

Prevalence and Associations of Myopic Anisometropia in Chinese Adults

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Purpose: To investigate the prevalence and associations of myopic anisometropia in Chinese adults.

Methods: A total of 3,791 Chinese refractive surgery candidates with myopia (25.15 ± 7.09 years old, Mean $\pm$ SD) were recruited. All eyes underwent a standardized ophthalmological examination. Associations between myopic anisometropia and age, gender, spherical ametropia, astigmatism, and axial length (AL) were analyzed by means of the chi-squared test, nonparametric Kruskal–Wallis or Mann–Whitney test, binomial logistic regression analyses, and multivariate logistic regression analysis.

Results: The mean myopic anisometric level was 0.96 D and prevalence of myopic anisometropia was 29.62% (defined as myopic anisometropia ≥ 1.00 D). The prevalence and severity of myopic anisometropia increased with age, larger interocular AL difference, and higher cylindrical power (all $P < 0.001$). Myopic anisometropia showed a U-shaped correlation with spherical equivalent (SE) refractive error and V-shaped correlations with AL, J0 and J45. Myopic anisometropia was most strongly associated with interocular AL difference ($P < 0.001$).

Conclusions: Compared with previous reports, this study revealed an even higher prevalence of myopic anisometropia and showed a U-shaped correlation with SE and a V-shaped correlation with AL. These results indicate that the formation of myopic anisometropia could be related to neural control in the binocular AL growth balance. Further study is needed to clarify this presumption.

Key Words: Myopia—Anisometropia—Refractive error.

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Myopic anisometropia is usually defined only when the interocular difference of myopia for an individual is at least 1.00 diopter (D),¹ which can cause diplopia, aniseikonia, decreased

stereopsis, visual fatigue, and even amblyopia in the more myopic eye.^{2–4} These symptoms usually become obvious when the degree of anisometropia is 2.50 D or more.^{2–4} According to Linke et al.,⁵ myopic anisometropia (spherical equivalent [SE] difference 1.00 D or more) demonstrated a prevalence of 18.7% in myopic subjects ($n=9,832$) above 18 years old. In a 23-year follow-up study, Pärssinen et al.⁶ found that the prevalence of anisometropia (SE ≥ 1.00 D) increased from 5% in childhood to 22.6% in adulthood. In another study of Pärssinen et al.,⁷ the prevalence of anisometropia was 17.7% among 66- to 79-year-old female twins. In a longitudinal study of Haegerstrom-Portnoy et al.,⁸ SE anisometropia (≥ 1.00 D) changed from 16.1% to 32.2% at two time points separated by approximately 12 years in 118 older observers. Therefore, it was a significant vision-related issue causing reduced quality of life for adults.

Most of the previous studies of anisometropia were from western countries, and studies investigating its prevalence for the general adult population in mainland China where there is a very large population have been insufficient until most recently. The Shandong Children Eye Study assessed the prevalence and associations of anisometropia in a school-based study of children 4 to 18 years old in the Eastern Chinese province of Shangdong.⁹ Nevertheless, studies focusing on adults over 18 years old are still rare thus far. In addition, most of the previous studies^{1,5,9} have not measured or correlated axial length (AL) with the prevalence and severity of anisometropia.

The rate of myopia in China has risen in recent years with an estimated prevalence of 72.8% in 18-year-old teenagers;¹⁰ however, to date, there has not been any study on myopic anisometropia among Chinese adults with a large sample size. Therefore, we conducted the present hospital-based study to measure the prevalence and severity of myopic anisometropia in southeast China, and to assess the associations of myopic anisometropia with demographic and ocular parameters including age, gender, refractive error, and AL.

MATERIALS AND METHODS

Subjects

This study is a cross-sectional epidemiological investigation about myopic anisometropia based on hospital-based population, which conducted a noninvasive ocular examination. It was approved by the Office of Research Ethics, Wenzhou Medical University, and conducted according to the tenets of the Declaration of Helsinki of the World Medical Association regarding scientific research on human subjects. Written informed consent was obtained from the patients for participation.

