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Original Article

Systolic blood pressure, choroidal thickness, and axial length in patients with myopic maculopathy

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Abstract

Background: In the population-based Shihpai Eye Study, patients aged >65 years with myopic maculopathy were found to have higher systolic blood pressure. This finding deserved further exploration because this is the only correctable factor for preventing maculopathy in patients with high myopia. Therefore, we investigated the association between myopic maculopathy and systolic blood pressure, as well as other ocular parameters in this study.
Methods: A clinic-based, retrospective cross-sectional study at a medical center was conducted between February 2011 and October 2012. Patients with high myopia were included and medical charts were reviewed. High myopia was defined as axial length ≥26.5 mm in at least one eye. Myopic maculopathy was defined as the presence of lacquer cracks, focal areas of deep choroidal atrophy, diffuse chorioretinal atrophy, and macular choroidal neovascularization or geographic atrophy in the presence of high myopia. Systolic blood pressure measurements were collected, and fundus photography and optical coherence tomography were performed. Subfoveal choroidal thickness (SFCT) shown on optical coherence tomography was measured and recorded.
Results: The medical records of 187 high-myopic patients (87 without and 100 with maculopathy) were reviewed. Patients with maculopathy were older (56.96 years vs. 42.95 years, $p < 0.01$), had longer axial length (29.96 mm vs. 27.31 mm, $p < 0.01$), thinner SFCT (49.71 μm vs. 155.77 μm, $p < 0.01$), higher systolic blood pressure (132.28 mmHg vs. 125.31 mmHg, $p < 0.05$), greater prevalence of hypertension (31% vs. 16%, $p < 0.05$), and longer history of hypertension (2.34 years vs. 0.59 years, $p < 0.01$) compared to patients without maculopathy. After multivariate adjustment, SFCT and axial length were the only significant factors for maculopathy.
Conclusion: Thinner SFCT and longer axial length are significant risk factors for myopic maculopathy. Unlike previous epidemiological surveys, results of this clinic-based study suggested that systolic blood pressure is not a significant factor for maculopathy.

Keywords: axial length; choroidal thickness; high myopia; hypertension; myopic maculopathy

1. Introduction

The prevalence of myopia is increasing worldwide and has become an extensive public health problem, especially in East Asian countries.[1–5] Among myopia, high myopia, also termed "pathologic myopia" or "degenerative myopia", is associated with multiple ocular morbidities. One of the most important complications of high myopia is myopic maculopathy, which often causes significant visual impairment.[6] The signs of

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maculopathy may include tessellated change at the posterior retina, posterior staphyloma, lacquer cracks, patchy atrophy, choroidal neovascularization (CNV), and geographic atrophy.[7] Clinic-based studies have shown that increased severity of maculopathy is associated with increased axial length and age.[8,9]

In the population-based Shihpai Eye Study, patients aged >65 years with myopic maculopathy were found to have higher systolic blood pressure after multivariate adjustment including age and other systemic factors.[10] Higher systolic blood pressure is associated with thinner choroidal thickness in normal individuals,[11,12] therefore, the authors suggested that increased systolic blood pressure may play a role in the pathogenesis of maculopathy by decreasing choroidal circulation from the back of the eye.[10] However, that study had a small sample size and important ocular parameters such as axial length and choroidal thickness were not analyzed. This finding deserved further exploration because systolic blood pressure might be the only correctable factor for preventing maculopathy in patients who already have high myopia. The purpose of the present study was to clarify the risk factors associated with myopic maculopathy in a clinic-based study with more complete data, namely systolic blood pressure, axial length, choroidal thickness, and age.

2. Methods

2.1. Patients

This was a clinic-based, retrospective cross-sectional study that reviewed the medical records of 187 highly myopic Chinese patients from February 2011 to October 2012 at the Medical Center, Taipei Veterans General Hospital, Taipei, Taiwan. The Institutional Review Board approved the protocols of this study prior to initiation. High myopia was defined as axial length $\geq$26.5 mm. Myopic maculopathy was defined as the presence of lacquer cracks, focal areas of deep choroidal atrophy, and macular CNV or geographic atrophy in the presence of high myopia.[10] When eyes of a patient were discrepant for the severity of myopic maculopathy, the more severe eye was assigned for the study. However, if the more severe eye had any retinal disorder other than myopic maculopathy or foveoschisis, or had ever received ocular surgery other than intravitreal injection and cataract surgery, the less severe eye was assigned. Eyes with macular pucker, diabetic retinopathy, age-related macular degeneration, retinal vein occlusion, retinal artery occlusion, retinal detachment, and eyes that had ever received vitrectomy and scleral buckling were excluded.

