How to Determine Premyopia and Myopia: Comparison among Non-Cycloplegic Predictors in Chinese Children

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Abstract: This study evaluated the predictive efficiency of non-cycloplegic ocular parameters for premyopia and myopia in children. Data from 493 patients aged 3-17 were retrospectively analyzed. AL/ACRC demonstrated the strongest predictive performance for premyopia and myopia, with an area under the receiver operating characteristic curve (ROC) of 0.956 (95% CI: 0.934-0.973). A combined predictor using NCSER≤0 and AL/ACRC > 2.95 achieved a higher Youden index than AL/ACRC alone (0.85 vs. 0.813). In the absence of cycloplegic refraction, AL/ACRC alone or in combination with NCSER may serve as effective alternative predictors for premyopia and myopia.

Keywords: Premyopia; Myopia; Axial Length; Spherical Equivalent Refraction; Predictors

1. Introduction

Myopia, defined as a refractive error of ≤-0.50 D [1], has been a prevalent eye disease and public health concern in East Asia, especially China, for years [2]. Early-onset myopia often progresses to high myopia, increasing the risk of irreversible blinding eye conditions. Delaying myopia onset is clinically important, necessitating early implementation of myopia prevention strategies for children.

The International Myopia Institute defines premyopia as a refractive state between >-0.50D and ≤+0.75D, accompanied by additional myopia risk factors [1]. For Chinese children, education is an unavoidable risk factor for myopia [3]. A study has shown that premyopia is the dominant refractive status among Chinese preschool children, with a prevalence of 52% [4], and that premyopia is significantly associated with an elevated risk of subsequent myopia development in children[5, 6]. Several studies have focused on Chinese children with cycloplegic spherical equivalent refraction (CSER) ≤+0.75D for myopia intervention, utilizing methods like low-dose atropine [5] or repeated low-level red light [7]. Therefore, myopia prevention strategies should target the myopic children (CSER≤-0.50D) as well as those with premyopia (CSER > -0.50D and ≤+0.75D).

In clinics, premyopia and myopia (CSER≤+0.75D) were based on cycloplegic refraction. Many children are not suitable for cycloplegia due to various factors inclding ocular side effects and exsting systemic diseases. Cycloplegic refraction is not available for everyone in practice, and doctors may only operate that when necessary.

Alternatively, a few studies have estimated the non cycloplegic predictor for premyopia and myopia. Research from Peking [8] in northern China and Nanjing [9] in southern China indicated that the axial length to average corneal radius of curvature (AL/ACRC) ratio can serve as a predictor for premyopia and myopia. Findings from the Shanghai cohort indicated that the combination of nocycloplegic spherical equivalent refraction (NCSER) and AL/ACRC provides the optimal predictive indicator for premyopia [10]. The conclusions of these studies were inconsistent. This study aimed to identify optimal noncycloplegic predictors for premyopia and myopia when cycloplegic refraction is unavailable, facilitating early intervention decisions.

2. Material and Methods

2.1 Research Methodology and Participant Selection

This research employed an observational cross-sectional design. Participants visiting the

eye clinic at the Chongqing Shapingba District People's Hospital from April to October 2024 were collected for analysis.

2.2 Ophthalmic Examination and data Collection

All examinations were conducted following the optometric routine procedure. Uncorrected visual acuity (UCVA) was assessed using a Standard Logarithmic visual acuity chart (ACP-8, Topcon, Japan). Spherical equivalent refraction and corneal curvature were determined via autorefraction (KR.8900, Topcon, Japan), while axial length (AL) was measured with IOL master-700 (Carl Zeiss, Germany). Age, sex, height, and weight in the medical recordings were also collected in this study. Topical anesthesia was routinely administered using 1% Cyclopentolate ophthalmic solution (Alcon, USA).

Children included in this study met the criterion of having a monocular best corrected visual acuity of 1.0 decimal (6/6); the monocular intraocular pressure was below 21mmHg; Ocular conditions that were not deemed to affect refractive status. Most Chinese children undergo their initial myopia screening at age 3, as required by the Chinese government. After 18 years, the children would be considered adults with minimal need for myopia control. Then, we chose 3-17 year range for practical use. Children with a history of systemic diseases, including hypertension, autoimmune disorders, convulsions, cardiovascular and central nervous system disorders, as well as those lacking cycloplegic refraction recordings, were excluded from the study. Finally, 493 pediatric patients were enrolled in the analysis.

