Change in Peripheral Refraction over Time in Singapore Chinese Children

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Purpose. Relative peripheral hyperopia has been associated with central myopia. This study was conducted to determine whether baseline relative peripheral hyperopia is associated with an increased risk of developing myopia or myopia progression in young Singapore Chinese children.

Methods. One hundred eighty-seven children who participated in the Peripheral Refraction in Preschool Children (PREP) Study at baseline underwent a follow-up examination. Autorefraction was performed at five eccentricities with an infrared autorefractor after cycloplegia: central axis and 15° and 30° eccentricities in the nasal and temporal visual fields. The primary outcomes were development of myopia among children who were nonmyopic at baseline, and myopia progression in those who were myopic at baseline.

Results. The mean age of the children at baseline was 7.2 ± 3.0 years, and the mean duration of follow-up was 1.26 years. At baseline, 96 children were myopic (mean central spherical equivalent [SE] −2.75 ± 1.72 D) and 91 were nonmyopic (mean central SE 0.76 ± 0.81 D). Baseline relative peripheral hyperopia was not associated with a greater likelihood of becoming myopic or myopia progression. At follow-up, children who remained nonmyopic (n = 24) retained relative peripheral myopia at all eccentricities, whereas those who became myopic (n = 67) developed relative peripheral hyperopia at the nasal (+0.44 ± 0.72 D) and temporal 30° (+0.13 ± 0.74 D). The mean change in central SE was −1.51 ± 0.63 D/y for children who developed myopia, −0.82 ± 0.76 D/y for children who were myopic at baseline, and −1.05 ± 0.80 D/y for all children.

Conclusions. Baseline peripheral refraction did not predict the subsequent onset of myopia or influence the progression of myopia. (*Invest Ophthalmol Vis Sci.* 2011;52:7880–7887) DOI:10.1167/iovs.11-7290

The prevalence of myopia is increasing worldwide and is particularly high among the Chinese.[1–6] Refractive eye development is affected by genetic and environmental factors, and it has been speculated that the visual experience at the periphery after birth can influence emmetropization.[7–9] The emerging evidence that the peripheral retina may play a key role in the process of emmetropization[9–14] has received significant interest. In studies of infant monkeys, foveal ablation resulted in emmetropia,[15] but the imposition of a hyperopic defocus in the retinal periphery and not on the fovea resulted in myopia.[16,17]

Human studies have also found an association between relative peripheral hyperopia, defined as a more hyperopic peripheral refraction compared to the central refraction and central myopia. In the Orinda Longitudinal Study of Myopia conducted in a predominantly Caucasian population, Mutti et al.[18] found that myopic children had relative peripheral hyperopia, whereas children who were emmetropic and hyperopic had relative peripheral myopia. Relative peripheral hyperopia reflects the relatively more prolate ocular shape in myopic eyes,[18–20] in which the axial length exceeds the equatorial diameter. It has also been reported in Chinese subjects with myopia,[21,22] and we have previously reported an association between relative hyperopia in the periphery with central myopia in 250 young Singaporean Chinese children.[22]

Most of the previous studies on peripheral refraction and human myopia were cross-sectional; hence, they were unable to establish the temporal relationship between relative peripheral hyperopia and the onset of myopia.[11,18,21–25] Only three previous studies on peripheral refraction and human myopia were longitudinal.[10,14,26] Hoogerheide et al.[10] measured the refraction of more than 400 young adults older than 18 years who were being trained as pilots over 120° of the horizontal visual field, of whom 41 became myopic during the course of the study. They found that relative hyperopia in the periphery was associated with a 40% probability of developing myopia over a few years, compared with a 4% probability of myopia if there was relative peripheral myopia. This result first implicated relative peripheral hyperopia in the development of myopia. Subsequently, Mutti et al.[14] showed that relative peripheral hyperopia preceded the onset of myopia by 2 years in 605 children aged 6 to 14 years recruited into the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) study. However, they recently reported that relative peripheral hyperopia had little consistent influence on the risk

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of myopia onset, and on the rate of myopia progression in 2817 children who participated in the CLEERE study.[26] Regardless, these studies were conducted on predominantly non-Asian subjects, and the association between relative peripheral refractive errors and the risk of myopia onset has been found to vary by ethnic group.[26] In the CLEERE study, Asian children who became myopic had more relative peripheral hyperopia before the onset of myopia than did children of other ethnicities.[14] In addition, the association between more hyperopic relative peripheral error in the third grade and the risk of myopia onset by the eighth grade was significant only in Asian children in the CLEERE study (OR = 1.56),[26] suggesting that relative peripheral refraction may be more significant in the pathogenesis of myopia development in Asians than in other ethnic groups. However, the ethnicity of the Asian children was not defined in the previous studies, and the role of peripheral refraction on the onset of myopia has not been investigated in Chinese children solely.