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The study subjects comprised 3,791 Chinese subjects with myopia (25.15 ± 7.09 years, Mean $\pm$ SD) recruited from The Affiliated Eye Hospital of Wenzhou Medical University between January 2009 and August 2015. All of the subjects were candidates for under-going refractive surgery to correct myopia. The study subjects were divided into two groups: myopic anisometropia ($n=1,123$) and nonanisometropia ($n=2,668$). All subjects showed at least -0.50 D of SE myopia in one eye and emmetropia or myopia in the other eye. The subjects with an interocular difference of SE refractive error of at least 1.00 D were assigned to the myopic anisometropia group. Each eye in this group was assigned to one of the three anisometropia severity sub-groups, which was defined as mild anisometropia (1.00 – 1.99 D); moderate anisometropia (2.00 – 2.99 D); and severe anisometropia (≥ 3.00 D). The subjects in the nonanisometropia group demonstrated a difference of SE less than 1.00 D between the two eyes. All subjects were free of previous ocular surgery and other known ocular or systemic diseases.

First, subjects were stratified into one of five age categories (18 – 19 , 20 – 29 , 30 – 39 , 40 – 49 , 50 – 59 years old) and two gender categories. Second, myopes were stratified into groups with an interval of 1.00 D in SE and 1.00 mm in AL in the less ametropic eye. Third, subjects were classified with 1.00 D intervals for J0 and cylinder power (0.50 D intervals for J45) in the less ametropic eye, where both vectorial (J0, J45) and nonvectorial approaches were studied.

Measurement of Refractive Status and Axial Length of the Eye

Cycloplegic refraction of all subjects were measured with an auto-refractometer (RM-8800, Topcon corporation, Japan) with the initial refractive data refined by subjective refraction. The SE of refractive error was calculated as the spherical component plus half of the cylindrical component. For astigmatism, subjective refraction in conventional script notation (sphere [S], cylinder [C], axis [α]) was converted to power vector coordinates by the following formulas:

$$J0 = (-C/2) \cos(2\alpha) \text{ and } J45 = (-C/2) \sin(2\alpha)$$

Axial length of the eye was measured using an IOL Master

system (Carl Zeiss Meditec, Jena, Germany). The mean of five consecutive measurements was recorded as the final result.

Statistical Analysis

All data were analyzed using the SPSS 21.0 software (Inc Chicago, IL) and significant differences between groups were defined as P value less than 0.05 . The chi-square test or, depending on expected values of the cells, the Fisher exact test (expected value <5) was used for comparisons of categorical data between groups. The Kruskal–Wallis or Mann–Whitney test was used for comparisons of continuous measures between groups. Binomial logistic regression analysis was performed to identify risk factors that were independently associated with myopic anisometropia in this hospital-based population. We also performed a multivariate stepwise regression analysis to drop all those parameters which were no longer significantly associated with myopic anisometropia and examine the associations between the severity of myopic anisometropia and other remaining parameters.

RESULTS

Demographics and Prevalence of Myopic Anisometropia

Among 3,791 eligible participants, the mean age was 25.15 ± 7.09 years (median: 23.00 years, range: 18–59 years). The mean myopic anisometropia level in the overall study population was 0.96 D (median: 0.50 D, range: 0.25 – 1.13 D). The prevalence of myopic anisometropia defined as ≥ 1.00 D was 29.62% . Mild myopic anisometropia was observed in 17.35% , moderate myopic anisometropia in 5.94% , and severe myopic anisometropia in 6.33% of the study subjects. Clinical characteristics and descriptive statistics of parameters for the myopes are shown in Table 1.