2.2. Ophthalmic examinations

Ophthalmic examinations included measurements of visual acuity with Snellen charts at a distance of 6 m, autorefraction (RK-8100; Topcon, Tokyo, Japan), non-contact tonometry (CT-60; Topcon), slit-lamp biomicroscopy (Model BQ900; Haag-Streit, Bern, Switzerland), and indirect ophthalmoscopy (Model 12500; Welch Allyn, Skaneateles Falls, NY, USA) through a dilated pupil with 1% tropicamide (Alcon, Couvreur, Puurs, Belgium). Lens status was recorded as phakic, pseudophakic, and aphakic. In addition, ultrasound biometry (AL-1000; Tomey Corporation, Aichi, Japan) was performed in all patients. Both eyes of each participant were photographed using a monoscopic fundus camera (CF-60UD; Canon, USA) at least 30 minutes after pupil dilatation. Two photographic fields were taken in each eye, with one centered at the fovea and the other at the optic disc. Optical coherence tomography (OCT) imaging of both eyes was performed using RTVue OCT (Optovue Inc., Fremont, CA, USA). Subfoveal choroidal thickness (SFCT) was measured using the calipers within the OCT machine software and positioning them from the outer aspect of Bruch's membrane to the border of the sclera.[11] With the participant in a seated position, blood pressure was measured in the right arm using an electronic sphygmomanometer (ES-P2000; Terumo, Japan) and the average of at least three measurements was recorded. History of hypertension, diabetes mellitus, stroke, and cardiovascular disease was defined as a positive medical record and treatment with medications for such conditions.

2.3. OCT imaging

RTVue OCT uses the technology of spectral-domain OCT. The scanning pattern was set to produce a cross-line scan that obtained 16 individual B scans of 1024 pixels each at the same location for a total of 16,384 data points per line. The B scan was viewed as an averaged composite image that reduced OCT noise and enhanced the image sharpness. The SFCT was measured at the center of the fovea in the horizontal and vertical line pattern (Fig. 1). The horizontal data[13] were used

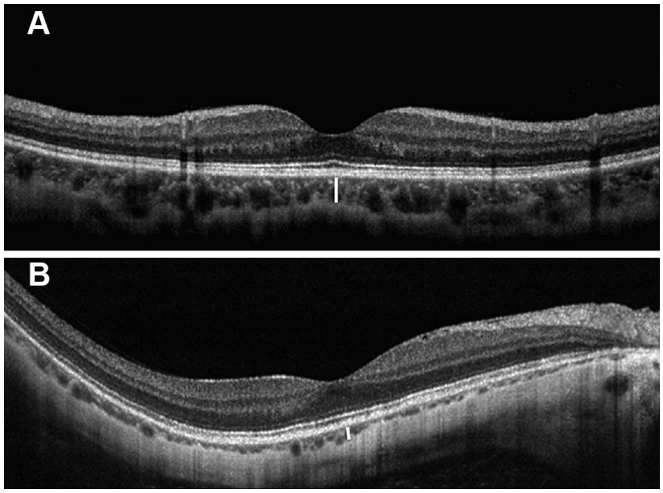

Fig. 1. SFCT is measured from Bruch's membrane to the sclera at the center of the fovea perpendicular to the Bruch's membrane plane. The image color was changed to increase the contrast between the choroid and the sclera. (A) OCT of a 32-year-old woman without maculopathy. The axial length is 26.62 mm and SFCT is 140 μm (as shown by the white line). (B) OCT of a 41-year-old man with myopic maculopathy. His axial length is 30.34 mm and SFCT is 63 μm (as shown by the white line). OCT = optical coherence tomography; SFCT = subfoveal choroidal thickness.

for analysis; however, in cases of unclear or questionable images, the vertical data were used.

