Location of Ocular Tessellations in Japanese: Population-Based Kumejima Study

Takehiro Yamashita,[1] Aiko Iwase,[2] Yuya Kii,[1] Hiroshi Sakai,[3] Hiroto Terasaki,[1] Taiji Sakamoto,[1] and Makoto Araie[4]

[1]Department of Ophthalmology, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan
[2]Tajimi Iwase Eye Clinic, Gifu, Japan
[3]Department of Ophthalmology, University of the Ryukyus Faculty of Medicine, Okinawa, Japan
[4]Department of Ophthalmology, Kanto Central Hospital, Tokyo, Japan

PURPOSE. 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.

METHODS. A cross-sectional, population-based study. Residents of Kumejima older than 40 years were studied. The subjects filled out a comprehensive questionnaire, had their body height (BH) measured, and had an ocular examination. The location of the tessellation was classified into 6 patterns. Correlations between each pattern and the axial length (AL), age, and BH were statistically determined.

RESULTS. Reliable measurements of the AL and fundus photographs of the right eyes were obtained from 1670 subjects. Nine hundred eleven eyes had no tessellation, 113 eyes had tessellation in the posterior pole, 118 eyes had tessellation in the macular area, 383 eyes had tessellation in the peripapillary region, 6 eyes had tessellation in the nasal region, and 239 eyes had tessellation in the inferior region. The AL of the "no tessellation" group was significantly shorter than that of the posterior pole and macular groups ($P < 0.01$). The individuals of the posterior pole and peripapillary groups were significantly older than in all other groups ($P < 0.05$) except for the nasal group. The individuals in the inferior tessellation group were significantly taller than those in the no tessellation, posterior pole, and peripapillary groups ($P < 0.01$).

CONCLUSIONS. The location distribution of the tessellation is important in correctly interpreting and predicting myopic changes.

Keywords: myopia, tessellation, axial length, tigroid fundus

High myopia and its associated complications is a common cause of blindness throughout the world. It has become a more serious global issue because of the increased prevalence of myopia.[1–4] A posterior staphyloma is a representative change in highly myopic eyes, and they are often found at the advanced stage of pathologic myopia. Staphylomas are usually associated with different types of retinochoroidal atrophy and are observed in 90% of individuals ≥50 years of age with pathologic myopia.[5,6] A staphyloma can cause severe deformation or stretching of the outer wall of the eye, which then leads to pathological changes of the retina and choroid. In the mild stages, however, these changes cannot be detected by conventional ophthalmological examinations.[5]

A tessellated fundus is another common characteristic of myopic eyes.[6–8] In healthy eyes, a tessellated fundus represents an area where the choroid is thin.[9–11] A tessellated fundus is observed at a younger age and has been recently classified as one type of myopic maculopathy.[6,7] Some tessellations at a younger age may be involved in the progression to pathologic retinochoroidal alterations or staphylomas in advanced stages of pathologic myopia. Importantly, tessellation is a sign that the choroid has been severely stretched. Atrophic changes of the retinochoroidal tissue in older individuals might enhance the tessellation-like appearance of the eye's entire posterior pole.[10]

There are several types of staphylomas present in highly myopic eyes. Curtin has classified staphylomas into 10 categories based on their locations.[8,12] In an earlier study, we classified tessellations into 8 groups, similar to Curtin's staphyloma classification in young, healthy eyes.[13] However, that study was a small case series that was slightly myopia-skewed. Considering the increasing prevalence of myopia worldwide and its association with serious retinochoroidal changes, it is important to learn more about tessellated fundi in a population study.

The Kumejima study is population-based and focused on ocular diseases in individuals who live on Kumejima in southwestern Japan.[14,15] Sequential stereo fundus photographs were taken with a nonmydriatic digital fundus camera during a screening examination, with the results analyzed using computer-assisted planimetry.[16]

The purpose of this study was to determine the locations of tessellations in the fundus of individuals of Kumejima, concentrating on the relationships of their location and the axial length (AL) of the eye, age, and body height (BH).

METHODS

Study Population

The procedures used for the Kumejima study conformed to the tenets of the Declaration of Helsinki and regional regulations, and the Ethics Board of the Regional Council approved the study protocol (May 17, 2005). All participants provided written informed consent before the examinations.

