Visual impairment in highly myopic eyes: the ZOC-BHVI high myopia cohort study

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ABSTRACT

Importance: Understanding visual impairment (VI) under different definitions and potential risk factors in high myopia is important for future myopia control.

Background: Limited studies exist investigating the VI among high myopic and with varying VI definitions.

Design: Registry cohort Study

Participants: 884 participants from ZOC-BHVI Study

Methods: Subjects aged 7-70 years with high myopia were enrolled. Uncorrected and best-corrected visual acuity (UCVA & BCVA), cycloplegic refraction, axial length (AL), corneal curvatures, anterior chamber depth and lens thickness were measured. Axial length/Corneal radius of curvature ratio (AL/CR ratio) was calculated. Fundus lesions were graded into 5 categories. VI and blindness were defined based on the better-seeing eye according to the World Health Organization (WHO) criteria and United States (US) criteria. Multiple logistic regression analysis was used to assess risk factors for VI.

Main outcome measures: Rates of VI and blindness

Results: A total of 884 participants were included, with mean (SD) age 18.5 (12.4) years and 46.4% male. Rate of UCVA/blindness were 72.6%/27.3% and 17.9%/82.1% based on WHO and US criteria. With respect to BCVA, 4.1%/5.9% of participants had BCVI using two definitions, while the rate for blindness was 0.2% and 0.6%. After adjusting confounders, multiple logistic regression showed that more severe fundus lesions, greater AL/CR ratio were at a higher risk of being VI, both in two definitions ($p < 0.005$).

Conclusions and Relevance: The rate of VI and blindness in highly myopic patients varies significantly using different definition. Severe fundus lesions and greater AL/CR ratios were associated with a higher risk of VI.

Keywords: visual impairment, blindness, rate, high myopia, WHO criteria, US criteria, risk factors

1. INTRODUCTION

Myopia is the most common refractive disorders in the world, with the myopia prevalence continuing to increase globally in recent decades.^{1,2} It is estimated that more than 4.82 billion or 50% of the population worldwide will be affected by myopia by 2050, among which 63% are Asian.³ Meanwhile, the prevalence of high myopia is also increasing dramatically, evidenced by previous reports that the prevalence of high myopia ranged 10%-16% in South Korea,⁴ Japan,⁵ and Singapore,⁶ even reach as high as 20% among school-aged Chinese populations in mainland China,^{7,8} Hongkong⁹ and Taipei.¹⁰ It is no surprise that high myopia has becoming a growing public health concern, especially for regions where myopia prevalence are high.

According to the World Health Organization (WHO) , there were 253 million people with visual impairment (VI) and 36 million with blindness worldwide in 2017.¹¹ High myopia related retinal degeneration has been reported to be the major cause of legal blindness in the Beijing Eye Study in China,¹² the Tajimi Study in Japan⁵ and the Shihpai Eye Study in Taiwan,¹³ as well as a frequent cause of blindness in western countries.^{14,15} Unlike myopia, high myopia cannot simply be treated with a pair of spectacles, especially when pathologic ocular changes occur such as glaucoma, retinal detachment, and myopic maculopathy, all of which can cause irreversible vision loss.^{16,17}

With the ever-increasing prevalence and higher risk of VI and blindness, high myopia is posing significant healthcare challenges around the world, especially in China which has the world's largest population and a rapidly increasing

prevalence of high myopia. A greater understanding of VI status in those with high myopia is urgently needed to better guide preventative measures and future eyecare needs. However, few studies have reported the rate of VI and blindness among high myopes in China. Therefore, it is critical to explore the rate and related risk factors to enable adjustments to current public health strategies. The aim of this study is to assess VI in highly myopic eyes and the associated risk factors of those participating the ZOC-BHVI High Myopia Cohort Study in China.

2. METHODS

2.1 Statement of ethics

This study was approved by the institutional ethics committee of Zhongshan Ophthalmic Centre (2012KYNL002) and adhered to the Declaration of Helsinki for experimentation on human subjects. All participants or guardians of the participating children were informed of the study details and signed informed consent.