The purpose of this 1-year longitudinal study was to determine whether relative peripheral refractive errors at baseline were associated with an increased risk of the development of myopia in young Singapore Chinese children.

METHODS

Study Population

The present study is a follow-up report of the Peripheral Refraction in Preschool children (PREP) study, which examined peripheral refraction and refractive error in Singapore Chinese children. The PREP study was designed as a single-visit study; details have been published.[22,27] The 250 children who participated in the PREP study were contacted approximately 1 year after their initial assessment and were invited to attend a clinic examination at the Jurong Medical Center. The baseline visit was the initial assessment for the PREP study, and the follow-up visit is the assessment for this present study. Data were used from both the baseline and the follow-up visits. We excluded children who had ocular disease, who had chronic medical and mental conditions, or whose parents refused to allow the administration of cycloplegic eye drops. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from the parents of all participants. Ethical approval was obtained from the Institutional Review Board of the Singapore National Healthcare Group.

Eye Examination

A trained optometrist performed refraction in a dimly illuminated room. Cycloplegic autorefraction was performed with a minimum pupil size of 6.0 mm, approximately 30 minutes after topical instillation of 3 drops of 1% cyclopentolate and 2.5% phenylephrine, administered 5 minutes apart. An open-field, infrared autorefractor (Autorefractor/Keratometer model WAM-5500; Grand Seiko Co. Ltd., Hiroshima, Japan), which was calibrated once every fortnight, was used to refract the right eye of participants while the left eye was occluded. Previous studies have used the same autorefractor for the measurement of peripheral refractive errors along the horizontal visual field.[22,23,28–30] Refraction was performed only on the right eye as many participants were young and could not cooperate with refraction of both eyes.

The fixation targets consisted of five LED targets arranged horizontally: one located along the central visual axis, and two at either side of the central target. The separation between each LED target and the adjacent target was 15°, measured from the participant, and the distance between the targets and the patient's corneal vertex was 33 cm. A trained optometrist first obtained three autorefractor measurements with the participants fixating on the central LED target through an open-view mirror. All measurements were within 0.25 D of each other, and the average of the three measurements was calculated. The open-view mirror allowed the optometrist to monitor the participants' fixation, so as to ensure that the participant was fixating on the correct target. To obtain measurements of the peripheral eccentricities, the participant fixated on each nasal and temporal target by moving their eyes, with the head remaining stationary.[31] Measurements of the nasal visual field were obtained when the participant fixated on the targets on the right side, and measurements of the temporal visual field were obtained when the participant fixated on the targets on the left side. Realignment of the pupil along the instrument axis was necessary because of the translation of the eye on rotation, so as to position the alignment mire in clear focus over the center of the pupil. Measurements of the peripheral refraction were then obtained in the same way as the central refraction.

Definitions

From the measurements of spherical and cylindrical error obtained with the autorefractor, power vectors were calculated using these equations[32]:

$$\mathrm{SE} = S + C/2$$

$$J_{180} = -(C/2)\cos(2\alpha)$$

$$J_{45} = -(C/2)\sin(2\alpha)$$

where SE is the spherical equivalent, S is the spherical power, C is the cylindrical power, α is the cylindrical axis, and J_{180} and J_{45} are the power of the two Jackson cross-cylinder components. We performed averaging in terms of these power vectors.

We defined myopia as central SE ≤ -0.5 D, emmetropia as central SE between -0.49 to $+1.0$ D, and hyperopia as central SE $> +1.0$ D. The absolute peripheral refraction at a particular eccentricity was the SE at that eccentricity. The relative peripheral refraction at a particular eccentricity was calculated by the SE at that eccentricity with the central SE subtracted.

"Myopic at baseline " refers to the children who were myopic at the baseline visit. We defined the following outcomes at follow-up: "became myopic, " the primary outcome, refers to the children who were emmetropic or hyperopic at the baseline visit and myopic at the follow-up visit; and "remained nonmyopic" refers to the children who were emmetropic or hyperopic at both the baseline and the follow-up visits.

Statistical Analysis

We compared the mean difference in absolute and relative SE at all eccentricities between the baseline and follow-up visit with the paired-samples *t*-test. The independent-samples *t*-test was used to compare the absolute and relative SE between became-myopic and the remained-nonmyopic children. Linear regressions were performed to estimate the effect of (1) the relative peripheral SE at the temporal and nasal 15° and 30° at baseline, (2) the absolute peripheral SE at the temporal and nasal 15° and 30°, and (3) J_{45} and J_{180} at the temporal and nasal 15° and 30° at baseline, on the shift in central SE (in diopters per year), adjusting for age and sex. To examine the relationship between baseline central SE and relative peripheral SE in children who were myopic at baseline and children who became myopic, linear regression was also performed for baseline relative peripheral SE with baseline central SE as the dependent variable. The association between the absolute SE at the baseline and that at the follow-up visits was examined for each eccentricity with linear regression analysis, with adjustment for age and sex (SPSS ver. 18.0; SPSS Inc., Chicago, IL). Statistical significance was set at $P < 0.05$.

