• Clinical Research •

Accuracy of IOL power calculation in pediatric aphakia secondary implantation

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Abstract

● **AIM:** To evaluate the accuracy of intraocular lens (IOL) power calculation formulas with/without preoperative aphakic anterior chamber depth (aph-ACD) in pediatric aphakia.

● **METHODS:** A total of 102 pediatric patients (150 eyes) undergoing secondary IOL implantation were divided into two groups (in-the-bag or ciliary sulcus). Prediction error was calculated for 9 IOL power calculation formulas, including: 1) not requiring ACD: Hoffer Q, Holladay 1, SRK/T; 2) usable without or with entering ACD: Barrett Universal II (BUII), Emmetropia Verifying Optical (EVO) 2.0, and Ladas Artificial Intelligence Super (Ladas AI); 3) requiring ACD: Haigis, Kane, and Pearl-DGS. Mean prediction error (ME), mean absolute error (MAE), median absolute error (MedAE) and the percentage of eyes within ±0.25, ±0.50, ±0.75, and ±1.00 D were calculated.

● **RESULTS:** For the BUII, EVO 2.0, and Ladas AI, with aph-ACD demonstrated a higher MedAE compared to without aph-ACD (BUII: 1.27 *vs* 1.13 D, EVO 2.0: 1.26 *vs* 1.06 D, Ladas AI: 1.30 *vs* 1.10 D; all $P<0.05$). Formulas requiring ACD (Haigis, Kane, and Pearl-DGS) exhibited larger MedAE than those not requiring aph-ACD (Hoffer Q, Holladay 1, and SRK/T; $P<0.05$). In the capsular group, the percentage of eyes within ±1.00 D ranged from 44.83% to 74.14%, and it was 19.57% to 32.61% in the sulcus group.

● **CONCLUSION:** The introduction of aph-ACD does not improve the accuracy of IOL calculation for pediatric aphakia, regardless of in-the-bag or sulcus IOL secondary implantation. The relationship between aph-ACD and effective lens position in pediatric aphakia warrants further study.

● **KEYWORDS:** intraocular lens calculation; pediatric aphakia; secondary intraocular lens implantation; aphakic anterior chamber depth

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INTRODUCTION

Secondary intraocular lens (IOL) implantation is a common refractive treatment for pediatric aphakia, where accurate IOL power prediction is crucial[1-2]. While current IOL formulas, based on adult phakic eyes, achieve high accuracy in adults [96.4% to 98.2% within ±1.00 diopter (D) of prediction error][3], they perform poorly in pediatric aphakia (16.7% to 70.8% within ±1.00 D of prediction error)[4-5]. In pediatric aphakic patients, the unavailability of phakic anterior chamber depth (ACD; the distance from corneal epithelium to the anterior surface of the lens) and lens thickness (LT) greatly impedes the application of several IOL power calculation formulas. Furthermore, the target refraction range for some formulas limited their applications in young children, who may require initial high hypermetropia to offset future myopic shifts, for instance, the newer-generation PEARL-DGS formula provides refractive predictions only within a target range up to +1.50 D[1].

In our previous study, we found that the preoperative aphakic anterior chamber depth (aph-ACD, which was measured from the corneal epithelium to the inferior margin of undilated pupil) in pediatric aphakia impacts on the prediction error. Specifically, deeper aph-ACD before IOL implantation [β: 0.304, 95% confidence interval (CI): -0.010 to 0.617, $P=0.057$] could lead to hyperopic shift (prediction error >0) in the mixed effects linear regression model[1].

We hypothesized that incorporating aph-ACD could enhance IOL calculation accuracy for these eyes. Thus, in this study, we compared the accuracy of various formulas with/without aph-ACD using a large pediatric aphakia dataset, categorized by ACD necessity: 1) ACD not needed: such as Hoffer Q[6-7], Holladay 1[7-8] and SRK/T[7,9]; 2) ACD optional: Barrett Universal II (BUII)[10-11], Emmetropia Verifying Optical (EVO) 2.0[12-13], and Ladas Artificial Intelligence Super (Ladas AI)[14-15]; 3) ACD required: Haigis[7,16], Kane[17-18], and Pearl-DGS[3,19].

PARTICIPANTS AND METHODS

Ethical Approval This retrospective consecutive case-series study was performed under the approve of the Zhongshan Ophthalmic Center (Guangzhou, China) Institutional Review Board (2022KYPJ099-4) and conformed to the tenets of Declaration of Helsinki. Details of study protocol and subject eligibility have been described previously[1,20-21].

