Ophthalmol Ther (2023) 12:3159–3175
https://doi.org/10.1007/s40123-023-00802-0

ORIGINAL RESEARCH

# Clinical Features of Fundus Tessellation and Its Relationship with Myopia: A Systematic Review and Meta-analysis

Xuan-Yu Chen · Hai-Long He · Jie Xu · Yi-Xin Liu · Zi-Bing Jin

Received: July 28, 2023 / Accepted: August 22, 2023 / Published online: September 21, 2023


## ABSTRACT

***Introduction***: This study aims to assess the existing literature on fundus tessellation (FT), focusing on its prevalence, associated factors, distribution, and progression.

***Methods***: Systemic methods were employed to search and gather published literature on FT from databases such as the National Library of Medicine (PubMed), Web of Science (WOS), and Elsevier on July 1, 2023. The quality of the studies was evaluated using the Newcastle–Ottawa Scale (NOS) and the Healthcare Research and Quality (AHRQ) criteria. A meta-analysis was conducted to compare tessellated and normal fundus with respect to age, gender, axial length, and spherical equivalent.

***Results***: The systematic review included 23 articles, encompassing a total of 3053 eyes in the meta-analysis. The prevalence of FT varied from 43.00 to 94.35%. The severity of FT was significantly associated with older age, male sex, lower body weight index, longer axial length, larger peripapillary atrophy, thinner choroid, thinner sclera, and larger corneal radius of curvature, suggesting a potential progression pattern. Notably, FT was observed predominantly in the macular and peripapillary regions. The meta-analysis revealed that tessellated fundus tended to be associated with older age (mean difference [MD] 4.76, 95% confidence interval [CI] 1.71–7.80, $P < 0.01$), longer axial length (MD 0.86, 95% CI 0.70–1.02, $P < 0.01$), and a lower spherical equivalent (MD − 1.16, 95% CI − 1.68 to 0.65, $P < 0.01$) compared to normal fundus. However, there was no significant difference in the proportion of males between individuals with tessellated and normal fundus (odds ratio [OR] 1.12, 95% CI 0.89–1.42, $P = 0.32$).

***Conclusions***: Overall, this systematic review and meta-analysis shed light on the prevalence, characteristics, and factors associated with FT, offering valuable insights for clinicians and researchers in the field of ophthalmology.

***Study Registration***: The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023442486).

Xuan-Yu Chen and Hai-Long He contributed equally to this work.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s40123-023-00802-0.

X.-Y. Chen · H.-L. He · J. Xu · Y.-X. Liu · Z.-B. Jin (✉)
Beijing Institute of Ophthalmology, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing 100005, China
e-mail: jinzibing@foxmail.com

**Keywords:** Fundus tessellation; Prevalence; Disease progression; Myopic maculopathy; Meta-analysis

**Key Summary Points**

***Why carry out this study?***

As an initial stage of myopic maculopathy, fundus tessellation holds the potential to serve as an indicator for subsequent myopic fundus changes. Previous studies have explored various aspects of fundus tessellation, including its prevalence, associated factors, distribution, and progression patterns of this condition.

In this study, we conducted a systematic review and meta-analysis to assess the prevalence, identify associated factors, analyze different locations of fundus tessellation, and examine its progression. This comprehensive investigation aims to enhance our understanding of fundus tessellation and illuminate its clinical implications.

***What was learned from the study?***

These results suggest that the prevalence of fundus tessellation varies significantly based on population characteristics. Furthermore, when compared with a normal fundus, a tessellated fundus exhibits several notable differences, including an older age demographic, longer axial length, and lower spherical equivalent.

The study could serve as a crucial resource for better understanding and treatment strategies in the realm of myopic maculopathy.

## INTRODUCTION

Fundus tessellation (FT) is a phenomenon characterized by the increased visibility of large choroid vessels surrounding the fovea and arcade vessels, accompanied by thinning of the retinal epithelium and choriocapillaris [1]. This condition holds the potential to serve as an indicator for subsequent myopic fundus changes [1], and the choroid assumes a crucial role in providing an elevated flow rate to fulfill the metabolic demands of the retina, particularly the photoreceptor layer, thus resulting in an abundance of blood vessels in this region [2]. Extensive research has been conducted on FT, ranging from the successful identification of associated factors to the development of reliable quantitative evaluation methods [3–19]. Nonetheless, it is essential to note that the current literature on FT exhibits significant variations in terms of content and research direction, and there may also be conflicting outcomes reported across different studies.

Several studies have been conducted to obtain a quantitative assessment of FT, focusing on specific characteristics, particularly choroidal thickness. Yoshihara et al. proposed a method for objective analysis of tessellation degree and choroidal thickness using the tessellated fundus index. Their approach involved detecting a circular area of 250-pixel diameter between the fovea and the optic disc, based on an initial study that revealed the most prominent changes in tessellation within this detected region [9]. Fang et al. conducted a study on the diagnostic criteria for different stages of myopic maculopathy using optical coherence tomography (OCT). They utilized choroidal thickness measurements for each type of myopic maculopathy and concluded that progressive and continuous choroidal thinning played a pivotal role in the transition from no maculopathy to tessellation and subsequently to diffuse atrophy [10]. Shao et al. employed artificial intelligence to quantitatively assess fundus tessellated density and related factors in fundus images. Their findings indicated that fundus tessellated density could serve as a promising new quantitative biomarker for subfoveal choroidal thickness, thereby holding potential for widespread use in population screening [16]. These studies contribute significantly to the advancement of knowledge concerning FT and choroidal thickness analysis, potentially

enhancing early detection and understanding of myopic maculopathy.

As a category of myopic maculopathy proposed by the International Photographic Classification and Grading System for myopic maculopathy, fundus tessellation has been identified as a relatively stable stage in comparison to other myopic maculopathies, such as diffuse chorioretinal atrophy, patchy chorioretinal atrophy, and macular atrophy, and these conditions can lead to irreversible visual impairment, imposing significant burdens on both patients and society [1]. In light of the aforementioned considerations, this systematic review will specifically focus on the distinctive differences between normal fundus and tessellated fundus. Furthermore, the review will explore the unique characteristics and progression patterns of FT compared to other myopic maculopathies. The primary objectives of this review encompass evaluating the prevalence, identifying associated factors, analyzing the distribution of FT, and examining its progression. To achieve these objectives, a rigorous systematic review and meta-analysis of existing literature will be conducted, enabling a comprehensive synthesis of current knowledge on FT. This comprehensive investigation aims to deepen our understanding of FT and shed light on its clinical implications.