RESULTS

Of the 250 children who participated in the PREP Study, we were able to recruit 187 children (75.2%) with a mean age of

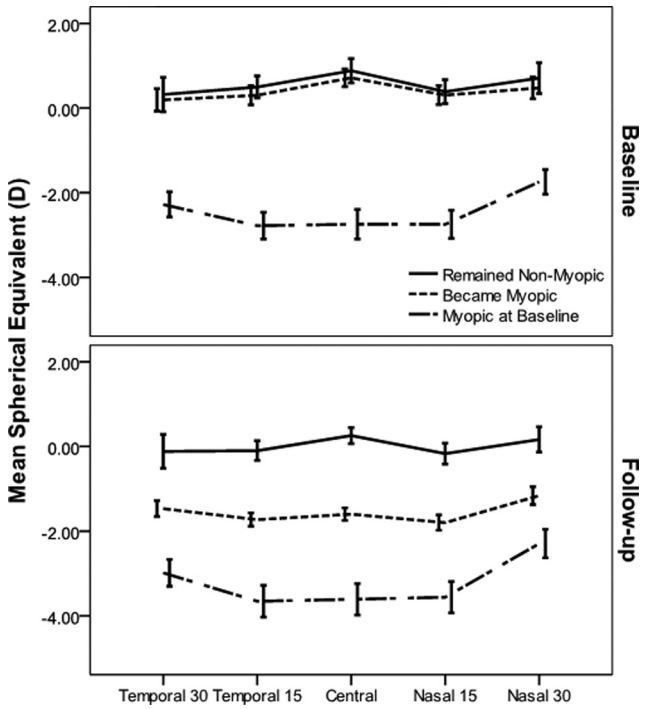

FIGURE 1. Means of SE as a function of visual field angle for became-myopic, remained-myopic, and remained-emmetropic children. Error bars, 95% CI of mean SE.

7.2 years (range, 3.4–15.8 years). We were unable to contact 5 children, and the parents of 58 children declined participation in the study. The mean duration of follow-up was 1.26 years (range, 0.5–2.0 years). The absolute SE was significantly more myopic at the follow-up visit than at the baseline visit at all eccentricities (all $P < 0.001$), and the mean change in central SE was -1.05 ± 0.80 D/y. There were 96 myopic-at-baseline children who were myopic at both the baseline and follow-up visits; 67 became-myopic children who were emmetropic or hyperopic at the baseline visit and myopic at the follow-up visit; and 24 remained-nonmyopic children who were emmetropic or hyperopic at both the baseline and follow-up visits. At the baseline visit, the mean central SE was -2.75 ± 1.72 D for the myopic children, and 0.76 ± 0.81 D for the nonmyopic children ($P < 0.001$). Compared with the children who were included in the study, those who did not participate in the study were younger (73.1 ± 34.9 vs. 86.5 ± 36.0 months; $P = 0.01$) and had a less myopic mean central SE at baseline (-0.36 ± 2.04 vs. -1.04 ± 2.21 D; $P = 0.04$).

The mean absolute SEs of became-myopic and remained-nonmyopic children were emmetropic at all eccentricities at the baseline visit (Fig. 1). At the follow-up visit, children who remained nonmyopic were nonmyopic at all eccentricities, whereas children who became myopic were myopic at all eccentricities (all $P < 0.001$). Children who became myopic were more myopic at the follow-up visit at all eccentricities (all $P < 0.001$) than at the baseline visit (all $P < 0.001$). Children who were myopic at baseline were significantly more myopic at all eccentricities at the follow-up visit (all $P < 0.001$). The became-myopic children had a larger myopic shift in the central refraction than did the myopic-at-baseline children (-0.13 ± 0.05 vs. -0.07 ± 0.06 D/y; $P < 0.001$).

At the baseline visit, the became-myopic and remained-nonmyopic children had relative peripheral myopia at all four peripheral eccentricities (Table 1). At the follow-up visit, the remained-nonmyopic children retained relative peripheral myopia at all four peripheral eccentricities. However, the became-myopic children had relative peripheral hyperopia at the nasal and temporal 30°, which was significantly more hyperopic than the remained-nonmyopic children ($+0.44 \pm 0.74$ vs. -0.09 ± 0.72 D, $P = 0.003$ and $+0.13 \pm 1.08$ vs. -0.37 ± 0.93 D, $P = 0.01$, respectively). The children who were myopic at baseline had baseline relative peripheral hyperopia at the nasal and temporal 30° ($+1.00 \pm 1.25$ and $+0.47 \pm 1.00$, respectively) and follow-up relative peripheral hyperopia at the nasal 15° ($+0.05 \pm 0.68$) and the nasal and temporal 30° ($+1.32 \pm 1.42$ and $+0.63 \pm 1.08$, respectively).

