Intraocular Pressure in General and Diabetic Populations From Southern China: the Dongguan Eye Study

Ying Cui,[1] Xiaohong Yang,[1] Guanrong Zhang,[2] Haike Guo,[1,3] Min Zhang,[4] Lixin Zhang,[5] Jin Zeng,[1] Qingyang Liu,[4] Liang Zhang,[1] and Qianli Meng[1]

[1]Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, Guangdong, China
[2]Information and Statistical Center, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, Guangdong, China
[3]Xiamen Eye Centre of Xiamen University, Xiamen, China
[4]Department of Ophthalmology, Dongguan People's Hospital, Dongguan, Guangdong, China
[5]Department of Ophthalmology, Hengli Hospital, Dongguan, Guangdong, China

Correspondence: Qianli Meng, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, 106 Zhongshan Er Road, Guangzhou 510080, PR China; mengqly@163.com.
Liang Zhang, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, 106 Zhongshan Er Road, Guangzhou 510080, PR China; 13602721773@139.com.

YC and XY contributed equally to the work presented here and should therefore be regarded as equivalent authors.

Submitted: July 12, 2018
Accepted: January 25, 2018

Citation: Cui Y, Yang X, Zhang G, et al. Intraocular pressure in general and diabetic populations from southern China: the Dongguan Eye Study. *Invest Ophthalmol Vis Sci*. 2019;60:761–769. https://doi.org/10.1167/iovs.18-25247

Purpose. To investigate the distribution and risk factors for intraocular pressure (IOP) among general and diabetic populations in Southern China.

Methods. The study participants aged 40 years or older were enrolled from the Dongguan Eye Study, a population-based cross-sectional study from September 2011 to February 2012. Systemic and ophthalmic examinations were performed, and diabetes status was screened based on the American Diabetes Association diagnostic criteria (2010). IOP was measured by a noncontact tonometer per standardized protocol. Regression analyses were used to assess the association between potential risk factors and IOP.

Results. A total of 2112 subjects were included with a median age of 55 years. IOP for general population showed a near normal distribution with an average of 15.58 ± 3.27 mm Hg. Multiple regression analyses revealed that higher IOP was significantly correlated with younger age, higher body mass index (BMI), shorter height, higher blood pressure (BP), higher fasting blood glucose (FBG), higher low-density lipoprotein cholesterol (LDL-C), lower high-density lipoprotein cholesterol (HDL-C), and thicker central corneal thickness (CCT). There was no association between diabetes status and IOP after adjusting for possible confounders. IOP for diabetic participants showed a right-skewed distribution. Risk factors for IOP elevation in diabetes included female, younger age, higher BP, higher LDL-C, lower HDL-C, and thicker CCT.

Conclusions. The present study identifies risk factors for elevated IOP in general and diabetic populations. Younger age and lower HDL-C, as well as higher BP, LDL-C, and CCT were significant factors contributing to higher IOP, especially in the female diabetic population.

Keywords: intraocular pressure, distribution, risk factors, diabetes mellitus

Intraocular pressure (IOP) is the fluid pressure inside the eye and an important ophthalmic physiological parameter. High IOP is widely acknowledged as the most important risk factor for glaucoma, and IOP reduction therapy is the only proven effective treatment.[1,2] Thus it is of pragmatic significance to understand the distribution and risk factors of IOP for glaucoma prevention and prognosis. Many factors, such as age,[3–6] body mass index (BMI),[7] blood pressure (BP),[5,8] blood glucose,[9,10] central corneal thickness (CCT),[4] have been reported to associate with IOP, but their results were not entirely consistent in all studies, and the potential risk factors in their analysis were failed to account due to lack of data. Therefore, population-based studies with larger sample size and detailed information are needed to better understand these issues.

To be noted, diabetes has become a global epidemic problem. It has been estimated that there were 451 million (age 18–99 years) people with diabetes in 2017, and these figures were expected to increase to 693 million by 2045.[11] It remains equivocal whether diabetic populations have different distribution or risk factors for IOP, and the association of diabetes with glaucoma has still been controversial, despite the fact that people with diabetes are twice likely to develop glaucoma compared with nondiabetes.[12] Therefore, data on IOP distribution and risk factors in diabetic populations are needed to clarify the relationship between glaucoma and diabetes and plan effective prevention strategies.

In view of the above issues, we conducted a large scale cross-sectional study based on the Dongguan Eye Study (DES) to investigate: (1) the distribution of and risk factors for IOP in general Southern Chinese population; (2) the difference in IOP distribution between diabetic and nondiabetic populations and risk factors for IOP in diabetes.