This study employed a congenital cataract cohort utilized in our preceding publication. Briefly, inclusion criteria were 1) diagnosed with congenital cataract and underwent cataract extraction before age 24mo; 2) received secondary in-the-bag or sulcus IOL implantation. Exclusion criteria were 1) preexisting ocular comorbidities which might interfere with the selection of method and outcome of secondary IOL implantation, such as aphakic glaucoma, corneal disease, microcornea, retinal disease, persistent fetal vasculature, or trauma; 2) suture fixation or other methods of secondary IOL implantation were used.

Two experienced professors performed all surgical procedures, deciding on in-the-bag or sulcus placement intraoperatively. A 4-5 mm anterior and 3.5-4 mm posterior capsulectomy preserved the lens capsule for a volumized Soemmerring ring, aiding in-the-bag IOL implantation. Before IOL insertion, viscoelastic was used to assess the Soemmerring ring's suitability for in-the-bag implantation. If sufficient capsule was present without leaflet adhesion, a cystotome or radiofrequency diathermy reopened the ring for in-the-bag IOL placement. Otherwise, the IOL was placed in the sulcus. Single-piece monofocal lens with anti-vaulting haptics (970C or 920H, Rayner, Worthing, West Sussex, UK) or three-piece monofocal lens with PMMA C-loop haptics (AR40e, Sensar, Abbott Medical Optics, Santa Ana, CA, USA) were used for sulcus implantation.

Prior to IOL implantation, patients underwent biometry using the IOL-Master 700 (Version 1.88.1.64861, Carl Zeiss Meditec AG, Jena, Thuringia, Germany) to collect axial length (AL), flat keratometry (K1), steep keratometry (K2), and central corneal thickness (CCT). Additionally, aph-ACD was measured by Scheimpflug tomography (Version 6.10r59, Pentacam HR, Oculus, Wetzlar, Hessen, Germany). Other data, including sex, ocular and systemic comorbidities, age at cataract surgery, age at IOL implantation, surgical procedures, type and power of inserted IOLs, preoperative and postoperative logarithm of the minimum angle resolution best-corrected visual acuity, and subjective refraction at 3mo after IOL implantation were also recorded.

The following formulas were evaluated using optimized constants from the User Group for Laser Interference Biometry (http://ocusoft.de/ulib/c1.htm, accessed on November 2, 2019): BUII, EVO 2.0, Haigis, Hoffer Q, Holladay 1, SRK/T, Kane, LSF and PEARL-DGS. The target refractive ranges supported by each formula were as follows: BUII and LSF, –10.00 to +10.00 D; EVO 2.0, –5.00 to +5.00 D; Kane, –6.00 to +2.00 D and PEARL-DGS, –4.00 to +1.50 D. No explicit restrictions on the calculable target refraction range were specified for the other formulas. For each formula, the predicted error (PE) was calculated as the difference between the actual (refraction at 3mo postoperatively) and predicted postoperative refraction (calculated as spherical equivalent). The mean predicted error (ME), mean absolute predicted error (MAE), and median absolute predicted error (MedAE), as well as the percentage of eyes within a PE of ±0.25, ±0.50, ±0.75 and ±1.00 D were calculated. Subgroup analyses were performed based on the different IOL implanted position (capsular group and sulcus group).

Statistical Analysis Statistical analyses followed the published protocol[22]. Data normality was assessed with the Kolmogorov-Smirnov test. Demographic comparisons used Chi-square or *t*-tests. If both eyes were included within the same person, the linear mixed model was used to adjust the correlation between two eyes for biometric characteristics. The repeat measurement variance analysis was used for PE and the Friedman test was used to evaluate the absolute PE among the formulas. The Friedman test with the Bonferroni correction was used for multiple comparisons of the absolute PE among the formulas. The percentage of eyes within a PE of ±0.25, ±0.50, ±0.75 and ±1.00 D were compared by the Cochran *Q* test. All statistical analyses were performed using SPSS Statistics software (version 25.0, IBM Corp., Armonk, NY, USA) with $P<0.05$ indicating significance.