TABLE 1. Peripheral Spherical Equivalent at the Baseline and Follow-up Visits in the Study Participants

	Became Myopic			Myopic at Baseline			Remained Nonmyopic		Total	
Field Angle	***n***		***P****	***n***		***P*†**	***n***		***n***	
Baseline absolute SE, D										
T30	67	+0.19 (1.09)	0.62	96	−2.28 (1.47)	<0.001	24	+0.32 (0.96)	187	−1.06 (1.79)
T15	66	+0.30 (0.93)	0.35	95	−2.78 (1.55)	<0.001	24	+0.50 (0.62)	186	−1.25 (2.01)
Central	67	0.71 (0.85)	0.39	96	−2.75 (1.72)	<0.001	24	0.88 (0.68)	187	−1.04 (2.21)
N15	66	+0.31 (0.91)	0.69	96	−2.75 (1.65)	<0.001	24	+0.39 (0.67)	187	−1.25 (2.03)
N30	67	+0.47 (1.04)	0.33	96	−1.75 (1.44)	<0.001	24	+0.71 (0.86)	188	−0.63 (1.68)
Followup absolute SE, D										
T30	67	−1.47 (0.77)	<0.001	96	−2.99 (1.56)	<0.001	23	−0.12 (0.92)	187	−2.08 (1.61)
T15	67	−1.73 (0.65)	<0.001	96	−3.66 (1.84)	<0.001	24	−0.10 (0.55)	186	−2.50 (1.90)
Central	67	−1.60 (0.61)	<0.001	96	−3.61 (1.83)	<0.001	24	+0.26 (0.45)	187	−2.39 (1.94)
N15	66	−1.80 (0.73)	<0.001	96	−3.56 (1.82)	0.001	24	−0.17 (0.58)	187	−2.49 (1.84)
N30	67	−1.16 (0.87)	<0.001	96	−2.30 (1.67)	<0.001	24	+0.16 (0.71)	188	−1.57 (1.57)
Refraction shift, D/y										
T30	67	−1.08 (0.70)	<0.001	96	−0.68 (0.76)	0.14	23	−0.29 (0.65)	187	−0.77 (0.76)
T15	66	−1.31 (0.67)	<0.001	95	−0.92 (0.94)	0.13	24	−0.50 (0.66)	186	−1.00 (0.86)
Central	67	−1.51 (0.63)	<0.001	96	−0.86 (0.76)	0.15	24	−0.52 (0.77)	187	−1.05 (0.80)
N15	66	−1.38 (0.72)	<0.001	96	−0.82 (0.92)	0.17	24	−0.39 (0.50)	187	−0.96 (0.87)
N30	67	−1.06 (0.64)	<0.001	96	−0.51 (1.17)	0.98	24	−0.35 (0.84)	188	−0.68 (1.01)

Data are the mean (SD). Refraction shift = (SE at Follow-up visit − SE at Baseline)/time difference between two visits in years.

* Based on *t*-test to compare the refractive error between *Became-Myopic* and *Remained-Nonmyopic* subjects.

† Based on *t*-test to compare the refractive error between *Myopic-at-baseline* and *Remained-Nonmyopic* subjects.

In the linear regression model of baseline relative peripheral SE, with baseline central SE as the dependent variable, every 1-D increase in relative peripheral SE at the temporal and nasal 30° and 15° eccentricities was associated with −0.89 (95% CI, −1.19 to −0.59; $P < 0.001$), −0.78 (95% CI, −1.01 to −0.55; $P < 0.001$), −1.10 (95% CI, −1.56 to −0.64; $P < 0.001$) and −0.80 (95% CI, −1.34, −0.27; $P = 0.004$) change in central SE respectively in children who were myopic at baseline, after adjustment for age and sex. In children who became myopic, there was no significant association between relative peripheral SE with central refraction at the baseline visit (all $P > 0.05$).