Methods

Design, Procedures, and Participants of DES

The DES, a large population-based cross-sectional study in Southern China, was established to investigate the frequency and risk factors for visual impairment and major vision-threatening eye diseases in an adult rural population. This study complied with the Declaration of Helsinki, and was approved by the Medical Ethics Committee of Dongguan People's Hospital and Research Ethics Committee of Guangdong Provincial People's Hospital. Each step in the study was verbally explained to the participants, and informed consent was obtained from each participant.

The methodology in detail has been reported elsewhere.[13,14] In brief, residents aged 40 years or older from Hengli Town of Dongguan were recruited from September 2011 to February 2012. A total of 11,357 participants were eligible for inclusion and 8952 (78.8% of eligible) participants were successfully enrolled for the systemic and ophthalmic examinations. Demographic, socioeconomic status, and health- and vision-related quality of life data were collected during interviews. Height, weight, waist and hip circumference, heart rate, and BP were measured per standardized protocol. Waist-hip ratio was defined as the quotient of waist circumference divided by hip circumference. BMI was calculated as weight in kilograms divided by height in meters squared. Body surface area (BSA) was calculated using the following formula: BSA (m^2) = 0.0061 × height (cm) + 0.0124 × weight (kg) − 0.0099. Venous blood was collected and laboratory tests, including fasting blood glucose (FBG), hemoglobin A1c, serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C), were conducted. A comprehensive ophthalmic examination included visual acuity, autorefraction, slit-lamp examination, IOP measurement, ocular biometry, gonioscopy, fundus photography, etc.

Every third person examined as part of the DES was systematically sampled to undergo an ocular biometric measurement. Subjects with glaucoma or other ocular diseases affecting measurement (e.g., pterygium, corneal opacity, severe trichiasis, strabismus, nystagmus, severe cataract, and lens subluxation) or history of ocular surgery (including cataract surgery) and trauma or unable to cooperate with the examination were excluded. A total of 2602 individuals were invited to take part in this examination, and 2112 (81.2% of invited) participants with available data on ocular biometry were included in this study. Moreover, according to the American Diabetes Association diagnostic criteria (2010),[15] 370 of the 2112 study participants were found to have type 2 diabetes with a corresponding prevalence of 17.52%.

Measurement of Ocular Biometry

The Lenstar LS900 optical biometer (Haag-Streit, Koeniz, Switzerland) was used to measure ocular biometry. Data on axial length (AL), CCT, anterior chamber depth (ACD), lens thickness (LT), corneal curvature, horizontal corneal diameter, and pupil diameter were obtained for analysis.

Measurement of IOP

IOP was measured by a noncontact tonometer (NCT, AT80, Topcon, Japan) for each eye. Three measurements were taken for each eye, and a retest was performed after 5-minute rest if the standard error of the three measurements exceeded 2 mm Hg. The final data of each eye was recorded as the average of three valid independent readings. When IOP was not measurable (e.g., due to corneal scar), it was estimated by digital tonometry and excluded in this study. IOP measurements were normally undertaken between 9 AM to 11 AM, and instrument calibration for the NCT was performed after finishing examination for each village.

Quality Control and Statistical Analysis

All data analysis was performed using SPSS software (version 20.0; SPSS, Inc., Chicago, IL, USA). Measurements from the right eye were selected for analysis because of the high correlation between the two eyes (Spearman rank correlation analysis). Distributions of IOP and other examination parameters were assessed for normality with Kolmogorov-Smirnov test and were considered significantly different from normal when the P value was ≤ 0.10. Normally distributed continuous variables were presented as mean ± standard deviation, and nonnormally distributed continuous data were presented as the median (interquartile range [IQR]). Differences between groups were compared using unpaired t-test/1-way ANOVA (normally distributed variables) or Wilcoxon/Kruskal-Wallis test (nonnormally distributed variables), as appropriate. Age was divided into four age groups 10 years apart: 40 to 49, 50 to 59, 60 to 69, and ≥70 years. Demographic and laboratory variables were also divided into subgroups for association analysis. Trend analysis was used to assess the association between IOP and age. Univariable and multiple linear regressions were used to assess the associations between potential risk factors and IOP. A 2-tailed P value of less than 0.05 was considered statistically significant for all analysis.