RESULTS

From January 2013 to December 2017, 81 participants (148 eyes) were excluded for lacking preoperative aph-ACD and being outside target refraction range of the formulas. Ultimately, 150 eyes from 102 participants were included, with 58 eyes in capsular group and 92 in sulcus group. Participants' demographic and biometric characteristics before secondary IOL implantation were noted in Table 1. All other variables were normally distributed. There were more males in capsular group (n=30) than in sulcus group (n=35, P=0.014). Mean ages at cataract surgery and IOL implantation were 7.28±4.07mo

Table 1 Demographic and biometric characteristics of the participants

Parameters	Total	In-the-bag implantation	Sulcus implantation	*P*
Cases (eyes), *n*	102 (150)	38 (58)	64 (92)	
Bilateral enrolled, *n* (eyes)	89 (137)	36 (56)	53 (81)	0.124[a]
Males, *n* (%)	65 (63.73)	30 (78.95)	35 (54.69)	0.014[a]
Characteristics of 150 eyes, mean±SD (range)				
Age at cataract surgery, mo	7.28±4.07 (2.37-18.59)	7.05±4.17 (2.96-16.58)	7.43±4.02 (2.37-18.59)	0.760[b]
Age at IOL surgery, mo	50.96±18.45 (16.03-106.18)	42.49±16.22 (16.03-81.50)	56.30±17.84 (26.48-106.18)	0.477[b]
Parameters before IOL implantation				
AL, mm	22.93±1.63	22.68±1.49	23.09±1.71	0.208[b]
K1, D	43.70±2.02	43.49±1.68	43.83±2.21	0.890[b]
K2, D	45.51±2.24	45.08±1.78	45.78±2.45	0.421[b]
aph-ACD, mm	3.80±0.37	3.80±0.34	3.80±0.40	0.945[b]
CCT, μm	565.38±76.98	568.88±89.25	563.17±68.56	0.661[b]

[a]Chi-square test; [b]Linear mixed model with adjustment of correlation between two eyes within same person. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil; AL: Axial length; CCT: Central corneal thickness; K1: Flat keratometry; K2: Steep keratometry; SD: Standard deviation.

Table 2 Predictive outcomes of formulas without/with preoperative aph-ACD in total

Prediction error (D)	BUII		EVO 2.0		Ladas AI		*P*
	without aph-ACD	with aph-ACD	without aph-ACD	with aph-ACD	without aph-ACD	with aph-ACD	
ME±SD	-0.90±1.27	-1.10±1.24	-0.81±1.15[a]	-1.09±1.11	-0.93±1.17	-1.13±1.18	<0.001[d]
MAE (range)	1.28±0.88 (0.02, 4.13)	1.38±0.91 (0.01, 4.00)	1.16±0.78 (0.01, 3.59)	1.32±0.83 (0, 3.72)	1.23±0.84 (0.01, 3.98)	1.36±0.91 (0.01, 4.37)	
MedAE (P_{25}, P_{75})	1.13[b] (0.59, 1.86)	1.27 (0.75, 1.97)	1.06[b] (0.51, 1.57)	1.26 (0.65, 1.93)	1.10[b] (0.58, 1.71)	1.30 (0.63, 1.91)	<0.001[e]
Percentage (%)							
±0.25 D	12.67	10.00	11.33	9.33	10.67	11.33	0.788[f]
±0.50 D	20.67	19.33	24.00[c]	16.00	20.67	19.33	0.028[f]
±0.75 D	34.00[c]	26.00	34.00[c]	28.67	32.00	28.00	0.007[f]
±1.00 D	43.33[c]	42.00	48.00[c]	38.67	45.33[c]	35.33	<0.001[f]

[a]The repeat measurement variance analysis with the Bonferroni correction: EVO 2.0 without aph-ACD<other formulas (adjusted *P*<0.05); BUII without aph-ACD, Ladas AI without aph-ACD<BUII with aph-ACD, EVO 2.0 with aph-ACD formula, Ladas AI with aph-ACD formula (adjusted *P*<0.05). [b]The Friedman test with the Bonferroni correction: EVO 2.0 without aph-ACD<other formula (adjusted *P*<0.05); Ladas AI without aph-ACD<BUII with aph-ACD, EVO 2.0 with aph-ACD, Ladas AI with aph-ACD formula (adjusted *P*<0.05); BUII without aph-ACD<BUII with aph-ACD, Ladas AI with aph-ACD formula (adjusted *P*<0.05). [c]The Cochran *Q* test with the Bonferroni correction: ±0.50 D (%): EVO 2.0 without aph-ACD>EVO 2.0 with aph-ACD (adjusted *P*<0.05); ±0.75 D (%): EVO 2.0 without aph-ACD, BUII without aph-ACD>BUII with aph-ACD (adjusted *P*<0.05); ±1.00 D (%): EVO 2.0 without aph-ACD>EVO 2.0 with aph-ACD (adjusted *P*<0.05); BUII without aph-ACD, EVO 2.0 without aph-ACD, Ladas AI without aph-ACD>Ladas AI with aph-ACD (adjusted *P*<0.05). [d]The repeat measurement variance analysis, [e]The Friedman test, [f]The Cochran *Q* test. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil; D: Diopter; MAE: Mean absolute error; ME: Mean prediction error; MedAE: Median absolute error; SD: Standard deviation; BUII: Barrett Universal II; EVO 2.0: Emmetropia Verifying Optical; Ladas AI: Ladas Super artificial intelligence formula.

and 50.96±18.45mo respectively. No statistically significant differences were observed in laterality, AL, K1, K2, aph-ACD, and CCT between groups (*P*>0.05).