2.2 Study Participants

The study participants were enrolled in the ZOC-BHVI High Myopia Cohort Study and details of this cohort study have been described previously.¹⁸ In brief, it was a registry study in Zhongshan Ophthalmic Centre and initiated in 2011, which aimed to determine the development patterns of pathologies in highly myopic eyes. The optometry clinic with sufficiently resources, provides optical services for the public with nearly 300,000 visits per year. Nearly all patients with refractive problems need to go through an optometry clinic before being

visited by an ophthalmologist. Thus, participants aged 7–70 years with bilateral high myopia (defined as less than -6.00 D spherical power and no astigmatic cut-off was used) were invited to register for the study. Those with systemic or ocular disease (such as autoimmune conditions, cataracts, keratoconus, or myopia secondary to systemic disease), abnormal binocular vision including amblyopia and strabismus, history of intraocular or refractive surgery or myopia-control treatment were excluded from the study. Baseline data was collected from 2011 to 2012.

2.3 Ophthalmic Examinations

All subjects underwent a series of ophthalmic evaluations. Uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) were examined for each eye using the Early Treatment Diabetic Retinopathy Study (ETDRS) logMAR illiterate E VA chart (Precision Vision, Villa Park, Illinois, USA). Biometry measurements were carried out in a room with low ambient illumination by trained nurses. Axial length (AL), corneal curvature (CC), lens thickness (LT) and central anterior chamber depth (ACD) were measured before cycloplegia using an optical low-coherence reflectometry (Lenstar LS-900; Haag-Streit AG, Koeniz, Switzerland). If AL exceeded the valid range of measurement in Lenstar (≥ 32 mm), a repeated measurement was conducted using a partial coherence interferometry (IOLMaster, Carl Zeiss Meditec, Oberkochen, Germany). The mean of five AL measurements was taken as the final AL. Axial length/Corneal radius of curvature ratio (AL/CR ratio) was calculated. Cycloplegia was conducted using two drops of 0.5 per cent tropicamide five minutes apart for three times. A pupil size of more than 6 mm was considered successful dilation. Both objective and subjective

refraction were examined 10 to 20 minutes after cycloplegia. Objective refraction was conducted with an auto-refractor (KR8800, Topcon, Tokyo, Japan), followed by a trial frame subjective refraction by an optometrist.

2.4 Fundus Photography and Grading

For all participants, two 45° color fundus photographs centered at the macula and optic nerve were obtained using a digital retinal camera (Canon CX-1) after cycloplegia. Fundus photographs were graded according to the International Photographic Classification and Grading System for Myopic Maculopathy.¹⁹ Myopic maculopathy was classified into 5 categories of “no myopic retinal lesions” (category 0, C0), “tessellated fundus only” (category 1, C1), “diffuse chorioretinal atrophy” (category 2, C2), “patchy chorioretinal atrophy” (category 3, C3), and “macular atrophy” (category 4, C4). In addition, lesions including lacquer cracks, myopic choroidal neovascularization and Fuchs’ spot were noted. Presence of staphyloma was identified based on fundus photographs by two independent graders who were masked to refraction data.

2.5 Definition of Visual impairment and blindness

According to the WHO definition, VI was defined as visual acuity (VA) $<20/60$ & $\geq 20/400$ and blindness was defined as $VA < 20/400$ in the better-seeing eye. VI and blindness were defined according to the United States (US) Standard in the same fashion, except that the cutoff for VI was $20/40$ & $20/200$ and for blindness was $20/200$. We calculated uncorrected visual impairment (UCVI) and best corrected visual impairment (BCVI) based on uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA), respectively.

2.6 Statistical Analysis

Refractive error was calculated using the spherical equivalent (SE), calculated as spherical power plus half the cylindrical power. Age was categorized into 7-18 years, 19-39 years and ≥ 40 years. High myopia was classified into 3 categories: -6.00 to -7.99 D, -8.00 to -9.99 D, and ≥ -10.00 D. Axial length was classified into 3 categories: < 28.00 mm, 28.00 to 29.99 mm and ≥ 30.00 mm.

Median and 25th–75th percentile was used to describe the non-normal distribution parameters. Logistic regression analysis was used to assess the odds ratio (OR) of risk factors for VI and blindness. Univariate logistic regression analysis was conducted to examine the relationship between BCVI and confounders such as age, gender, SE, AL, LT, fundus lesion severity and staphyloma. Since AL is significantly related to the SE in individuals,²⁰ AL was arbitrarily selected into the multiple analysis models to avoid collinearity. Similarly, fundus lesion severity is significantly related to staphyloma, so only fundus lesion level was included into the multiple regression analysis models. A p-value of < 0.05 was considered statistically significant. All statistics were performed using STATA (V.14.0, Stata, College Station, Texas, USA).