2.3 Statistical Analysis

The average corneal curvature (ACC) was calculated using the horizontal and vertical cornea curvature. The spherical equivalent refraction was calculated as sphere power plus 0.5*cylinder power. The AL/ACRC ratio was determined by dividing AL by ACRC, which stands for the average corneal radius of curvature. Body mass index (BMI) was computed as weight (kg) divided by the squared value of height (m). Assuming the retrospective observation data were missing randomly, the Predictive Mean Matching method for multiple imputation was applied in the final analysis. SPSS 30.0 (IBM, Armonk, NY, USA) and MedCalc 23.0 (MedCalc Software Ltd., Belgium) were applied to the right eye of each participant because of the high correlation between eyes. The Shapiro-Wilk test assessed normality. Cycloplegic refraction was used to define premyopia and myopia, categorizing the cohort into CSER >+0.75D and CSER≤+0.75 D groups. Predictors within CSER subgroups or by gender were assessed. Using CSER≤+0.75 D as the criterion for premyopia and myopia, univariate logistic regression identified potential predictors, while multiple logistic regression confirmed the predictors for these conditions. The predicted probability values were calculated by logistic regression with the combined test, which was used as a predictor for premyopia and myopia. The performance of ocular biometric parameters in detecting premyopia and myopia was assessed by calculating sensitivity, specificity, the area under the curve (AUC). We subsequently assessed the optimal cutoff value, sensitivity, specificity, and Youden Index by sequentially combining NCSER with AL/ACRC, referring children only if they failed both predictors. A two-tailed *P*-value less than 0.05 was statistically significant.

3. Results

3.1 Characteristics of the Participants

Of the 493 participants aged 3-17, 13.99% (69 of 493) of case items were missing from the recordings. The analysis included 493 participants with a median age of 9 years, following multiple imputations. There were 256(51.93%) girls and 237(48.07%) boys. Among all participants, 398 (80.73%) had CSER≤+0.75D demanding myopia intervention. In the CSER >+0.75 D group, the median values for age, AL, AL/ACRC, height, weight, and BMI were significantly lower, whereas the median values for UCVA, NCSER, and CSER were higher compared to the CSER≤+0.75 D group. There was no statistical difference between CSER ≤+0.75 D and CSER >+0.75 D groups in No.Girls and ACC. Table 1 shows the detailed characteristics of detected parameters by gender, revealing that boys have a significantly higher mean axial length (AL) compared to girls. However, the degree of myopia, measured by median CSER, shows no significant statistical difference between genders, though it is slightly higher in girls (-1.25D) than in boys (-1.00D).

Table 1. General Characteristics of Participants of Imputation Data

Parameters	Total, N=493		CSER>+0.75D N=95	CSER≤+0.75D N=398	P value	Girls,N=256	Boys, N=237	P value
	Mean(SD) or Median (P25, P75)	Range	Mean(SD) or Median (P25, P75)	Mean(SD) or Median (P25, P75)		Mean(SD) or Median (P25, P75)	Mean(SD) or Median (P25, P75)	
Age (years)	9.00 (6.50,11.00)	3 to 17	5.00(4.00,7.00)	10.00(8.00,11.00)	P<0.001	9.00(7.00,1.00)	9.00(6.00,11.00)	P=0.222
UCVA	0.40 (0.20,0.60)	0.02 to 1.50	0.70(0.50,0.90)	0.40(0.20,0.50)	P<0.001	0.20(0.40,0.60)	0.20(0.40,0.60)	P=0.140
ACC	43.25 (42.25,44.50)	38.50 to 47.50	43.32±0.16	43.34±0.07	P=0.878	43.50(42.50,44.75)	43.00 (42.13,43.88)	***P<0.001***
NCSER (D)	-1.25 (-2.50,0.00)	-11.63 to 5.00	0.50(0.13,1.25)	-1.69(-3.00, -0.88)	P<0.001	-1.38(-1.38, -0.03)	-1.23(-2.32,0.00)	P=0.167
CSER (D)	-1.13 (-2.31,0.38)	-11.5 to 8.130	1.75(1.25,2.50)	-1.50(-2.75, -0.75)	P<0.001	-1.25(-2.38,0.13)	-1.00(-2.25,0.57)	P=0.302
AL (mm)	23.84 ±0.06	19.35 to 28.81	22.19±0.10	24.19 (23.53,24.89)	P<0.001	23.64±0.08	24.05±0.08	***P<0.001***
AL/ACRC	3.06± 0.01	2.55 to 3.52	3.07(2.94,3.16)	3.11(3.03,3.18)	P<0.001	3.05±0.01	3.06±0.01	P=0.553
height (cm)	139.00 (125.00,151.00)	95 to 182	115.00(109.00,128.00)	143.00 (131.00,154.00)	P<0.001	140.00 (126.00,151.00)	138.00 (124.00,151.75)	P=0.722
weight (kg)	31.00 (24.00,43.00)	12 to 85	21.50(18.00,27.00)	34.00 (26.00,45.63)	P<0.001	31.00(24.00,41.75)	31.00 (24.00,45.25)	P=0.284
BMI	16.52 (15.03,18.89)	11.11 to 38.14	15.58(14.61,17.09)	16.92 (15.33,19.31)	P<0.001	16.39(14.88,18.22)	17.09 (15.31,19.71)	***P=0.003***
NO. girls	256(51.9%)		47(49.5%)	209(52.5%)	P=0.594	209(81.64%)	189.00(79.75%)	P=0.594