Prediction Outcomes of BUII, EVO 2.0, and LSF Formulas without/with aph-ACD The prediction outcomes of BUII, EVO 2.0, and LSF formulas overall were shown in Table 2. Significant differences were found in PE and the absolute PE among formulas (*P*<0.001). For the BUII, EVO 2.0 and Ladas AI, with aph-ACD demonstrated higher ME and MedAE than without aph-ACD (adjusted *P*<0.05). The EVO 2.0 without aph-ACD showed the lowest ME and MedAE among formulas (adjusted *P*<0.05). The percentage of eyes within a PE of ±0.50, ±0.75 and ±1.00 D differed significantly among formulas (*P*=0.028, *P*=0.007, *P*<0.001), ranging from 16.00% to 24.00% for ±0.50 D and 35.33% to 48.00% for ±1.00 D. The formulas with 24.00% eyes within a PE of ±0.50 D and 48.00% eyes within a PE of ±1.00 D were both EVO 2.0 without aph-ACD.

In capsular group, the prediction outcomes of BUII, EVO 2.0, and LSF formulas were shown in Figures 1A and 2A. There was statistically significant difference in PE (*P*<0.001), but no significant difference in the absolute PE across formulas (*P*=0.099). For the BUII, EVO 2.0, and Ladas AI, with aph-ACD exhibited a higher ME and MedAE than without aph-ACD (all adjusted *P*<0.05). In all formulas, the percentage of eyes within a PE of ±1.00 D differed significantly among

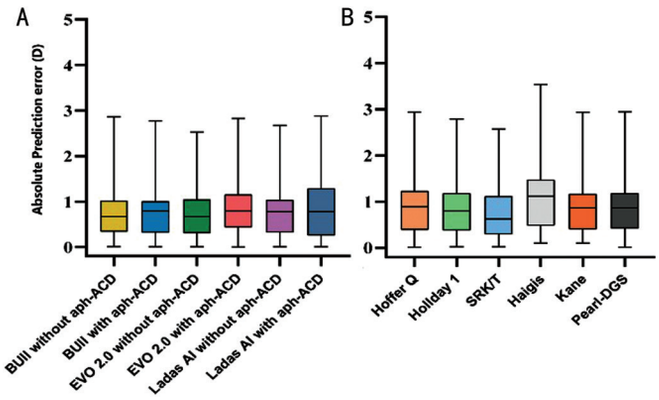

Figure 1 Box plots showing the absolute prediction error of intraocular lens calculation formulas in capsular group (38 persons, 58 eyes) A: BUII, EVO 2.0, and LSF formulas without/with aph-ACD; B: Formulas not requiring aph-ACD *vs* requiring aph-ACD. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil.

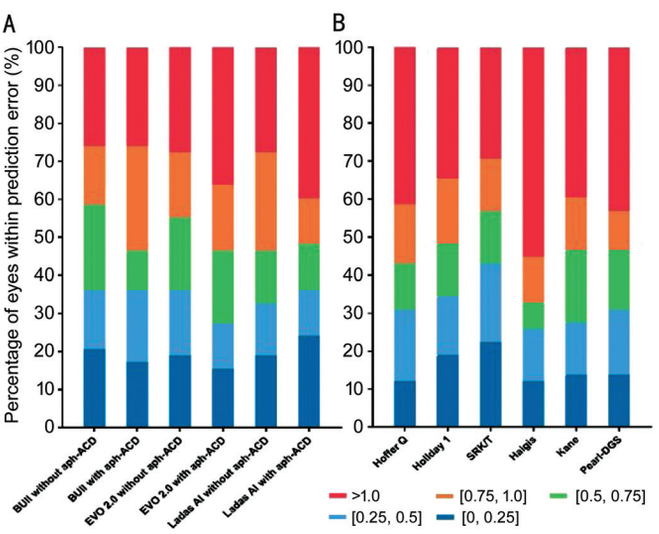

Figure 2 Stacked histogram showing percentage of eyes within ±0.25, ±0.50, ±0.75, ±1.0, and >1.0 D range of prediction error in capsular group (38 persons, 58 eyes) A: BUII, EVO 2.0, and LSF formulas without/with aph-ACD; B: Formulas not requiring aph-ACD *vs* requiring aph-ACD. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil.

formulas (P=0.026), ranging from 27.59% to 36.21% for ±0.50 D and 60.34% to 74.14% for ±1.00 D. The formulas with 74.14% eyes within a PE of ±1.00 D were BUII without and with aph-ACD.