Myopic Anisometropia and Its Association With Age and Gender

The prevalence and severity of myopic anisometropia increased significantly with age in this clinically selected group of myopes from 18 to 59 years (both $P < 0.001$). In logistic regression analysis,

TABLE 1. Characteristics of Nonanisometropia and Anisometropia in the Study Population ($n=3,791$)

	Nonanisometropia (<1.00 D)		Anisometropia (≥ 1.00 D)		Total	
	Number	%	Number	%	Number	%
Patients	2,668	70.38	1,123	29.26	3,791	100.00
Male	1,323	49.59	508	45.24	1,831	48.30
Female	1,345	50.41	615	54.74	1,960	51.70
Age (yrs)	24.65 ± 6.74 (18–59)		26.33 ± 7.34 (18–56)		25.15 ± 7.09 (18–59)	
SE of LAE (D)	-6.26 ± 3.20 ($-27.00/-0.50$)		-6.65 ± 4.24 ($-26.50/0.00$)		-6.38 ± 3.54 ($-27.00/0.00$)	
Spherical power of LAE (D)	-5.84 ± 3.10 ($-27.00/-0.50$)		-6.08 ± 4.13 ($-26.00/0.00$)		-5.91 ± 3.44 ($-27.00/0.00$)	
Cylinder power of LAE (D)	-0.83 ± 0.73 ($-6.50/0.00$)		-1.14 ± 0.91 ($-5.75/0.00$)		-0.92 ± 0.80 ($-6.50/0.00$)	
J0 of LAE (D)	0.30 ± 0.41 ($-1.97/3.20$)		0.40 ± 0.53 ($-1.88/2.70$)		-0.33 ± 0.45 ($-1.97/3.20$)	
J45 of LAE (D)	-0.02 ± 0.21 ($-1.20/1.35$)		-0.03 ± 0.31 ($-1.74/1.52$)		-0.03 ± 0.25 ($-1.74/1.52$)	
AL of LAE (mm)	26.12 ± 1.81 (11.20/34.13)		26.15 ± 1.78 (13.40/33.05)		26.13 ± 1.80 (11.20/34.13)	
AL of MAE (mm)	26.25 ± 1.76 (11.20/34.64)		27.05 ± 2.42 (6.65/34.99)		26.49 ± 2.01 (6.65/34.99)	
Difference in AL (mm)	0.25 ± 1.20 (0.00/15.99)		1.00 ± 1.62 (0.00/19.33)		0.47 ± 1.38 (0.00/19.33)	
BCVA of LAE (logmar)	-0.02 ± 0.10 ($-0.18/1.30$)		0.02 ± 0.12 ($-0.18/1.00$)		-0.01 ± 0.11 ($-0.18/1.30$)	
BCVA of MAE (logmar)	-0.02 ± 0.10 ($-0.18/1.30$)		0.06 ± 0.20 ($-0.18/1.30$)		-0.01 ± 0.14 ($-0.18/1.30$)	

Mean $\pm$ SD, range inside the parenthesis.

AL, axial length; BCVA, best corrected visual acuity; Difference in AL, difference in AL between eyes; LAE, less ametropic eye; MAE, more ametropic eye; SE, spherical equivalent.

TABLE 2. Binomial Logistic Regression Analysis for the Presence of Anisometropia (≥ 1.00 D Difference in MSE of Both Eyes) With Age Modeled as a Continuous Variable ($n=3,791$)

Model	Variable	Regression Coefficient	SE of Coefficient	Significance	Odds Ratio	95% CI of OR
Myopes, all age, $n=3,791$	Age (yrs)	0.016	0.006	0.007	1.016	1.004–1.028
	Sex (male)	−0.148	0.094	0.115 (NSD)	0.863	0.718–1.037
	Spherical power (D)	0.014	0.019	0.483 (NSD)	1.014	0.976–1.053
	Cylindrical power (D)	−0.256	0.053	<0.001	0.774	0.697–0.859
	J0 cylinder (D)	−0.213	0.155	0.170 (NSD)	0.80	0.596–1.095
	J45 cylinder (D)	−0.294	0.167	0.078 (NSD)	0.745	0.537–1.033
	AL of LAE (mm)	−1.557	0.073	<0.001	0.211	0.183–0.243
	AL of MAE (mm)	1.569	0.072	<0.001	4.804	4.168–5.536
	Difference in AL (mm)	1.630	0.075	<0.001	5.103	4.407–5.908

AL, axial length; CI, confidence interval; Difference in AL, difference in AL between eyes; LAE, less ametropic eye; MAE, more ametropic eye; NSD, not significantly different; OR, odds ratio; SE, spherical equivalent.

age was independently associated with myopic anisometropia in the study subjects as shown in Table 2 ($P=0.007$). Multivariate Analysis also revealed that more severe myopic anisometropia was independently associated with older age as shown in Table 3 ($P<0.001$).