In the linear regression model of the effect of relative peripheral refraction at the baseline visit on the shift in the central refraction (Table 2) in all subjects, a 1-D decrease in baseline relative peripheral SE at the nasal 30° was associated with a more myopic central SE by 0.12 (95% CI, 0.01, 0.23; $P = 0.03$) D/y, and a 1-D decrease in baseline relative peripheral SE at temporal 30° was associated with a more myopic central SE by 0.17 D/y (95% CI, 0.04–0.29; $P = 0.01$), after adjustment for age and sex. No significant associations were found between the relative SE at the temporal and nasal 15°, and the shift in central refraction ($P = 0.25$ and 0.06 respectively). Within the became-myopic, myopic-at-baseline, and remained-nonmyopic children, there was no significant association between the relative peripheral refraction at baseline and the shift in central refraction. In the linear regression model of the effect of absolute peripheral refraction at the baseline visit on the shift in the central refraction (Table 2) in became-myopic subjects, every 1-D increase in absolute SE at the temporal and nasal 30° and 15° was associated with a more myopic central SE by 0.27 (95% CI, 0.40–0.14), 0.41 (95% CI, 0.54–0.27), 0.38 (95% CI, 0.53–0.24), and 0.31 (95% CI, 0.44, 0.18) D/y, respectively (all $P < 0.001$), after adjustment for age and sex.

The absolute cylindrical power in terms of the astigmatic vectors J_{45} and J_{180} was generally small (less than ±0.5 D) at all the eccentricities in the became-myopic, myopic-at-baseline, and remained-nonmyopic children, at both baseline and follow-up visits (Table 3). Compared with the remained-nonmyopic children, absolute J_{45} and J_{180} at the baseline and follow-up visits were not significantly different in the became-myopic children. At the baseline visit, the myopic-at-baseline children had a more hyperopic absolute J_{45} (0.10 ± 0.33 vs. −0.05 ± 0.24 D, $P = 0.046$) and J_{180} (0.33 ± 0.57 vs. 0.06 ± 0.42 D, $P = 0.04$) at the nasal 15° compared with the remained-nonmyopic children. At the follow-up visit, myopic-at-baseline children had a more hyperopic absolute J_{180} (0.30 ± 0.65 vs. 0.09 ± 0.33 D, $P = 0.04$) at the nasal 15° compared with the remained-nonmyopic children. In the linear regression model, there was no significant effect of absolute J_{45} and J_{180} at the baseline visit on the shift in central refraction, after adjustment for age and sex (all $P > 0.05$).

Discussion

We present longitudinal data over a 1-year interval on relative peripheral refractive errors in relation to the onset of myopia in Chinese children that have not been previously described. Our results indicate that children who were myopic at baseline or who became myopic had relative peripheral hyperopia at the follow-up visit, while children who remained nonmyopic (emmetropic or hyperopic) throughout the study had relative peripheral myopia at baseline and follow-up. However, the differences between the central and peripheral refractions are small (less than ± 1.50 D), and relative peripheral hyperopia and astigmatism did not predict progression to myopia. Those who became myopic during the course of the study had baseline relative peripheral refractions that were similar to children who remained nonmyopic. Each diopter decrease in baseline relative SE at the nasal and temporal 30° was associated with a 0.12- and 0.17-D decrease in the central SE, respectively.

Our results in Chinese children should be compared to the few previous studies on relative peripheral refraction in Caucasian subjects. These were largely cross-sectional and hence were unable to determine the temporal relationship between relative peripheral hyperopia and central myopia.[11,18,21–25] In the PREP study, we previously demonstrated that relative peripheral hyperopia was associated with central myopia in young Chinese children from Singapore (<0.001), whereas children with central emmetropia and hyperopia had relative peripheral myopia ($P < 0.001$).[22] We now show that that the development of myopia was associated with a change from relative peripheral myopia to relative peripheral hyperopia in Singapore Chinese children. This suggests that there is an alteration in ocular shape with axial elongation, as the axial length increases to a larger extent than the equatorial diameter, resulting in a relatively more prolate ocular shape.[19,20,33,34] This is unlike emmetropic or hyperopic eyes, which have an oblate ocular shape as the equatorial diameter exceeds axial length.[34] The precise mechanism responsible for a relatively more prolate ocular shape in myopic eyes is unknown. Animal studies suggest that the eye elongates by synthesis of new scleral tissue in the posterior pole of the eye, and this may be an important factor contributing to the relatively more prolate shape in myopic eyes.[35,36] External forces, such as extraocular muscles and the bony dimensions of the orbit, may also explain the slow ocular equatorial expansion, as suggested by the rabbit model of myopia.[37]