2.4. Statistical analysis

The significance of the differences between characteristics reported as mean values in patients with or without myopic maculopathy was assessed using the *t* test. The χ^2 test was used to assess the significance of differences between characteristics expressed as proportions in patients with or without myopic maculopathy. Logistic regression was used to examine the relationships between myopic maculopathy and the selected characteristics. Pearson's correlation coefficient was used to measure the strength and direction of the linear relationship between two variables. Statistical analyses were performed with commercially available software (SPSS version 19.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Univariate and multivariate analyses of ocular characteristics in high-myopic eyes with or without maculopathy

Records from 187 high myopic patients (87 without and 100 with maculopathy) were included in the analyses. Demographic, ocular, and systemic data of the included patients grouped by presence of maculopathy are summarized in Table 1. There were five asymmetric cases with high myopia in only one eye. However, the following results did not change even after excluding these five cases. Patients with maculopathy were older (56.96 years vs. 42.95 years, $p < 0.01$), had poorer corrected visual acuity (logMAR: 0.60 vs. 0.10, $p < 0.01$), longer axial length (29.96 mm vs. 27.31 mm, $p < 0.01$), thinner SFCT (49.71 μm vs. 155.77 μm, $p < 0.01$), and higher systolic blood pressure (132.3 mmHg vs. 125.3 mmHg, $p < 0.05$) compared with patients without maculopathy. Overall, 24% (45/187) of the patients had a positive history of hypertension (31% vs. 16% in patients with and without maculopathy, respectively, $p < 0.05$). In patients who had a history of hypertension, patients with maculopathy had longer history of hypertension than patients without maculopathy (2.34 years vs. 0.59 years, respectively, $p < 0.01$). We also found that patients with a history of hypertension had higher blood pressure than those without hypertension (systolic blood pressure: 143 mmHg vs. 124.5 mmHg, $p < 0.01$). Patients with a history of hypertension had higher systolic blood pressure measured in the hospital even if they had antihypertensive medication. However, after multivariate adjustment by logistic regression, positive history and duration of hypertension, as well as systolic blood pressure, were no longer significantly different between patients with and without myopic maculopathy (Table 1). SFCT (odds ratio = 0.977, $p < 0.01$) and axial length (odds ratio = 1.686, $p < 0.01$) were the two significant factors for myopic maculopathy after multivariate adjustment.

3.2. Relationships of age, axial length, SFCT, and systolic blood pressure

In these high-myopic patients, SFCT was negatively correlated with axial length ($r = -0.61$, $p < 0.01$; Fig. 2A),

Table 1
Univariate and multivariate analyses of ocular parameters and risk factors in high-myopic eyes with or without maculopathy.

Parameter	Univariate			Multivariate			
	Without maculopathy ($n = 87$)	With maculopathy ($n = 100$)	p*	OR	95% CI for OR		p*
					Lower	Upper	
Age[b] (y)	42.95 ± 15.06	56.96 ± 12.89	**< 0.001**	1.03	0.98	1.09	0.196
Sex[c] (M/F)	27/60	22/78	0.161				
VA[a,b] (logMAR)	0.10 ± 0.21	0.60 ± 0.60	**< 0.001**				
Lens[c] (P/PS/A)	65/19/3	84/14/2	0.288				
AL[b] (mm)	27.31 ± 1.67	29.96 ± 1.95	**< 0.001**	1.69	1.19	2.39	**0.003**
SFCT[b] (μm)	155.77 ± 79.13	49.71 ± 34.29	**< 0.001**	0.98	0.96	0.99	**0.001**
SBP[b] (mmHg)	125.31 ± 21.07	132.28 ± 19.13	**0.020**	0.99	0.97	1.03	0.943
DBP[b] (mmHg)	78.13 ± 13.93	79.23 ± 11.12	0.551				
HTN (y)[b]	0.59 ± 2.08	2.34 ± 4.91	**0.003**	1.10	0.87	1.40	0.421
HTN history[c]	14/87	31/100	**0.017**	0.72	0.13	4.07	0.707
DM[c]	6/87	7/100	0.978				
Smoking[c]	2/87	1/100	0.598				
CV disease[c]	6/87	9/100	0.597				
Stroke[c]	0/87	1/100	> 0.99				

Data are presented as mean ± standard deviation.
AL = axial length; CI = confidence interval; CV disease = cardiovascular disease; DBP = diastolic blood pressure; DM = diabetes mellitus; HTN = hypertension; Lens (P/PS/A) = Lens (phakia/pseudophakia/aphakia); OR = odds ratio; SBP = systolic blood pressure; SFCT = subfoveal choroidal thickness; VA = visual acuity.
The *p* values in bold font indicate statistical significance.
* A *p* value <0.05 was considered statistically significant.
[a] Visual acuity was checked with Snellen chart and transformed to logMAR data.
[b] *t* test.
[c] χ^2 test.