The prevalence of myopic anisometropia was higher in female subjects than male subjects ($P=0.014$). Myopic anisometropia was also slightly more severe in women than men (1.01 ± 1.52 D in female vs. 0.90 ± 1.46 D in male; $P=0.001$). However, after correcting for multiple testing, the results showed no clinically significant difference in the prevalence between the two genders (Table 2; $P=0.115$) or level of myopic anisometropia between the genders (Table 3; $P=0.099$).

Myopic Anisometropia and Its Association With Spherical Equivalent and Axial Length

Myopic anisometropia showed a U-shaped correlation with SE refractive error (Fig. 1A, B) and a V-shaped correlation with AL (Fig. 1C, D) in the subjects' less myopic eye. There was a rough linear trend of decreasing myopic anisometropia prevalence and severity with increasing myopia up to a maximum of approximately -5.00 D (both $P<0.001$) and increasing AL up to a maximum of approximately 26.00 mm ($P \leq 0.006$). For very high myopia (< -9.00 D) and longer AL (≥ 26.00 mm), we observed an increasing tendency of myopic anisometropia with increasing myopia and AL (all $P=0.001$). However, the prevalence and severity of myopic anisometropia remained relatively stable for SE power increasing from -5.00 to -9.00 D ($P \geq 0.103$). In the subjects' more ametropic eye, we also observed an increasing myopic anisometropia prevalence and severity with increasing AL (both $P<0.001$). The prevalence and severity of myopic anisometropia increased significantly (Fig. 1E; both $P<0.001$) as the interocular AL difference got bigger (Fig. 1F; $P<0.001$).

Myopic Anisometropia and Cylindrical Power

In vectorial analysis, the prevalence of myopic anisometropia was lowest when the cylindrical power was 0 for both J0 and J45 in the less ametropic eye (Fig. 2A, C), as was the severity of myopic anisometropia (Fig. 2B, D). A V-shaped prevalence and severity of myopic anisometropia with a minimum for J0 was found ($J0 \leq 0$: both $P \leq 0.002$; $J0 > 0$: both $P<0.001$), as was for J45 ($J45 \leq 0$: both $P<0.001$; $J45 > 0$: both $P<0.001$). In nonvectorial analysis, the relationship between myopic anisometropia and cylindrical power was also evident. The prevalence and severity of myopic anisometropia increased significantly as cylindrical power increased in the less myopic eye (Fig. 2E, F; both $P<0.001$).

Logistic and Multivariate Regression Models

The binomial logistic regression model described the associations between myopic anisometropia (≥ 1.00 D) and the explanatory variables age, SE, spherical power, cylindrical power, J0, J45, AL of the less ametropic eye, AL of the more ametropic eye, and difference in AL, along with gender as a binary independent variable in these myopic subjects (Table 2). Difference in AL was the parameter most strongly associated with myopic anisometropia (odds ratio [OR]=5.103, $P<0.001$). Age (OR=1.016, $P<0.007$), cylindrical power (OR=0.774, $P<0.001$), AL of less ametropic eye (OR=0.211, $P<0.001$), and AL of the more ametropic eye (OR=4.804, $P<0.001$) also showed significant independent association with myopic anisometropia. In the multivariate stepwise regression analysis (Table 3), higher myopic anisometropia was associated with older age ($P<0.001$), more myopic spherical refractive error ($P<0.001$), longer AL in more ametropic eye ($P<0.001$), larger interocular difference in AL ($P<0.001$), lower cylindrical power ($P<0.001$), lower J0 cylinder ($P=0.017$), and shorter AL in the less ametropic eye ($P<0.001$).