UCVA: uncorrected visual acuity; ACC: average corneal curvature; NCSER: non-cycloplegic spherical equivalent refraction; CSER: cycloplegic spherical equivalent refraction; AL: axial length; AL/ACRC: axial length to average corneal radius of curvature; BMI: body mass index; D: diopter.

P values were tested between boys and girls with chi-square test for No. Myopia, and Student t test, or Mann-Whitney U test for other variables.

3.2 Regression Analysis of Parameters for Premyopia and Myopia

As table 2 showed, we did the collinear diagnosis of the variables for permyopia and myopia. Height, weight, BMI, and age were excluded from further analysis due to multicollinearity, as indicated by a variance inflation factor (VIF) greater than 5 or a tolerance less than 0.1.

Table 2. Collinear Diagnosis of the Variables that P<0.05 in Univariate Analysis

Variables	variance inflation factor	Tolerance
Age	7.878	0.127
UCVA	**1.727**	**0.579**
NCSER(D)	**2.916**	**0.343**
height (cm)	25.411	0.039
weight (kg)	40.147	0.025
AL (mm)	**3.523**	**0.284**
AL/ACRC	**4.356**	**0.230**
BMI	12.537	0.080

UCVA: uncorrected visual acuity; NCSER: non-cycloplegic spherical equivalent refraction; D: diopter; AL: axial length; AL/ACRC: axial length to average corneal radius of curvature; BMI: body mass index

Table 3 showed that age, UCVA, NCSER, height, weight, AL, AL/ACRC, and BMI were the risk factors highly associated with CSER ≤+0.75 D other than ACC and gender in the univariate logistic analysis. After excluding collinear variables, the subsequent multiple logistic regression analysis incorporated UCVA, NCSER (D), AL, and AL/ACRC. Finally, the association among the UCVA, NSCER, AL, AL/ACRC, and CSER≤+0.75D was unchanged after multivariate adjustment. NCSER (OR=0.413, P=0.003), UCVA (OR=0.168, P=0.054), AL (OR=2.181, P=0.005), and AL/ACRC (OR=255426.629, P<0.001) were identified as risk factors for CSER≤+0.75 D. According to the multiple logistic regression analysis in Table 3, the formula to predict the probability of premyopia and myopia is: logit(p) =−52.64−1.786×UCVA −0.885×NCSER(D)+0.78×AL(mm)+12.451×AL /ACRC.

Table 3. Logistic Regression Analysis of Noncycloplegic Predictors for Pemyopia and Myopia (Imputation Data)

Parameters		Univariate logistic analysis							Multiple logistic analysis (Backward LR logistic regression)						
		B	S. E	Wald	ORs	95%CI for OR s lower	95%CI for ORs upper	*P*-Valu e	B	S. E	Wald	ORs	95%CI for ORs lower	95%CI for ORs upper	*P*-Value
Premyopia	Intercept								-52.64	8.842	35.441				<.001

and myopia (CSER≤+0.75 D)	Age	0.568	0.06	88.549	1.765	1.568	1.987	<0.001							
	UCVA	-4.449	0.519	73.454	0.012	0.004	0.032	<0.001	-1.786	0.925	3.724	0.168	0.027	1.028	**0.054**
	NCSER(D)	-2.031	0.235	74.98	0.131	0.083	0.208	<0.001	-0.885	0.296	8.963	0.413	0.231	0.737	**0.003**
	height (cm)	0.081	0.009	82.331	1.085	1.066	1.104	<0.001							
	weight（kg）	0.113	0.016	52.131	1.119	1.086	1.154	<0.001							
	AL (mm)	2.112	0.217	94.895	8.269	5.406	12.648	<0.001	0.78	0.276	7.958	2.181	1.269	3.749	**0.005**
	AL/ACRC	22.579	2.42	87.06	63966 73031	55736226.7 32	73412622 7453.123	<0.001	12.451	3.147	15.657	255426 .629	535.647	121801894.4	**<.001**
	BMI	0.116	0.04	8.203	1.123	1.037	1.216	0.004							

CSER: cycloplegic spherical equivalent refraction; UCVA: uncorrected visual acuity; NCSER: non-cycloplegic spherical equivalent refraction; D: diopter; AL: axial length; AL/ACRC: axial length to average corneal radius of curvature; BMI: body mass index. B: Beta coefficient; OR: odds ratio; CI: Confidence Interval; S.E: Standard Error

3.3 ROC Curve Analysis for Premyopia and Myopia

The effectiveness of the single predictor and combined predictor were analyzed for premyopia and myopia (Figure 1).