3. RESULTS

A total of 890 subjects were enrolled in the ZOC-BHVI high myopia cohort study. Among these participants, 6 with co-existing retinal pathology in the best seeing eyes were excluded and the data from the remaining 884 subjects' best seeing eye were analyzed. The characteristics of the study population are presented in Table 1. Among 884 subjects, 410 (46.4%) were male. The median age was 18.5 years (range, 7–70 years) and the median SE was -9.9 D

(range, -6 to -23.9 D). The median corneal curvature (CC), axial length (AL), central anterior chamber depth (ACD) and lens thickness (LT) were 43.7 D, 27.4 mm, 3.2 mm and 3.6 mm, respectively. The median Axial length/Corneal radius of curvature ratio (AL/CR ratio) was 3.5 (range, 3.3-4.2).

Rates of BCVI and blindness are listed in Table 2. The rate of BCVI and blindness using the WHO definition were 4.1% (2.8-5.4) and 0.2% (0-0.5), while that for the US criteria were 5.9% (4.3-7.4) and 0.6% (0.1-1.1), respectively. No significant difference was observed between gender for BCVI ($p=0.525$ and $p=0.886$) and blindness ($p=0.713$ and $p=0.668$) under both WHO and US definition. The rates of BCVI were higher in subjects with myopia severe than -10.0D and longer axial length (with all $p<0.001$).

Comparable results of the rates of UCVI and blindness are shown in Table 3. Using the WHO definition, 72.6% (69.7-75.6) participants fulfilled the criteria for UCVI, while 27.3% (24.3-30.2) subjects were blind. Using the U.S. definition, 17.9% (15.3-20.4) participants had UCVI, while 82.1% (79.6-84.7) were blind. Participants older than 18 years of age presented a higher rate of blindness but lower rate of BCVI (with all $p<0.001$). The rate of blindness increased with more myopic SE and longer AL under both WHO and US criteria (with all $p<0.001$). Other results about rates of BCVI/UCVI and blindness in the worse-seeing eye are showed in Supplement table 1 & 2.

Figure 1 shows distribution of BCVA in different myopic maculopathy lesion categories (C0-C4) under WHO and US definitions according to age. In Figure

1A, the proportion of BCVI and blindness as the severity of myopic maculopathy lesion categories increased. An age-dependent increase in the proportion of BCVI was also observed in each classification lesion. For blindness in C2 and C3+C4 group, no patient was observed in older age group. In Figure 1B, similar distributions of BCVI were also observed under US definition. But more proportion of blindness were observed in C2 and C3+C4 group. "Plus" lesions, which supplemented the Meta-PM categories, comprised lacquer cracks, choroidal neovascularization (CNV), and Fuchs spot. Among 884 participants, the occurrence of "plus" lesions were rare, present in only 18 (2.0%) participants. Lacquer cracks, Fuchs spot, and CNV were found in 14 (1.6%), 2 (0.23%), and 2 (0.23%) participants, respectively.

The relationship between BCVI and associated risk factors are shown in Table 4. Univariate logistic regression models showed that BCVI were significantly associated with increasing age, more myopic SE, larger CC, longer AL, greater AL/CR ratio, thicker LT, presence of staphyloma and more severe fundus lesions under both WHO and US criteria (with all $p < 0.05$). No association was found between BCVI and gender (WHO: OR=0.991, $p=0.788$; US: OR=0.968, $p=0.148$) in neither criterion. Multiple regression models showed that subjects of female gender, with a greater AL/CR ratio had a higher risk of having BCVI under WHO definition. Similar significant associations were found between BCVI and aforementioned confounders (with all $p < 0.05$), except for gender ($p=0.388$) when using US definition. Fundus lesion was an important risk factor since patients with fundus lesions had up to 10.5 or 26.7 times of higher risk of being visually impaired under US and WHO definition, respectively.

4. DISCUSSION

Among 884 participants with high myopia in this study, we found that 4.1% - 5.9% of high myopes had BCVI and 0.2 - 0.6% had blindness based on BCVA under the WHO and US criteria. As for UCVA, the rate of VI and blindness was 72.6% and 27.3% using the WHO criteria and 17.9% and 82.1% using the US criteria, respectively. More severe fundus lesions, longer AL and larger CC were significant risk factors for both BCVI and UCVI.