TABLE 3. Associations (Multivariate Analysis) Between the Severity of Refractive Anisometropia (Spherical Equivalent; Diopters) and Age and Ocular Parameters ($n=3,791$)

Parameter	P	Standardized Correlation Coefficient β	Standardized Regression Coefficient B	95% Confidence Interval of B
Age (yr)	<0.001	0.120	0.025	0.019 to 0.031
Spherical power (D)	<0.001	0.079	0.035	0.016 to 0.053
Cylindrical power (D)	<0.001	−0.152	−0.286	−0.375 to −0.196
J0 cylinder (D)	0.017	−0.058	−0.192	−0.349 to −0.034
AL of LAE (mm)	<0.001	−0.289	−0.240	−0.279 to −0.202
AL of MAE (mm)	<0.001	0.373	0.277	0.241 to 0.313
Difference in AL (mm)	<0.001	0.253	0.450	0.238 to 0.309

AL, axial length; Difference in AL, difference in AL between eyes; LAE, less ametropic eye; MAE, more ametropic eye.

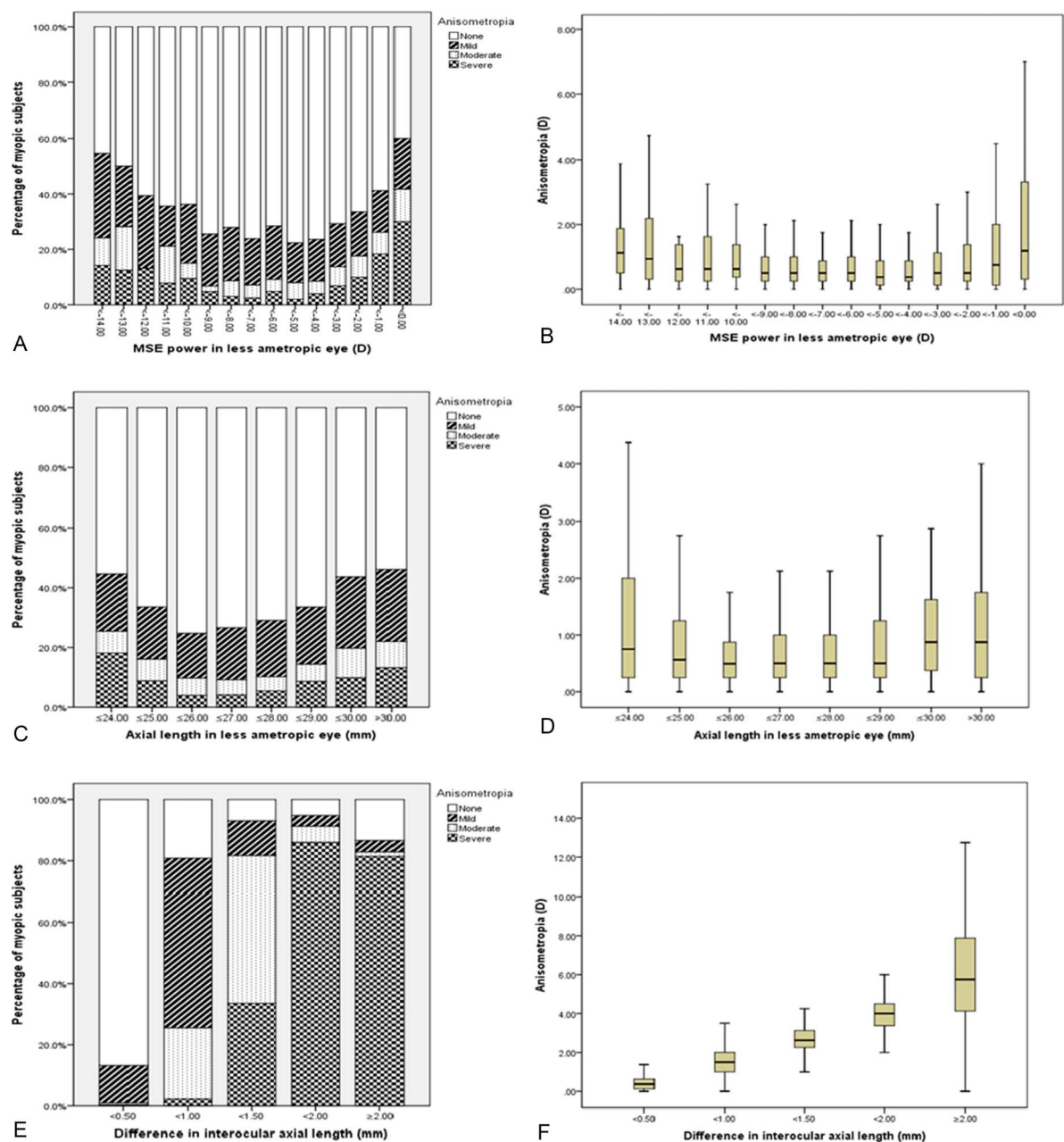


FIG. 1. (A–F) Prevalence and severity of myopic anisometropia with the level of myopia (A and B: MSE, mean spherical equivalent) in the less ametropic eye of the study population. Prevalence and severity of myopic anisometropia with axial length (AL) in the less (C and D) ametropic eye of the study population. Prevalence and severity of myopic anisometropia with the interocular AL difference (E and F) of the study population. Subjects are stratified