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Original article

Axial length and subfoveal choroidal thickness in individuals with age-related macular degeneration

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ABSTRACT

Purpose: To compare axial length (AL) and subfoveal choroidal thickness (SFCT) between individuals with age-related macular degeneration (AMD) and controls with no lesions.
Methods: This was a case-control study. In total, 853 eyes of 484 patients (>65 years), including 397 eyes at various AMD stages and 456 eyes with no fundus lesions (controls) were recruited. Using color fundus photography, eyes were grouped according to AMD degree. AL was automatically measured using IOL Master and SFCT was manually measured by two independent observers. The associations among age, AL, SFCT, and each AMD grade were analyzed.
Results: Out of 853 eyes, 456 had no lesions, 217 contained drusen only, 134 had early AMD, and 46 had late AMD. The eyes with late AMD were older ($p = 0.007$) and had longer AL ($p < 0.001$) and thinner SFCT ($p < 0.001$) compared with groups of no fundus lesions, drusen only, and early AMD. SFCT in eyes with late AMD decreased by 19.20 μm ($p = 0.049$), 24.78 μm ($p = 0.029$), and 15.56 μm ($p = 0.162$) compared with groups of no fundus lesions, drusen only, and early AMD, respectively. SFCT decreased by 14.18 μm/mm increase in AL ($p < 0.001$). The odds ratio (OR) for late AMD by longer AL (≥25 mm) and thinner SFCT (<240 μm) was 4.54 ($\chi^2 = 9.36$; $p = 0.002$) and 4.86 ($\chi^2 = 17.62$; $p < 0.001$), respectively, and was 9.57 ($\chi^2 = 18.07$; $p < 0.001$) when both AL ≥ 25 mm and SFCT < 240 μm.
Conclusion: Eyes with late AMD have distinct reduced SFCT and elongated AL. Eyes with thinner SFCT and longer AL showed high ORs for late AMD and even higher ORs when both factors were simultaneously present. These findings illustrate the crucial pathophysiological role of these two important ocular factors and arouse our attention to patients with both characteristics, especially in Asian countries where the prevalence of myopia are disturbingly high.

1. Introduction

Age-related macular degeneration (AMD) is a leading cause of blindness in the elderly,[1] and is the most common cause of legal blindness in the Western world and in industrialized nations.[2–7] AMD can lead to loss of central vision; it can be associated with several environmental factors[8,9] including cigarette smoking,[3,10] higher body mass index,[11,12] and dietary carotenoids.[13,14] A genetic effect was suggested on the basis of clinical observations, familial aggregation, and linkage studies,[15,16] and has been confirmed with studies showing the associations between AMD and several genetic loci.[17]

Besides the genetic and environmental factors, previous population-based studies among Caucasians have identified the possible associations of various ocular factors with AMD.[18–20] The Los Angeles Latino Eye Study also evaluated the associations between various ocular factors and AMD in Latinos. These factors

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included iris color, lens opacity, retinal pigment epithelium (RPE) depigmentation, and longer axial length (AL).[21] Some early histological studies[22,23] showed a decrease in the density of choroidal blood vessels and thinning of the choroid in AMD eyes. Some small scale image studies[24,25] also confirmed decreased subfoveal choroidal thickness (SFCT) in exudative AMD eyes. The choroidal circulatory status seems to play an important role. For example, the findings of choroidal hypoperfusion were seen on indocyanine green angiography in eyes with neovascular AMD.[26] It is reasonable to assume that the disruption of the integrity of the choroidal circulation is part of the pathophysiology of wet AMD. Choriocapillaris dysfunction and insufficient blood supply to the RPE cells may allow the RPE cells to be more prone to harmful oxidants or insults; this initiates the accumulation of waste within Bruch's membrane, resulting in the progression of AMD.[27,28]

Although anatomical choroid thickness is not necessarily indicative of choroidal blood volume, flow, and function, measurement of SFCT is currently the most rational and accessible method to evaluate choroidal function. To the best of our knowledge, this study is the largest population-based survey comparing SFCT and AL both together in normal eyes and in eyes at different stages of AMD in an Asian population. We analyzed the relationship between age, AL, and SFCT in different groups. All of these factors may play a crucial pathophysiological role in the development of late AMD in aging people.

2. Methods

This study is a case-control observational study based on our prior population-based cross-sectional study, the Puzih Eye Study.[29] From January 2010 to March 2012, a total of 708 volunteers (aged > 65 years) who lived in Puzih City participated in the Puzih Eye Study. Puzih is also the area with the highest concentration of aging population in Taiwan.

The study adhered to the Declaration of Helsinki, and ethics approval was obtained from the Institutional Review Board of Chang Gung Memorial Hospital at Chiayi, Taiwan. Written informed consent was obtained from all participants after a verbal explanation by study researchers.