In sulcus group, the prediction outcomes of BUII, EVO 2.0, and LSF formulas were shown in Figures 3A and 4A. Significant differences were found in PE and the absolute PE among formulas (P<0.001). For the BUII, EVO 2.0, and Ladas AI, with aph-ACD demonstrated a higher ME and MedAE than without aph-ACD (adjusted P<0.05). The EVO 2.0 without aph-ACD showed lowest ME and MedAE (adjusted P<0.05). In all formulas, the percentage of eyes within a PE

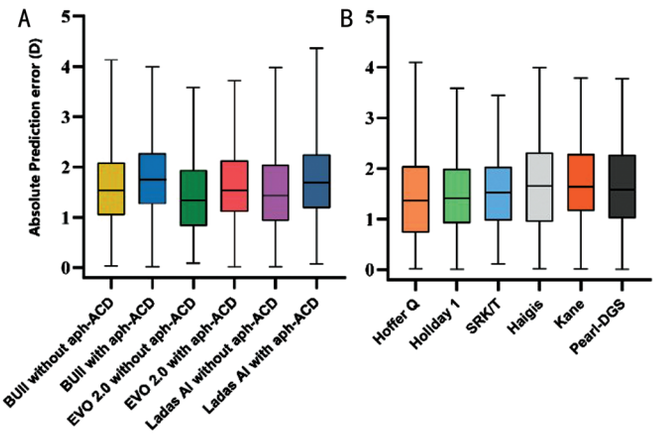

Figure 3 Box plots showing the absolute prediction error of intraocular lens calculation formulas in sulcus group (64 persons, 92 eyes) A: BUII, EVO 2.0, and LSF formulas without/with aph-ACD; B: Formulas not requiring aph-ACD *vs* requiring aph-ACD. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil.

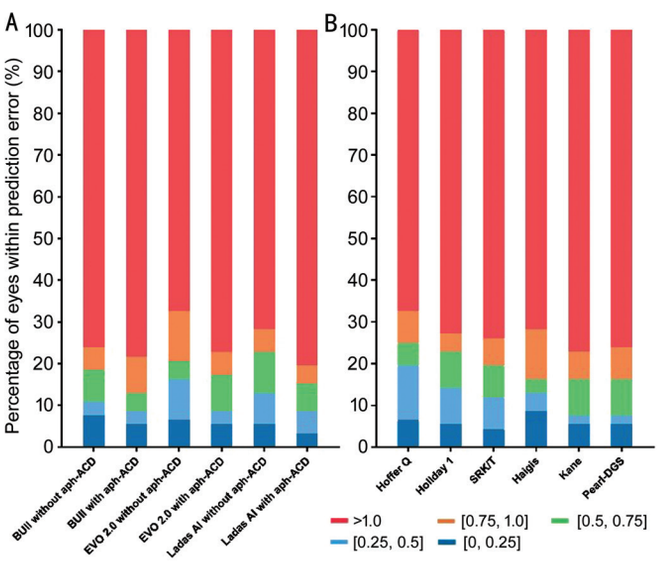

Figure 4 Stacked histogram showing percentage of eyes within ±0.25, ±0.50, ±0.75, ±1.0, and >1.0 D range of prediction error in sulcus group (64 persons, 92 eyes) A: BUII, EVO 2.0, and LSF formulas without/with aph-ACD; B: Formulas not requiring aph-ACD *vs* requiring aph-ACD. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil.

of ±0.50, ±0.75, and ±1.00 D differed significantly among formulas (P<0.001, P=0.001, P<0.001), ranging from 8.70% to 16.30% for ±0.50 D and 19.57% to 32.61% for ±1.00 D. The formulas with 16.30% eyes within a PE of ±0.50 D and 32.61% eyes within a PE of ±1.00 D were both EVO 2.0 without aph-ACD.