by 1.00-D intervals of SE power in the less or more ametropic eye. (A and B) Myopic anisometropia showed a U-shaped correlation with SE refractive error. There was a roughly linear trend of decreasing myopic anisometropia prevalence and severity with increasing myopia up to a maximum of approximately -5.00 D (both $P < 0.001$). For very high myopia (< -9.00 D), we observed an increasing tendency of myopic anisometropia with increasing myopia (both $P < 0.001$). However, the prevalence and severity of myopic anisometropia remained relatively stable for SE power increasing from -5.00 to -9.00 D (both $P \geq 0.103$). (C and D) Myopic anisometropia showed a V-shaped correlation with AL in the subjects' less myopic eye. There was a roughly linear trend of decreasing myopic anisometropia prevalence and severity with increasing AL up to a maximum of approximately 26.00 mm (both $P < 0.001$). For longer AL (≥ 26.00 mm), we observed an increasing tendency of myopic anisometropia with increasing AL ($P < 0.001$). (E and F) The prevalence and severity of myopic anisometropia increased significantly as the interocular AL difference got bigger (both $P < 0.001$).

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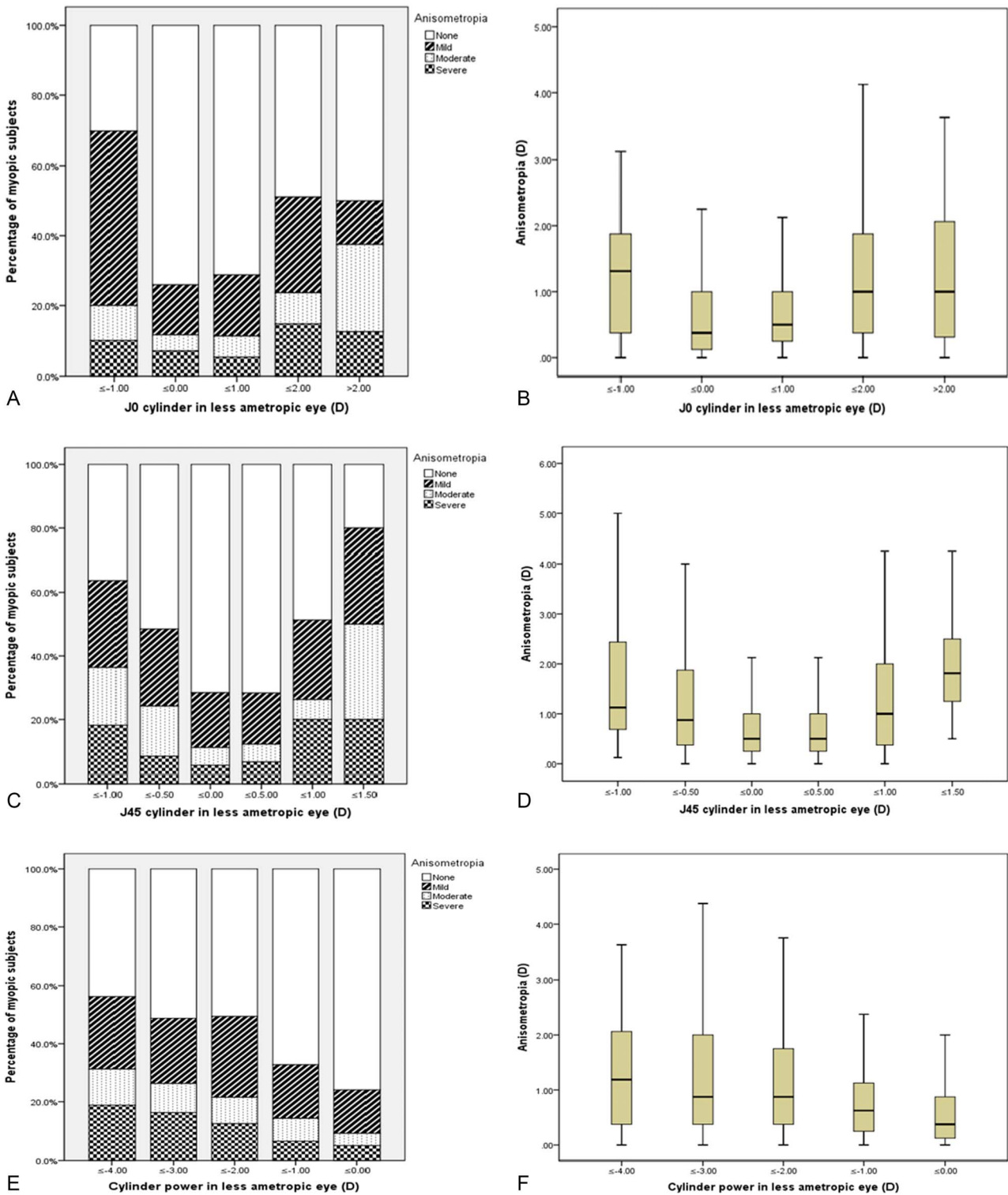