2.1. Patient selection and grouping

Among the 708 volunteers, 680 (96.04%) had at least one fundus photograph of either eye, whereas 673 (95.05%) had recognizable fundus photographs. After excluding eyes with retinopathy or maculopathy other than AMD (e.g., diabetic retinopathy, retinal vessel occlusion disease, high myopic maculopathy, and polypoidal choroidal vasculopathy), 853 eyes from 484 patients using qualified optical coherence tomography (OCT) images were enrolled in our present study. The 853 eyes were grouped using color fundus photographs according to the different stages of AMD: no fundus lesions, drusen only, early AMD, and late AMD (Fig. 1).

The grading of the AMD stage was determined by two independent retinal specialists, according to the Wisconsin Age-Related Maculopathy Grading System,[30] using the color fundus photograph that had been taken using a fundus camera (CF-60UD, Canon Inc, Tokyo, Japan). The two specialists were masked from all general data for the volunteers; all equivocal photos were reviewed together with senior retina specialists.

2.2. Parameters measurement

AL of each eye was measured using optical biometry (IOL Master; Zeiss, Jena, Germany) for each eye by averaging five measurements. SFCT was manually measured by two observers using 1-line raster scans OCT image (Stratus OCT, Carl Zeiss Meditec, Inc, Dublin, CA, USA) taken through the foveal center horizontally. The subfoveal choroid was defined as the choroid beneath the concave central retinal depression 1500 μm in diameter. A single choroidal thickness measurement was obtained for the horizontal raster from the outer border of the RPE to the inner scleral border. The manual caliper was used to sequentially measure 250-μm distances in both radial directions encompassing 1500 μm centered on the foveola by each observer and the average of these measurements were calculated as SFCT (Fig. 2). The observers were masked from patients' clinical data. Intraobserver/interobserver repeatablility was also calculated.

2.3. Statistical analysis

One-way analysis of variance and *post-hoc* test (Scheffe's procedure) were used to calculate and compare the age, AL, and SFCT of each AMD-grading group. The association between age and AL, age and SFCT, and AL and SFCT were analyzed using univariate regression, and the Pearson's correlation coefficient was calculated. Using multivariate regression, the effect on SFCT by age, AL, and AMD grading was analyzed. Finally, the odds ratio (OR) for late AMD with a certain cut-off value (22 mm and 25 mm of AL, and 240 μm of SFCT) was calculated. The generalized estimating equation model was used to estimate the strength of the relationship between the outcome and the risk factors, while appropriately taking into account the magnitude of the correlation between fellow eyes.[19,31] A p value ≤ 0.05 was considered statistically significant. All statistics were calculated using SPSS version 16.0 (SPSS Inc, Chicago, IL, USA).

3. Results

The study enrolled 853 eyes from 484 patients, including 456 eyes with no lesion, 217 with drusen only, 134 with early AMD, and 46 with late AMD. Four hundred and eighty-three eyes (56.6%) were of male participants. The mean age of the participants was 73.51 ± 6.02 years (range, 65–90 years). The mean AL and SFCT were 23.42 ± 1.22 mm and 282.7 ± 45.16 μm (Table 1).

3.1. Analysis between age, AL, and SFCT

The single linear regression analysis of age, AL, and SFCT revealed no significant correlation between age and SFCT ($r = -0.002$; $p = 0.967$), a very weak negative correlation between age and AL ($r = -0.077$; $p = 0.043$; Figs. 3A and 3B), and a moderately negative correlation between AL and SFCT ($r = -0.455$; $p < 0.001$). The linear equation of AL versus SFCT showed that SFCT decreased by 16.15 μm for every mm increase in AL (Fig. 4).

In a stepwise multiple regression model analysis of the effect on SFCT, AL had the most effect on SFCT after adjustment for age and AMD grading; SFCT decreased by 14.18 μm for every mm increase in AL ($p < 0.001$). Age showed a nonsignificant effect, whereas SFCT increased 0.55 μm for each additional year of age ($p = 0.082$).

3.2. Age, AL, and SFCT of each subgroup

The mean age in the late AMD group was 76.73 ± 6.32 years, which was higher than that in the other groups ($p = 0.007$). The mean AL in the late AMD group (24.32 ± 2.88 mm) was longer than that in the other groups ($p < 0.001$). The mean SFCT in the late AMD group (250.7 ± 68.2 μm) was thinner than that in the other groups ($p < 0.001$). The mean SFCT in the no lesions, drusen only, and early AMD groups were 282.2 ± 42.5 μm, 292.1 ± 44.1 μm, and 280.5 ± 40.7 μm, respectively. There were no significant differences