The size of Kumejima is 63.2 km², and it is located in the southwestern part of Japan (eastern longitude of 126° 48′ and northern latitude of 26° 20′) west of the main island of Okinawa. Its population is approximately 9000 with most residents originating from the Okinawa prefecture. The study was conducted between May 2005 and August 2006, and all residents who were ≥40 years were informed on the protocol and invited to participate. According to the official household registration database, Kumejima had 5249 residents ages ≥40 years in 2005, but 617 were identified as nonresidents, were deceased, or had relocated during the screening period. Of the remaining 4632 eligible residents, 3762 (participant rate, 81.2%) completed the screening examination in the Public Kumejima Hospital (3572 subjects) or in their own or nursing homes (190 subjects).[14]

Examinations and Diagnosis

The screening examination consisted of a structured interview about occupation, health history, prior surgery and trauma, smoking habits, and measurements of body weight, height, and systemic blood pressure. The weight and height were determined with an analog stadiometer and a digital weight scale, respectively.

Ocular examinations were performed by experienced ophthalmologists and examiners, and measurements were made of the uncorrected and best-corrected visual acuity (BCVA), refractive error (spherical equivalent), intraocular pressure, central corneal thickness, anterior chamber depth, AL, slit-lamp biomicroscopy, gonioscopy, ophthalmoscopy, fundus photography, and perimetry.[14,15] Sequential stereoscopic color fundus photographs (30° and 45°) were obtained with a nonmydriatic digital ocular fundus camera system (Image Net TRC-NW7; Topcon, Tokyo, Japan). The refractive error was measured with an autorefractometer (ARK-730; Topcon), the IOP with a Goldmann applanation tonometer and the median value was used, the CCT by specular microscopy (SP-2000; Topcon), and the central ACD and AL using the IOLMaster (Carl Zeiss Meditec, Jena, Germany). The peripheral ACD was scored according to the van Herick method and the gonioscopic findings according to Shaffer's grading system using a Goldmann two-mirror lens. The VF was examined with the frequency doubling technology (FDT) perimetry with the C-20-1 screening program (Carl Zeiss Meditec).

Participants were referred for a more comprehensive examination if there was suspicion of ocular abnormalities. Glaucoma was suspected if one or more of the following criteria were found during the screening examination; BCVA <20/30, IOP >19 mmHg, vertical cup/disc (vC/D) ratio ≥0.6, superior (11–1 o'clock) or inferior (5–7 o'clock) rim width/disc diameter of ≤0.2, bilateral asymmetry of the vC/D of 0.2 or more, a nerve fiber layer defect or splinter disc hemorrhage, abnormal findings on slit-lamp examinations or fundus photographs, angle width of grade ≤2 (van Herick method), and at least one abnormal test point ($P < 0.05$) in the C-20-1 test results of FDT perimetry. The comprehensive examination included detailed slit-lamp biomicroscopy, gonioscopy, and fundus examinations and VF testing with the Humphrey Field
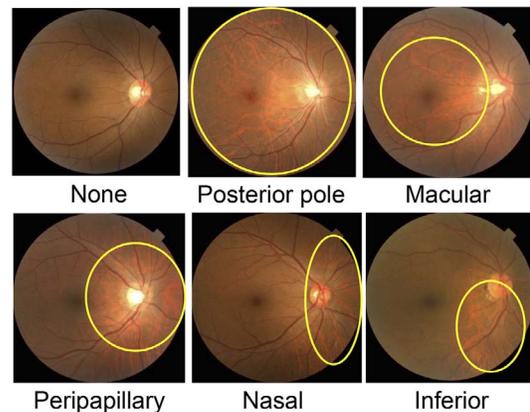

FIGURE 1. Five locations of the tessellations in an older individual from a semi-closed population. The location of the tessellations was based on Curtin's classification: no tessellation, posterior pole, macular, peripapillary, nasal, and inferior.

Analyzer Central 24-2 Swedish interactive threshold algorithm standard program (Carl Zeiss Meditec).

The details of the disc, fundus, and VF examinations and the diagnosis of glaucoma have been reported elsewhere.[14,15] The diagnosis was based on the clinical results obtained from examinations including slit-lamp biomicroscopy, gonioscopy, ophthalmoscopy of the optic disc, retinal nerve fiber layer and VFs; and the International Society of Geographic and Epidemiologic Ophthalmology criteria.[17]

Classification of Lesions in Tessellated Fundus

The fundi of all subjects were photographed using the digital sequential stereoscopic color fundus photographs with a 45° field of view (Image Net TRC-NW7; Topcon). The lesions were classified into 5 primary types based on Curtin's classification of the location of posterior staphylomas: in the posterior pole, macular region, peripapillary, nasal, or inferior (Fig. 1).[8,13] Classifications were made by 2 independent masked examiners (TY, YK). If the raters disagreed, they discussed reasons for their classification with a third rater (HT), and the final classification was determined by an agreement of at least 2 of the 3 graders. If a consensus was not reached, the eye was excluded.