Prediction Outcomes of Formulas not Requiring aph-ACD *vs* Requiring aph-ACD Prediction outcomes overall were shown in Table 3. Significant differences in PE and the absolute PE were observed among formulas (P<0.001). ACD-requiring formulas (Haigis, Kane, and Pearl-DGS) displayed

Table 3 Predictive outcomes of formulas requiring aph-ACD or not in total (150 eyes)

Prediction error (D)	Not requiring aph-ACD			Requiring aph-ACD			*P*
	Hoffer Q	Holladay 1	SRK/T	Haigis	Kane	PEARL-DGS	
ME±SD	-0.99±1.13	-0.93±1.11	-0.89±1.17	-1.28±1.11[a]	-1.15±1.17	1.16±1.12	<0.001[d]
MAE (range)	1.24±0.85 (0.01, 4.10)	1.22±0.79 (0.01, 3.58)	1.23±0.80 (0.02, 3.44)	1.44±0.89 (0.02, 3.99)	1.39±0.87 (0.01, 3.79)	1.36±0.86 (0.004, 3.77)	
MedAE (P_{25}, P_{75})	1.15[b] (0.53, 1.67)	1.19[b] (0.58, 1.67)	1.15[b] (0.55, 1.76)	1.40 (0.79, 1.91)	1.27 (0.68, 2.03)	1.21 (0.71, 1.96)	<0.001[e]
Percentage (%)							
±0.25 D	8.67	10.67	11.33	10.00	8.67	8.67	0.845[f]
±0.50 D	24.00[c]	22.00	24.00[c]	18.00	15.33	16.67	0.003[f]
±0.75 D	32.00[c]	32.67[c]	34.00[c]	22.67	28.00	28.00	0.001[f]
±1.00 D	42.67	42.00	43.33	34.67	37.33	36.67	<0.001[f]

[a]The repeat measurement variance analysis with the Bonferroni correction: Hoffer Q, Holladay1, SRK/T<Kane, PEARL-DGS<Haigis formula (adjusted *P*<0.05). [b]The Friedman test with the Bonferroni correction: Hoffer Q, Holladay1, SRK/T<Haigis, Kane, PEARL-DGS formula (adjusted *P*<0.05). [c]The Cochran *Q* test with the Bonferroni correction: ±0.50 D (%): Hoffer Q, SRK/T>Kane formula; ±0.75 D (%): Hoffer Q, Holladay1, SRK/T>Haigis formula (adjusted *P*<0.05); ±1.00 D (%): all *P*>0.05. [d]The repeat measurement variance analysis, [e]The Friedman test, [f]The Cochran *Q* test. aph-ACD: Aphakic anterior chamber depth, the depth from corneal epithelium to the inferior margin of undilated pupil; D: Diopter; MAE: Mean absolute error; ME: Mean prediction error; MedAE: Median absolute error; SD: Standard deviation.

larger ME and MedAE than non-ACD formulas (Hoffer Q, Holladay 1, and SRK/T; adjusted *P*<0.05). In all formulas, the percentage of eyes within a PE of ±0.50, ±0.75, and ±1.00 D differed significantly (*P*=0.003, *P*=0.001, *P*<0.001), ranging from 15.33% to 24.00% for ±0.50 D and 34.67% to 43.33% for ±1.00 D. Hoffer Q and SRK/T had 24.00% within ±0.50 D PE, and SRK/T had 43.33% within ±1.00 D PE.

In capsular group, prediction results were presented in Figures 1B and 2B. Significant differences in PE and absolute PE were found among formulas (*P*<0.001). ACD-requiring formulas had larger ME than non-ACD formulas (adjusted *P*<0.05). SRK/T showed the lowest ME (adjusted *P*<0.05) and Haigis showed highest MedAE among formulas (adjusted *P*<0.05). The percentage of eyes within a PE of ±0.50, ±0.75, and ±1.00 D differed significantly among formulas (*P*=0.037, *P*=0.004, *P*=0.001), ranging from 25.86% to 43.10% for ±0.50 D and 44.83% to 70.69% for ±1.00 D. SRK/T had 43.10% within ±0.50 D PE, and 70.69% within ±1.00 D PE.

In sulcus group, prediction outcomes were shown in Figures 3B and 4B. Significant differences in PE and absolute PE were observed among formulas (*P*<0.001). ACD-requiring formulas had larger ME and MedAE than non-ACD formulas (all adjusted *P*<0.05). In all formulas, the percentage of eyes within a PE of ±0.50, ±0.75, and ±1.00 D differed significantly (*P*<0.001, *P*=0.001, *P*=0.032), ranging from 7.61% to 19.57% for ±0.50 D and 22.83% to 32.61% for ±1.00 D. The formulas with 19.57% eyes within a PE of ±0.50 D and 32.61% eyes within a PE of ±1.00 D were both Hoffer Q formula.

