• Clinical Research •

Cycloplegia is required for accurate refraction of young adults in epidemiologic studies

Xiao-Jie Feng[1], *Yuan-Zhen Liu*[1], *Wen-Jia Cai*[1], *Xiao-Qian Deng*[1], *Ian G Morgan*[1,2], *Ming-Guang He*[1,3,4,5], *Xiao-Hu Ding*[1]

[1]State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangdong Provincial Key Laboratory of Ophthalmology and Visual Science, Guangdong Provincial Clinical Research Center for Ocular Diseases, Guangzhou 510060, Guangdong Province, China

[2]Research School of Biology, College of Medicine, Biology and Environment, Australia National University, Canberra 2601, Australia

[3]School of Optometry, The Hong Kong Polytechnic University, Kowloon, Hong Kong 999077, China

[4]Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Kowloon, Hong Kong 999077, China

[5]Centre for Eye and Vision Research (CEVR), 17W Hong Kong Science Park, Kowloon, Hong Kong 999077, China

Correspondence to: Xiao-Hu Ding. Zhongshan Ophthalmic Center, Sun Yat-sen University, #54 S. Xianlie Rd, Guangzhou 510060, Guangdong Province, China. dingxiaohu@gzzoc.com

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Abstract

● **AIM:** To quantify the impact of the measurement of non-cycloplegic refraction on estimates of refraction and classification of refractive status in young adults.

● **METHODS:** This cross-sectional analysis included 825 young adults (mean age 26.6±3.3y; 56.7% female) from the Guangzhou Twin Eye Study. All participants underwent both non-cycloplegic and cycloplegic autorefraction. Error in refraction was defined as the difference between cycloplegic and non-cycloplegic spherical equivalent refraction (SER).

● **RESULTS:** Using a cut-off of -0.50 D for non-cycloplegic refraction to diagnose myopia, the prevalence of myopia was overestimated (90.2% *vs* 87.0%), resulting in the identification of 3.2% (26/825) pseudo-myopes. After increasing the threshold to -0.75 D, the overall prevalence (87.5%) was approximately equivalent to that with cycloplegic refraction, 9 of the 26 pseudo-myopes would have been re-classified correctly as emmetropes, but 13 genuine myopes would have been re-classified incorrectly as emmetropes. Lack of cycloplegia resulted in a significant myopic shift compared to cycloplegic refraction. Notably, 25.6% of participants exhibited a clinically significant myopia refractive shift of ≥0.50 D, and 5.7% demonstrated a large shift of ≥1.00 D.

● **CONCLUSION:** At a threshold of -0.75 D, the calculated prevalence of myopia is close to that obtained with cycloplegic refraction. However, threshold adjustment does not solve the mis-classification problem, because while it will eliminate some pseudo-myopes, it will also eliminate some genuine myopes. Our study confirms that non-cycloplegic refraction leads to significant measurement errors in young adults, highlighting the necessity of cycloplegia for accurate epidemiologic assessment of myopia prevalence.

● **KEYWORDS:** cycloplegic refraction; myopia; emmetropia; hyperopia; refractive error

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INTRODUCTION

Over the past sixty years, the global prevalence of myopia has increased dramatically in younger, better-educated generations, resulting in a rising burden of adult myopia worldwide[1-2]. With myopia becoming more prevalent, there has been a disproportionately rapid increase in the prevalence of high myopia—a condition that continues to progress until young adulthood. This trend has substantially broadened the scope of clinical practice to encompass both myopia prevention and control, thereby rendering the accurate measurement of spherical equivalent refraction (SER) an increasingly critical clinical challenge.

Cycloplegic refraction is widely regarded as the gold standard for obtaining objective SER measurements, particularly in children[3-4]. Whether cycloplegia is required for adults is more controversial. Some studies have suggested that cycloplegia may be required up to the age of 50[5-6], but this position has been contested. Krantz *et al*[7] have argued that cycloplegia in adults is not essential, if the study is only interested in myopia, or if the prevalence of hyperopia in the sample is low. However, the results presented showed that under the age of 50, many emmetropes and hyperopes are mis-classified, as was also found by Fotouhi *et al*[5], suggesting that cycloplegia is necessary for a comprehensive epidemiological survey in adults. The importance of cycloplegic refraction in young adults has been particularly contentious[8-9]. Sanfilippo *et al*[10] have argued that cycloplegia is not necessary in young adults, although other evidence suggests that it is required[11-13].

While Duane's[14] classical curves and Hofstetter's[15] linear approximations have long set the research agenda in accommodative decline, recent work with objective measurements suggests that early subjective measurements of accommodation over-estimate accommodative capacity in younger children, leading to a picture of large declines in accommodative capacity during childhood. However, more objective measurement techniques show a more stable level of accommodative capacity that persists throughout childhood and well into young adulthood, followed by a decline in the 30–50 age bracket. As a result, over this age range, accommodation leads to masking of emmetropia and hyperopia without cycloplegia[16-17].