# METHODS

## Study Protocol

We completed our systematic review followed by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023442486), on July 15, 2023. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

## Inclusion and Exclusion Criteria

Types of studies included cohort study, case series study, and cross-sectional study. Subjects included normal subjects, patients with FT, and other patients with myopic maculopathy. Outcome indicator: age, gender, axial length (AL), spherical equivalent (SE), or refractive error (RE). Exclusion criteria: studies for which data could not be accurately extracted or data were missing, and for duplicate published studies, the study reporting the most comprehensive data was selected.

## Search and Selection Criterion

We searched PubMed, Web of Science, and Elsevier on July 1, 2023. For PubMed, the search strategy was (Fundus Tessellation) AND ("Cohort Studies"[Mesh] OR "Prevalence"[Mesh] OR "Incidence"[Mesh] OR "Case–Control Studies"[Mesh] OR "Cross-Sectional Studies"[Mesh]) AND ("Myopia"[Mesh] OR "Myopia Degenerative"[Mesh]). In the Web of Science search engine, the search strategy was TS = (Fundus Tessellation) AND (TS = (Cohort Studies) OR TS = (Prevalence) OR TS = (Incidence) OR TS = (Case–Control Studies) OR TS = (Cross-Sectional Studies)) AND (TS = ( Myopia) OR TS = (Myopia Degenerative)). In Elsevier search strategy, the search strategy was fundus tessellation AND (Cohort Studies OR Prevalence OR Incidence OR Case–Control Studies OR Cross-Sectional Studies) AND (Myopia OR Myopia Degenerative). We also searched the reference lists of articles identified by this search strategy and selected those relevant articles based on the quality of the data. Review articles, meta-analyses, and summary articles were also included to provide readers with more details.

First, we excluded certain articles based on their titles and abstracts. Next, we thoroughly read the full texts of the remaining articles to ascertain if they met the criteria, and duplicate articles were removed. Following this, we imported the essential information of the remaining articles into Table 1.

### Literature Screening and Data Extraction

Two researchers independently screened the literature and then extracted and cross-checked the data (XY C and HL H). If there was any disagreement, the dispute was resolved by discussion, or the third researcher would assist with the judgment (J X). For literature that lacked information, efforts were made to contact the original authors to obtain the necessary data for supplementation. The extracted data included the following: basic information about the included studies, such as the first author's name, publication year, and study type; basic characteristics of the subjects, including the number of subjects and relevant information about them, such as age, AL, and RE; main data of interest and key elements of bias risk assessment.

### Assessment of the Quality of the Study

Since the original studies included in our research were all observational studies, encompassing cohort, case series, and cross-sectional designs, we utilized the Newcastle–Ottawa Scale (NOS) to assess the quality of the cohort and case series studies, and SELECTION, COMPARABILITY, and EXPOSURE were used to evaluate the quality. A study with a score higher than 6 could be included for meta-analysis, more than 7 will be considered as being of high quality. The Agency for Healthcare Research and Quality (AHRQ) was used to assess the following aspects of the cross-sectional study [20] and detailed information of ARHQ was presented in the Supplementary Materials. In case of any disagreements among researchers regarding individual ratings, a consensus will be reached through discussions involving the third reviewer (J X).

### Statistics and Analysis

RevMan 5.3 statistical software was used for meta-analysis. For the outcome indicator of sex, which was a dichotomous variable, we utilized the odds ratio (OR) as the effect indicator for analysis, and for the outcome indicators of age, AL, and RE, which were continuous variables, we used the mean difference (MD) as the effect indicator. For each effect size, we provided the point estimate along with its corresponding 95% confidence intervals (CI). This approach allowed us to appropriately analyze and present the results for these continuous outcome measures. The median, maximum, and minimum data mentioned in the included studies were transformed according to the formula and then combined for analysis [21, 22]. The heterogeneity of the included studies was analyzed by $\chi^2$ test ($\alpha = 0.1$) and evaluated by $I^2$ statistic. If the heterogeneity test result $I^2 > 50\%$, it indicated that there was statistical heterogeneity among the results of each study and implemented the removal of studies with notably elevated heterogeneity. Egger's test was further tested for publication bias by the R program when needed. A $P$ value $< 0.05$ was considered statistically significant.

## RESULTS

### Characteristics of the Included Articles

According to our systematic retrieval, we obtained 33 articles from PubMed, 30 articles from Web of Science, and 83 articles from Elsevier, making a total of 146 articles. After a rigorous screening process based on the titles and abstracts, we excluded a total of 104 articles that did not meet the inclusion criteria. After removing duplicates, we were left with 38 articles, for which we retrieved the full-text articles for further detailed screening and evaluation. During this process, we made efforts to contact the authors via e-mail to obtain the missing information. However, we faced challenges as only a few e-mails were answered. Ultimately, we identified 23 articles that specifically mentioned the prevalence of tessellated fundus, which was the primary focus of our study. The flow chart of the selection process is shown in Fig. 1. Seven articles contained detailed information on both normal fundus and tessellated fundus cases, resulting in a total of 3053 eyes being included in our meta-analysis. The sample sizes in the seven studies varied, ranging

**Table 1** Characteristics of included studies

| Study ID | Type | Purpose of study | Race | No | Participants | Prevalence of FT (%) |
|---|---|---|---|---|---|---|
| Hayashi et al. 2010 | Case series study | To investigate the long-term progression pattern of myopic maculopathy and to determine the visual prognosis of each progression stage | Japanese | 806 eyes | Age: 41.1 ± 16.7<br>AL: 28.7 ± 1.9<br>RE: − 13.4 ± 4.9 | 34.24 |
| Chen et al. 2012 | Case series study | To describe the severity and morphological features of high myopic maculopathy in Chinese patients and to evaluate their association with age, refractive error, and visual acuity | Chinese | 604 eyes | Age: 40.6 ± 17.1<br>AL: missing<br>RE: − 11.40 ± 4.80 | 9.27 |
| Koh et al. 2013 | Case series study | This study describes the pathologic changes in the retina of a group of young Asian subjects with myopia worse than – 10 diopters spherical equivalent (SE) refraction | Chinese/ Indian | 21 eyes | Age: 21.8 ± 1.3<br>AL: 27.43 ± 1.20<br>RE: − 10.88 ± 1.28 | 85.71 |
| Yoshihara et al. 2014 | Cross-sectional study | We determined the degree of tessellation in fundi objectively in normal, non-pathological myopic eyes, and correlated the degree of tessellation and the choroidal thickness (CT) and axial length (AL) | Japanese | 100 eyes | Age: 25.8 ± 3.9<br>AL: 25.3 ± 1.4<br>RE: − 4.6 ± 3.3 | 43.00 |
| Terasaki et al. 2016 | Cross-sectional study | To determine the locations of the tessellations in the ocular fundus of young healthy eyes, and to determine relationships between their locations and morphological parameters of the eyes | Japanese | 126 eyes | Age: 26.0 ± 4.1<br>AL: 25.43 ± 1.45<br>RE: − 4.71 ± 3.41 | 65.08 |