Our results suggest that relative peripheral hyperopia was not an important factor in the development of myopia, as it did not precede the onset of myopia, but rather occurred in parallel with axial elongation as the ocular shape changed from oblate to relatively more prolate. In the linear regression model, we found that a myopic shift in the central refraction was associated with baseline absolute peripheral hyperopia and relative peripheral myopia, rather than baseline relative peripheral hyperopia. The became-myopic children, who had absolute peripheral hyperopia and relative peripheral myopia at the baseline visit (Table 1), had a larger myopic shift in the central refraction compared with the myopic-at-baseline children, who had baseline absolute peripheral myopia and relative peripheral hyperopia. In an earlier study, the myopic shift in the central refraction was also found to be larger just prior to the onset of myopia compared to subsequent myopia progression.[14] Our results are consistent with the recent findings of Mutti et al.,[26] who showed that relative peripheral hyperopia had little consistent influence on the risk of myopia onset, myopia progression, or axial elongation in 2817 children who participated in the CLEERE study. However, the ethnicity of the Asian children was not defined, hence could have differed from our cohort of Chinese children. In addition, two different autorefractors were used in that study, and the measurements may not be comparable because of the poor agreement between these autorefractors.[38] Nevertheless, these findings are consistent with our results that baseline peripheral refraction does not predict the subsequent onset of myopia.

These recent data do not agree with previous studies in predominantly Caucasian subjects, which found that relative peripheral hyperopia precedes and increases the risk of myopia onset.[10,14] Hoogerheide et al.[10] found that relative peripheral hyperopia in trainee pilots was associated with a 10-fold increase in the probability of subsequently development of central myopia. However, this study was lacking in details on how peripheral refraction was measured and how the different types of skiagrams were derived. In a longitudinal study of 605

Table 2. Linear Regression Model for Relative and Absolute Peripheral Refraction at the Baseline Visit with the Shift in the Central Refraction as the Dependent Variable

	Became Myopic (n = 67)		Myopic at Baseline (n = 96)		Remained Nonmyopic (n = 24)		All Subjects (n = 187)	
	B (95% CI)	*P*	B (95% CI)	*P*	B (95% CI)	*P*	B (95% CI)	*P*
Relative peripheral refraction at baseline								
Crude								
Relative SE at T30	0.14 (−0.08 to 0.37)	0.22	0.04 (−0.11 to 0.19)	0.62	0.09 (−0.27 to 0.45)	0.62	0.14 (0.03 to 0.26)	0.01
Relative SE at T15	−0.03 (−0.39 to 0.32)	0.86	−0.02 (−0.23 to 0.21)	0.89	0.46 (−0.14 to 1.07)	0.13	0.11 (−0.08 to 0.30)	0.23
Relative SE at N15	0.19 (−0.09 to 0.48)	0.18	−0.05 (−0.30 to 0.19)	0.66	0.88 (0.36 to 1.41)	<0.001	0.18 (−0.01 to 0.37)	0.06
Relative SE at N30	0.09 (−0.17 to 0.34)	0.49	0.01 (−0.11 to 0.13)	0.9	−0.15 (−0.64 to 0.34)	0.54	0.10 (0.001 to 0.20)	0.047
Age-sex adjusted								
Relative SE at T30	0.12 (−0.11 to 0.35)	0.3	0.07 (−0.09 to 0.23)	0.36	0.29 (−0.05 to 0.63)	0.1	0.17 (0.04 to 0.29)	0.01
Relative SE at T15	−0.02 (−0.37 to 0.33)	0.91	0.007 (−0.22 to 0.23)	0.95	0.45 (−0.10 to 1.00)	0.11	0.12 (−0.08 to 0.31)	0.25
Relative SE at N15	0.18 (−0.10 to 0.46)	0.21	−0.01 (−0.26 to 0.24)	0.92	0.80 (0.31 to 1.29)	0.001	0.19 (−0.01 to 0.38)	0.06
Relative SE at N30	0.08 (−0.18 to 0.33)	0.56	0.04 (−0.09 to 0.18)	0.52	−0.22 (−0.67 to 0.22)	0.33	0.12 (0.01 to 0.23)	0.03
Absolute peripheral refraction at baseline								
Crude								
SE at T30	−0.24 (−0.37 to −0.11)	<0.001	0.05 (−0.06 to 0.15)	0.38	−0.23 (−0.57 to 0.11)	0.18	−0.10 (−0.16 to −0.03)	0.003
SE at T15	−0.40 (−0.53 to −0.26)	<0.001	0.02 (−0.08 to 0.12)	0.72	−0.44 (−0.96 to 0.08)	0.09	−0.10 (−0.15 to −0.04)	0.001
SE at N15	−0.36 (−0.50 to −0.21)	<0.001	0.02 (−0.08 to 0.11)	0.75	−0.15 (−0.66 to 0.36)	0.55	−0.09 (−0.15 to −0.04)	0.001
SE at N30	−0.29 (−0.42 to −0.16)	<0.001	0.04 (−0.07 to 0.14)	0.51	−0.45 (−0.79 to −0.11)	0.01	−0.11 (−0.18 to −0.05)	0.001
Age-sex adjusted								
SE at T30	−0.27 (−0.40 to −0.14)	<0.001	0.03 (−0.09 to 0.14)	0.63	−0.14 (−0.49 to 0.21)	0.41	−0.12 (−0.19 to −0.05)	0.002
SE at T15	−0.41 (−0.54 to −0.27)	<0.001	−0.004 (−0.12 to 0.11)	0.94	−0.51 (−0.99 to −0.30)	0.04	−0.13 (−0.20 to −0.07)	<0.001
SE at N15	−0.38 (−0.53 to −0.24)	<0.001	−0.01 (−0.11 to 0.10)	0.88	−0.26 (−0.75 to 0.23)	0.28	−0.13 (−0.19 to −0.06)	<0.001
SE at N30	−0.31 (−0.44 to −0.18)	<0.001	0.02 (−0.09 to 0.13)	0.7	−0.53 (−0.82 to −0.23)	0.001	−0.13 (−0.21 to −0.06)	0.001