Results

Baseline Characteristics of Participants

A total of 2112 participants were included in the current analysis with a median age of 55 years (IQR, 47–62 years), 90.3% of the participants were aged 40 to 69 years old and 58.3% were female. Table 1 presents the baseline demographic, laboratory characteristic, ocular biometric parameters, and IOP for participants and nonparticipants of the current study. Most of systemic parameters were significant differences between the two groups, but without marked clinical significance, possibly due to the large sample size and the exclusion criteria. In view of strong correlations between the eyes for all biometric parameters and IOP (all with $P < 0.001$; Supplementary Table S1), the characteristics of ocular biometric parameters and the distribution of IOP from the right eye were analyzed. The mean IOP for the general population was 15.58 ± 3.27 mm Hg. IOP showed a near normal distribution with the majority of participants having an IOP value within the normal clinical range of 10 to 21 mm Hg (skewness: 1.139 [0.053], kurtosis: 5.849 [0.106]) (Fig. 1A).

IOP Distribution and Risk Factor in the General Population

The mean IOP was 15.60 ± 3.08 mm Hg in female participants and 15.55 ± 3.53 mm Hg in male participants, respectively. The distribution of IOP approximated normal distribution in both sexs while showing a slightly bigger variance in female participants (Figs. 1B, 1C). IOP for female and male participants were similar within the same age group, while IOP in younger age groups were higher compared with older age groups. Trend analysis showed a significant decreasing trend of IOP with increasing age (Supplementary Table S2, P for trend < 0.001).

Table 1. Baseline Demographic, Laboratory Characteristic, Ocular Biometric Parameters, and IOP for Participants and Nonparticipants of the Current Study

Variables	Participants, No. of Persons (%) or Mean ± SD	Nonparticipants, No. of Persons (%) or Mean ± SD	*P* Value
n	2112	6840	
Sex, male	881 (41.7)	2763 (40.4)	0.281
Age, y*	55 (47–62)	55 (47–63)	0.031
Height, cm	157.3 (7.9)	156.3 (8.4)	<0.001
Weight, kg	61.3 (10.7)	60.2 (11.3)	<0.001
BMI, kg/m^2	24.7 (3.5)	24.6 (4.0)	0.268
BSA, m^2	1.71 (0.17)	1.69 (0.18)	<0.001
Waist circumference, cm	82.6 (9.2)	82.1 (9.8)	0.038
Hip circumference, cm	94.4 (6.8)	93.4 (7.1)	<0.001
Waist-hip-ratio	0.87 (0.07)	0.88 (0.07)	<0.001
Mean SBP, mm Hg	132.3 (18.5)	133.7 (19.7)	0.003
Mean DBP, mm Hg	75.8 (10.6)	76.3 (10.7)	0.060
Mean heart rate, /minute	80.7 (12.4)	79.8 (12.5)	0.001
FBG, mmol/L*	5.57 (5.17–6.07)	5.47 (5.10–5.93)	<0.001
TC, mmol/L	5.27 (1.04)	5.22 (1.03)	0.052
TG, mmol/L*	1.21 (0.87–1.75)	1.27 (0.91–1.80)	0.014
LDL-C, mmol/L	3.08 (0.89)	3.04 (0.92)	0.079
HDL-C, mmol/L	1.52 (0.44)	1.49 (0.43)	0.005
AL, mm	23.28 (1.01)	–	–
CCT, mm	0.529 (0.030)	–	–
ACD, mm	2.57 (0.34)	–	–
LT, mm	4.41 (0.40)	–	–
LAF	1.90 (0.20)	–	–
RLP	2.27 (0.16)	–	–
Vitreous cavity length, mm	15.80 (1.04)	–	–
R1, mm	7.71 (0.26)	–	–
R2, mm	7.58 (0.26)	–	–
Corneal curvature, R, mm	7.65 (0.26)	–	–
Horizontal corneal diameter, mm	11.57 (0.52)	–	–
Pupil diameter, mm	4.07 (0.72)	–	–
AL/corneal curvature	3.05 (0.12)	–	–
Spherical equivalent, D*	0.25 (−0.88 to 1.13)	–	–
IOP, mm Hg	15.58 (3.27)	–	–

SBP, systolic BP; DBP, diastolic BP. BMI (kg/m^2) = weight (kg) / height (m^2); BSA (m^2) = 0.0061 × height (cm) + 0.0124 × weight (kg) − 0.0099; waist-hip-ratio = waist circumference (cm) / hip circumference (cm); LAF = (lens thickness /axial length) × 10; RLP = [(central corneal thickness + aqueous depth + 1/2 lens thickness) / axial length] × 10; vitreous cavity length = axial length − central corneal thickness − aqueous depth − lens thickness; R = (R1+R2) / 2.