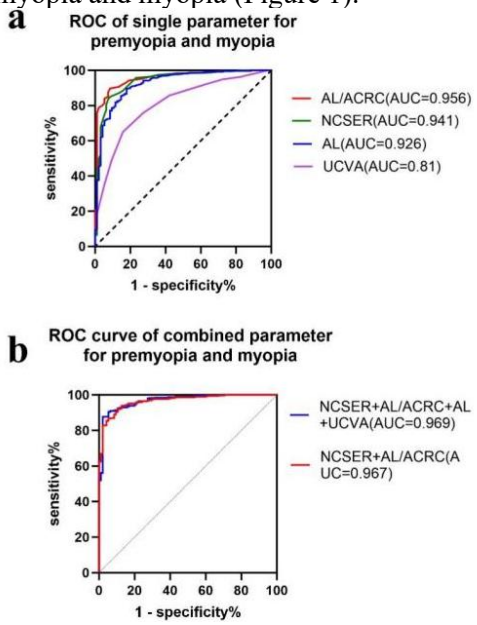

Figure 1. ROC Curve for Premyopia and Myopia (Imputation Data)

UCVA: uncorrected visual acuity; NCSER: non-cycloplegic spherical equivalent refraction; AL: axial length; AL/ACRC: axial length to average corneal radius of curvature; AUC: the area under the curve; ROC: receiver operating characteristic

Using AL/ACRC as a single predictor for premyopia and myopia yielded the highest AUC of 0.956 (95% CI: 0.934 to 0.973) with a cutoff value of AL/ACRC > 2.95 (Table 4).

Using a two-combined predictor for premyopia and myopia, the combination of NCSER and AL/ACRC achieved an AUC of 0.967 (95% CI: 0.947 to 0.981). The combination of NCSER and AL/ACRC showed a significantly larger AUC compared to AL/ACRC alone (P=0.01). The combination of UCVA, NSCER, AL, and AL/ACRC achieved the highest prediction efficiency with an AUC of 0.969; however, it was not statistically significant compared to NCSER and AL/ACRC (P=0.512). Thus, the NCSER and AL/ACRC combination was the optimal predictor for CSER≤+0.75D. Various combinations of NCSER and AL/ACRC were tested sequentially, with referrals made for children who did not meet both criteria. As listed in Table 5, the best combination was NCSER≤0 and AL/ACRC ＞ 2.95. Compared with AL/ACRC>2.95 as referral criteria, the NCSER and AL/ACRC combination had a higher Youden Index than AL/ACRC alone (0.85 vs. 0.813).

Table 4. The ROC Analysis for CSER ≤+0.75D (Imputation Data)

CSER	Variables	AUCs	Cut-off value	Sensitivity	Specificity	Youden index	95% Confidence interval
	UCVA	0.81	≤0.4	64.08%	84.21%	0.493	0.764 to 0.856
premyopia and myopia (CSER≤ +0.75 D)	NCSER(D)	0.941	≤-0.38	84.92%	91.58%	0.765	0.916 to 0.960
	AL/ACRC	**0.956**	**>2.95**	**89.70%**	**91.58%**	**0.813**	**0.934 to 0.973**
	AL (mm)	0.926	>22.9	89.45%	82.11%	0.716	0.899 to 0.948
	AL/ACRC+AL	0.962	>0.919	82.41%	98.95%	0.814	0.941 to 0.977
	NCSER+AL	0.960	>0.823	87.44%	94.74%	0.822	0.939 to 0.975
	NCSER+AL/ACRC	**0.967**	**>0.708**	**91.96%**	**89.47%**	**0.814**	**0.947 to 0.981**
	UCVA+NCSER	0.946	>0.739	89.45%	90.53%	0.799	0.922 to 0.964
	UCVA+AL/ACRC	0.959	>0.884	83.67%	96.84%	0.805	0.938 to 0.975
	UCVA+AL	0.947	>0.791	86.93%	93.68%	0.806	0.924 to 0.965
	NCSER+AL+UCVA	0.963	>0.749	90.70%	93.68%	0.844	0.942 to 0.978
	UCVA+AL/ACRC+NCSER	0.968	>0.858	86.43%	95.79%	0.822	0.948 to 0.982
	NCSER+AL/ACRC+AL	0.968	>0.824	89.20%	95.79%	0.850	0.949 to 0.982

