Title:
High magnitude with-the-rule astigmatism and myopic progression in children

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ABSTRACT:
Purpose: To investigate high magnitude with-the-rule astigmatism (WTRA, plus cylinder with axis between 75 and 105 degrees) as a risk factor for myopic progression in children.
Methods: Retrospective case-control study. Medical records were screened using CPT codes and age of visit. Subjects were included if the age at initial and final refractive visits were < 8 years and ≥ 10 years, respectively, and had at least five years of follow up. Exclusion criteria include a history of intraocular/oculoplastic pathologies, surgeries, lasers, presence of pathologic myopia (magnitude ≥ 8 diopters). Eyes were categorized based on the initial refraction: no astigmatism (NA), non-WTRA (cylinder outside of 75-105 degree range), low-WTRA (cylinder < 2 D) or high-WTRA (cylinder ≥ 2 D).
Results: A total of 2974 records were screened. 202 eyes of 110 patients were included; 79 (39%) were NA, 81 (40%) were low-WTRA, 24 (12%) eyes were high-WTRA, and 18 (9%) were non-WTRA. High-WTRA had the least hyperopic initial spherical equivalence (0.5 +/- 6.4 D) compared to NA (2.2 +/- 3.0 D), non-WTRA (2.3 +/- 3.2 D), and low-WTRA (3.2 +/- 2.7 D, $P = 0.009$). When comparing the rates of myopic refractive change per year, patients with high-WTRA demonstrated a significantly greater rate (-0.24 +/- 0.21 D/year) than those without high-WTRA (-0.13 +/- 0.22 D/year, $P = 0.0041$).
Conclusions: Compared to cohorts with NA, non-WTRA or low-WTRA, children with high-WTRA show a significantly higher rate of myopic progression when followed for five or more years.

Key words – myopic progression, high magnitude astigmatism, children

1. INTRODUCTION:

Myopia is the most common cause of visual impairment worldwide, and its prevalence is increasing, especially in Asian countries.[1] The cause of myopic progression is unknown. Thus far, genetic studies suggest a heterogeneous etiology[2], and many risk factors have been identified, including family history, intense near work, presence of image blur during critical periods of visual development, and certain well-characterized syndromes.[3] High myopia is a common finding in children with poorly controlled infantile glaucoma due to distension and elongation of the globe, while the stabilization of axial length in these children after treatment suggests that intraocular pressure (IOP) may play a role in mediating globe size and myopic progression during development.[4]
Animal studies have demonstrated dynamic high-frequency IOP fluctuations during the blink cycle, the magnitude of which is presumably attributed to eyelid biomechanics.[5]
With-the-rule astigmatism (WTRA), when uncorrected, introduces image blur, an established stimulus for myopic progression. Furthermore, it may be marker of abnormal eyelid biomechanics[6] and globe/eyelid interaction and results in intermittent, high frequency fluctuations in IOP.[5] We hypothesize that high amount of WTRA may be associated with a greater rate of myopic progression in children.

2. PATIENTS AND METHODS:

The medical records from the Pediatric Ophthalmology Service at Vanderbilt Eye Institute were screened using Current Procedural Terminology (CPT) code for any levels of new patient office visit or consultation (99201-99205, 92002, 92004, and 99241-5) that occurred between 1998 and 2006. All available records resulted from the screening were reviewed.

Patients were enrolled into the study based on the inclusion/exclusion criteria outlined in Table 1.

Table 1. Inclusion and exclusion criteria for enrollment in the study.

Inclusion criteria – • Age < 8 years at the time of initial cycloplegic refraction • Age > 10 at the time of final cycloplegic refraction
Exclusion criteria – • Any history of intraocular surgery or laser • Any history of intraocular pathology • Any history of surgical procedures on the eyelids • Any history of eyelid pathology (e.g. congenital ptosis, capillary hemangioma, etc) • Follow up < 5 years • Presence of pathologic myopia (magnitude ≥ 8 diopters) at initial visit

Cycloplegic refractions from the initial and final visits were recorded in positive-cylinder format and the spherical equivalence (SE) calculated. The patients were categorized based on the characteristics of their initial refraction:

- No astigmatism (NA, cylinder magnitude < 0.25 D)
- Non-with the rule astigmatism (Non-WTRA, axis of plus cylinder

astigmatism outside of 75- 105 degree range, cylinder of any magnitude)

- Low-with the rule astigmatism (Low-WTRA, axis of plus cylinder astigmatism between 75-

105 degree range, cylinder magnitude < 2 D)

- High-with the rule astigmatism (High-WTRA, axis of plus cylinder astigmatism between 75- 105 degree range, cylinder magnitude ≥ 2 D)

The rate of myopic change (in diopters [D]/year) was calculated for each group by dividing the total change in spherical equivalence between final and initial visits by the total follow-up time in years.

The study protocol was reviewed and exempted by the Institutional Review Board at Vanderbilt University and carried out in compliance with the requirements of the Health Insurance

Portability and Accountability Act (HIPAA).

Analysis of variance and unpaired *t*-test were used to compare the rates of myopic progression amongst the four groups.