Data are expressed as the shift in refraction (SE) in diopters/year. Relative SE = Peripheral SE − Central SE.

TABLE 3. The Distribution of Absolute J_{45} and J_{180} at the Baseline and Follow-up Visits

Field Angle	Total (n = 187)	Became Myopic (n = 67)	Myopic at Baseline (n = 96)	Remained Nonmyopic (n = 24)
Baseline absolute J_{180}				
T30	−0.31 (0.70)	−0.30 (0.68)	−0.28 (0.73)	−0.47 (0.65)
T15	0.15 (0.56)	0.09 (0.41)	0.24 (0.66)	0.01 (0.44)
Central	0.37 (0.48)	0.25 (0.37)	0.47 (0.57)	0.27 (0.28)
N15	0.21 (0.52)	0.09 (0.44)	0.33 (0.57)	0.06 (0.42)
N30	0.01 (0.58)	−0.14 (0.43)	0.15 (0.67)	−0.11 (0.41)
Follow-up absolute J_{180}				
T30	−0.42 (0.65)	−0.47 (0.51)	−0.38 (0.75)	−0.48 (0.57)
T15	0.16 (0.51)	0.02 (0.37)	0.28 (0.61)	0.06 (0.30)
Central	0.35 (0.52)	0.19 (0.47)	0.50 (0.58)	0.24 (0.27)
N15	0.18 (0.58)	0.05 (0.52)	0.30 (0.65)	0.09 (0.33)
N30	−0.07 (0.57)	−0.24 (0.43)	0.09 (0.65)	−0.28 (0.42)
Difference*				
T30	−0.11 (0.51)	−0.17 (0.62)	−0.10 (0.44)	−0.02 (0.44)
T15	0.01 (0.32)	−0.06 (0.29)	0.04 (0.33)	0.05 (0.33)
Central	−0.02 (0.32)	−0.04 (0.22)	0.03 (0.31)	−0.04 (0.22)
N15	−0.02 (0.40)	−0.04 (0.43)	−0.02 (0.38)	0.03 (0.41)
N30	−0.09 (0.40)	−0.10 (0.36)	−0.05 (0.43)	−0.17 (0.34)
Baseline absolute J_{45}				
T30	0.04 (0.34)	0.04 (0.31)	0.03 (0.38)	0.02 (0.29)
T15	0.001 (0.22)	0.05 (0.18)	−0.03 (0.25)	0.004 (0.19)
Central	−0.04 (0.20)	−0.05 (0.18)	−0.03 (0.23)	−0.02 (0.14)
N15	0.06 (0.31)	0.02 (0.29)	0.10 (0.33)	−0.05 (0.24)
N30	0.07 (0.33)	0.02 (0.34)	0.10 (0.34)	0.06 (0.23)
Follow-up absolute J_{45}				
T30	0.07 (0.34)	0.07 (0.29)	0.07 (0.38)	0.10 (0.31)
T15	0.02 (0.24)	0.01 (0.24)	0.01 (0.27)	0.06 (0.14)
Central	−0.04 (0.22)	−0.05 (0.20)	−0.03 (0.25)	−0.03 (0.13)
N15	0.05 (0.33)	0.005 (0.27)	0.10 (0.38)	0.24 (−0.02)
N30	0.04 (0.32)	0.001 (0.32)	0.08 (0.34)	−0.02 (0.22)
Difference				
T30	0.04 (0.25)	0.03 (0.25)	0.03 (0.26)	0.08 (0.19)
T15	0.01 (0.21)	−0.04 (0.23)	0.04 (0.20)	0.05 (0.23)
Central	−0.002 (0.16)	−0.005 (0.20)	0.001 (0.14)	−0.005 (0.14)
N15	−0.005 (0.30)	−0.02 (0.30)	0.004 (0.31)	0.02 (0.27)
N30	−0.02 (0.24)	−0.02 (0.25)	−0.02 (0.24)	−0.08 (0.19)