**Table 1** continued

| Study ID | Type | Purpose of study | Race | No | Participants | Prevalence of FT (%) |
|---|---|---|---|---|---|---|
| Yokoi et al. 2016 | Case series study | To search for a morphologic biomarker to differentiate between pathologic myopia and simple childhood myopia | Japanese | 56 eyes | Age: 10.2 ± 3.6 to 36.0 ± 7.6<br>AL: 27.0 ± 1.4 to 29.7 ± 2.0<br>RE: − 9.6 ± 4.8 to − 16.6 ± 4.5 | 33.93 |
| Zhou et al. 2018 | Cross-sectional study | To investigate the choroidal thickness (CT) and retinal thickness (RT) in highly myopic tessellated eyes | Chinese | 115 eyes | Age: older than 18 years<br>AL: missing<br>RE: worse than − 6 D | 80.87 |
| Choudhury et al. 2018 | Cross-sectional study | To characterize and provide population-based prevalence estimates of myopic degeneration (MD) among Chinese Americans, the fastest-growing minority population in the United States in the last decade | Chinese American | 1519 patients | Age: 50 years and older<br>AL: missing<br>RE: missing | 31.73 |
| Xiao et al. 2018 | Cohort study | The purpose of this study was to document the distribution of the severity of myopic maculopathy in a cohort of patients that are highly myopic and to explore the associated risk factors | Chinese | 884 eyes | Age: 7 to 70<br>AL: missing<br>RE: − 6 D or worse in both eyes | 20.02 |
| Yan et al. 2018 | Cross-sectional study | To investigate the progression pattern of myopic maculopathy and associated factors in a population-based study | Chinese | 110 eyes | Age: 56.2 ± 9.5<br>AL: 26.8 ± 2.0<br>RE: − 9.53 ± 3.68 | 71.82 |

**Table 1** continued

| Study ID | Type | Purpose of study | Race | No | Participants | Prevalence of FT (%) |
|---|---|---|---|---|---|---|
| Yamashita et al. 2018 | Cross-sectional study | Tessellation of the ocular fundus is commonly found at a mild stage in myopic eyes, and their locations vary among individuals. We conducted this study to determine the distribution of tessellation locations in a population study | Japanese | 1670 eyes | Age: 53.6 ± 10.3<br>AL: 23.50 ± 0.88<br>RE: − 0.14 ± 1.62 | 45.45 |
| Wong et al. 2018 | Cohort study | To examine the progression pattern of disc and retinal lesions in highly myopic Chinese adolescents over a 10-year period in Singapore | Chinese | 88 eyes | Age: 14.0 ± 1.0 to 24.0 ± 1.0<br>AL: 25.8 ± 1.0 to 26.5 ± 1.0<br>RE: − 6.2 ± 1.3 to − 7.5 ± 1.8 | 54.55 |
| Fang et al. 2019 | Cross-sectional study | To analyze the choroidal thickness (CT) of each type of myopic maculopathy, and to establish an OCT-based classification of myopic maculopathy | Japanese | 1487 eyes | Age: 58.4 ± 16.3<br>AL: 29.87 ± 1.99<br>RE: − 13.2 ± 4.0 | 17.89 |
| Hopf et al. 2019 | Cross-sectional study | To determine the prevalence of myopic maculopathy in the general population in Germany and to analyze potential associations with ocular and systemic factors | German | 801 eyes | Age: 51.0 ± 9.77<br>AL: missing<br>RE: ≤ − 6 D | 55.31 |
| Wong et al. 2019 | Case series study | To characterize the choriocapillaris (CC) in highly myopic eyes with myopic maculopathy, using optical coherence tomographic angiography | Singaporean | 42 eyes | Age: 59.2 ± 11.0<br>AL: 28.69 ± 1.89<br>RE: − 10.09 ± 4.23 | 40.48 |
| Li et al. 2019 | Cohort study | To evaluate the 2-year changes in myopic maculopathy and its associations in highly myopic eyes | Chinese | 657 eyes | Age: 21.6 ± 12.2<br>AL: 27.55 ± 1.56<br>RE: − 10.18 ± 3.38 | 20.40 |

**Table 1** continued

| Study ID | Type | Purpose of study | Race | No | Participants | Prevalence of FT (%) |
|---|---|---|---|---|---|---|
| Guo et al. 2019 | Cross-sectional study | To determine the prevalence of fundus tessellation and associations with ocular and systemic parameters among junior students from Greater Beijing | Chinese | 1430 eyes | Age: 12.7 ± 0.71<br>AL: 24.48 ± 1.17<br>RE: − 2.39 ± 2.17 | 48.11 |
| Zhao et al. 2020 | Case series study | To investigate the morphological feature, visual acuity, and prevalence of macular complications in highly myopic eyes with different categories of myopic maculopathy (MM) according to the META-PM classification system | Chinese | 1841 eyes | Age: 18 years and older<br>AL: ≥ 26.5 mm<br>RE: ≤ − 6.0 D | 42.31 |
| Lyu et al. 2021 | Cross-sectional study | To explore the characteristics and associated factors of fundus tessellation, especially the alternation of choroidal thickness among different degrees of tessellated fundus in young adults | Chinese | 796 eyes | Age: 19.82<br>AL: 25.27<br>RE: − 4.18 | 90.20 |
| He et al. 2021 | Cross-sectional study | To describe the methodology and pilot data of the Shanghai Child and Adolescent Large-scale Eye Study (SCALE-HM) | Chinese | 134 eyes | Age: 12.32 ± 3.14<br>AL: 26.91 ± 1.07<br>RE: − 9.40 ± 1.77 | 50.00 |
| Shao et al. 2021 | Cross-sectional study | This study aimed to quantitative assess the fundus tessellated density (FTD) and associated factors on the basis of fundus photographs using artificial intelligence | Chinese | 3468 eyes | Age: 64.1 ± 9.7<br>AL: 23.22 ± 1.09<br>RE: − 0.13 ± 1.96 | 88.64 |
| Cheng et al. 2021 | Cross-sectional study | To investigate the prevalence and associated factors of fundus tessellation in highly myopic children and adolescents | Chinese | 513 eyes | Age: 13.47 ± 3.13<br>AL: 26.63 ± 1.04<br>RE: − 8.34 ± 1.91 | 94.35 |

**Table 1** continued

| Study ID | Type | Purpose of study | Race | No | Participants | Prevalence of FT (%) |
|---|---|---|---|---|---|---|
| Gong et al. 2022 | Cross-sectional study | To assess the role of the corneal radius of curvature (CR) in the identification of fundus tessellation in children with low myopia | Chinese | 1127 people | Age: 10.29 ± 0.60<br>AL: 24.17 ± 0.74<br>RE: − 1.44 ± 0.69 | 52.44 |

