Prevalence and Characteristics of Choroidal Nevi in an Asian vs White Population

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Objective: To describe the prevalence and characteristics of choroidal nevi in an Asian population and compare this with findings from a white population.

Methods: The Singapore Malay Eye Study (SiMES) examined a population-based, cross-sectional, age-stratified, random sample of 3280 Malay persons (78.7% participation rate) aged 40 to 80 years living in Singapore. Comprehensive examination of participants included bilateral retinal photography. Choroidal nevi were graded from photographs using the Blue Mountains Eye Study (BMES) protocol.

Results: The person-specific prevalence of choroidal nevi was 1.4%, with 50 nevi found in 45 participants. This is lower than the 6.5% prevalence seen in white persons in the BMES. However, characteristics of nevi in Malay persons in the SiMES were similar to those of white persons in the BMES by size (SiMES, 1.27 mm; BMES, 1.25 mm; \( P = .35 \)), shape (\( P = .58 \)), color (\( P = .39 \)), location within posterior pole or periphery (\( P = .30 \)), and nevus margin proximity to the optic disc (\( P = .29 \)). Features previously identified as indicating growth or malignant potential (including diameter >6 mm, posterior margin touching optic disc, orange pigment, pigment clumping, and retinal edema) were not found in this sample.

Conclusion: Choroidal nevi were detected in 1.4% of Malay persons. There were no significant racial or ethnic differences in nevus characteristics between Malay and white persons.
participants of Helsinki, with written informed consent obtained from approved the study, conducted in accordance with the Declaration of Helsinki. Details of the SiMES design and methodology are reported elsewhere.29-34 Age-stratified random sampling of all Malay adults residing in the southwestern part of Singapore was conducted, selecting 1400 names from each decade (ages 40-49, 50-59, 60-69, and 70-79 years), with an initial 5600 names selected. Of these, 4168 individuals (74%) were eligible to participate. Persons were ineligible if they had moved from their residential address, had not lived there in the last 6 months, or were deceased or terminally ill. Of 4168 eligible individuals, 3280 participated in the study (78.7%); 831 nonparticipants were deceased or terminally ill. Of 4168 eligible individuals, 1400 names from each decade (ages 40-49, 50-59, 60-69, and 70-79 years), with an initial 5600 names selected. Of these, 4168 individuals (74%) were eligible to participate. Persons were ineligible if they had moved from their residential address, had not lived there in the last 6 months, or were deceased or terminally ill. Of 4168 eligible individuals, 3280 participated in the study (78.7%); 831 nonparticipants (20%) declined and 57 (1%) were not contactable. Nonparticipants tended to be in the older age group (70-79 years) compared with participants.

All participants underwent a standardized interview and detailed clinical slitlamp examination. Sociodemographic and medical information was obtained, including smoking history and comorbidities.29,31,34,35 The hospital institutional review board approved the study, conducted in accordance with the Declaration of Helsinki, with written informed consent obtained from participants.

RETNAL PHOTOGRAPHY, NEVUS DEFINITIONS, AND GRADING

A standardized protocol was used for retinal photography.29,36 After pharmacological pupil dilation, two 45° photographs were taken of each eye, one centered at the optic disc and another centered on macula, using a digital retinal camera (Canon CR-DGi with 10D SLR back; Canon, Tokyo, Japan).

A choroidal nevus was defined as an unequivocal pigmented slate blue or green-gray choroidal lesion measuring at least 500 µm in diameter. Choroidal lesions resembling nevus that were partially depigmented were graded as patchy hypomelanotic nevi. Congenital hypertrophy of the retinal pigment epithelium, pigment clumps, and pigmented scars were excluded. There were no melanomas detected in this Malay population.

The nevus features recorded included the number, shape (oval, round, or irregular), color (slate blue, green-gray, or hypomelanotic), location (posterior pole, periphery or overlap of posterior pole, or periphery), position relative to fovea, proximity of posterior margin to the optic disc, quadrantal distribution relative to the optic disc, and presence of orange pigment, pigment clumping, retinal edema, and drusen. Nevus diameter and surface area were measured using Adobe Photoshop CS2, with micrometer per pixel conversion calculated using 4500 µm as the standard distance from the center of the optic disc to the center of the fovea. Nevus were assessed as being macular, subfoveal, or subfoveal when positioned within a 3000-µm, 750-µm, or 175-µm radius from the fovea, respectively. Drusen characteristics assessed included maximum size (63 µm, C6 [distinct and indistinct]; 125 µm, C1; and 250 µm, C2), as used for grading of drusen in age-related maculopathy25), area of nevus involved by drusen, and placement of drusen over the nevus (central, peripheral, or both).