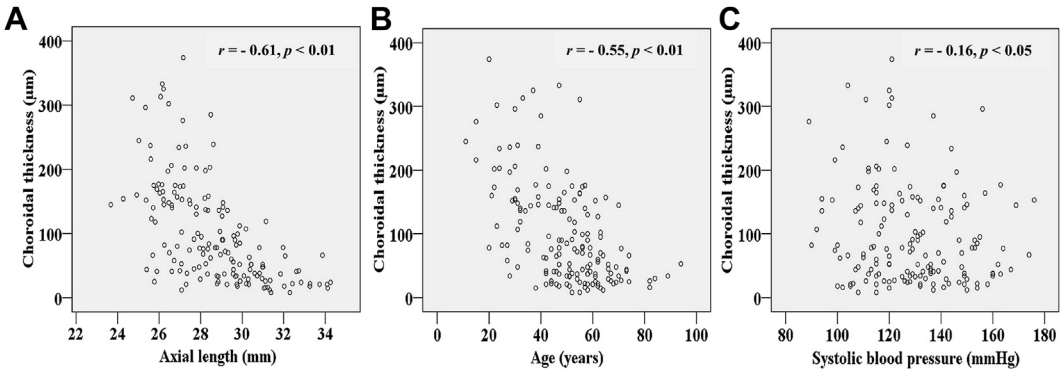

Fig. 2. Pearson correlation showing negative correlation between: (A) subfoveal choroidal thickness and axial length ($r = -0.61$, $p < 0.01$); (B) age ($r = -0.55$, $p < 0.01$); (C) systolic blood pressure ($r = -0.16$, $p < 0.05$).

age ($r = -0.55$, $p < 0.01$; Fig. 2B), and systolic blood pressure ($r = -0.16$, $p < 0.05$; Fig. 2C). However, after linear regression, only age and axial length contributed to the variance of SFCT (21.6% and 36.5%, respectively). In addition, age was positively correlated with systolic blood pressure ($r = 0.38$, $p < 0.01$; Fig. 3A) and axial length ($r = 0.19$, $p < 0.01$; Fig. 3B). After stepwise analysis with logistic regression hierarchically as shown in Table 2, systolic blood pressure was no longer a significant factor after adding age as a factor into the model, suggesting that the effect of increased blood pressure on maculopathy was no greater than the effect of age.

4. Discussion

Our results showed that myopic maculopathy was mostly associated with decreased SFCT and increased axial length. These results were consistent with the study of Wang et al,[14] showing choroidal thickness was the most significant predictive factor for lacquer cracks. A thinner choroidal vascular complex may compromise blood flow, which can result in the development of lacquer cracks. Moreover, lacquer cracks may extend the area of choriocapillary atrophy as well as increase the chances of CNV ingrowth from a ruptured Bruch's membrane.[15,16] When removing the factor of SFCT in multivariate adjustment analysis, we found age and axial length were still significant factors for maculopathy, as in previous studies.[8,9] We also found that SFCT was correlated with axial length and age. Aging and increased axial length together would make the choroid vascular complex become thinner, which increases the risk of myopic maculopathy.

In our study, although systolic blood pressure was associated with myopic maculopathy, it was no longer a significant factor after multivariate adjustment. In the population-based Shihpai Eye Study, patients aged >65 years with myopic maculopathy were found to have higher systolic blood pressure after multivariate adjustment, including age and other systemic factors.[10] The authors proposed that high systolic blood pressure may compromise the thinner choroid in highly myopic patients, increasing the severity of maculopathy. However, choroidal thickness was not available and axial length was not used for multivariate adjustment in the Shihpai Eye Study. Also, the age range was limited to elderly patients in that study.