*AL* axial length, *RE* refractive error, *FT* fundus tessellation, *D* diopter, *CT* choroidal thickness, *SE* spherical equivalent, *RT* retinal thickness, *MD* myopic degeneration, *CC* choriocapillaris, *MM* myopic maculopathy, *FTD* fundus tessellated density, *CR* curvature

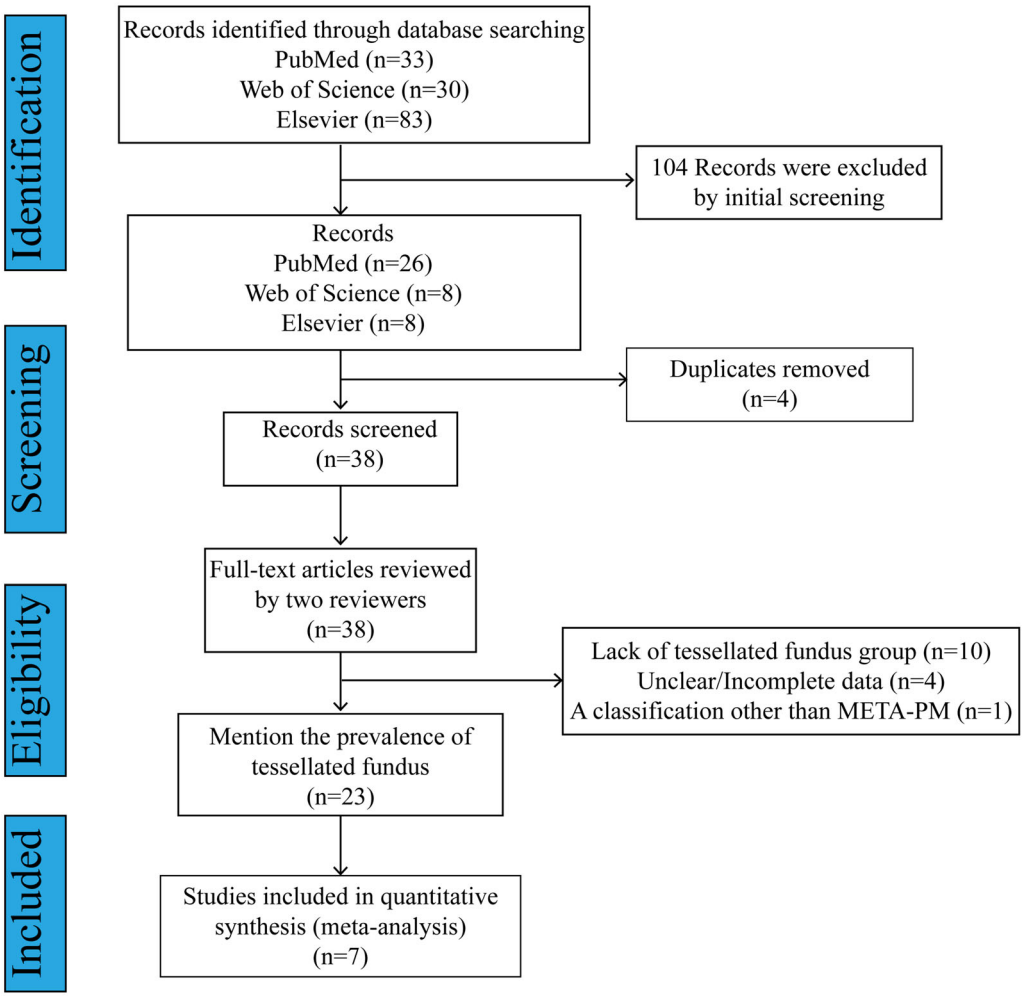



**Fig. 1** PRISMA flowchart of studies included in this review and meta-analysis

**Table 2** Quality of the included studies assessed by Newcastle–Ottawa Scale

| Study | Year of publication | SELECTION (4) | COMPARABILITY (2) | OUTCOME (3) | NOS Score (9) |
|---|---|---|---|---|---|
| Cohort study | | | | | |
| Xiao et al. | 2018 | 4 | 1 | 3 | 8 |
| Wong et al. | 2018 | 3 | 1 | 3 | 7 |
| Li et al. | 2019 | 3 | 2 | 3 | 8 |
| **Study** | **Year of publication** | **SELECTION (4)** | **COMPARABILITY (2)** | **EXPOSURE (2)** | **NOS Score (8)** |
| Case series study | | | | | |
| Hayashi et al. | 2010 | 3 | 1 | 2 | 6 |
| Chen et al. | 2012 | 3 | 1 | 2 | 6 |
| Koh et al. | 2013 | 3 | 2 | 2 | 7 |
| Yokoi et al. | 2016 | 3 | 2 | 2 | 7 |
| Wong et al. | 2019 | 3 | 2 | 2 | 7 |
| Zhao et al. | 2020 | 3 | 2 | 2 | 7 |

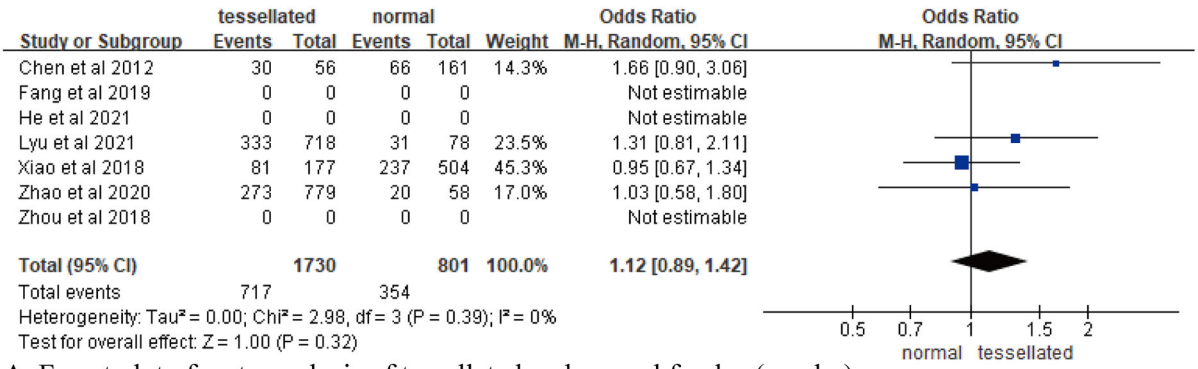
from 115 to 837 eyes. These studies were conducted in two countries, with six studies conducted in China and one in Japan. The assessment of the quality of the study is summarized in Table 2 and Supplementary Table 1.