Prediction Outcomes of All Selected Formulas In total, the EVO 2.0 without aph-ACD showed lowest ME among formulas (adjusted *P*<0.05). For MedAE, the EVO 2.0 without aph-ACD was lower than Hoffer Q, Haigis, Kane and PEARL-DGS formula (adjusted *P*<0.05). The BUII without aph-ACD was lower than Haigis and Kane formula (adjusted *P*<0.05). The Ladas AI without aph-ACD showed lower MedAE than Haigis, Kane and PEARL-DGS formula (adjusted *P*<0.05). The Hoffer Q was lower than BUII and Ladas AI with aph-ACD formula (adjusted *P*<0.05). The Holladay 1 and SRK/T formula was lower than EVO 2.0 with aph-ACD, BUII with aph-ACD and Ladas AI with aph-ACD formula (adjusted *P*<0.05). Significant differences in the percentage of eyes within ±0.50, ±0.75, and ±1.00 D PE were found among formulas (*P*=0.002, *P*<0.001, *P*<0.001), ranging from 15.33% to 24.00% for ±0.50 D and 34.67% to 48.00% for ±1.00 D. EVO 2.0 without aph-ACD, Hoffer Q, and SRK/T had 24.00% within ±0.50 D PE, and EVO 2.0 without aph-ACD had 48.00% within ±1.00 D PE. The BUII without aph-ACD, EVO 2.0 without aph-ACD, Hoffer Q, Holladay 1, Ladas AI without aph-ACD, SRK/T formula demonstrated higher percentage of eyes within a PE of ±0.75 D than Haigis formula (adjusted *P*<0.05). The Ladas AI without aph-ACD formula had more eyes within ±1.00 D of PE than Haigis (adjusted *P*<0.05).

In capsular group, the BUII with/without aph-ACD, EVO 2.0 without aph-ACD, Ladas AI without aph-ACD, SRK/T formula showed lower ME than other formulas (adjusted *P*<0.05). BUII without aph-ACD showed lower ME than SRK/T formula (adjusted *P*<0.05). The BUII, EVO 2.0 and Ladas AI without/with aph-ACD demonstrated lower MedAE than Haigis formula (adjusted *P*<0.05). Significant differences in the percentage of eyes within ±0.75 and ±1.00 D PE were found among formulas (*P*=0.002 and *P*<0.001), ranging from 44.83% to 74.14% for ±1.00 D. BUII with and without aph-ACD had 74.14% within ±1.00 D PE. BUII with and without aph-ACD, EVO 2.0 without aph-ACD, and Ladas AI without aph-ACD had more eyes within ±1.00 D PE than Haigis (adjusted *P*<0.05).

In sulcus group, the statistically significant results are as follows (adjusted *P*<0.05). For ME, the EVO 2.0 without

aph-ACD was lower than Hoffer Q, SRK/T, Haigis, Kane and PEARL-DGS formula. The Ladas AI without aph-ACD was lower than Haigis, Kane and PEARL-DGS formula. The Hoffer Q and Holladay 1 were lower than BUII without/with aph-ACD and EVO 2.0 with aph-ACD formula. The SRK/T showed lower ME than BUII with aph-ACD and EVO 2.0 with aph-ACD formula. The Holladay 1 and SRK/T were lower than Ladas AI with aph-ACD formula and EVO 2.0 with aph-ACD showed lower ME than Kane and PEARL-DGS formula. The Ladas AI without aph-ACD was lower than Haigis, Kane, and PEARL-DGS formula. The Hagis showed lower MedAE than BUII with aph-ACD formula. The Hoffer Q and Holladay1 showed lower MedAE than BUII without/with aph-ACD, EVO 2.0 with aph-ACD and Ladas AI with aph-ACD formula. In all formulas, the percentage of eyes within a PE of ±0.50, ±0.75, and ±1.00 D differed significantly among formulas (P<0.001). The percentage of eyes within a PE of ±0.50 and ±1.0 D was ranged from 7.61% to 19.57% and 19.57% to 32.61%, respectively. Hoffer Q formula had 19.57% within ±0.50 D PE, and EVO 2.0 without aph-ACD and Hoffer Q formula had 32.61% within ±1.00 D PE. The Hoffer Q displayed higher percentage of eyes within a PE of ±0.50 D than BUII with/without aph-ACD, EVO 2.0 with aph-ACD, Ladas AI with aph-ACD formula and the EVO 2.0 without aph-ACD outperformed Kane and PEARL-DGS in the same outcome. The Holladay 1 showed higher percentage of eyes within a PE of ±1.00 D than BUII with aph-ACD formula. Both EVO 2.0 without aph-ACD and Hoffer Q had more eyes within ±1.00 D of PE than BUII with aph-ACD, EVO 2.0 with aph-ACD, Kane, and Ladas AI with aph-ACD formula.