This study aims to conduct a systematic comparison of cycloplegic and non-cycloplegic refractive measurements in a sample of young adults. Our investigation leverages a substantial cohort to better characterize accommodative influence in young adulthood. We hypothesize that in a substantial proportion of emmetropic/hyperopic young adult eyes, non-cycloplegic refraction will result in a significant mis-classification of refractive status.

PARTICIPANTS AND METHODS

Ethical Approval Ethics approval for this study was obtained from the Zhongshan Ophthalmic Center Ethics Review Board (Approval No.2023KYPJ212). The study was conducted in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from their parents or legal guardians.

Participants Data for this analysis were derived from the Guangzhou Twin Eye Study, a population-based longitudinal cohort study initiated in 2006. Detailed descriptions of the study design and baseline characteristics have been published previously[18-20]. Briefly, twins aged 7–15y at enrollment were followed annually. This study included data from the 2023 follow-up of individuals aged ≥18y, with specific exclusion of those with manifest strabismus, amblyopia, or nystagmus to avoid confounding effects on refractive measurements.

Data Collection Both cycloplegic and non-cycloplegic refraction assessments were performed. Non-cycloplegic refraction was performed prior to cycloplegia by an experienced optometrist using an autorefractor (Topcon KR8800; Japan). Subsequently, cycloplegia was induced using 2 drops of 1% tropicamide (Shengyang Xingqi, Corp. China) administered 5min apart, followed by a third drop after 20min. After an additional 15min, pupil diameter (>6 mm) and light response were confirmed by a trained ophthalmologist using a pupil gauge and handheld light source. Cycloplegic autorefraction was then performed using the same device and operator. Three consecutive measurements were taken for each procedure. If the difference between any two readings exceeded 0.5 diopters (D), the outlier was discarded and an additional measurement was taken.

Statistical Analysis Only data from the right eye were analyzed due to high interocular correlation. Refraction was evaluated by cycloplegic SER defined as spherical power +0.5 cylindrical power. Refractive change was defined as the difference between cycloplegic and non-cycloplegic refractive measurements (cycloplegic SER minus non-cycloplegic SER). The distribution of continuous variables was assessed for normality using the Shapiro-Wilk test. Data are presented as mean±standard deviation (SD) for normally distributed parameters or median and interquartile range (IQR) for non-normally distributed parameters. Categorical data are presented as frequencies and percentages (*n*, %).

The unadjusted association between refractive change and the underlying cycloplegic SER was visualized using a scatter plot. A nonparametric smoothing curve was fitted using the Locally Estimated Scatterplot Smoothing (LOESS) algorithm to elucidate the potential complex, non-linear trend without imposing a predefined model. For all analyses, a two-sided P-value <0.05 was considered statistically significant. Statistical analyses were conducted using R software (version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 825 participants were included in the current analysis. The mean age was 26.6±3.3y, and 468 (56.7%) were female. The change in SER, cylinder power, and corneal power before and after cycloplegia are summarized in Table 1. It shows a statistically and clinically significant change in SER after cycloplegia (P<0.001). In contrast, the change in cylinder power was not statistically significant (P=0.969). Although the change in corneal power was statistically significant (P=0.01), it was not clinically meaningful (0.02±0.22 D).

Overall, the prevalence of myopia under cycloplegia was 87.0%. Next, we evaluated the myopia prevalence by using different thresholds for non-cycloplegic refraction. For the thresholds of -0.5, -0.75, -1.0, -1.25, and -1.5 D, the estimated prevalence was 90.2%, 87.5%, 84.4%, 80.8%, and 78.8%, respectively. Among them, the threshold of -0.75 D applied to non-cycloplegic data (87.5%) gave a prevalence value very close to that obtained with cycloplegic refraction.

Of the overall population, using a cut-off of -0.50 D for non-cycloplegic refraction to diagnose myopia, 718 genuine myopic and 26 pseudo-myopic were identified. After changing the threshold to -0.75 D, 13 genuine myopes would have been re-classified incorrectly as emmetropes, while 9 of the 26 pseudo-myopes would have been re-classified correctly as emmetropes. Thus, the myopic population defined without cycloplegia still consisted of a mixture of genuine myopes and pseudo-myopes.

Figure 1 presents the scatter plot of the change in SER before and after cycloplegia in young adults against cycloplegic refraction. LOWESS smoothing curve was used to fit the trend, which revealed a notable increase in the difference as the refractive error shifted toward hyperopia, particularly evident among individuals with hyperopic refractions.

