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Lens Power, Axial Length–to–Corneal Radius Ratio, and Association with Diabetic Retinopathy in the Adult Population with Type 2 Diabetes

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Purpose: To calculate crystalline lens power and to determine the relationship between ocular biometry and diabetic retinopathy (DR) in an adult population with type 2 diabetes mellitus (T2DM).

Design: Cross-sectional, population-based study.

Participants: Patients with T2DM from the Beixinjing community, Changning district, Shanghai.

Methods: Random clustering sampling was used to identify adults with T2DM in the Beixinjing community. Spherical equivalent (SE) was determined by subjective refraction that achieved the best corrected vision. Axial length (AL), corneal power (CP), and anterior chamber depth (ACD) were measured using the IOLMaster. Diabetic retinopathy and diabetic macular edema (DME) were assessed according to the international DR classification.

Main Outcome Measures: The crystalline lens power was calculated using the Bennett–Rabbetts formula. The AL–to–corneal radius ratio (AL/CR ratio) was defined as the axial length divided by the mean corneal radius of curvature.

Results: A total of 4011 eyes of 2057 subjects with T2DM were included in the analysis. In multivariate logistic models adjusting for age, sex, duration of diabetes, glycosylated hemoglobin A1c, serum creatinine, body mass index, systolic blood pressure, and cataract, after categorizing values into quartiles, there were trend associations between lens power and any DR ($P = 0.01$), between AL/CR ratio and any DR ($P = 0.02$), and between AL and any DR ($P = 0.03$), between lens power and moderate DR ($P = 0.02$), and between AL and moderate DR ($P = 0.02$); eyes with higher AL/CR ratio were less likely to have any DR (odds ratio [OR], 0.43; 95% confidence interval [CI], 0.24–0.78; $P = 0.01$ per 1 increase) and moderate DR (OR, 0.44; 95% CI, 0.21–0.93; $P = 0.03$ per 1 increase), eyes with longer AL were less likely to have any DR (OR, 0.88; 95% CI, 0.81–0.95; $P = 0.002$ per millimeter increase) or moderate DR (OR, 0.89; 95% CI, 0.80–0.98; $P = 0.02$ per millimeter increase), and eyes with higher SE were more likely to have any DR (OR, 1.08; 95% CI, 1.03–1.13; $P = 0.003$ per diopter increase).

Conclusions: In persons with T2DM, lens power, AL/CR ratio, and AL were associated with the presence of any DR and moderate DR. These findings suggested that globe elongation plays a major role in protective effects against DR, with contributions from lens power and other refractive components. *Ophthalmology 2016;■:1–10 © 2016 by the American Academy of Ophthalmology*

The growing burden of diabetes globally has been accompanied by an increase in numbers of patients with type 1 diabetes and particularly type 2 diabetes (T2DM).[1,2] The World Health Organization estimated that by 2025, 300 million people worldwide will have diabetes mellitus (DM), including 270–285 million (90%–95%) people with T2DM.[1,3]

Diabetic retinopathy (DR) is a potentially sight-threatening microvascular complication of diabetes and an important cause of preventable blindness.[4–8] The risks of retinopathy onset and its progression are modified by a variety of systemic and ocular factors, and an understanding of these factors aids in prognosis and risk stratification.[7–11] Several studies have shown that DM has a major impact on lens biometry, and the lens has been found to become even thicker and more convex.[12–17] More importantly, no population-based studies have investigated the relationship between crystalline lens power and DR.

Because lens power cannot be measured in vivo, calculation of the power of the lens inside the eye is not straightforward,[18] but can only be calculated based on other ocular components. Rabbetts[19] presented an in vivo formula to calculate crystalline lens power, based on distance refraction, corneal power (CP), anterior chamber depth (ACD), and axial length (AL). In this formula, certain constants have been revised recently.[20] Furthermore, this improved formula could be used to calculate the mean values of crystalline lens power in cases of studies performed using IOLMaster biometry. The accuracy of such formulas depends on the validity of

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measurements of biometric parameters, which are included in the formula. Such formulas ensure the realization of large-scale epidemiology research studies investigating the relationship between lens power and DR.

Longer AL has been suggested to have a protective effect against DR.[21,22] However, it remains unclear whether the protective association of longer AL against DR is related to the axial dimensions of the eye or to other refractive components, such as corneal curvature. The AL−to−corneal radius ratio (AL/CR ratio) can synthetically determine the refractive state of the human eye and describe the shape of the globe.[23] It is necessary to assess the relationships of AL/CR ratio and other refractive parameters with DR.

Therefore, we conducted this population-based investigation in Shanghai to measure ocular biometry and serum biometry in subjects with T2DM, and we calculated crystalline lens power using the Bennett−Rabbetts formula. This calculation enabled an investigation of a compensation mechanism for the changes in the refractive system caused by DR. Finally, we studied the relationships between crystalline lens power, refractive errors, AL/CR ratio, and AL and DR, adjusting for diabetes duration, serum parameters, and other ocular parameters.