	AL/ACRC+AL+UCVA	0.965	>0.887	85.43%	98.95%	0.8437	0.945 to 0.980
	NCSER+AL/ACRC+AL+UCVA	**0.969**	**>0.839**	**87.69%**	**97.89%**	**0.856**	**0.949 to 0.982**

CSER: cycloplegic spherical equivalent refraction; UCVA: uncorrected visual acuity; NCSER: non-cycloplegic spherical equivalent refraction; D: diopter; AL: axial length; AL/ACRC: axial length to average corneal radius of curvature.

Table 5. Combination of NCSER and AL/ACRC for CSER ≤+0.75D. (Imputation Data)

CSER	Criteria	Sensitivity	Specificity	Youden index
premyopia and myopia (CSER≤+0.75 D)	AL/ACRC>2.95	0.897	0.916	0.813
	NCSER≤0 and AL/ACRC >2.95	0.882	0.968	0.85

Combination means combined use of NCSER and AL/ACRC in serial order. CSER: cycloplegic spherical equivalent refraction; NCSER: non-cycloplegic spherical equivalent refraction; D: diopter; AL/ACRC: axial length to average corneal radius of curvature

4. Discussion

The study identified AL/ACRC as the most effective single predictor for premyopia and myopia. However, the cutoff value of AL/ACRC>2.95 had a slightly lower Youden Index than that of the NCSER≤0 and AL/ACRC >2.95 combination (0.813 vs. 0.85).These findings indicated that AL/ACRC or combined AL/ACRC and NSCER and their cutoff values could be used as alternative predictors for premyopia and myopia so that eyecare providers may consider myopia intervention ahead.

There were a few studies aimed at exploring the predictors of premyopia and myopia. A longitudinal study cohort from NanJing suggested that AL/ACRC, other than AL, had an enormous effect on survival in myopia [9], similar to the cross-sectional study from a Peking hospital [8]. Our study's conclusion aligns with the Shanghai cohort, showing that combining NCSER and AL/ACRC yields positive outcomes for premyopia and myopia [10]. The discrepancy among these studies may be attributed to the specific predictor was being considered in research. To our knowledge, only one of the previous studies[8] explored the cutoff value of premyopia and myopia for direct clinical use, and it explored CSER ≤+0.50 D instead of the standard of CSER≤+0.75 D from the International Myopia Institute. The cutoff value of CSER ≤+0.50 was 2.955 in the Peking cohort [8], close to that of CSER in premyopia≤+0.75D as 2.95 in our study. According to the association analysis in previous studies [8, 11, 12], AL/ACRC was negatively correlated with the CSER, CSER≤+0.50 with AL/ACRC cutoff value of 2.955 in other study was higher than CSER ≤+0.75 with AL/ACRC cutoff value of 2.95 in our study was reasonable.

Several limitations were applied to our study. Firstly, the study was retrospective and hospital-based, bearing the risk of potential bias. However, we attempted to attenuate the risk through multiple regression and sensitive analyses. Secondly, age was correlated to AL/ACRC and NCSER, although age was not the independent risk factor for premyopia and myopia. Children of different ages may have different cutoff values in relevant predictors; however, CSER ≤+0.75 with AL/ACRC cutoff value of 2.95 in our study was comparable to the CSER ≤+0.50 with AL/ACRC cutoff value of 2.955 in the cohort aged 4-6 years old[8]. Thirdly, since sensitivity and specificity vary with disease prevalence, the predictor outcomes in our study may not be applicable to populations with differing prevalence rates of premyopia and myopia. The study's findings could be applicable in clinical settings. Therefore, longitudinal studies with large sample sizes will be conducted to establish the different criteria according to different age groups in the future.

5. Conclusion

We observed the ocular parameter for detecting premyopia and myopia in a hospital-based cohort aged 3-17. Although AL/ACRC was the optimal single parameter for premyopia and myopia, the combination of AL/ACRC and NCSER was recommended to achieve satisfactory accuracy. These predictors' cutoff values can be used to determine preventive intervention for myopia.

Ethical statement

This research adhered to the principles of the Declaration of Helsinki. The Chongqing Shapingba District People's Hospital's medical ethics committee granted approval (KY202241).Due to its retrospective nature and few risks, the requirements for informed consent were waived.

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