To further explore refractive discrepancies across refractive status, participants were further stratified into four refractive categories: high myopia (SER≤-6.0 D), mild-to-moderate myopia (-6.0 D<SER≤-0.5 D), emmetropia (-0.5 D<SER≤0.5 D), and mild and severe hyperopia (SER>0.5 D; Table 2). Across all groups, cycloplegic refractions were more hyperopic than non-cycloplegic refractions. The magnitude of refractive change varied significantly by refractive status. Hyperopic participants demonstrated the largest mean shift (0.68±0.38 D), followed by emmetropic (0.38±0.38 D), high myopic (0.37±0.47 D), and mild-to-moderate myopic participants (0.27±0.32 D).

Next, we examined the clinically significant myopia refractive shift (SER shift ≥0.50 D). A total of 25.6% (211/825) of participants experienced such a shift. Furthermore, 5.7% of participants exhibited a large shift of SER ≥1.0 D. As expected, this prevalence also varied considerably among the refractive groups (Figure 2). This effect was most pronounced in hyperopic young adults (SER>0.50 D), where the majority, 75.0% exhibited a shift of ≥0.50 D. Interestingly, a relatively high proportion of significant refractive shifts was also observed at both extremes of the remaining spectrum, with 35.2% of high myopes (SER≤-6.00 D) and 34.6% of emmetropic individuals (-0.50 D<SER≤0.50 D) demonstrating a shift of ≥0.50 D. In contrast, participants with mild-to-moderate myopia (-6.00 D<SER≤-0.50 D) were the least susceptible to non-cycloplegic measurement errors, with only 19.5% experiencing a shift ≥0.50 D. These findings clearly illustrate that the magnitude and prevalence of accommodation-induced errors are highly dependent on the individual's baseline refractive status.

DISCUSSION

In this study, we demonstrated that non-cycloplegic refraction

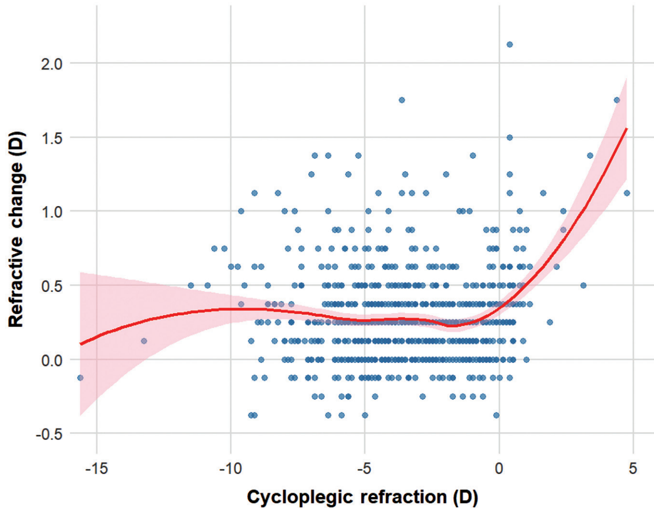

Figure 1 Scatter plot and LOWESS smoothing curve showing the relationship between cycloplegic refraction and refractive change in young adults The horizontal axis represents the cycloplegic SER in diopters (D), which serves as the baseline diagnostic standard. The vertical axis represents the refractive change (D), calculated as the cycloplegic SER minus the non-cycloplegic SER. LOWESS: Locally Weighted Scatterplot Smoothing; SER: Spherical equivalent refraction.

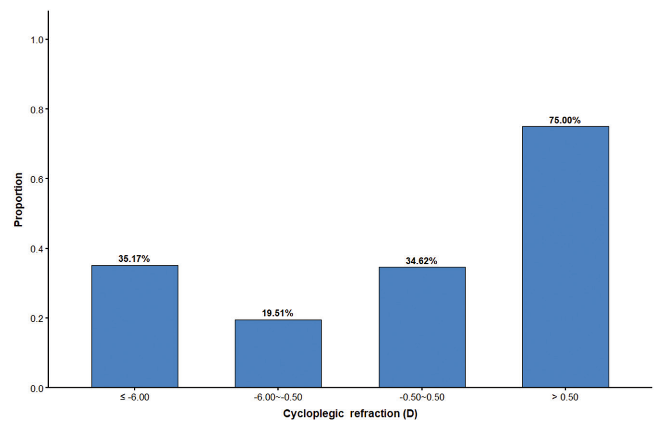

Figure 2 Proportion with refractive change ≥0.50 D.

Table 1 Comparison of SER, cylinder power, and corneal power before and after cycloplegia mean±SD

Parameters	Cycloplegic	Non-cycloplegic	*P*
SER (D)	-3.64±2.81	-3.96±2.81	<0.001
Cylindrical power (D)	-1.02±0.85	-1.02±0.86	0.969
Corneal power (D)	43.69±1.56	43.67±1.56	0.01

SER: Spherical equivalent refraction; SD: Standard deviation; D: Diopter.