STATISTICAL ANALYSIS

Choroidal nevi were analyzed as a binary outcome variable. Associations with age and sex were analyzed using χ² tests and reported as numbers and proportions. Age-standardized prevalence rates for men and women were computed using direct standardization of our study sample to the Singapore 2000 Census data of Malay citizens and permanent residents.28 Nevus characteristics such as size, shape, color, and location were reported in numbers and percentages. Findings were compared with raw data obtained from the BMES in participants of the same age by using the χ² test of proportion for each category. The Fisher exact test was used for any cell frequencies less than 5. Nevus associations with other variables (including cataract, age-related macular degeneration, diabetes, and smoking) were assessed using logistic regression. The association between nevus size and age was assessed using the χ² test. P ≤ .05 was regarded as statistically significant. All analyses were performed in SPSS version 16.0 (SPSS Inc, Chicago, Illinois).

Table 1. Age and Sex Distribution of Participants With Choroidal Nevi in the Singapore Malay Eye Study

<table>
<thead>
<tr>
<th>Age, y</th>
<th>No./Total (%)</th>
<th>P Value a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Men</td>
</tr>
<tr>
<td>40-49</td>
<td>12/812 (1.5)</td>
<td>7/379 (1.8)</td>
</tr>
<tr>
<td>50-59</td>
<td>19/954 (2.0)</td>
<td>14/429 (3.3)</td>
</tr>
<tr>
<td>60-69</td>
<td>10/774 (1.3)</td>
<td>5/374 (1.3)</td>
</tr>
<tr>
<td>70-79</td>
<td>4/720 (0.6)</td>
<td>2/386 (0.5)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.
a P value for sex.
b P value for age.
c Age standardized to the 2000 Singapore Malay population (citizens and permanent residents).

The final study sample consists of 3280 persons aged 40 to 80 years (some participants were aged 80 years at the time of examination). Of these, 20 participants without retinal photographs or with photographs of insufficient quality for grading were excluded, leaving 3260 participants with gradable photographs for analysis. A total of 45 (1.4% of 3260) had 1 or more choroidal nevi. Two subjects (4.4%) had bilateral nevi, 24 (53.3%) had nevi in the right eye only, and 19 (42.2%) had nevi in the left eye only. The maximum number of nevi seen per eye was 2, found in 3 subjects (6.7%). The age and sex distribution of participants with choroidal nevi in this population are outlined in Table 1. In men, a slightly higher prevalence of persons with choroidal nevi was seen in...
Table 2. Features of Choroidal Nevi in Malay (Singapore Malay Eye Study) and White (Blue Mountains Eye Study) Persons Aged 49 to 80 Years