Few researches have reported the rate of VI and blindness in high myopes. Shih et al²¹ included 552 high myopes in Taiwan and reported that the rate of BCVI was 10% in patients aged 40 to 59 and 56% in those older than 60. The Handan Eye Study found that in high myopes (SE < -5.0D), BCVI existed in 14 participants (24.6%) over 30 years of age using the WHO definition.²² The rate of BCVI was 4.1% in our study, which is much lower than that in the above two studies. This may be attributed to differences in the studied populations, since participants in our study were much younger (6-70 vs. >40 & >30 years old) when myopia and related pathologic changes were still likely to be progressing. We would expect to see a rise in BCVI in our study population as they continue to age. But with increasing public awareness and scientific advances in the treatment of high myopia around the world, myopia-related complications and BCVI will decrease in the future.

It's worth mentioning that the rate of blindness based on UCVA under US criteria was much higher than the WHO criteria (72.6% vs. 17.9%), which suggests that most subjects VA ranged from 20/60 to 20/200 and using a

different criterion for VI and blindness would have a significant impact on rate estimates. For UCVI, more studies are required to verify this. We need take precautions when comparing prevalence among different countries and regions. The US definition better reflects the visual demands of modern urban life, such as driving a car and viewing a screen, which require a higher level of vision and therefore require a stricter definition of VI.

Older age has been considered a major risk factor for BCVI in many studies,^{12,23} which is inconsistent with our study. The difference may be largely attributed to the skewed distribution of age in our population, since half of the population were under 19 years of age. Compared to patients with older age and longer duration of high myopia, young patients are less likely to develop myopic maculopathy which is one of the most important causes of vision impairment. What's more, age is significantly associated with ocular biometrics such as AL and ACD in the growth stage. Therefore, collinearity may severely affect the estimation for the relationship between age and visual impairment, evidenced by the fact that the association between age and BCVI became insignificant after adjusting ocular biometrics and the severity of fundus lesions. However, future follow-up studies are required to confirm this association.

In the present study, we found that the risk of BCVI in high myopia was 2.4 times higher in females than males ($p=0.048$). Some studies also revealed a stronger association between female and VI,²⁴ but not in others.^{23,25} A possible explanation is that Asian women tend to avoid direct sun exposure and spend more time performing near tasks indoors compared to men. Meanwhile, the effect of sex hormones on ocular structures may be another potential

mechanism. Estrogen is related to myopia progression, possibly due to scleral remodeling through metalloproteinases.²⁶ So higher prevalence of myopia and high myopia in woman are more likely related to higher VI.

A higher risk of myopic maculopathy or VI was associated with severe myopia levels among adults in other studies.^{27,28} Similarly, our findings indicate that individuals with more severe myopia have a higher risk of BCVI. Its rate increased markedly with higher levels of myopia.

AL was significantly associated with VI among high myopes, which has also been reported in previous studies.^{29,30} A number of reports have shown a negative relationship between AL and SE. A higher risk of myopic maculopathy, which can cause irreversible VI, was associated with greater myopic SE among adults.³⁰ AL reflects the sum of the anterior chamber depth (ACD), lens thickness (LT) and vitreous chamber depth (VCD). Research has shown that part of the heritability of AL is mediated by ACD.²⁰ So ACD and LT as two of the influencing factors were included in the analysis and were significantly associated with BCVI in the univariate logistic regression model. But they were not identified as a risk factor for BCVI in our study population. It is suggested that VCD has the greatest contributing effect, when individual components of AL are evaluated and this is also supported by previous studies.³¹ We found that a higher risk of BCVI was associated with larger CC in our study, which is similar to the study by Wu et al (CIEMS; 4711 adults).³² And AL/CR ratio is a strong predictor for BCVI in our study. The AL/CR ratio is a more robust measure of the refractive status of the eye because it minimizes the variability between them. Thus, it can be a useful marker of the onset and the progression

of myopia, especially among high myopia patients.³³ The correlation between AL and CC, SE and CC are strong and positive, while the correlation between AL/CR ratio and SE are negative. With the progression of myopia and AL elongation, corneal radius of curvature becomes steeper and corneal refractive power increases.³⁴

Age is an important factor for myopic maculopathy and therefore we analyzed the BCVA in two age subgroups, 7-39 yrs and older than 40 yrs.³⁰ We found that BCVI and blindness tended to be more common for patients older than 40 years of age than younger age group in C0, C1, C2 group both definitions. But in C3+C4 group of our study, a small number of total patients led us to fail to reach the same conclusion yet. In addition, our results indicated that severer myopic maculopathy group had more BCVI and blindness, similarly to other studies.^{27,28}

