Axial Myopia and Low HbA1c Level are Correlated and Have a Suppressive Effect on Diabetes and Diabetic Retinopathy

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Purpose: The aim of this study was to investigate whether axial myopia has a suppressive effect on diabetes and diabetic retinopathy.

Methods: This retrospective, cross-sectional study used propensity-score matching to explore the correlations between axial myopia and diabetes and diabetic retinopathy. This study included patients who underwent ophthalmic surgery, including cataract surgery, between April 2009 and July 2016.

Results: With an increase of the axial length (AL < 24 mm; 24 mm ≤ AL < 26 mm; and AL ≥ 26 mm) in axial myopia, the prevalence of diabetes (35.9%, 27.9%, and 20.1%, respectively) and diabetic retinopathy (43.3%, 31.2%, and 24.1%, respectively) decreased (p < 0.001 and = 0.001, respectively). Similarly, glycosylated hemoglobin (HbA1c) level (7.00%, 6.67%, and 6.44%, respectively) decreased with an increase of AL in axial myopia (p < 0.001). Axial length and HbA1c level were significantly and negatively correlated, as determined by partial correlation analysis after adjusting for age and sex (\(r = -0.127, p < 0.001\)).

Conclusions: Axial myopia and low HbA1c level are correlated and have a suppressive effect on diabetes and diabetic retinopathy.

Keywords: Axial length; Diabetes mellitus; Diabetic retinopathy; Glycosylated hemoglobin; Myopia

Introduction

The worldwide prevalence of diabetes has been increasing steadily and is expected to increase more dramatically than previously estimated [1,2]. The prevalence of diabetes among Korean adults is approximately 10%, and it gradually increases with age until 60 years, at which point, the prevalence has been reported to range between 20% and 25% [3,4]. The prevalence of diabetic retinopathy (DR) increases with duration of diabetes and has been reported to be approximately 15% among Koreans with diabetes [5,6].

Several recent studies have suggested that myopia has a protective effect against DR [7-12]. Decreased blood flow in eyes with greater axial length (AL) has been suggested to be
protective against the development of DR [9,13]. However, a subsequent experimental study reported that reduced retinal blood flow was not a major factor for progression of DR [14], and a population-based study failed to demonstrate any association between axial myopia and DR [15].

There are fewer studies on the correlation between myopia and diabetes than there are on the correlation between myopia and DR. Pierro et al. reported that, among patients with AL < 24 mm, those with diabetes exhibited a shorter AL than those without [16]. Herse conducted experiments in rabbits and reported that chronic hyperglycemia impedes axial development [17]. Li et al. reported that hyperglycemia induces lenticular swelling and causes myopic changes by increasing refractive power [18]. However, no study to date has clarified the exact relationship between axial myopia and diabetes. The present study aimed to evaluate the hypothesis that patients with axial myopia exhibit a relatively low prevalence of diabetes.

Materials and Methods

This study adhered to the tenets of the Declaration of Helsinki. The study protocol was approved by the institutional review board of Severance Hospital, Yonsei University, which waived the requirement for informed patient consent because of the retrospective study design.

Study population

This study retrospectively reviewed the data of 12,628 patients (18,449 eyes) who underwent extracapsular cataract extraction (ECCE) with intraocular lens (IOL) implantation at Severance Hospital, Seoul, South Korea, between April 1, 2009, and July 31, 2016. Data regarding patient age at the time of surgery, presence of hypertension, diabetes, DR, and intraoperative AL of both eyes were retrieved from medical records of physical and ophthalmologic examinations. For patients who underwent bilateral surgery, only data from the eye that was operated first were included. After excluding 465 patients under 40 years of age, 61 patients above 90 years of age, 57 patients with confirmed type I diabetes, and 100 patients with suspected secondary diabetes, the study finally included 11,945 patients. In addition, patients with data available for glycated hemoglobin (HbA1c) level, systolic blood pressure (SBP), diastolic blood pressure (DBP), height, and weight were grouped separately (n = 4,795; Fig. 1).