## Prevalence of Fundus Tessellation

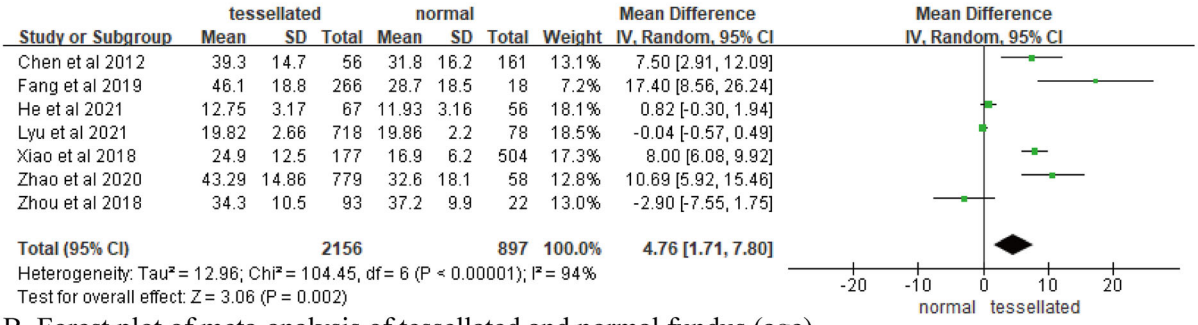
The current studies on FT primarily focus on population-based studies and retrospective, observational case series. In Table 1, we have summarized the various studies on FT, including the basic participant information, the number of participants, the prevalence of FT, and the purpose of each study [3–19, 23–28]. Some studies included other myopic maculopathies, such as diffuse atrophy and patchy lesions, where the reported prevalence of FT represented FT only [5, 6, 8, 10, 12, 14, 15, 18, 19, 23, 26–28], while other studies specifically focused on comparing tessellated fundus and normal fundus cases [3, 4, 7, 9, 11, 13, 16, 17, 24, 25].

The prevalence of FT varied among the studies based on normal fundus and tessellated fundus, ranging from 43.00 to 94.35%. Interestingly, there was a difference in the prevalence of FT observed among different regions based on Table 1 from different articles. Studies conducted in China consistently demonstrate a higher prevalence of FT (71.82%, age 56.2 ± 9.5 years old) compared to other regions such as Japan (45.45%, age 53.6 ± 10.3 years old) and Germany (55.31%, age 59.2 ± 11.0 years old) within a similar age range [3, 4, 9, 10, 13, 14, 16, 24, 25].

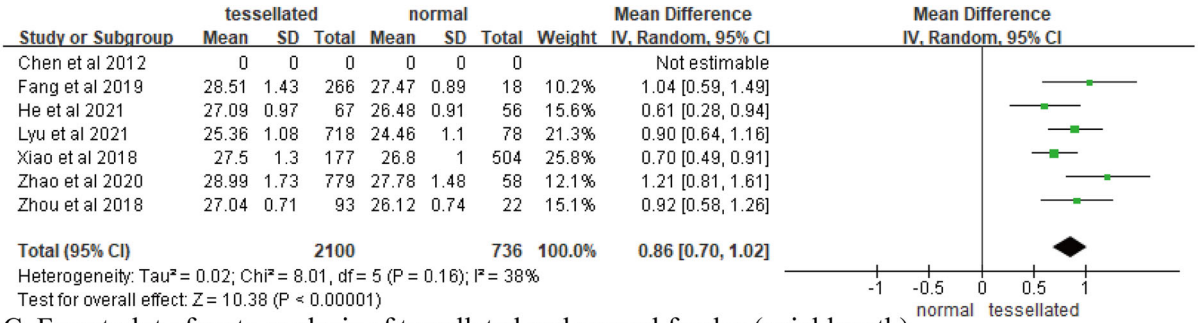
Meanwhile, one interesting observation is that the prevalence of FT in some adolescents was higher than that in the elderly. For instance, studies conducted by Cheng et al. and Shao et al. in China found that the prevalence of FT in adolescents (mean age 13.47 ± 3.13 years, age range 4–19 years) and the elderly (mean age 64.1 ± 9.7 years, age range 50–93 years) was 94.35 and 88.64%, respectively [13, 16]. This suggests that environmental factors may play a crucial role in the prevalence of FT. Additionally, myopia was found to have a significant influence on FT [13, 17]. Two studies on this topic found that the prevalence of FT in children with myopia



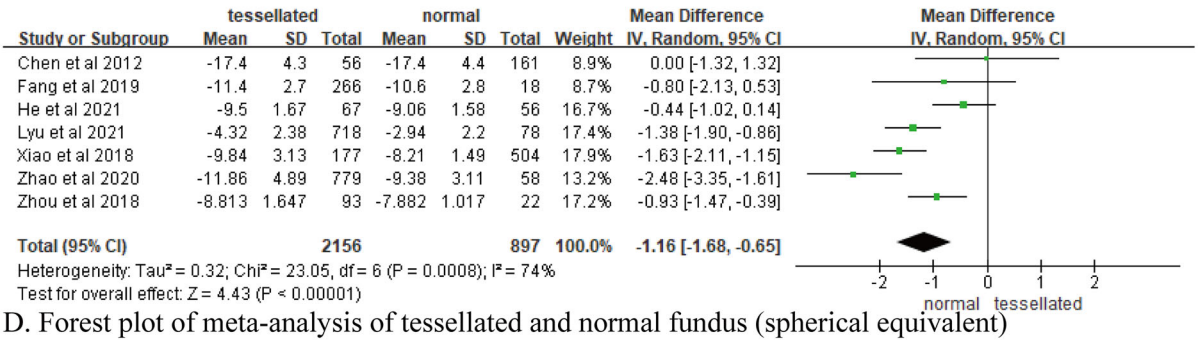

A. Forest plot of meta-analysis of tessellated and normal fundus (gender)




B. Forest plot of meta-analysis of tessellated and normal fundus (age)




C. Forest plot of meta-analysis of tessellated and normal fundus (axial length)




D. Forest plot of meta-analysis of tessellated and normal fundus (spherical equivalent)

**Fig. 2** Forest plot of meta-analysis of tessellated and normal fundus with respect to **A** gender, **B** age, **C** axial length, and **D** spherical equivalent. *CI* confidence interval, *SD* standard deviation

was significantly lower than that in highly myopic children (94.35 and 52.44%, respectively) [13, 17]. These findings suggest that myopia severity may impact the presence of FT.

Overall, these studies shed light on the prevalence and potential contributing factors of FT in various populations, with particular attention to the role of myopia and regional differences.