The presence of any myopic maculopathy was associated with BCVI in our study, which is supported by previous studies.^{27,30} It is the main risk factor of BCVI in myopic eyes. We also found that there is a non-linear increase in the risk of BCVI from C0 to C4. Morphologic changes in the posterior region of the eye, such as diffuse and localized chorioretinal atrophic lesions are often associated with choroidal thinning, making it susceptible to retinal degeneration, retinal holes, and choroidal neovascularization (CNV) and other fundus lesions which may result in loss of central vision. High myopes have thinner sclera that may be due to both reduced collagen synthesis and increased collagen degradation. All this suggests that prevention of VI requires more attention to myopic

macular retinopathy. Staphyloma presents more stretching of the macular lesion, which may explain the higher VI of more severe myopic maculopathy.³⁵

The strengths of this study include a large sample size of high myopes from South China, standardized methodology for data collection and comprehensive ophthalmic examinations including refraction, ocular biometry assessment and fundus photography. We employed the latest standardized International photographic classification and grading system classification¹⁸ to categorize myopic maculopathy, enhancing the comparability of other findings.³ Furthermore, the rate of VI and blindness was reported in detail using BCVA and UCVA under the WHO and US definitions, which provides a better understanding of the VI in high myopes.

There are several limitations of our study that should be taken into consideration. Firstly, our research was conducted based on a previous registry study rather than a population-based study. However, considering the low prevalence of high myopia in Southern China, a registry study is a relatively more efficient and cost-effective design to investigate risk factors for VI in high myopia. Secondly, specific causes of VI and blindness in highly myopic patients were not determined in this study. However, we tried to explore the risk factors of VI in respect to ocular structures and fundus lesions, which provides information on cause analysis. We found C0 to C4 were significantly associated with BCVI, which is supported by findings from previous studies.³⁰ We believe the main cause of BCVI to be pathological fundus lesions. Using the US definition, 94.1% of the study participants could achieve VA $\geq$ 20/40 with best refractive correction, meaning refractive error is the primary cause of UCVI.

Lastly, no additional variables such as educational level, family income, near work time were added to the analysis.

4.1 Conclusion

We observed high rate of UCVI and BCVI among high myopes in China, which is expected to increase with the aging population. Greater AL/CR ratio and more severe fundus lesions were associated with a higher risk of BCVI. Increased efforts are required to promote eye care services for high myopes who are at higher risk of VI.

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Table 1: Study population characteristics

Variables	Median	25%-75% Percentiles	Range
Male (%)	410 (46.4)		
Age (yrs)	18.5	14.2~27.6	7~70
SE (D)	-9.9	-11.0~-7.5	-23.9~-6.0
AL (mm)	27.4	26.3~28.2	23.8~34.3
CC (D)	43.7	42.8~44.8	38.6~50.5
AL/CR ratio	3.5	3.4~3.6	3.3~4.2
ACD (mm)	3.2	3.0~3.3	1.9~3.9
LT (mm)	3.6	3.4~3.8	2.8~5.5

D: Diopter; mm: millimeter; CC: Corneal Curvature; AL: Axial Length; SE: Spherical Equivalent; ACD: Anterior Chamber Depth; LT: Lens Thickness

AL/CR ratio: Axial Length (mm) / Corneal radius (mm)

Table 2: Rates of best-corrected visual impairment and blindness in better-seeing eye (Defined by WHO criteria and US criteria) by gender, age, spherical equivalent and axial length.

Group	Visual Acuity in the Better-Seeing Eye (WHO)						Visual Acuity in the better-Seeing Eye (US)					
	<20/400			<20/60 and ≥20/400			<20/200			<20/40 and ≥20/200		
	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P
Gender												
Male (n=410)	1	0.2 (0-0.7)	0.713	17	4.1 (2.2-6.1)	0.525	3	0.7 (0-1.6)	0.668	23	5.6 (3.4-7.8)	0.886
Female (n=474)	1	0.2 (0-0.6)		19	4.0 (2.2-5.8)		2	0.4 (0-1.0)		29	6.1 (4.0-8.3)	
Age												
7-18 (n=426)	0	0	0.101	4	0.9 (0-1.9)	<0.001	0	0	<0.001	12	2.8 (1.2-4.4)	0.001
19-39 (n=362)	1	0.3 (0-0.8)		23	6.4 (3.8-8.9)		1	0.3 (0-0.8)		32	8.8 (5.9-11.8)	
40+ (n=96)	1	1.0 (0-3.1)		9	9.4 (3.4-15.3)		4	4.2 (0-8.2)		7	7.3 (2.0-12.6)	
Spherical equivalent (D)												
-6.00 to -7.99 (n=299)	0	0	0.225	3	1.0 (0-2.2)	<0.001	0	0	0.091	3	1.0 (0-2.2)	<0.001
-8.00 to -9.99 (n=287)	0	0		2	0.7 (0-1.7)		1	0.3 (0-1.0)		4	1.4 (0-2.8)	
<-10.00 (n=294)	2	0.7 (0-1.6)		27	9.1(5.8-12.4)		4	1.3 (0-2.7)		41	13.8 (9.9-17.8)	
Missing(n=4)												
Axial Length (mm)												
<28.00 (n=620)	0	0		7	1.1 (0.3-2.0)		0	0		15	2.4 (1.2-3.6)	