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Malay (n = 37)</th>
<th>White (n = 244)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>11 (30)</td>
<td>84 (34)</td>
<td>.35</td>
</tr>
<tr>
<td>1-2</td>
<td>23 (62)</td>
<td>123 (51)</td>
<td></td>
</tr>
<tr>
<td>&gt;2</td>
<td>3 (8)</td>
<td>36 (15)</td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Round</td>
<td>15 (41)</td>
<td>80 (33)</td>
<td>.58</td>
</tr>
<tr>
<td>Oval</td>
<td>13 (35)</td>
<td>105 (44)</td>
<td></td>
</tr>
<tr>
<td>Irregular</td>
<td>9 (24)</td>
<td>56 (23)</td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slate blue or green-gray</td>
<td>37 (100)</td>
<td>233 (96)</td>
<td>.37</td>
</tr>
<tr>
<td>Hypomelanotic</td>
<td>0 (0)</td>
<td>11 (4)</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior pole</td>
<td>19 (51)</td>
<td>110 (45)</td>
<td>.30</td>
</tr>
<tr>
<td>Posterior periphery</td>
<td>14 (38)</td>
<td>120 (49)</td>
<td></td>
</tr>
<tr>
<td>Overlap of pole and periphery</td>
<td>4 (11)</td>
<td>14 (6)</td>
<td></td>
</tr>
<tr>
<td>Posterior margin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Touching disc</td>
<td>0 (0)</td>
<td>15 (6)</td>
<td>.29</td>
</tr>
<tr>
<td>Relative to optic disc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 Disc diameters</td>
<td>15 (40)</td>
<td>88 (36)</td>
<td></td>
</tr>
<tr>
<td>&gt;2 Disc diameters</td>
<td>22 (60)</td>
<td>141 (58)</td>
<td></td>
</tr>
<tr>
<td>Quadrant relative to optic disc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper temporal</td>
<td>24 (65)</td>
<td>100 (41)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Upper nasal</td>
<td>9 (25)</td>
<td>17 (7)</td>
<td></td>
</tr>
<tr>
<td>Lower temporal</td>
<td>2 (6)</td>
<td>108 (44)</td>
<td></td>
</tr>
<tr>
<td>Lower nasal</td>
<td>2 (6)</td>
<td>19 (8)</td>
<td></td>
</tr>
<tr>
<td>Presence of drusen</td>
<td>8 (22)</td>
<td>244 (100)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Our study found a 1.4% prevalence of choroidal nevi in a Malay population in Singapore. A key feature of this study was the ability to compare findings with the white population from the BMES, as similar definitions were used for grading choroidal nevi. We found a substantially lower prevalence in Malay persons compared with the 6.5% prevalence reported in the BMES. Similarly, the only other report of choroidal nevi in an Asian population, the Beijing Eye Study, also found a substantially lower prevalence in adult Chinese persons (2.9%) compared with white persons in the BMES.

Importantly, despite the differences in prevalence, we show that the key characteristics of nevi were similar in Malay persons in the SiMES and white persons in the BMES. The mean nevus diameter in our population was 1.27 mm, similar to the mean diameter of 1.25 mm found in the BMES. Nevi in both studies were also similar in terms of shape (P = .58), color (P = .39), location within posterior pole or periphery (P = .30), and proximity of nevus margin to the optic disc (P = .29). The only significant difference was in the frequency of drusen in the nevi (22% in the SiMES and 100% in the BMES; P < .001).

There is a wide range in the reported prevalence of choroidal nevus from previous studies, mostly conducted in white persons. These differences are likely owing to different examination methods used and sample variations across studies. There are few data in the literature on choroidal nevi from populations that are not white. After correcting for limitations of the photographic field, with the estimation that 25% of nevi would likely be missed on photography, a prevalence of 1.8% in the SiMES can be estimated. This adjustment was derived from Naumann et al, who suggested from combined clinical and...
histopathologic investigations that 75% of choroidal nevi are located in the posterior pole and its immediate surroundings, an area comparable with our photographic field.

A limitation of our study is that, as grading was performed by one author (C.H.N.) with adjudication provided by a retinal specialist (A.H.), intragrader or intergrader reproducibility of the grading of nevi was not assessed. There were also differences in the photographic fields used in the SiMES and the BMES. In the SiMES as well as in the Beijing Eye Study,14 two 45° photographic fields centered on the disc and macula were used, whereas six 30° photographic fields were used in the BMES (disc, macula, lateral macula, upper and lower temporal arcade, and nasal retina).3 The decision to obtain only 2 standard photos in the SiMES was based on the primary aim of SiMES to investigate age-related eye diseases, principally macular diseases29; however, we acknowledge that a wider photographic field would have been ideal in terms of detecting choroidal nevi.

Figure 1 and Figure 2 show composite views of the photographic fields obtained in the SiMES and the BMES. The illustrations enable subjective comparison of field differences, although we are unable to comment on the exact proportion of nevi that would have been undetected in the SiMES owing to field differences. However, despite the differences in photographic fields and quadrant distributions outlined in Table 2, the proportion of nevi found involving the posterior pole (SiMES, 51%; BMES, 45%), midperiphery (SiMES, 38%; BMES, 49%), and overlapping the posterior pole and midperiphery (SiMES, 11%; BMES, 6%) was not significantly different. These findings suggest that differences in the fields photographed alone may partially contribute to, but are insufficient to account for, such a large disparity in prevalence, so that racial differences are likely contributors to the observed differences in nevi prevalence.