DISCUSSION

Our study assessed accuracy of 9 IOL formulas in a large pediatric aphakia cohort and found that regardless of aph-ACD introduction, the percentage of eyes within a PE of ±0.50 and ±1.0 D overall was less than 25% and 50% respectively, highlighting the need for a new IOL formula tailored for pediatric secondary IOL implantation. The capsular group showed higher accuracy than sulcus group, indicating that ELP varies by implant position and requires different IOL power calculations.

In the pediatric aphakic population, aph-ACD is accessible instead of phakic ACD as originally defined in the formulas, but its inclusion did not enhance the accuracy of new generation formulas in this study. The BUII, EVO 2.0 and Ladas AI without aph-ACD outperformed their corresponding ones with aph-ACD, aligning with prior studies. Formulas based on aphakic refraction showed higher MedAE (1.54 D for in-th-bag group and 2.90 D for sulcus-implanted group) than formulas without aph-ACD (the maximum MedAE was 1.40 and 0.98 D, respectively)[4,23]. The poor performance of the newer formulas with aph-ACD might indicate unreliable ACD measurements. The preoperative ACD definition varied[24-27], with this study using the measurement from the corneal epithelium to the inferior margin of undilated pupil. However, the relationship between aph-ACD and ELP needs further investigation for new aphakic IOL formulas. Future studies should focus on standardizing its definition and improving the reliability of its measurement in pediatric aphakia. Additionally, incorporating aph-ACD into the development of pediatric aphakia-specific IOL formulas through data-driven modeling approaches, such as machine learning or regression-based ELP estimation algorithms, may improve the accuracy of refractive outcomes.

In general, when preoperative aph-ACD is unavailable or IOL position is uncertain, the new-generation formulas (BUII, EVO and LSF) and the third-generation formulas like (SRK/T) can be considered. For secondary capsular implantation with available aph-ACD, BUII is a viable option. The change of ELP will affect the PE, with sulcus implantation is more prone to prediction errors than capsular implantation[1,28]. Liu *et al*[20] proposed a protocol for adjusting sulcus-IOL power using SRK/T formula based on original capsular predictions. Some researchers proposed aphakic refraction formulas and concluded that aphakic refraction formulas may be aiding in confirming IOL power prediction, especially when biometry is challenging[4,29-31].

Our study found that the target refraction range for some formulas limited their applications in young children, who may require initial high hypermetropia to offset future myopic shifts. A targeted postoperative refraction of +4.00 to +6.00 D is recommended for children aged 1-5y[32-34]. However, some formulas, like RBF 3.0, Kane, pearl DGS, and EVO, have maximum predictable hyperopia of only +1.00, +2.00, +3.00, and +5.00 D, respectively. This limitation resulted in only 102 participants meeting the criteria for analysis.

In our study, we used a hydrophilic acrylic single-piece IOL with anti-vaulting haptics and a spherical hydrophobic acrylic three-piece IOL with PMMA C-loop haptics. In our previous study, the single-piece IOLs showed significantly less dislocation (4.17% *vs* 15.22%, P=0.046) and were preferred for secondary IOL sulcus implantation in pediatric aphakia due to better long-term stability. There were no significant differences in glaucoma-related adverse events (P=0.845), iris synechiae, discoria and/or chronic iridocyclitis (P=0.700), or visual axis opacification (P=0.774)[35]. Thus, the surgeons in our study chose single-piece hydrophilic acrylic IOL with anti-vaulting haptics for sulcus implantation in some eyes.

The main highlight of this study is comparing the accuracy of 9 IOL power formulas in pediatric aphakia, including the traditional and new-generation formulas. And this

study pioneered the analysis of aph-ACD's impact on new-generation formulas accuracy in this population. A limitation was the absence of IOL power adjustment for secondary sulcus placement due to a lack of consensus.

In conclusion, new-generation formulas (BUII, EVO and LSF) and the third-generation formulas (SRK/T) were recommended for IOL power calculation in secondary pediatric capsular implantations. The accuracy of sulcus-IOL calculation in pediatric aphakic eyes demands further refinement. Current IOL formulas, while accurate in adults including specific patients with highly myopic eyes or keratoconus eyes, are less so in children because they are derived from stable adult eyes, not growing juvenile ones[36-39]. Future studies should aim to improve prediction accuracy by developing formulas tailored to pediatric aphakia, considering their anterior chamber features, IOL positions, and the high hyperopic target refraction required for developing eyes.

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