28.00-29.99 (n=199)	0	0	14	7.1 (3.5-10.7)	2	1.0 (0-2.4)	17	8.6 (4.7-12.6)
≥30.00 (n=63)	2	3.0 (0-7.2)	15	22.4 (12.1-32.6)	3	4.5 (0-9.6)	20	29.9 (18.6-41.1)
Missing(n=2)								
		0.010		<0.001		0.001		<0.001
			1					
Total (N=884)	2	0.2 (0-0.5)	37	4.1 (2.8-5.4)	5	0.6 (0.1-1.1)	53	5.9 (4.3-7.4)

D: Diopter; WHO: World Health Organization criteria; US: United States criteria

Table 3: Rates of uncorrected visual impairment and blindness in better-seeing eye (Defined by WHO criteria and US criteria) by gender, age, spherical equivalent and axial length in ZOC-BHVI High Myopia Cohort Study.

Group	Visual Acuity in the Better-Seeing Eye (WHO)						Visual Acuity in the better-Seeing Eye (US)					
	<20/400			<20/60 and ≥20/400			<20/200			<20/40 and ≥20/200		
	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P
Gender												
Male (n=410)	116	28.3 (23.9-32.7)		294	71.7 (67.3-76.1)		331	80.7 (76.9-84.6)		79	19.3 (15.4-23.1)	
Female (n=474)	125	26.4 (22.4-30.4)		348	73.4 (69.4-77.4)		395	83.3 (80.0-86.7)		79	16.7 (13.3-20.0)	
			0.545			0.597			0.333			0.333
Age												
7-18 (n=426)	76	17.8 (14.2-21.5)		349	81.9 (78.3-85.6)		323	75.8 (71.7-79.9)		103	24.2 (20.1-28.3)	
19-39 (n=362)	134	37.0 (32.0-42.0)		228	63.0 (58.0-68.0)		320	88.4 (85.1-91.7)		42	11.6 (8.3-14.9)	

40+ (n=96)	31	32.3 (22.8-41.8)		65	67.7 (58.2-77.2)		83	86.5 (79.5-93.4)		13	13.5 (6.6-20.5)	
			<0.00			<0.00			<0.00			<0.00
			1			1			1			1
Spherical equivalent (D)												
-6.00 to -7.99 (n=299)	44	14.8 (10.8-18.9)		252	84.8 (80.7-88.9)		215	72.4 (67.3-77.5)		82	27.6 (22.5-32.7)	
-8.00 to -9.99 (n=287)	61	21.3 (16.6-26.1)		225	78.7 (73.9-83.4)		239	83.6 (79.2-87.9)		47	16.4 (12.1-20.8)	
<-10.00 (n=294)	133	44.8 (39.1-50.5)		164	55.2 (49.5-60.9)		268	90.2 (86.8-93.6)		29	9.8 (6.4-13.2)	
Missing(n=4)												
			<0.00			<0.00			<0.00			<0.00
			1			1			1			1
Axial Length (mm)												
<28.00 (n=620)	122	19.7 (16.6-22.9)		495	80.1 (76.9-83.3)		486	78.6 (75.4-81.9)		132	21.4 (18.1-24.6)	
28.00-29.99 (n=199)	75	38.1 (31.2-44.9)		122	61.9 (55.1-68.8)		172	87.3 (82.6-92.0)		25	12.7 (8.0-17.4)	
≥30.00 (n=63)	42	62.7 (50.8-74.6)		25	37.3 (25.4-49.2)		66	98.5 (95.5-100.0)		1	1.5 (0-4.5)	
Missing(n=2)												
			<0.00			<0.00			<0.00			<0.00
			1			1			1			1
Total (N=884)	241	27.3 (24.3-30.2)		642	72.6 (69.7-75.6)		726	82.1 (79.6-84.7)		158	17.9 (15.3-20.4)	