## Characteristics and Associated Factors of Fundus Tessellation

According to the results of the meta-analysis (Fig. 2), individuals with tessellated fundus were found to be older than those with normal fundus [mean difference (MD) = 4.76, 95% CI 1.71–7.80, $P < 0.01$]. In addition, tessellated fundus was associated with longer axial length in comparison to normal fundus (MD = 0.86, 95% CI 0.70–1.02, $P < 0.01$) and a lower spherical equivalent (MD = − 1.16, 95% CI − 1.68 to 0.65, $P < 0.01$) [3–6, 8, 10, 19]. However, there was no significant difference in the proportion of gender between individuals with tessellated and normal fundus [males, odds ratio (OR) = 1.12, 95% CI 0.89–1.42, $P = 0.32$]. The result of Egger's test was shown that there is no publication bias for the included studies ($P = 0.34$, 0.21, 0.13, and 0.38). In addition to these findings, previous studies have reported that individuals with tessellated fundus exhibit worse best-corrected visual acuity, thinner choroid, and thinner sclera in the center fovea [3]. It is noteworthy that there are conflicting findings on the thickness of the retina in individuals with tessellated fundus. Some studies, like Lyu et al., reported a thinner retina in the tessellated fundus, while others found no significant difference in retinal thickness between tessellated and normal fundus [3, 4].

The severity of FT has been associated with several factors, including age, gender, body weight index, axial length, peripapillary atrophy size, choroidal and scleral thickness, and corneal radius of curvature [3, 4, 9, 11, 13, 17, 29]. However, there are discrepancies regarding the gender-based association with FT. Some studies, like Shao et al., found that male sex was associated with more severe tessellated fundus, while others suggested that female sex may play a role [13, 16]. Furthermore, correlation analysis indicated a significant increase in fundus tessellation density with age, with a 33.1% increase for each decade of life [16]. Moreover, the correlation between FT density and SE appeared to be negative in myopic participants, while no such correlation was observed in hypermetropic and emmetropic participants [16].

These findings highlight the complexity of factors influencing the presence and severity of FT and suggest the need for further research to understand the underlying mechanisms and potential clinical implications.

## Fundus Tessellation of Different Locations

To gain a more comprehensive understanding of the specific distribution of FT at different locations, we summarized the findings from various studies [3, 4, 7, 24, 25]. In a study with a sample size of 1670 eyes, the location of FT was categorized based on Curtin's classification, which includes the posterior pole, macular, peripapillary, nasal, and inferior regions. The prevalence of FT in these locations was reported as follows: 6.8% in the posterior pole, 7.1% in the macular region, 22.9% in the peripapillary area, 0.4% in the nasal region, and 8.3% in the inferior region [24]. Notably, among people over 80 years of age, no individuals had FT in the macular, nasal, or inferior regions [24]. Additionally, the study revealed that individuals in the posterior pole and peripapillary groups were significantly older than those in the other groups, except for the nasal group [24]. Terasaki et al. employed Curtin's classification to categorize FT into eight distinct groups: no tessellation, temporal, infra-temporal, inferior, nasal, peripapillary, whole, and unclassified tessellations. They studied the correlations between FT in each location and various factors, including AL, the area of the optic disc plus conus, and optic disc tilt. Among the eyes examined, 44 were assigned to the no tessellation group, 12 to the temporal group, 21 to the infra-temporal group, nine to the inferior

group, eight to the nasal group, 15 to the peripapillary group, 11 to the whole group, and six to the unclassified group. The investigation revealed significant disparities; for instance, the AL of the infra-temporal and whole groups was notably longer than that of the no tessellation group, while the optic disc tilt in the infra-temporal group exhibited a significantly larger measurement than the no tessellation group, as well as the inferior, nasal, and peripapillary groups [25].

Lyu et al. used the early treatment of diabetic retinopathy study (ETDRS) grid to grade FT based on fundus photographs, evaluating the relative location between FT and the fovea [3]. As FT becomes more visible and approaches the center fovea of the ETDRS grid, the grade of FT increases from Grade 0 (no large choroidal vessels visible) to Grade 4 (FT visible in the center fovea of ETDRS grid) [3]. The results showed that among all subfields of the macular and peripapillary regions, the center fovea and the region between the center fovea and optic disc exhibited the most significant decrease in choroidal thickness [3]. Additionally, another study reported a horizontal decrease in choroidal thickness from the temporal to nasal positions [4].

These studies offer valuable insights into the location-specific distribution of FT and its associations with various ocular factors, providing a more nuanced understanding of this unique fundus feature. However, further research may be required to explore the clinical implications and underlying mechanisms related to FT at different locations.

## Progression of FT and Its Association with Myopic Maculopathy

The development of pathological myopia and its connection to myopic maculopathy has been studied carefully. The META-PM study classifies myopic maculopathy into five categories: no lesions (category 0), tessellated fundus (category 1), diffuse chorioretinal atrophy (category 2), patchy chorioretinal atrophy (category 3), and macular atrophy (category 4) [1]. As myopic maculopathy worsens, patients tend to be older and have worse vision [3]. The severity, from category 0 to 3, is associated with longer axial length and a greater spherical equivalent, with exceptions from category 3 to 4 [8]. Gender also plays a role in myopic maculopathy, with males having a higher incidence, while cardiovascular risk and socioeconomic factors do not seem to play a role [14]. The study in Table 1 supports the above findings, except for axial length in Chen et al.'s study, where the study population was specifically selected to have high myopia [19]. Additionally, Xiao et al. found that the proportion of diffuse chorioretinal atrophy or greater in children aged 7 to 11 years was higher than in those aged 12 to 18 years (20.9 vs. 11.0%), which indicated children with early onset high myopia have disproportionately increased risk [6]. Subfoveal and parafoveal choroidal thicknesses thickness decrease with more severe myopic maculopathy [8]. However, subfoveal choroidal thickness does not significantly differ between certain stages [8]. Furthermore, the complications associated with myopic maculopathy can vary across different categories and include foveoschisis, choroidal neovascularization, hemorrhage, lacquer cracks, Fuchs spot, dome-shaped macula, and epiretinal membrane [8].

The progression of FT varies among different articles. Over 10 years, Hayashi et al. reported 10.1% of eyes with FT progressed to diffuse chorioretinal atrophy, 2.9% developed lacquer cracks, and 0.4% had choroidal neovascularization [26]. Yan et al. found that over the years, 15% of eyes with FT progressed to diffuse chorioretinal atrophy, 1% developed lacquer cracks, 1% had patchy atrophy, and 1% developed macular atrophy [18]. Li et al. observed that over 2 years, 24 eyes progressed to a higher category, with 2.6% progressing from no maculopathy to FT, 0.9% from FT to diffuse atrophy and 0.2% from diffuse to patchy atrophy [15].