The subjects were divided into three groups based on mean AL (AL < 24 mm, 24 mm ≤ AL < 26 mm, and 26 mm ≤ AL). Differences among the three groups were determined based on age at the time of surgery, sex, and presence of hypertension, diabetes and DR. Propensity-score matching (PSM) analysis was performed in order to adjust for statistical bias (selection bias) and to confirm whether the same results would be obtained with other analytical methods. The model was used to obtain a 1:1 match using the nearest neighbor matching method. After matching the “24 mm ≤ AL < 26 mm” group with the “26 mm ≤ AL” group, the “AL < 24 mm” group was matched with the “24 mm ≤ AL” group.

Statistical analysis

Data for numeric variables are expressed as mean ± standard deviation. Biases due to differences in age, sex, and presence of hypertension were adjusted by PSM. Continuous
Results

The 11,945 patients included in this study were grouped based on AL as follows: AL < 24 mm, 7,684 patients; 24 mm ≤ AL < 26 mm, 2,965 patients; and 26 mm ≤ AL, 1,116 patients. After PSM, these three groups included 2,232, 1,116, and 1,116 patients, respectively. There was no significant difference in age, sex, or presence of hypertension among the three groups after PSM. However, the prevalence of diabetes (35.9%, 27.9%, and 20.1%, respectively) and DR (43.3%, 31.2%, and 24.1%, respectively) decreased significantly (both, p < 0.001; Table 1) with increasing AL (AL < 24 mm; 24 mm ≤ AL < 26 mm; and AL ≥ 26 mm).

The 4,795 patients with data available for HbA1c level, SBP, DBP, height, and weight were grouped based on AL as follows: AL < 24 mm, 3,325 patients; 24 mm ≤ AL < 26 mm, 1,120 patients; and 26 mm ≤ AL, 250 patients. After PSM, these three groups contained 500, 250, and 250 patients, respectively. There was no significant difference in age, sex, or presence of hypertension among the three groups after PSM. However, the prevalence of diabetes (78.8%, 70.0%, and 60.0%, respectively) and DR (49.5%, 38.9%, and 28.0%, respectively) decreased significantly (both, p < 0.001) with increasing AL (AL < 24 mm; 24 mm ≤ AL < 26 mm; and AL ≥ 26 mm). Similarly, the HbA1c level was found to decrease significantly with increasing AL (p < 0.001; Table 2).

The results of partial correlation analysis for associations between AL, HbA1c level, height, weight, SBP, and DBP revealed that AL and HbA1c were significantly negatively correlated (p < 0.001), while AL, height, and weight were significantly and positively correlated with each other (all, p
The results of multinomial logistic regression analysis for evaluating the effects of axial myopia on diabetes and DR revealed that the odds ratio (OR) of both diseases decreased with an increase in axial myopia (Table 4). However, the results of multinomial logistic regression analysis performed using all parameters, including HbA1c, revealed no significant effects of axial myopia on diabetes or DR (Table 5).

**Discussion**

Diabetes remains one of the leading causes of morbidity and mortality worldwide [19]. The prevalence of diabetes has been projected to reach 69% in developing countries and 20% in developed countries by the year 2030 [1,2]. Risk factors for diabetes include obesity, hypertension, lifestyle
Table 3. Partial correlation analysis among the study variables

| Control          | Variable | Axial length | HbA1c   | Height | Weight | SBP       | DBP       |
|------------------|----------|--------------|---------|--------|--------|-----------|-----------|
| Age, sex         | Axial length | r   | -0.127 | 0.184 | 0.114 | -0.018 | 0.042     |
|                  | p        |   | <0.001 | <0.001| <0.001| 0.209   | 0.004     |
| HbA1c            | r        | - | -0.021 | 0.405 | -0.032 | -0.034 |
|                  | p        |   | <0.001 | 0.001 | 0.027 | 0.018 |
| Height           | r        | - | -0.145 | 0.405 | -0.032 | -0.034 |
|                  | p        |   | <0.001 | 0.001 | 0.027 | 0.018 |
| Weight           | r        | - | -0.114 | 0.184 | -0.018 | -0.034 |
|                  | p        |   | <0.001 | 0.004 | 0.018 |        |
| SBP              | r        | - | -0.018 | 0.209 | 0.042 | 0.004   |
|                  | p        |   | 0.209  | 0.042 |       |          |
| DBP              | r        | - | -0.034 | 0.018 |       |          |
|                  | p        |   | 0.018  |       |        |          |