Our study had several limitations. First, a selection bias may have existed because all included patient records were

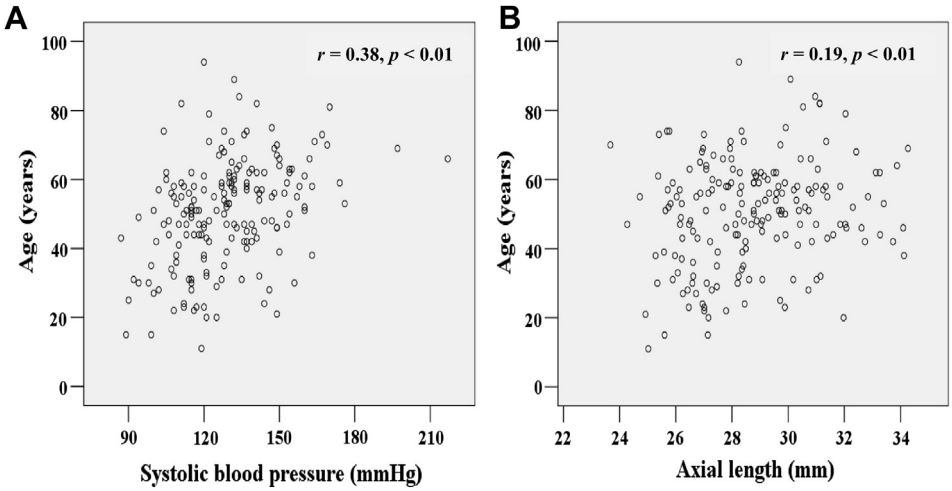

Fig. 3. Pearson correlation showing positive correlation between (A) age and systolic blood pressure ($r = 0.38$, $p < 0.01$) and (B) axial length ($r = 0.19$, $p < 0.01$).

Table 2
Hierarchical regression analysis of factors associated with myopic maculopathy which includes step-wise adding of SBP, age, axial length and SFCT.[a]

Parameter	Step 1 beta	Step 2 beta	Step 3 beta	Step 4 beta
SBP	0.018*	0.000	−0.05	0.004
Age		0.071***	0.096***	0.035
AL			0.895***	0.518**
SFCT				−.023**
Variance explained (R2)	0.040	0.258	0.608	0.670
R2 change	0.040	0.254	0.35	0.062

*$p < 0.05$ for beta value.
**$p < 0.01$ for beta value.
***$p < 0.001$ for beta value.
AL = axial length; SBP = systolic blood pressure; SFCT = subfoveal choroidal thickness.
[a] The explained variance for myopic maculopathy ranged from 0.04 of SBP alone to 0.67 with all factors adjusted.

Table 3
Ocular characteristics and other parameters in patients >65 years of age with maculopathy compared with those with maculopathy in the Shihpai Eye Study.

Parameter	Patients in current study ($n = 22$)	Shihpai Eye Study patients ($n = 32$)	p
Age (y)	74.14 ± 8.10	74.31 ± 6.62	0.930
Sex (male)	27.27	50.00	0.095
Positive hypertension history	54.55	46.88	0.580
Systolic blood pressure (mmHg)	140.91 ± 22.67	146.44 ± 16.20	0.305
Axial length (mm)[a]	29.85 ± 1.95	28.27 ± 2.08	**0.037**
M3/M4/M5 (no.)[a]	3/4/15	7/8/17	0.535

Data are presented as mean ± SD or % unless otherwise indicated.
M3 = lacquer cracks; M4 = patchy atrophy or diffuse atrophy; M5 = geographic atrophy or choroidal neovascularization.
[a] Only the more severe eye was included in each person in the current and Shihpai Eye studies.

collected from clinics. To evaluate the presence of selection bias, the differences in demographics and ocular parameters between the elderly patients (≥65 years) in this clinic-based study and those of the population-based Shihpai Study were examined (Table 3). Patients in the current study had a comparable degree of maculopathy ($p = 0.535$), percentage of positive hypertension history (54.5% vs. 46.9%, $p = 0.580$), and blood pressure (141 mmHg vs. 146 mmHg, $p = 0.305$) with the population-based Shihpai Study. The axial length, however, was longer in the current study (29.85 mm vs. 28.27 mm, $p = 0.037$). These findings suggest that the selection bias in the current study was minimal. Second, we used a strict definition of high myopia (axial length ≥26.5 mm) for phakic or aphakic eyes. However, the cutoff was adopted in several studies.[8,10,17]

In conclusion, thinner SFCT and longer axial length were the two most important risk factors for myopic maculopathy in this study. After multivariate adjustment, age and systolic blood pressure were not significant factors for maculopathy. Longitudinal studies are warranted to clarify the relationship between blood pressure and maculopathy.

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