Data Analyses

The intra-rater correlation coefficients of the classification of the tessellated fundus was assessed with the Cohen's κ method. The Kruskal-Wallis 1-way analysis of variance and Steel-Dwass multiple comparison tests were used to determine the significance of the differences in the AL, age, and BH among the groups. All statistical analyses were performed with the statistical programming language R (version 3.0.2; The R Foundation for Statistical Computing, Vienna, Austria). A P value of <0.05 was considered statistically significant.

RESULTS

Of the 7524 eyes of the 3762 participants, acceptable stereo fundus photographs in which the fundus diseases were determined to be reliable. These types of photographs could not be obtained from 376 right and 421 left eyes because of cataract, corneal opacity, large pterygium, or a small pupil. Pseudophakic or aphakic (453 right, 443 left) eyes were excluded because an accurate refractive error was unavailable.

TABLE 1. Demographic Information of the Right Eyes of Eligible Subjects

Category	Mean ± Standard Deviation (Range)
Men/women	842/828
Age (years)	53.6 ± 10.3 (40–88)
Body height (cm)	157.4 ± 8.8 (133.1–186.4)
Refractive error (spherical equivalent; diopters)	−0.14 ± 1.62 (−7.63 to 5.50)
Axial length (mm)	23.50 ± 0.88 (20.92–27.55)

Eyes also were excluded when the spherical equivalent refraction was less than −8 or greater than +5 diopters (14 right eyes, 11 left eyes) or when optic disc diseases or glaucoma or retinal or brain diseases were present in either eye (711 right eyes, 679 left eyes). As a result, both eyes of 2208 subjects were judged normal. Detailed demography of these eyes was described in our earlier report.[18]

Only right eyes were used to determine the location of the tessellation. Five hundred and thirty-eight eyes were excluded because of difficulty in judging the tessellation location due to lack of clarity of the peripheral area of the fundus or were unclassified tessellations. In the end, 1670 right eyes were used for the classification of the tessellations. The demographic data of the right eyes of eligible subjects are shown in Table 1.

The inter-rater agreement in the classification of the location of the tessellations was high with a Cohen's κ of 0.92. Tessellations were not found in 911 eyes (54.6%), that is, the "no tessellation" group, and found in 759 eyes (45.4%). Among the 759 eyes, 113 (6.8%) eyes with tessellation were placed in the posterior pole group, 118 (7.1%) eyes in the macular group, 383 (22.9%) eyes in the peripapillary group, 6 eyes (0.4%) in the nasal group, and 139 (8.3%) eyes in the inferior group. The number and the locations of the tessellation in different age groups is shown in Table 2.

We compared the AL, age, and BH relative to the location of the tessellations. The comparisons of the tessellation groups by a Kruskal-Wallis 1-way analysis of variance revealed significant differences among them in AL, age, and BH ($P < 0.001$). The AL in the posterior pole tessellation group ($P < 0.001$) and the macular tessellation group ($P = 0.003$) were significantly longer than those in the "no tessellation" group (Fig. 2A). The AL of the eyes in the posterior pole tessellation group was significantly longer than those in the peripapillary group ($P < 0.001$) and the inferior tessellation group ($P = 0.002$; Fig. 2A). The subjects in the posterior pole and peripapillary tessellation groups were significantly older than those in the other groups (all $P < 0.05$; Fig. 2B), except that in nasal group. The subjects in the inferior group were significantly taller than those in the "no tessellation" group ($P = 0.008$), the posterior pole tessellation group ($P < 0.001$), and the peripapillary tessellation group ($P = 0.002$; Fig. 2C).

DISCUSSION

To the best of our knowledge, this is the first study to classify the locations of tessellations in normal eyes in an epidemiological survey. The localization of the tessellations was determined from the fundus photographs, and the reproducibility was very good.