Methods

Sampling and Enumeration

This study was performed in a randomly selected sample of diabetic residents of the Beixinjing community of Shanghai. Since 2003, our study group has been helping residents with diabetes in this community to prevent and control DR progression through glucose control.[24] In 1999, a local Chronic Diseases Prevention and Control System, including almost all of the residents with T2DM, was created by the government, and it has been updated annually by the Beixinjing Community Health Service Centers. According to this system, T2DM is defined as age at onset ≥30 years old without insulin dependence, and by the end of 2014, 7756 residents with T2DM were living in the Beixinjing community. This project was approved by the ethics committee of Shanghai General Hospital, Shanghai Jiao Tong University, in accordance with the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant at the examination site.

Eye Examination and Calculation

Field work was performed by 2 ophthalmologists, 10 optometrists, and 4 general health practitioners. Additionally, an ophthalmologist with sufficient experience in epidemiology studies supervised the entire work. Eligible participants were examined at local community facilities, and those who did not visit the examination site on schedule were contacted by telephone to encourage participation.

All of the participants underwent a comprehensive eye examination, including a detailed questionnaire (including age, sex, diabetes onset age and duration, years of education, general and eye disease history), refractive error assessment using an autorefractor machine (model KR-8900; Topcon, Tokyo, Japan), ACD, CP, and AL of the globe using an IOLMaster (version 5.02; Carl Zeiss Meditec, Oberkochen, Germany), slit-lamp biomicroscopic examination of the anterior segment (model YZ5X1; 66 Vision-Tech Co., Ltd, Suzhou, China), fundus examination before and after pupil dilation, retinal photography centered on the optic disc and the macula using a digital, nonmydriatic retinal camera (model CR-DGi; Canon, Tokyo, Japan), and retinal map and retinal nerve fiber layer thickness measurements using optical coherence tomography (iVue; Optovue, Fremont, CA). Subjective refraction was performed by a trained optometrist for all of the subjects. Ophthalmic examination of the eyelid, globe, pupillary reflex, and lens was performed by an experienced ophthalmologist. For subjects with aphakia/pseudophakia, the surgical history, including the type of surgery and surgical complications, was obtained. Participants with best-corrected visual acuity ≤20/63 or any sign of DR had their pupils dilated for slit-lamp biomicroscopic fundus examination with Volk 90-diopter (D) lenses, followed by retinal photography. For subjects with an anterior chamber angle of grade I or less using the van Herick technique, the fundus was photographed through an undilated pupil under dim illumination. The clinical data, including fundus photography and optical coherence tomography results, were collected and stored through the local area network, and the participants received treatment recommendations immediately after the examination.

The patients' heights, weights, and systolic (SBP) and diastolic (DBP) blood pressures were measured by trained physicians. The body mass index (BMI) was calculated as the weight in kilograms divided by the height in meters squared. Fasting (≥8 hours) venous blood samples were collected and sent for analysis of hemoglobin A1c (HbA1c), serum creatinine (SCr), cholesterol, and triglyceride levels at Labway Clinical Laboratory Shanghai, Ltd.

Lens Opacity Classification System II standard color photographs were used as the reference for cataract grading, and the grading nomenclature of nuclear color, nuclear opalescence, and cortical and posterior subcapsular cataract was adopted.[25] A nuclear, cortical, and posterior subcapsular lens opacity was considered no cataract or an early cataract when the opacity was lower than Lens Opacity Classification System II grade NII, CII, or PSCII, respectively. The 3 types of cataract were classified as advanced if the grade of the opacity was equal to or greater than grade NII, CII, or PSCII, respectively.[26]

Diabetic retinopathy and diabetic macular edema (DME) were assessed by 2 ophthalmologists according to the international DR classification.[27] Three categories were defined for analyses. Any DR was defined as minimal nonproliferative DR (NPDR) or worse, moderate DR was defined as moderate NPDR or worse, and vision-threatening retinopathy was defined as the presence of severe NPDR, proliferative DR (PDR), or clinically significant macular edema, using the Eye Diseases Prevalence Research Group definition.[28] If an eye was ungradable, it was excluded from that particular analysis.

The refraction data were converted to spherical equivalents (SEs; SE = sphere +1/2 cylinder). Myopia was defined as SE less than −0.5 D; mild myopia was further defined as SE between −0.5 and −3 D; moderate myopia was defined as SE between −3 and −6 D, and high myopia was defined as SE less than −6 D. Hyperopia was defined as SE >0.5 D. The AL/CR ratio was defined as the AL divided by the mean corneal radius of curvature. Education level was divided into 5 grades: postgraduate (12−15 years); high school (9−11 years); middle school (6−8 years); primary school (1−5 years); and less than primary school (<1 year). These definitions were chosen to compare the data with other available data.

The refractive power of the lens was calculated using the modified Bennett−Rabbetts formula:

$$P_{L,BR} = \frac{\mathrm{L}(\mathrm{S_{CV}} + \mathrm{K}) - 1000\mathrm{n}}{(\mathrm{L} - \mathrm{ACD} - \mathrm{C_{BR}})\left(\frac{\mathrm{ACD}+\mathrm{C_{BR}}}{1000\mathrm{n}}(\mathrm{S_{CV}} + \mathrm{K}) - 1\right)}$$