D: Diopter; WHO: World Health Organization criteria; US: United States criteria

Table 4: Logistic regression analysis of risk factors for visual impairment. (BCVA<20/60 and ≥20/400, WHO; BCVA<20/40 and ≥20/200)

Factors	WHO		US	
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	Univariate model		Adjusted Model †		Multiple regression		Univariate model		Adjusted Model †		Multiple regression	
	OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
Age, yrs	1.047	<0.001	1.047	<0.001	0.99	0.788	1.024	0.011	1.024	0.012	0.968	0.148
Male	0.965	0.918	0.915	0.798	0.488	0.100	1.097	0.749	1.057	0.845	0.735	0.388
Spherical Equivalent (D)	0.721	<0.001	0.729	<0.001	-	-	0.730	<0.001	0.725	<0.001	-	-
Axial Length (mm)	1.882	<0.001	1.772	<0.001	-	-	1.777	<0.001	1.787	<0.001	-	-
Corneal Curvature (D)	1.438	0.001	1.449	0.002	-	-	1.369	<0.001	1.371	0.001	-	-
AL/CR ratio	310.923	<0.001	228.527	<0.001	67.765	<0.001	231.59	<0.001	271.43	<0.001	58.763	<0.001
Anterior Chamber Depth (mm)	0.182	0.005	0.412	0.198	0.310	0.213	0.380	0.064	0.579	0.345	0.590	0.498
Lens Thickness (mm)	5.046	<0.001	3.042	0.154	1.984	0.864	2.977	0.002	3.188	0.084	1.510	0.648
Fundus grading												
C0	Ref				Ref		Ref		Ref		Ref	
C1	9.708	0.006	9.145	0.008	5.339	0.050	34.335	0.007	4.717	0.005	3.044	0.049
C2	35.685	<0.001	32.709	<0.001	6.288	0.023	19.007	<0.001	21.347	<0.001	5.985	0.002
C3 +C4	151.985	<0.001	132.757	<0.001	26.665	0.001	50.264	<0.001	63.132	<0.001	10.534	0.004
Staphyloma	9.552	<0.001	6.511	<0.001	-	-	9.005	<0.001	9.770	<0.001	-	-
D: Diopter												

† Adjusted by age, gender

‡ Adjusted by age, gender, AL/CR ratio, anterior chamber depth, lens thickness, fundus grading.

Figure 1: BCVA in different myopic maculopathy lesion categories under WHO and US definitions

Supplementary table 1: Rates of uncorrected visual impairment and blindness in worse-seeing eye (Defined by WHO criteria and US criteria) by gender, age, spherical equivalent and axial length.

Group	Visual Acuity in the Worse-Seeing Eye (WHO)						Visual Acuity in the Worse -Seeing Eye (US)					
	<20/400			<20/60 and ≥20/400			<20/200			<20/40 and ≥20/200		
	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P
Gender												
Male (n=410)	166	40.5 (35.7-45.3)		244	59.5 (54.7-64.3)		370	90.2 (87.4-93.1)		79	19.3 (15.4-23.1)	
Female (n=474)	199	42.0 (37.5-46.4)		274	57.8 (53.3-62.3)		424	89.5 (86.7-92.2)		79	16.7 (13.3-20.0)	
			0.652			0.608			0.698			0.333
Age												
7-18 (n=426)	127	29.8 (25.5-34.2)		298	69.9 (65.6-74.3)		361	84.7 (81.3-88.2)		103	24.2 (20.1-28.3)	
19-39 (n=362)	187	51.7 (46.5-56.8)		175	48.3 (43.2-53.5)		344	95.0 (92.8-97.3)		42	11.6 (8.3-14.9)	
40+ (n=96)	51	53.1 (43.0-63.3)		45	46.9 (36.7-57.0)		89	92.7 (87.4-98.0)		13	13.5 (6.6-20.5)	
			<0.001			<0.001			<0.001			<0.001
Spherical equivalent (D)												
-6.00 to -7.99 (n=299)	77	25.8 (20.8-30.7)		221	73.9 (68.9-78.9)		247	82.6 (78.3-86.9)		82	27.6 (22.5-32.7)	
-8.00 to -9.99 (n=287)	109	38.0 (32.3-43.6)		178	62.0 (56.4-67.7)		264	92.0 (88.8-95.1)		47	16.4 (12.1-20.8)	
<-10.00 (n=294)	176	59.9 (54.2-65.5)		118	40.1 (34.5-45.8)		279	94.9 (92.4-97.4)		29	9.8 (6.4-13.2)	
Missing(n=4)			<0.001			<0.001			<0.001			<0.001
			1			1			1			1