We first compared the results with our earlier study of young university students living in Kagoshima, Japan.[13] In the present study, 45.4% of the eyes were without tessellation, 22.9% of showed peripapillary type tessellation, 8.3% of the lower type, 7.1% of the macular type, 6.8% of the posterior pole type, and 0.4% of the nasal type. In our previous study, 34.9% of the eyes had no tessellation, 40.2% in the macular type, followed by 18.3% in peripapillary type, 13.4% in posterior pole type, 10.9% in inferior type, and 9.6% in nasal type.[13] That group had an average age of 26.0 ± 4.1 years, an average refractive errors was −4.71 ± 3.41 diopters, and an average ocular AL of 25.43 ± 1.45 mm, which differed from the present study of ≥40 years. More specifically, in young adults, there are many eyes with longer AL and macular type tessellation than the individuals in the Kumejima study. The subjects with macular type tend to have a longer AL and be more prevalent in younger subjects, so the results are consistent with each other. Second, our earlier study involved mainly young individuals in comparison to the Kumejima study. The younger individuals had good nutrition during their growing days and a different lifestyle, that is, more television viewing and computer use and fewer outdoor activities.[19,20] Previous studies have shown that younger individuals tend to be taller and their axial length longer, with significant and positive correlation between height and axial length.[21–28] Nutritional improvement may be one of the causes for longer axial length in the younger generation, and improvements in physique are due mainly to improvements in nutrition. This difference in the generations might affect the prevalence of tessellation type. Further, since Kumejima is isolated from its surroundings by the sea and interisland transport has been highly limited historically, it is considered a genetically different population from the people in the Kagoshima area.[14,15]

Tessellations are considered to be related to staphylomas because both are caused by excessive extension or deformation of eye. Hsiang et al.[6] reported on the distribution in the locations of staphylomas in a hospital-based Japanese population. They studied 209 eyes with high myopia, and they used locations similar to those used by Curtin in his classification of staphylomas. Ohno-Matsui found that 23.4% of the staphylomas were the posterior pole type, 52.7% the macular type, 4.3% the peripapillary type, 2.7% the inferior type, and 17% the complicated type.[6] In comparison, our results showed that the incidences of the posterior pole tessellation and macular tessellation were high, while those of the peripapillary tessellation type, nasal tessellation type, and inferior tessellation type were low. In a hospital-based study, eyes with visual disturbances—such as macular retinochoroidal atrophy and

TABLE 2. Distribution of the Location of the Tessellation in Different Age Groups

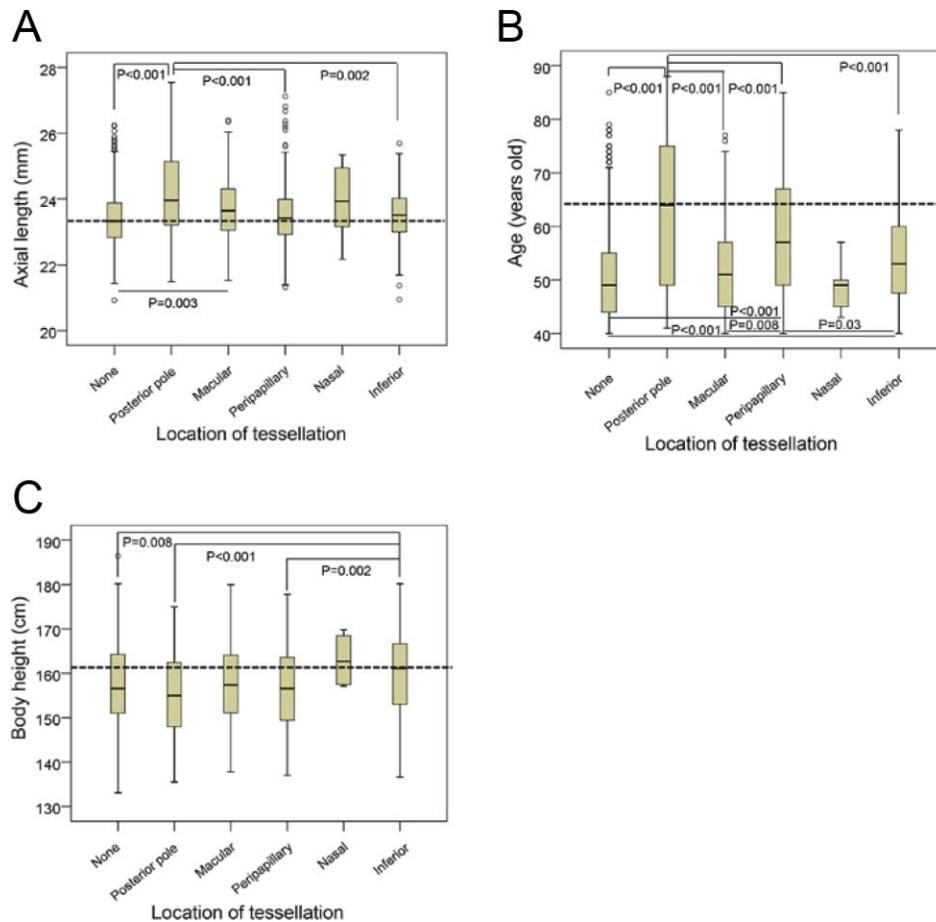| Age Group (years)	No Tessellation	Posterior Pole	Macular	Peripapillary	Nasal	Inferior
40–49	491 (53.9%)	30 (26.5%)	51 (43.2%)	98 (25.6%)	3 (50%)	41 (29.5%)
50–59	302 (33.2%)	17 (15.0%)	42 (35.6%)	125 (32.6%)	3 (50%)	62 (44.6%)
60–69	88 (9.7%)	18 (15.9%)	15 (12.7%)	83 (21.7%)	0 (0%)	24 (17.3%)
70–79	29 (3.2%)	37 (32.7%)	10 (8.5%)	66 (17.2%)	0 (0%)	12 (8.6%)
80+	1 (0.1%)	11 (9.7%)	0 (0%)	11 (2.9%)	0 (0%)	0 (0%)
Total	911 (54.6%)	113 (6.8%)	118 (7.1%)	383 (22.9%)	6 (0.4%)	139 (8.3%)