* Median (P_{25}–P_{75}).

Univariable analysis of the association between IOP and potential risk factors showed that subjects with presence of diabetes or hypertension, or with younger age, higher BMI, bigger waist-hip ratio, higher TG, higher LDL-C, lower HDL-C, thicker CCT, lower LT, higher relative lens position (RLP), and a pupil diameter level of 3.5 to 4.0 mm had higher IOP (Supplementary Table S3).

The parameters with *P* value less than 0.10 in univariable analysis and those considered risk factors for glaucoma in literature[16–18] were selected into multivariable analysis (Table 2). The results showed that sex was not significantly associated with IOP. IOP tended to decrease with the increase of age, height, HDL-C, but tended to increase with the increase of BMI, SBP, DBP, FBG, LDL-C, and CCT in

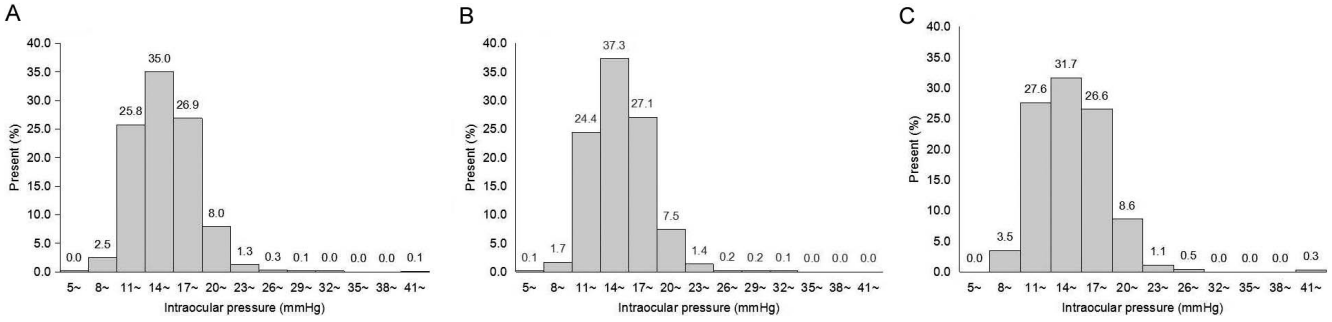

Figure 1. Distribution of IOP for the general participants (*right eye*). (**A**) All participants, (**B**) female participants, and (**C**) male participants. All participants: skewness is 1.139 (0.053), kurtosis is 5.849 (0.106); Females: skewness is 0.589 (0.070) and kurtosis is 1.212 (0.139); Males: Skewness is 1.645 (0.082) and kurtosis is 9.404 (0.165).

Table 2. Multiple Linear Regression Models of IOP in the Right Eye of All Persons Among Participants of the Current Study