As in the BMES,3 there was a trend toward decreasing prevalence with increasing age in our study, although this did not reach statistical significance. Ocular media opacity obscuring the view of subtle nevi could partly explain this finding, although it is unlikely to be a major reason owing to the high visibility of nevi. In our study, a higher prevalence of choroidal nevi was seen in younger age groups in men, but not in women. The prevalence of choroidal nevi was significantly higher in men than women only within the 50- to 59-year age group. We speculate that this is a random variation in the data due to small numbers after stratifying the sample into age groups. Interestingly, the Beijing Eye Study also reported that the overall prevalence of choroidal nevi was significantly higher in men than in women.14

Like their cutaneous counterparts, the main clinical concern with choroidal nevi is their rare potential for malignant transformation.1,8,15-22 Previous studies have estimated that one choroidal melanoma may result from 4300 to 8845 nevi per year in white persons.3,8,19 This risk gives rise to continuing efforts to identify reliable indicators of growth and malignant potential, as well as continuing surveillance of patients with choroidal nevi.27,40 Features associated with risk of transformation include orange pigment (lipofuscin), pigment clumping, and subretinal fluid, which are hypothesized to arise from retinal pigment epithelial damage resulting from enlargement of the underlying nevi.1,17,23,41 None of these features were observed in any participants in our study, consistent with the very low probability of detecting choroidal melanoma in a population-based sample at a single time point without longitudinal data. Importantly, the BMES 5-year follow-up data also showed no malignant changes over that period.22

Large elevated nevi have been found to have an increased risk of growth and malignant change.1,17,21,23,39,41 Past studies proposed that suspicious nevi should include those larger than 6 mm in diameter or thicker than 1 to 3 mm in elevation16,21,27 or those with posterior margins that touched the optic disc.16 Nevi in our study were relatively small, with a mean (SD) diameter of 1.27 (0.47) mm. In our sample, the largest lesion measured 2.55 mm in diameter, and no nevi had posterior margins touching the optic disc, suggesting that most lesions were benign without signs of potential malignancy. We were unable to measure the height of nevi from digital images, although we can subjectively com-
ment that the lesions photographed appeared not to be significantly elevated.

The presence of drusen overlying nevi has been postulated to imply low growth potential, although its significance is equivocal. Various percentages (26% to 98%) of choroidal nevi were reported to have overlying drusen in previous studies, using different grading methods. The presence of drusen overlying nevi has been associated with increasing subject age as well as increasing nevus size, suggesting that this sign relates to the chronicity of the nevus. We found no statistically significant associations between drusen and age or nevus size in this population. Our study found that only 20% of nevi had overlying drusen, substantially less than the 98% reported in the BMES. We cannot offer explanations for such a large discrepancy but speculate that both sample variations and differences in grading (as performed by different graders) could have contributed to this.

Choroidal nevi have been reported to be associated with visual impairment, especially subfoveal nevi. Gonder et al. reported decreased visual acuity in 11% of patients referred to an oncology clinic for assessment of choroidal tumors. Shields et al. noted decreased visual acuity in 6.3% of 3422 patients referred to an ocular oncology service at a tertiary referral center. In our population-based study in which 40% of nevi were within the macular area and 10% were subfoveal, there were no cases where impaired visual acuity was attributable to choroidal nevi, consistent with the BMES findings. Given that lesions in Gonder and colleagues' and Shields and colleagues' studies were much larger than those in ours and in the BMES, with an average diameter of 4.3 mm and 4.7 to 5.6 mm, respectively, it is possible that cases referred to oncology assessment centers are selected samples and are likely to have included relatively large nevi, which may not be representative of choroidal nevi found in a usual population.

In conclusion, our study in an Asian Malay sample is among the first reports of population-based data on choroidal nevi in a population that is not white. We documented that the prevalence of choroidal nevi in this Malay population was lower than that in an age-comparable white population. Most nevi were relatively small and did not affect visual acuity. Importantly, we show that characteristics of nevi were largely similar between Asian and white persons.

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