The most common patterns of development in eyes with myopic maculopathies were from FT to diffuse chorioretinal atrophy, followed by lacquer cracks [26]. Subsequently, the diffuse atrophy expanded and developed into patchy atrophy, while the width of lacquer cracks increased and progressed to patchy atrophy. Eyes with early patchy atrophy showed

expansion and fusion of the atrophy. Furthermore, eyes with FT, lacquer cracks, diffuse atrophy, and patchy atrophy were found to progress to the development of choroidal neovascularization, and this might eventually lead to macular atrophy. During the progression, the fusion of patchy atrophy, the development of choroidal neovascularization, and macular atrophy were associated with a significant decrease in visual acuity [26]. Moreover, it was noted that lacquer cracks can progress to different types of lesions, not just diffuse atrophy [26].

The studies also identified several risk factors associated with the progression of myopic maculopathy, including longer axial length, older age, a higher prevalence of staphylomas, smaller parapapillary γ-zone, and female gender [18]. These findings indicate the importance of monitoring and identifying potential risk factors to guide management and treatment decisions for individuals with myopic maculopathy.

## DISCUSSION

Fundus tessellation is a distinct subtype of myopic maculopathy characterized by the presence of large choroidal vessels in the fundus. This condition has the potential to progress to more severe forms of myopic maculopathy, leading to more serious manifestations, such as choroidal neovascularization and macular atrophy, which can cause significant visual impairment or even disability [1]. Early detection and appropriate management are crucial to prevent the progression and mitigate the impact on visual health.

In the systematic review, we primarily focused on the prevalence of FT, its characteristics, and the progression of myopic maculopathy. The unexpectedly high prevalence of FT in the studies was noteworthy. Among the 23 articles included in the review, 13 were conducted in China, reporting varying proportions of individuals with normal fundus without fundus tessellation, ranging from 5.65 to 57.01% [3–6, 8, 11, 13, 15–19, 23]. To gain a better understanding of the reasons for the substantial difference in prevalence between two specific studies by Cheng et al. (5.65%) and Xiao et al. (57.01%), a more detailed comparison was undertaken [6, 13]. It was found that Cheng et al. included children and adolescents aged 4–19 years with high myopia (spherical equivalent $< -5$ D) in Shanghai, whereas Xiao et al. recruited participants aged 7–70 years with a spherical power of − 6.00 D or worse in both eyes through optometry clinics and community screenings at Zhongshan Ophthalmic Center in Guangzhou, China. Another distinction was that Cheng et al.'s study was cross-sectional, while Xiao et al.'s was a cohort study [6, 13]. The perplexing finding was that the younger age group (Cheng et al.) exhibited a higher prevalence of fundus tessellation compared to the older group (Xiao et al.) [6, 13]. After accounting for the differences in examination methodologies (both studies utilized 45° fundus photographs for both macular-centered and disc-centered areas), researchers speculated that this disparity might be attributed to differences in eye usage and environmental factors [6, 13]. For instance, children and adolescents in China might spend more time reading books, leading to long-term eye fatigue, which could potentially influence the appearance of fundus tessellation [6, 13]. Further investigation into these environmental factors and their association with fundus tessellation prevalence could provide valuable insights into its development and progression. Understanding these factors may aid in implementing preventive measures and targeted interventions to reduce the incidence of myopic maculopathy and associated vision impairment.

In the meta-analysis conducted, the researchers explored the association between personal characteristics and tessellated fundus. The findings revealed that individuals with tessellated fundus tended to have older age, longer axial length, and a lower spherical equivalent. In the process of conducting a meta-analysis, a notable level of heterogeneity was observed pertaining to age and spherical equivalent. Despite the implementation of a method involving the systematic exclusion of individual studies to re-evaluate heterogeneity, it was found that heterogeneity did not exhibit a statistically significant reduction ($I^2 > 50\%$,

see Supplementary Fig. 1 for details). Concurrently, it is noteworthy that the conclusions drawn from each study remained consistent. We speculated that this phenomenon may predominantly stem from variances in sample characteristics among the included studies, encompassing factors such as age and refractive status. These disparities in sample attributes are postulated to potentially exert an influence on the outcomes of the studies, thereby giving rise to the manifestation of heterogeneity. While some articles contradicted these results and reported that tessellated fundus was associated with gender, particularly with male gender [8, 14]. This conflicting evidence highlights the need for further research to understand the relationship between gender and fundus tessellation better. Apart from the aforementioned factors, several other aspects were investigated about tessellated fundus. The analysis indicated that individuals with tessellated fundus tended to have worse best-corrected visual acuity, thinner choroid, and thinner sclera in the central fovea [3]. Nevertheless, there was an ongoing debate regarding the association between retinal thickness and fundus tessellation [3, 4]. One study in students found that tessellated fundus had a thinner average retinal thickness, while another study in adults did not observe a significant difference in foveal retinal thickness between tessellated and normal fundi [3, 4]. This discrepancy suggests that the association between retinal thickness and fundus tessellation may vary depending on the region of interest within the retina.

In contemporary practice, the diagnosis and assessment of FT can be accomplished using various imaging modalities, including fundus photography, OCT, OCT angiography, and fundus autofluorescence. These imaging techniques provide valuable information about the morphology and function of the retina, choroid, and sclera. Several methods have been proposed by different researchers to analyze and quantify FT, but the lack of a standardized classification system hampers comparability and generalizability of results across studies. Furthermore, the diverse research objectives regarding FT result in variations in the ages, genders, and refractive states of the study subjects. This complexity makes it difficult to conduct subsequent comparisons and summaries. For instance, comparing differences under different refractive states becomes unfeasible due to the varying ages within the different groups. To address this limitation, there is a need for a standardized classification system and a large-scale database to facilitate the diagnosis and management of myopic maculopathy. Such a system would enhance the consistency and accuracy of assessments, enabling better comparisons between studies and an improved understanding of the condition's progression and associated factors. Collaborative efforts among researchers and clinicians are essential in establishing a widely accepted classification system that can be used across various clinical and research settings.

## CONCLUSIONS

In summary, the study of fundus tessellation provides valuable insights into the complexities of myopic maculopathy and serves as a foundation for continued research to improve diagnostic precision and patient care for those vision-threatening conditions.

***Authorship*** All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

***Author Contributions.*** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Xuan-Yu Chen, Hai-Long He, Jie Xu, and Yi-Xin Liu. The first draft of the manuscript was written by Xuan-Yu Chen and Hai-Long He. Zi-Bing Jin and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

***Funding.*** This study is partly supported by the National Science Fund for Distinguished Young Scholars (82125007). The journal's Rapid

Service Fee was funded by the corresponding author (Zi-Bing Jin).

***Data Availability.*** The datasets generated during and analyzed during the current study are not publicly available due to the need for further research but are available from the corresponding author on reasonable request.

