showed that as many as 15% of patients required correction greater than ±1.0 D when IOL power was calculated according to the Hoffer Q formula. However, they used A-scan ultrasound to obtain AL, which is a less accurate method than IOLMaster. Studies based on preoperative and postoperative ultrasound biometry demonstrated that 54% of the errors in predicted refraction after IOL implantation can be attributed to AL measurement errors.[18] However, in the study by Gökce et al.,[4] after applying the method of optical low-coherence reflectometry to measure AL (Lenstar LS900), this rate was only 2.3% of 67 patients when using the Hoffer Q formula (and Holladay 1). The accuracy of AL, K, and ACD measurements is similar using Lenstar LS900 and IOLMaster 700. However, the IOLMaster 700 uses swept-source optical coherence tomography and demonstrates superior acquisition of biometric measurements compared with the widely used optical biometer IOLMaster 500.[19] On the other hand, there was reportedly no statistically significant difference in compared biometric parameters obtained with the IOLMaster 700 and the Pentacam AXL, which combines Scheimpflug technology with partial coherence interferometry.[20] In contrast, a recent study of 16 patients by Tang et al.[15] showed that up to 46.7% of patients (which was the best result, obtained with the Hill-RBF formula) required correction greater than ±0.5 D after phacoemulsification. However, the surgeries in their study were performed by resident ophthalmologists.

The methodology of this study is pioneering because of the use of ROC curve analysis. ROC curves are widely used to evaluate sensitivity and specificity in medicine.[16] However, they have not been used in previous studies of the effectiveness of IOL power calculation formulas. The ROC curve is plotted as:

$$ROC(\cdot) = \{(1-F(c), 1-G(c)): -\infty \le c \le \infty\}$$

It is a graph of variable x {x: x > c} with a changing threshold c. Since F (+1) = G (+1) = 1 and F (-1) = G (-1) = 0, the ROC curve joins the vertices (0, 0) and (1, 1) of the unit square (where F is the distribution function of the variable x in the group labeled 0 and G is the distribution function of the variable x in the group labeled 1). In practice, it is useful to calculate AUC.[16] Normally, an AUC of 0.5 represents a test with no discriminating ability (i.e., no better than chance), while an AUC of 1.0 represents a test with perfect discrimination.

In this study, the largest AUC (0.667) was obtained for the SRK/T formula and was statistically significant (p=0.028).

However, the AUC values achieved by Holladay 1 (0.649) and Hoffer Q (0.645) were very close to that obtained for SRK/T. Additionally, a cut-off point for AL was marked for each formula and ranged from 21.27 mm (the Hoffer Q formula) to 21.87 mm (the Barrett Universal II formula). The cut-off point for the Hoffer Q formula was the smallest, demonstrating that the Hoffer Q was more accurate for even shorter eyes than those tested. On the other hand, the median AL of the examined eyes was 21.49 mm and was the closest to the cut-off point of the SRK/T formula, which could favor this formula in terms of AUC. However, there are some papers proving the accuracy of the SRK/T formula in IOL power calculation. Doshi et al.[1] reported that the SRK/T formula achieved the largest percentage of patients with refraction up to ±0.5 D, while the Hoffer Q formula had the largest percentage with refraction up to ±1.0 D in short eyes. Aristodemou et al.[13] obtained the highest percentage of patients with refraction up to ±0.25 D and up to ±1.0 D for eyes with AL ranging from 21.5 mm to 21.99 mm using the SRK/T formula. The cut-off points determined in this study are very similar due to the small AL range of the studied eyes, although theoretically, based on these cut-off points one can try to determine the ranges of AL for which the given formula is the most accurate. The concept will probably work better with myopic eyes, where length differences are much larger. Although the ROC curve method seems intriguing, it did not give unequivocal results when assessing the sensitivity and specificity of the IOL power calculation formulas.

Study limitations

I recognize certain limitations of this study. The first one is the relatively small range of AL in the operated eyes (20.58-21.97 mm). Aristodemou et al.[13] obtained different mean AE results for certain length ranges, reporting the smallest mean AE in eyes with a length of 20.00-20.99 mm for the Holladay 1 formula, 21.00-21.49 mm for the Hoffer Q formula, and 21.50-21.99 mm for the SRK/T formula (AE=0.67, 0.50, and 0.43, respectively). In the present study, the median AL of the operated eyes was 21.49 mm, which could have resulted in the Hoffer Q formula obtaining the highest accuracy in terms of AE and the SRK/T formula in terms of ROC curve. This interpretation of the discrepancy in my results is similar to the observations of Aristodemou et al.[13] in their large study (457 eyes). Although the patient group in my study does not seem large, there are many published papers with even smaller samples.[9,12,18,21,22] Cook at el.[21] and Gavin et al.[22] studied 41 eyes, Wang et al. included 33 eyes,[18] Carifi et al. evaluated 28 eyes,[9] and Roh et al.[12] studied only 25 eyes. On the other hand, there have been a few studies with more eyes: 457 in the study by Aristodemou et al.,[13] 86 in the study by Gökce et al.,[4] and 75 in the study by Eom et al.[23] Another limitation of this study is that all patients received the same model of IOL, so these results may not be generalizable to IOL models of a different design. Similarly, all procedures being performed by the same eye surgeon limits generalization. Additionally, six patients participating in this study had both eyes operated on, which may also be a limitation of the study. However, they accounted for only 10% of operated eyes and should not affect the final result. Finally, pupil dilatation was not considered in the study. There are reports on the influence of pupil dilation on the accuracy of IOL power calculation formulas.[24]

Conclusion

In summary, this study shows that the Hoffer Q formula can be recommended for IOL power calculation for eyes with AL smaller than 22.0 mm in terms of AE, percentage of patients with full visual acuity without correction, and percentage of hyperopic patients. However, considering the results of ROC curve analysis, the SRK/T formula is the most accurate for these cases, followed by Holladay 1 and Hoffer Q. Although the reliability of the presented results may be limited due to the small sample size, the concept of using the ROC curve method seems promising.

Ethics

Ethics Committee Approval: It is retrospective study based on patients data.

Peer-review: Externally peer reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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