3. RESULTS:

A total of 2974 records were screened. 202 eyes of 110 patients were included. 123 of the 202 eyes (60.9%) had astigmatism; 79 (39%) were NA, 81 (40%) were low-WTRA, 24 (12%) eyes were high-WTRA, and 18 (9%) were non-WTRA. Background and initial refractive characteristics are reported in Table 2, and the mean length of follow up was 6.3 years. High- WTRA had the least hyperopic initial spherical equivalence (0.5 +/- 6.4 D) compared to NA (2.2 +/- 3.0 D), non-WTRA (2.3 +/- 3.2 D), and low-WTRA (3.2 +/- 2.7 D, P = 0.009). When comparing the rates of myopic refractive change per year, patients with high-WTRA demonstrated a significantly greater rate (-0.24 +/- 0.21 D/year) than those without high-WTRA (-0.13 +/- 0.22 D/year, P = 0.0041).

Table 2. Patient background, initial and final refractive characteristics, and rates of myopic changes.

	High-WTRA*	NA*	Non-WTRA*	Low-WTRA*	Total	P-value
N of eyes	24 (12%)	79 (39%)	18 (9%)	81 (40%)	202	
N of males (%)	12 (50%)	41 (52%)	8 (44%)	49 (61%)	110 (55%)	
Age at initial visit Mean (SD) years	5.6 (1.3)	4.5 (1.5)	2.8 (2.1)	4.7 (1.5)	4.7 (1.5)	0.019*
Initial astigmatism magnitude Mean (SD) diopters	2.7 (0.9)	0 (0)	1.1 (0.4)	0.9 (0.5)	0.8 (0.9)	<0.001*
Initial spherical equivalence Mean (SD) diopters	0.5 (6.4)	2.2 (3.0)	2.3 (3.2)	3.2 (2.7)	2.4 (3.6)	0.009*
Age at final visit Mean (SD) years	11.8 (1.6)	10.9 (1.1)	11.2 (1.1)	11.0 (1.0)	11.1 (1.2)	0.006*
Final spherical equivalence Mean (SD) years	-1.0 (6.0)	1.6 (3.4)	1.4 (4.1)	2.4 (3.7)	1.6 (4.0)	0.005*
Rate of refractive change Mean (SD) diopters/year***	-0.24 (0.21)	-0.11 (0.18)	-0.16 (0.26)	-0.14 (0.24)	-0.14 (0.22)	0.12*
Rate of refractive change Mean (SD) diopters/year***	-0.24 (0.21)		-0.13 (0.22), n = 178			0.027**

+WTRA = with-the-rule-astigmatism (axis 75 to 105 degrees); high $\geq$ 2 cylinders; NA = no astigmatism
*Analysis of variances
** Unpaired *t*-test
***A rate of change with negative value denotes myopic progression

4. DISCUSSION:

Myopia is the most common disorder of the eye affecting children and adults worldwide, affecting 25%-43% of children and adults in the United States and as high as 81% of adolescents in some Asian countries.[7, 8, 9] The relationship between various types of astigmatism and myopia is not well understood. In this cohort, astigmatism was present in 60.9% of eyes,

with the majority (65.9%) being low-WTRA, which is consistent with findings of several large, prospective, multi-centered surveys of pediatric eye disease prevalence.[10, 11] These surveys have established significant association between astigmatism and myopia. In Vision in Preschoolers (VIP) Study, myopia of 1 or more diopters is a significant risk factor for astigmatism, and more myopic progression[13] and the difference in racial composition between our cohort (children mostly Caucasians of European descent) and the Hong Kong study (children mostly of Asian ancestry) may account for the difference in the rates of myopic shift. Furthermore, our cohort was older than the cohort in Hong Kong, and the rate of myopic shift likely diminishes with age.

The mechanism relating astigmatism and myopic shift is a topic of speculation. While uncorrected astigmatism results in image blur, a known stimulus for axial elongation[14, 15], it may also be considered a marker of abnormal lid/globe interaction, as evidenced by changes in the axis and magnitude of astigmatism in adults after ptosis repair and blepharoplasty[6], which may play a role in myopic progression in children. To test this hypothesis, one needs to compare high-WTRA patients with a cohort of image blur in this process, as well as comparing large cohorts with WTRA and against-the-rule astigmatism of similar magnitude to explore the role of lid/globe interaction in refractive changes in children

similar magnitudes of astigmatism but at against-the-rule or oblique axes, which would introduce similar image blur independent of lid position or biomechanics. Non-WTRA comprised of a small proportion of our cohort (9%) and the magnitude was modest (1.1 +/- 0.4 D). The myopic progression rates between high-WTRA and non-WTRA in our cohort was insignificant possibly due to the small sample size.

There are several limitations to our study. The retrospective design is vulnerable to referral bias, especially in a tertiary care center, although our inclusion/exclusion criteria were designed to circumvent any inadvertent selection prejudice. The cohort size is modest, and statistical significance was only achieved when comparing high-WTRA with the aggregated remainder, while analysis of variance between each discreet subgroup failed to show significance, likely due to the small number of patients in each group. In summary, we performed a retrospective, case-control study which revealed high-WTRA to be associated with higher rate of myopic progression. Future efforts should be focused on comparing corrected with uncorrected astigmatic refractive error to elucidate role of astigmatic

CONFLICT OF INTEREST
None of the authors have any conflict of interest to declare.

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Not applicable.

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