FIG. 2. (A–F) Prevalence and severity of myopic anisometropia with the level of astigmatism in less spherical ametropia of the study population (A–D represented in vectorial notation, E and F represented in nonvectorial notation). Subjects are stratified by 1.00-D intervals of J0 and cylinder power (0.50-D intervals for J45) in the less ametropic eye. (A–D) A V-shaped prevalence and severity of myopic anisometropia with a minimum for J0 and J45 was found (all $P \leq 0.002$). (E and F) The prevalence and severity of myopic anisometropia increased significantly as cylindrical power increased in the less myopic eye (both $P < 0.001$).

DISCUSSION

In this clinically selected group of myopes from 18 to 59 years old, with a mean myopic anisometropia level of 0.96 D and prevalence of myopic anisometropia of 29.62%, the prevalence and severity of myopic anisometropia increased with older age, larger interocular AL difference, and higher cylindrical power (all $P < 0.001$). Myopic anisometropia showed a U-shaped correlation with SE refractive error and V-shaped correlation with AL, J0 and J45. Interocular AL difference was most strongly associated with myopic anisometropia (OR=5.103, $P < 0.001$).

Wu et al.¹¹ revealed an anisometropia prevalence of 14.4% in Singaporean males aged 16 to 25 years old. In the Blue Mountains Eye Study, Guzowski et al.¹² reported that anisometropia was present in 14.7% of all the participants older than 50 years. A prevalence of 19.3% anisometropia was reported in a cohort study of refractive surgery candidates in central Europe, which was higher than that reported for the general population of developed countries,^{12,13} but comparable to the approximately 17% prevalence of anisometropia reported by Qin et al.¹ However, the prevalence of myopic anisometropia of 29.62% in the present study is almost double of that in other studies.^{1,11–13} One possible reason explaining the much higher prevalence of anisometropia in this study maybe because of our selection of study subjects which only included myopes. It is known that anisometropia is more common in cases of high ametropia, particularly among individuals with a large amount of myopia; Wu et al.¹⁴ reported that the OR of anisometropia in myopic individuals was 2.7 times more than in nonmyopics, and many other studies have also corroborated these findings.^{12,15,16} In addition, differences in the definition of anisometropia and recruiting the refractive data should also be taken into consideration.⁵ Furthermore, differences in the age and refraction distribution in the cohort should also be taken into account.