HbA1c = glycated hemoglobin or glycohemoglobin; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Table 4. Multinomial logistic regression analysis of diabetes severity according to age, sex, hypertension, and AL

| Diabetes | Diabetes retinopathy |
|----------|----------------------|
| OR (95% CI) | p-value | OR (95% CI) | p-value |
| Before matching |         | 0.967 (0.961–0.973) | <0.001 |
| Age (years) | 1.020 (1.015–1.025) | <0.001 |
| Sex         | Reference           | 0.581 (0.516–0.655) | <0.001 |
| Male        | Reference           | 0.581 (0.516–0.655) | <0.001 |
| Female      | 0.678 (0.618–0.744) | <0.001 |
| Hypertension| No                  | 2.829 (2.584–3.097) | <0.001 |
| Yes         | 3.478 (3.083–3.923) | <0.001 |
| AL (mm)     | AL < 24             | Reference           | Reference |
| 24 ≤ AL < 26| 0.810 (0.727–0.901) | <0.001 |
| 26 ≤ AL     | 0.533 (0.444–0.639) | <0.001 |
| After propensity-score matching |         | 0.982 (0.972–0.992) | <0.001 |
| Age (years) | 1.028 (1.020–1.037) | <0.001 |
| Sex         | Reference           | 0.567 (0.464–0.693) | <0.001 |
| Male        | Reference           | 0.567 (0.464–0.693) | <0.001 |
| Female      | 0.791 (0.673–0.931) | 0.005 |
| Hypertension| No                  | 3.290 (2.787–3.883) | <0.001 |
| Yes         | 4.260 (3.464–5.239) | <0.001 |
| AL (mm)     | AL < 24             | Reference           | Reference |
| 24 ≤ AL < 26| 0.807 (0.666–0.978) | <0.001 |
| 26 ≤ AL     | 0.554 (0.452–0.679) | 0.029 |

AL = axial length; OR = odds ratio; CI = confidence interval.
Table 5. Multinomial logistic regression analysis of diabetes severity according to age, sex, hypertension, AL, height, weight, SBP, DBP, and HbA1c level

|                         | Diabetes | p-value | Diabetic retinopathy | p-value |
|-------------------------|----------|---------|-----------------------|---------|
|                         | OR (95% CI) |         | OR (95% CI)            |         |
| Before matching         |          |         |                       |         |
| Age (years)             | 1.003 (0.992–1.013) | 0.627   | 1.003 (0.992–1.013) | <0.001  |
| Sex                     | Reference |         | Reference             |         |
| Male                    |          |         |                       |         |
| Female                  | 0.797 (0.615–1.033) | 0.086   | 0.797 (0.615–1.033) | <0.001  |
| Hypertension            |          |         |                       |         |
| No                      | Reference |         | Reference             |         |
| Yes                     | 1.793 (1.505–2.137) | <0.001  | 1.793 (1.505–2.137) | <0.001  |
| AL (mm)                 |          |         |                       |         |
| < 24                    | Reference |         | Reference             |         |
| 24–25.99                | 0.864 (0.706–1.056) | 0.154   | 0.864 (0.706–1.056) | <0.001  |
| ≥ 26                    | 0.729 (0.508–1.047) | 0.087   | 0.729 (0.508–1.047) | <0.001  |
| Height (cm)             | 0.995 (0.979–1.011) | 0.752   | 0.995 (0.979–1.011) | 0.773   |
| Weight (kg)             | 1.013 (1.003–1.023) | 0.014   | 1.013 (1.003–1.023) | 0.743   |
| SBP (mmHg)              | 1.013 (1.006–1.020) | <0.001  | 1.013 (1.006–1.020) | <0.001  |
| DBP (mmHg)              | 0.979 (0.969–0.989) | <0.001  | 0.979 (0.969–0.989) | <0.001  |
| HbA1c level             | 12.578 (10.465–15.118) | <0.001  | 12.578 (10.465–15.118) | <0.001  |
| After propensity-score matching |          |         |                       |         |
| Age (years)             | 1.010 (0.988–1.032) | 0.387   | 1.010 (0.988–1.032) | <0.001  |
| Sex                     | Reference |         | Reference             |         |
| Male                    |          |         |                       |         |
| Female                  | 0.905 (0.489–1.676) | 0.751   | 0.905 (0.489–1.676) | 0.013   |
| Hypertension            |          |         |                       |         |
| No                      | Reference |         | Reference             |         |
| Yes                     | 1.678 (1.124–2.504) | 0.011   | 1.678 (1.124–2.504) | 0.001   |
| AL (mm)                 |          |         |                       |         |
| < 24                    | Reference |         | Reference             |         |
| 24–25.99                | 0.613 (0.379–0.992) | 0.046   | 0.613 (0.379–0.992) | <0.001  |
| ≥ 26                    | 0.837 (0.508–1.379) | 0.485   | 0.837 (0.508–1.379) | 0.076   |
| Height (cm)             | 1.002 (1.002–1.037) | 0.913   | 1.002 (1.002–1.037) | 0.454   |
| Weight (kg)             | 1.013 (0.989–1.037) | 0.287   | 1.013 (0.989–1.037) | 0.127   |
| SBP (mmHg)              | 1.020 (1.002–1.037) | 0.025   | 1.020 (1.002–1.037) | 0.001   |
| DBP (mmHg)              | 0.977 (0.953–1.002) | 0.068   | 0.977 (0.953–1.002) | 0.003   |
| HbA1c level             | 21.387 (13.226–34.584) | <0.001  | 21.387 (13.226–34.584) | <0.001  |