Table 2 Comparison of cycloplegic and non-cycloplegic refraction by refractive status

Parameters	Cycloplegic	Non-cycloplegic	*P*
High myopia (*n*=145)	-7.85±2.04	-8.22±2.17	<0.001
Mild-to-moderate myopia (*n*=574)	-3.34±1.52	-3.61±1.56	<0.001
Emmetropia (*n*=78)	0.09±0.31	-0.29±0.45	<0.001
Mild and severe hyperopia (*n*=28)	1.56±1.14	0.88±0.96	<0.001

systematically underestimated hyperopia and overestimated myopia[5,21-23], with the discrepancy most pronounced in individuals with cycloplegic SER≥0 D. Specifically, emmetropic and hyperopic participants showed clinically meaningful differences between cycloplegic and non-cycloplegic measurements, while the discrepancy was smaller in myopic participants. These findings stress the necessity of cycloplegic refraction in epidemiological studies of young adults.

Our results are consistent with previous studies[23-24], where cycloplegia is regarded as the gold standard for eliminating the confounding effects of accommodation. Compared with Mimouni *et al*[23] (young adults) and Fotouhi *et al*[5] (population samples), our proportion of eyes with ≥0.50 D shift is higher than some earlier young adult cohorts that included older participants or lower hyperopia prevalence. This difference is likely due to our younger mean age (26.6±3.3y), a higher proportion of emmetropic and hyperopic eyes in the relevant strata, and our use of a strict threshold for clinically meaningful change.

Previous studies on young adult populations have yielded inconsistent results. Some reported minimal differences between cycloplegic and non-cycloplegic refraction in young adults, leading to the assumption that cycloplegia may be unnecessary in young adults[24]. In contrast, other investigations have documented clinically relevant discrepancies, particularly in hyperopic individuals[5-6,11,25].

The International Myopia Institute has suggested shifting the non-cycloplegic myopia diagnostic cut-off in studies measuring noncycloplegic refraction[26]. The non-cycloplegic prevalence using the ≤-0.75 D cut-off (87.5%) closely approached the cycloplegic prevalence using ≤-0.50 D (87.0%), compared to an overestimation of 3.2% with an SER cut-off of ≤-0.5 D). In contrast, adopting a cut-off of ≤-1.0 D led to an over-estimation of 2.6%. Given the dependence of the difference between cycloplegic and non-cycloplegic refraction on baseline refractive status, which varies between populations and with age, and the possible impact of different cycloplegic agents such as tropicamide, cyclopentolate and atropine, an adjustment of threshold to get a close approximation to the cycloplegic prevalence probably needs to be empirically determined, and therefore, for epidemiological investigations, cycloplegia is essential.

In contrast, for large-scale school screening, the non-cycloplegic strategy can be adopted, but at the cost of over-referral, particularly of younger children where the prevalence of hyperopia tends to be high.

Threshold adjustment may enable a more accurate prevalence of myopia to be achieved without cycloplegia, but it is not a substitute for cycloplegic refraction in clinical practice. Even with the -1.00 D cut-off, 22.7% of participants exhibited a clinically significant refractive shift (≥0.50 D) after cycloplegia, with the greatest discrepancies observed in emmetropic and hyperopic individuals. For precise individual diagnosis, cycloplegic refraction remains indispensable.

From a practical clinical standpoint, the average refractive shift of approximately 0.50 D observed in our study has a tolerable impact on routine adult spectacle prescribing. Clinicians traditionally adhere to the principle of conservative prescribing, which inherently mitigates the influence of minor accommodative fluctuations without the need for routine cycloplegia. However, from an epidemiological perspective, reliance on non-cycloplegic measurements risks overestimating myopia prevalence while underestimating hyperopia, thereby distorting public health strategies for myopia prevention. Accurate refractive assessment is therefore crucial for both individual clinical care and for guiding public health policies on refractive error and myopia prevention[27].

Three limitations should be acknowledged. First, the study sample consisted of relatively young adults with a narrow age range, but other studies on older adults up to the age of 50 have given similar results. Second, while we identified a refractive threshold using Locally Weighted Scatterplot Smoothing (LOWESS) and curvature analysis, this cut-off may vary across populations and with the cycloplegic agents used[5,28]. Third, we exclusively utilized 1% tropicamide for cycloplegia. While tropicamide is widely preferred in adult epidemiologic surveys and clinical screenings due to its rapid onset and shorter duration of action, it is less potent than cyclopentolate or atropine. Consequently, our findings might represent a conservative estimate of the true accommodative capacity, and caution should be exercised when comparing our results with studies utilizing stronger cycloplegic agents. Despite these limitations, our study confirms that cycloplegic refraction is indispensable in epidemiological studies on myopia, even in young adults.

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