	Unadjusted Difference in IOP		Adjusted Difference in IOP					
			Model 1		Model 2		Model 3	
	β (95% CI), mm Hg	*P*	β (95% CI), mm Hg	*P*	β (95% CI), mm Hg	*P*	β (95% CI), mm Hg	*P*
Sex, male vs. female	−0.058 (−0.341 to 0.226)	0.690	−0.026 (−0.371 to 0.319)	0.883	−0.176 (−0.565 to 0.214)	0.377	−0.073 (−0.401 to 0.255)	0.663
Age, per 10 y	−0.580 (−0.717 to −0.442)	<0.001	−0.707 (−0.858 to −0.555)	<0.001	−0.506 (−0.703 to −0.309)	<0.001	−0.571 (−0.717 to −0.425)	<0.001
Diabetes, yes vs. no	0.614 (0.247 to 0.980)	0.001	0.078 (−0.346 to 0.501)	0.719	1.027 (0.572 to 1.482)	<0.001	0.016 (−0.387 to 0.418)	0.939
BMI, per 5 kg/m^2	0.713 (0.527 to 0.900)	<0.001	0.278 (0.085 to 0.471)	0.005	-	-	0.242 (0.059 to 0.426)	0.010
Height, per 10 cm	−0.056 (−0.223 to 0.111)	0.509	−0.256 (−0.458 to −0.053)	0.013	-	-	−0.276 (−0.474 to −0.079)	0.006
SBP, per 10 mm Hg	0.306 (0.230 to 0.382)	<0.001	0.271 (0.113 to 0.321)	<0.001	-	-	0.218 (0.119 to 0.317)	<0.001
DBP, per 10 mm Hg	0.795 (0.660 to 0.931)	<0.001	0.403 (0.221 to 0.586)	<0.001	-	-	0.382 (0.208 to 0.555)	<0.001
FBG, mmol/L	0.183 (0.092 to 0.273)	<0.001	0.113 (0.012 to 0.214)	0.029	-	-	0.129 (0.032 to 0.226)	0.009
LDL-C, mmol/L	0.410 (0.254 to 0.566)	<0.001	0.337 (0.186 to 0.487)	<0.001	-	-	0.276 (0.132 to 0.419)	<0.001
HDL-C, mmol/L	−0.678 (−0.993 to −0.363)	<0.001	−0.478 (−0.796 to −0.160)	0.003	-	-	−0.406 (−0.708 to −0.103)	0.009
CCT, per 20 μm	0.715 (0.626 to 0.805)	<0.001	-	-	0.490 (0.278 to 0.701)	<0.001	0.677 (0.590 to 0.764)	<0.001
R1	−0.423 (−0.958 to 0.111)	0.120	-	-	−1.016 (−2.020 to −0.012)	0.047	−0.490 (−0.999 to 0.019)	0.059
AL, mm	−0.023 (−0.162 to 0.117)	0.750	-	-	0.546 (−1.142 to 2.235)	0.526	-	-
ACD, mm	0.315 (−0.093 to 0.723)	0.130	-	-	−6.065 (−14.819 to 2.689)	0.174	-	-
LT, mm	−0.322 (−0.677 to 0.033)	0.075	-	-	2.494 (−3.213 to 8.201)	0.391	-	-
LAF	−0.481 (−1.183 to 0.221)	0.179	-	-	−12.327 (−26.786 to 2.131)	0.095	-	-
RLP	1.381 (0.515 to 2.246)	0.002	-	-	13.063 (−7.751 to 33.878)	0.218	-	-
Pupil diameter, mm	−0.021 (−0.222 to 0.180)	0.840	-	-	−0.159 (−0.420 to 0.102)	0.233	-	-
Spherical equivalent, D	−0.014 (−0.083 to 0.056)	0.705	-	-	0.042 (−0.065 to 0.150)	0.442	-	-
Adjusted R^2	-		0.116		0.115		0.204	

Unadjusted, results are from univariable regression models; Model 1, results from multivariable regression models adjusted for sex, age, diabetes, BMI, height, SBP, DBP, FBG, HDL-C, and LDL-C. Model 2, results from multivariable regression models adjusted for sex, age, diabetes, CCT, R1, AL, ACD, LT, LAF, RLP, pupil diameter, and spherical equivalent. Model 3, results from multivariable regression models adjusted for sex, age, diabetes, BMI, height, SBP, DBP, FBG, HDL-C, LDL-C, CCT, and R1. SBP, systolic BP; DBP, diastolic BP.

Table 3. Baseline Demographic, Laboratory Characteristic, Ocular Biometric Parameters, and IOP for Nondiabetic and Diabetic Participants