The prevalence and severity of anisometropia vary throughout life.¹⁷ Anisometropia is observed to decrease during the early years of life, followed by an increase from childhood to adulthood, which subsequently remains relatively stable between 30 and 50 years old. However, in older age (≥ 60 years), an increase is observed, which may be related to the development of age-related cataract.¹⁷ In this clinically selected group of myopes, we found that both the prevalence and severity of myopic anisometropia increased significantly with age (18–59 years old), which was in agreement with most of the other studies.^{5,15,18,19}

In accordance with the previous studies,^{15,18,20} after correcting for multiple testing, there was no difference in the prevalence or the severity of myopic anisometropia between the two genders.

The prevalence and severity of anisometropia significantly increased with myopic refractive error in the previous studies.^{1,5,9,15} In addition, Linke et al.¹ observed that there was a roughly linear trend of increasing anisometropia prevalence and severity with myopia up to approximately -7.00 D; however, for very high myopia (< -8.00 D), a decreasing tendency of anisometropia with myopia was observed. In contrast to the previous studies,^{1,5,9,15} one of the most interesting findings in this study was that myopic anisometropia showed a U-shaped correlation with SE refractive error and a V-shaped correlation with AL in the less myopic eyes, that is, a decreasing tendency of myopic anisometropia with myopia in low-to-moderate myopic eyes (Fig. 2A–D, SE > -5.00 D, AL < 26.00 mm), followed by a stable phase with SE

refractive error increasing from -5.00 to -9.00 D, and an increasing tendency with myopia in very highly myopic eyes (SE < -9.00 D, AL ≥ 26.00 mm).²¹ It appears that our results were more reasonable and explainable. As we already know, the correlation in refractive error between both eyes is high.^{1,22} Except for tight genetic control, both eyes are fine-tuned to the same emmetropic endpoint by visual feedback or a combination of the two mechanisms. In the present study, we found that both eyes tried to keep symmetry for low and moderate myopic eyes. When the eye progressed to severe myopia, the two eyes lost their balance of refractive error gradually. However, we found that myopic anisometropia was most strongly associated with the interocular difference in AL which was in agreement with the previous studies,^{9,23–25} suggesting that the development of myopic anisometropia mainly occurred through the influence of changes of the interocular difference in AL of the eye. Therefore, we presumed that the formation of myopic anisometropia could be related to the neural control in the binocular AL growth balance for the two paired eyes.^{2,26,27} Further study is needed to clarify this presumption.

Previous studies have assessed the extent to which anisometropia and nonvectorial astigmatism are independently associated.^{1,5} In this present study, both logistic and multivariate regression models were used to confirm the independent association between myopic anisometropia and nonvectorial astigmatism in myopes, which only analyzed the altitude of astigmatism. In vectorial analysis, similar to the results of Qin et al.,¹ we found a V-shaped prevalence and severity of myopic anisometropia with J0 and J45 which took into account both the altitude and axis of astigmatism. Positive values of J0 indicate with-the-rule (WTR) astigmatism, and negative values indicate against-the-rule (ATR) astigmatism. J45 refers to a Jackson cross-cylinder (JCC) set at 45° and 135° , representing oblique astigmatism. Positive values of J45 indicate a JCC set at 45° and negative values of J45 indicate a JCC set at 135° . To sum up, both prevalence and severity of myopic anisometropia were significantly related with WTR astigmatism, ATR astigmatism, and oblique astigmatism. These findings suggested that astigmatism was another main factor contributing to the development of myopic anisometropia.

One limitation of our study is hospital-based and only included subjects with myopia, thus our findings may be affected by “selection biases” compared with other population-based studies. Another limitation of this study is the retrospective design.

In conclusion, compared with the previous reports, this study revealed that the prevalence of myopic anisometropia was higher. Myopic anisometropia showed a U-shaped correlation with SE refractive error and a V-shaped correlation with AL. These results indicated that the formation of myopic anisometropia could be related to neural control in the binocular AL growth balance. Further study is needed to clarify this presumption.

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