AL = axial length; SBP = systolic blood pressure; DBP = diastolic blood pressure; HbA1c = glycated hemoglobin or glycohemoglobin; OR = odds ratio; CI = confidence interval.

changes, pancreatic dysfunction, and smoking [2,20].

Among patients with diabetes in the present study, the proportion of men and the frequency of hypertension were relatively high (data not shown). Several studies on the association between diabetes and sex have documented that men exhibit higher rates of diabetes than women, and that
male sex is a risk factor for diabetes [21-23]. In contrast, some studies have demonstrated a lack of association between these two factors [24]. With regard to this controversy, Nordström et al. [25] reported that the higher rates of diabetes among men was attributable to the higher proportion of visceral fat, and that being male was no longer a risk factor for diabetes after adjustment for visceral fat. Many studies on the association between hypertension and diabetes have found the former to be a risk factor for developing diabetes [20,26].

Myopia is known to induce nuclear and posterior sub-capsular cataract, causing patients with myopia to undergo early surgery [27,28]. In the present study, patients with a longer AL were younger than those with a shorter AL. In order to compensate for differences in age, sex, and hypertension due to AL, the AL groups in the present study were selected by PSM.

Previous studies have suggested that patients with relatively long AL exhibit decreased retinal perfusion, which is one of the factors contributing to the decreased incidence of DR. Therefore, some studies have described myopia as having a protective effect against DR [7-13]. However, in the present study, patients with axial myopia exhibited a relatively low prevalence of diabetes as well as DR. In addition, HbA1c levels were low among patients with axial myopia. The strength of the correlation between myopia and diabetes decreased after adjusting for HbA1c level. Based on the present findings, the authors suggest that axial myopia and low HbA1c level are correlated and have a suppressive effect on diabetes and DR (Fig. 2).

Further studies are warranted to investigate the mechanisms underlying the correlation between axial myopia and HbA1c level, as well as the suppressive effect of axial myopia on diabetes and DR. A follow-up study is being planned at our institute.

There are several limitations to the present study. First, the subjects in this study underwent ophthalmic surgery involving ECCE with IOL implantation at tertiary medical institutions. Second, the effects of socioeconomic status and education were not investigated. Consequently, the present findings on the prevalence of diabetes and hypertension might not be applicable in a population-based study. However, the aim of this study was not to evaluate the prevalence of diabetes or DR among patients with axial myopia, but rather to analyze differences based on the presence of axial myopia. This study was meaningful in that it included patients who underwent ECCE with IOL implantation over a period of more than seven years.

In conclusion, even after adjusting for age, sex, and hypertension, patients with axial myopia exhibited a gradual decrease both in the prevalence of diabetes and DR and HbA1c level with increasing AL. Patients with axial myopia exhibited relatively low ORs of diabetes and DR; however, after adjusting for HbA1c level, the relationship between axial myopia and diabetes and DR was no longer significant. The authors believe that a decrease in HbA1c level with an increase in AL is the reason for the decreased prevalence of diabetes and DR among patients with axial myopia (Fig. 2). These findings demonstrate that axial myopia and low HbA1c level are correlated and have a suppressive effect on diabetes and DR.

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**Conflicts of Interest**

The authors declare no conflicts of interest relevant to this article.
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