FIGURE 2. Box plot analysis and multiple comparisons of (A) the axial length, (B) age, and (C) body height among the different tessellation location groups.

choroidal neovascularization—dominate the subjects that would inevitably lead to a bias that posterior staphylomas are the dominant type. Nonetheless, those with tessellations or staphylomas in the inferior, nasal, and parapapillary regions may not have visited the hospital because they did not have any visual impairments.

Our results showed that posterior pole tessellations and macular tessellations had significantly longer AL than those of other groups. In posterior pole and macular tessellation groups, the tessellation contains the macular area, so the AL measured on the visual axis is longer than those in other groups. Conversely, the AL is shorter in the inferior, peripapillary, and nasal tessellation groups where tessellations do not cover the macular area.

In the Kumejima population, the subjects with the posterior pole tessellation type were older than in the other tessellation types. Additionally, the BCVA (logMAR) in the posterior pole type (mean −0.025) was significantly worse than in "no tessellation" group (mean −0.067; $P < 0.001$). This may be because atrophic changes of the retinochoroidal tissue in older individuals might enhance the tessellation-like appearance of whole posterior pole of the eye.[10]

Subjects with the inferior tessellation type were taller than the subjects with the other tessellation types, but the AL of their eyes was not longer than those of other types. In this study, the BH of the subjects was positively correlated with the AL ($r = 0.35$, $P < 0.001$), which is consistent with many earlier studies.[21-28] These results indicate that tessellation of the

inferior type may not be affected only by the AL. The upper half of the eye is not necessarily the mirror image of the lower half of eye.[29,30] It has been reported that in embryonic development of the eye, the inducer is different for each retinal quadrant, and these molecules also affect development of the body.[31] However, which molecules affect development of both the eye and body have not been determined. Further basic research is needed to determine which molecules affect the vertical asymmetry in the eyes with the inferior type of tessellation and BH.

There are limitations in this study. First, a number of eyes were excluded from analysis, which may have caused a selection bias. The fundus was photographed with a non-mydriatic camera to increase the number of participants and avoid the possibility of mydriatic-induced complications. As a result, there were cases in which the surrounding area was too dark for assessment, and they were excluded. Cases with media opacities (such as cataracts) were also excluded. Additionally, eyes with diseases (such as glaucoma and retinal diseases) were also excluded because tessellation can be exaggerated or obscured in such eyes. These may be selective biases and are the limitations of this research. Second, we classified the location of the tessellations subjectively. Although the inter-rater agreement of the two independent masked examiners was high, further study is needed using an objective method to classify the tessellations.

In conclusion, the results showed that the location of the tessellation based on the population-based data and revealed

that peripapillary location of the tessellations was most frequent in the individuals of Kumejima. The eyes with the posterior pole and macular tessellations had longer AL, the subjects with the posterior pole type were older, and the subjects with the inferior type were taller than other groups. This information can be used to compare future pathologic myopia studies. Determination of similar data in different races is needed.

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