* Difference = Follow-up value − Baseline value.

predominantly white children aged between 6 and 14 years, Mutti et al.[14] found that children who developed myopia had more hyperopic relative peripheral refractive errors than emmetropes from 2 years before the onset to 5 years after the onset of myopia ($P < 0.002$ for each year). However, they assessed only the relative peripheral refractive error in one eccentricity: 30° in the nasal visual field. In addition, their results may not be directly comparable with ours, as they defined myopia as a refraction of at least −0.75 D in each eccentricity, whereas myopia was defined as central SE ≤ −0.5 D in our study. It is likely that relative peripheral hyperopia was detected before this rigorous definition of myopia of −0.75 D in each eccentricity, but would essentially still be a result rather than a cause of increased axial elongation that commenced before the onset of myopia. This notion is consistent with the findings of Mutti et al.[14] that marked relative peripheral hyperopia only develops several years after myopic progression has started.

Taken in totality, human studies have so far been unable to confirm animal experiments that investigated the role of peripheral refraction in the process of emmetropization. In rhesus monkeys, a −3-D lens used to induce peripheral hyperopia beyond 15.5° eccentricity was able to cause axial elongation and myopia.[16,17] However, the animal studies have only shown that peripheral defocus can stimulate axial growth in the absence of foveal signals, but have not established that the peripheral retina is more important than the fovea in myopia development. In addition, human and animal studies are not directly comparable, as the human studies do not involve the imposition of peripheral hyperopia or foveal ablation. While human studies have assessed the effect of relative peripheral hyperopia on myopia's onset and progression, animal studies have evaluated the consequence of absolute rather than relative peripheral hyperopia. It is unclear what extent of defocus is necessary to alter foveal refraction in humans. Schmid and Wildsoet[39] have shown that imposing a 2-D interocular difference in refraction is sufficient to induce an average of 2.13 D of anisometropia in chick eyes, but their study pertains to central defocus rather than isolated peripheral defocus. In our study, the relative peripheral hyperopia in myopic children was less than +1.50 D, which may not be of sufficient magnitude to induce axial elongation. It has been speculated that the absence of relative peripheral hyperopia resulting in good peripheral image quality may inhibit ocular growth,[40,41] although its presence may not stimulate ocular growth. A recent study of 210 Chinese children by Sankaridurg et al.[42] showed that there were no statistically significant differences in the rates of myopia progression between children who wore one of three novel spectacle lenses that decreased relative peripheral hyperopia and those who wore the conventional single-vision spectacle lenses. However, in a subgroup analysis of younger children (aged 6–12 years) with a parental history of myopia (n = 100), one of the three

novel spectacle lenses was found to reduce myopia progression over 1 year. These results suggest that the improvement of peripheral image quality may inhibit axial elongation in a group of children who may have a higher risk of myopia progression, but the findings need to be validated in a larger, longer, and more targeted study.

In our 1-year study, there was no significant difference in the J_{180} and J_{45} astigmatic vectors between the remained-nonmyopic children, and the became-myopic or myopic-at-baseline children. Baseline peripheral astigmatism did not predict the subsequent development of myopia or influence myopia's progression. Furthermore, the magnitude of J_{180} and J_{45} was small at all eccentricities in our cohort of Chinese children. Bakaraju et al.[43] proposed that peripheral astigmatism may play a role in the progression of myopia, although conclusive evidence is lacking. Our results suggest that peripheral astigmatism is minimal in Chinese children and does not play a significant role in the development of myopia.

The strength of our study is the prospective evaluation of peripheral refraction in relation to myopia onset in very young Chinese children, which has not been previously studied. Other strengths include autorefraction under cycloplegia, the use of the same autorefractor for all measurements, and the assessment of peripheral refraction at several horizontal eccentricities. However, our study was limited by the small sample size, especially the small number of children in the remained-nonmyopic group. Secondly, we assessed only peripheral refraction in the horizontal plane; the vertical plane was not assessed. The peripheral refraction profile along the vertical plane has been evaluated in only a few studies,[21,23] and although they reported that there was no significant association with refractive status, further studies are needed to verify this. In addition, the prevalence of myopia and the rate of myopia onset were high in the participants of our study, who may not be representative of Chinese children in Singapore.

In summary, our longitudinal study of Chinese children in Singapore showed that the development of myopia was associated with a change from relative peripheral myopia to relative peripheral hyperopia. However, baseline relative peripheral hyperopia of less than +1.50 D and peripheral astigmatism did not predict the subsequent onset of myopia and hence did not play a significant role in the development of myopia. Our study provides additional insights into the interrelationship between the early refractive and shape changes in myopia development.

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