Axial Length (mm)										
<28.00 (n=620)	205	33.0 (29.3-36.7)		415	66.8 (63.1-70.5)		540	87.0 (84.3-89.6)		132 21.4 (18.1-24.6)
28.00-29.99 (n=199)	107	54.0 (47.0-61.0)		91	46.0 (39.0-53.0)		189	95.5 (92.5-98.4)		25 12.7 (8.0-17.4)
≥30.00 (n=63)	51	81.0 (71.0-90.9)		12	19.0 (9.1-29.0)		63	100.0 (100.0-100.0)		1 1.5 (0-4.5)
Missing(n=2)										
			<0.00			<0.00			<0.00	<0.00
			1			1			1	1
Total (N=884)	365	41.3 (38.0-44.5)		518	58.6 (55.3-61.9)		794	89.8 (87.8-91.8)		158 17.9 (15.3-20.4)

Supplementary table 2: Rates of best-corrected visual impairment and blindness in worse-seeing eye (Defined by WHO criteria and US criteria) by gender, age, spherical equivalent and axial length in ZOC-BHVI High Myopia Cohort Study.

Group	Visual Acuity in the Worse -Seeing Eye (WHO)						Visual Acuity in the Worse -Seeing Eye (US)					
	<20/400			<20/60 and ≥20/400			<20/200			<20/40 and ≥20/200		
	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P	No.	% (95% CI)	P
Gender												
Male (n=410)	3	0.7 (0-1.6)	0.858	37	9.0 (6.2-11.8)	0.729	7	1.7 (0.4-3.0)	0.587	56	13.7 (10.3-16.9)	0.946
Female (n=474)	3	0.6 (0-1.3)		46	9.7 (7.0-12.4)		6	1.3 (0.3-2.3)		64	13.5 (10.4-16.6)	
Age												
7-18 (n=426)	2	0.5 (0-1.1)	0.008	13	3.1 (1.4-4.7)	<0.001	3	0.7 (0-1.5)	<0.001	32	7.5 (5.0-10.0)	<0.001
19-39 (n=362)	1	0.3 (0-0.8)		50	13.8(10.2-17.4)		2	0.6 (0-1.3)		62	17.1 (13.2-21.0)	
40+ (n=96)	3	3.1 (0-6.7)		20	20.8 (12.6-29.1)		8	8.3 (2.7-14.0)		26	27.1 (18.0-36.1)	
Spherical equivalent (D)												
-6.00 to -7.99 (n=299)	0	0		5	1.7 (0.2-3.1)	1	0	0	1	10	3.3 (1.3-5.4)	
-8.00 to -9.99 (n=287)	2	0.7 (0-1.7)		8	2.8 (0.9-4.7)		4	1.4 (0-2.8)		17	5.9 (3.2-8.7)	
<-10.00 (n=294)	4	1.4 (0-2.7)		66	22.4(17.7-27.2)		7	2.4 (0.6-4.1)		91	31.0 (25.6-36.3)	
Missing(n=4)												

			0.251		<0.001					<0.001
					1				1	
Axial Length (mm)										
<28.00 (n=620)	2	0.3 (0-0.8)	25	4.0 (2.5-5.6)	3	0.5 (0-1.0)	47	7.6 (5.5-9.7)		
28.00-29.99 (n=199)	2	1.0 (0-2.4)	32	16.2 (11.0-21.3)	5	2.5 (0.3-4.7)	45	22.7 (16.9-28.6)		
≥30.00 (n=63)	2	3.2 (0-7.6)	26	41.3 (28.8-53.8)	5	7.9 (1.1-14.8)	28	44.4 (31.8-57.1)		
Missing(n=2)										
			0.062		<0.001				<0.001	
					1				1	
Total (N=884)	6	0.7 (0.1-1.2)	83	9.4 (7.5-11.3)	13	1.5 (0.7-2.3)	120	13.6 (11.3-15.8)		

D: Diopter; WHO: World Health Organization criteria; US: United States criteria

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