### *Declarations*

***Disclosures.*** Xuan-Yu Chen, Hai-Long He, Jie Xu, Yi-Xin Liu, and Zi-Bing Jin have nothing to disclose.

***Compliance with Ethics Guidelines.*** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.



## REFERENCES

1. Ohno-Matsui K, Kawasaki R, Jonas JB, Cheung CMG, Saw S-M, Verhoeven VJM, et al. International photographic classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015;159:877-883.e7.
2. Linsenmeier RA, Padnick L. Metabolic dependence of photoreceptors on the choroid in the normal and detached retina. 2000;41.
3. Lyu H, Chen Q, Hu G, Shi Y, Ye L, Yin Y, et al. Characteristics of fundal changes in fundus tessellation in young adults. Front Med. 2021;8: 616249.
4. Zhou Y, Song M, Zhou M, Liu Y, Wang F, Sun X. Choroidal and retinal thickness of highly myopic eyes with early stage of myopic chorioretinopathy: tessellation. J Ophthalmol. 2018;2018:1–9.
5. He X, Deng J, Xu X, Wang J, Cheng T, Zhang B, et al. Design and pilot data of the high myopia registration study: Shanghai Child and Adolescent Large-scale Eye Study (SCALE-HM). Acta Ophthalmol (Copenh) [Internet]. 2021. https://doi.org/10.1111/aos.14617.
6. Xiao O, Guo X, Wang D, Jong M, Lee PY, Chen L, et al. Distribution and severity of myopic maculopathy among highly myopic eyes. Investig Opthalmol Vis Sci. 2018;59:4880.
7. Wong Y-L, Ding Y, Sabanayagam C, Wong C-W, Verkicharla P, Ohno-Matsui K, et al. Longitudinal changes in disc and retinal lesions among highly myopic adolescents in Singapore over a 10-year period. Eye Contact Lens Sci Clin Pract. 2018;44:286–91.
8. Zhao X, Ding X, Lyu C, Li S, Liu B, Li T, et al. Morphological characteristics and visual acuity of highly myopic eyes with different severities of myopic maculopathy. Retina. 2020;40:461–7.
9. Yoshihara N, Yamashita T, Ohno-Matsui K, Sakamoto T. Objective analyses of tessellated fundi and significant correlation between degree of tessellation and choroidal thickness in healthy eyes. Vavvas D, editor. PLoS ONE. 2014;9: e103586.
10. Fang Y, Du R, Nagaoka N, Yokoi T, Shinohara K, Xu X, et al. OCT-based diagnostic criteria for different stages of myopic maculopathy. Ophthalmology. 2019;126:1018–32.
11. Guo Y, Liu L, Zheng D, Duan J, Wang Y, Jonas JB, et al. Prevalence and associations of fundus tessellation among junior students from greater Beijing. Investig Opthalmology Vis Sci. 2019;60:4033.
12. Choudhury F, Meuer SM, Klein R, Wang D, Torres M, Jiang X, et al. Prevalence and characteristics of myopic degeneration in an adult Chinese American population: the Chinese American eye study. Am J Ophthalmol. 2018;187:34–42.
13. Cheng T, Deng J, Xu X, Zhang B, Wang J, Xiong S, et al. Prevalence of fundus tessellation and its associated factors in Chinese children and

adolescents with high myopia. Acta Ophthalmol (Copenh) [Internet]. 2021. https://doi.org/10.1111/aos.14826.

14. Hopf S, Korb C, Nickels S, Schulz A, Münzel T, Wild PS, et al. Prevalence of myopic maculopathy in the German population: results from the Gutenberg Health Study. Br J Ophthalmol. 2019. https://doi.org/10.1136/bjophthalmol-2019-315255.

15. Li Z, Liu R, Xiao O, Guo X, Wang D, Zhang J, et al. Progression of myopic maculopathy in highly myopic Chinese eyes. Investig Opthalmology Vis Sci. 2019;60:1096.

16. Shao L, Zhang QL, Long TF, Dong L, Zhang C, Da Zhou W, et al. Quantitative assessment of fundus tessellated density and associated factors in fundus images using artificial intelligence. Transl Vis Sci Technol. 2021;10:23.

17. Gong W, Cheng T, Wang J, Zhang B, Chen J, Zhu J, et al. Role of corneal radius of curvature in early identification of fundus tessellation in children with low myopia. Br J Ophthalmol. 2022. https://doi.org/10.1136/bjo-2022-321295.

18. Yan YN, Wang YX, Yang Y, Xu L, Xu J, Wang Q, et al. Ten-year progression of myopic maculopathy. Ophthalmology. 2018;125:1253–63.

19. Chen H, Wen F, Li H, Zuo C, Zhang X, Huang S, et al. The types and severity of high myopic maculopathy in Chinese patients: types and severity of high myopic maculopathy. Ophthalmic Physiol Opt. 2012;32:60–7.

20. Leape LL. The government responds: the agency for healthcare research and quality. Mak Healthc Safe [Internet]. 2021. https://doi.org/10.1007/978-3-030-71123-8_10.

21. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Stat Methods Med Res. 2018;27:1785–805.

22. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14:135.

23. Wong CW, Teo YCK, Tsai STA, Ting SWD, Yeo YSI, Wong WKD, et al. Characterization of the choroidal vasculature in myopic maculopathy with optical coherence tomographic angiography. Retina. 2019;39:1742–50.

24. Yamashita T, Iwase A, Kii Y, Sakai H, Terasaki H, Sakamoto T, et al. Location of ocular tessellations in Japanese: population-based Kumejima Study. Investig Opthalmol Vis Sci. 2018;59:4963.

25. Terasaki H, Yamashita T, Yoshihara N, Kii Y, Tanaka M, Nakao K, et al. Location of tessellations in ocular fundus and their associations with optic disc tilt, optic disc area, and axial length in young healthy eyes. Vavvas DG, editor. PLoS ONE. 2016;11:e0156842.

26. Hayashi K, Ohno-Matsui K, Shimada N, Moriyama M, Kojima A, Hayashi W, et al. Long-term pattern of progression of myopic maculopathy. Ophthalmology. 2010;117:1595-1611.e4.

27. Koh VT, Nah GK, Chang L, Yang AH, Lin ST, Ohno-Matsui K, et al. Pathologic changes in highly myopic eyes of young males in Singapore. Ann Acad Med Singapore. 2013;42:216–24.

28. Yokoi T, Jonas JB, Shimada N, Nagaoka N, Moriyama M, Yoshida T, et al. Peripapillary diffuse chorioretinal atrophy in children as a sign of eventual pathologic myopia in adults. Ophthalmology. 2016;123:1783–7.

29. Yan YN, Wang YX, Xu L, Xu J, Wei WB, Jonas JB. Fundus tessellation: prevalence and associated factors. Ophthalmology. 2015;122:1873–80.