Variables	Nondiabetic Participants, $n = 1742$	Diabetic Participants, $n = 370$	$\chi^2/t/Z$	P
Average age	54.7 ± 10.0	58.8 ± 10.3	−7.141	<0.001
Sex, male	727 (41.7)	153 (41.4)	0.018	0.892
Height, cm	157.4 ± 7.9	156.6 ± 8.0	1.816	0.070
Weight, kg	60.6 ± 10.4	64.9 ± 11.5	−6.711	<0.001
BMI, kg/m^2	24.4 ± 3.4	26.4 ± 3.7	−9.617	<0.001
BSA, m^2	1.71 ± 0.17	1.76 ± 0.18	−4.810	<0.001
Waist circumference, cm	81.6 ± 8.9	87.3 ± 9.2	−11.099	<0.001
Hip circumference, cm	94.0 ± 6.6	96.7 ± 7.3	−6.628	<0.001
Waist-hip-ratio	0.87 ± 0.07	0.90 ± 0.06	−8.667	<0.001
Mean SBP, mm Hg	130.7 ± 18.0	140.0 ± 18.8	−8.736	<0.001
Mean DBP, mm Hg	75.3 ± 10.4	78.2 ± 11.1	−4.508	<0.001
Mean heart rate, /minute	80.3 ± 12.4	82.5 ± 12.2	−3.095	0.002
FBG, mmol/L*	5.45 (5.10∼5.84)	6.86 (6.11∼7.86)	−22.894	<0.001
TC, mmol/L	5.22 ± 1.00	5.48 ± 1.20	−3.848	<0.001
TG, mmol/L*	1.15 (0.85∼1.67)	1.52 (1.08∼2.27)	−8.765	<0.001
LDL-C, mmol/L	1.54 ± 0.45	1.43 ± 0.37	4.976	<0.001
HDL-C, mmol/L	3.05 ± 0.86	3.24 ± 1.02	−3.484	0.001
AL, mm	23.3 ± 1.0	23.2 ± 0.9	2.624	0.009
CCT, mm	0.53 ± 0.03	0.53 ± 0.03	−0.015	0.988
ACD, mm	2.58 ± 0.34	2.53 ± 0.37	2.104	0.036
LT, mm	4.40 ± 0.36	4.46 ± 0.52	−1.953	0.051
LAF	1.89 ± 0.19	1.93 ± 0.25	−2.439	0.015
RLP	2.27 ± 0.14	2.26 ± 0.24	0.820	0.412
Vitreous cavity length, mm	15.82 ± 1.02	15.73 ± 1.14	1.508	0.132
R1	7.71 ± 0.26	7.70 ± 0.26	0.905	0.365
R2	7.59 ± 0.26	7.56 ± 0.26	1.890	0.059
Corneal curvature, R, mm	7.65 ± 0.26	7.63 ± 0.25	1.423	0.155
Horizontal corneal diameter, mm	11.59 ± 0.51	11.50 ± 0.57	2.928	0.004
Pupil diameter, mm	4.09 ± 0.73	3.96 ± 0.66	3.321	0.001
AL/R	3.05 ± 0.12	3.04 ± 0.10	1.417	0.157
Spherical equivalent, D*	0.25 (−1.00∼1.25)	0.25 (−0.63∼1.13)	−0.998	0.318
IOP, mm Hg	15.47 ± 3.26	16.09 ± 3.29	−3.286	0.001

SBP, systolic BP; DBP, diastolic BP. BMI (kg/m^2) = weight (kg) / height (m^2); BSA (m^2) = 0.0061 × height (cm) + 0.0124 × weight (kg) − 0.0099; waist-hip-ratio = waist circumference (cm) / hip circumference (cm); LAF = (lens thickness /axial length) × 10; relative lens position = [(central corneal thickness + aqueous depth + 1/2 lens thickness) / axial length] × 10; vitreous cavity length = axial length − central corneal thickness − aqueous depth − lens thickness; R = (R1+R2) / 2.

* Median (P_{25}–P_{75}).

adjusted analyses. The age- and sex-adjusted mean IOP of the diabetic participants was significantly higher than that of nondiabetes (mean difference 0.849 [0.486–1.213] mm Hg; $P < 0.001$), but when adjusting for systemic factors (BMI, height, SBP, DBP, FBG, HDL-C, and LDL-C) at the same time, there was no association between diabetes status and IOP (Table 2, model 1, model 3). Moreover, although lower R1 tended to have higher IOP when adjusted for sex, age, and ocular parameters, there was no correlation when adjusted for systemic and ocular factors. The AL, ACD, LT, lens/axial length factor (LAF), RLP, pupil diameter, and spherical equivalent, however, showed to be not related to IOP after adjusting for possible confounders. The model 3 in Table 2 displayed better fitness when adjusting for both systemic and ocular factors (adjusted $R^2 = 0.204$) as compared to adjusting systemic factors (model 1: adjusted $R^2 = 0.116$) or ocular parameters (model 2: adjusted $R^2 = 0.115$).

IOP in the Diabetic Population

Table 3 shows the baseline demographic, laboratory characteristic, ocular biometric parameters, and IOP for participants with or without diabetes. The mean IOP for diabetic population was 16.09 ± 3.29 mm Hg. Compared with nondiabetic participants, those with diabetes were older and had a higher BMI, BSA, waist-hip ratio, BP, heart rate, FBG, and blood lipids levels. Furthermore, participants with diabetes had smaller AL, ACD, horizontal corneal diameter, and pupil diameter, but larger LAF. Of note, the CCT and spherical equivalent had no significant difference between the participants with and without diabetes, while the LT was higher in the diabetic participants with a borderline significance ($P = 0.051$). IOP showed a right-skewed distribution among diabetic participants and a nearly normal distribution among nondiabetic participants (Fig. 2).

Univariable analysis of the association between IOP and potential risk factors among diabetic participants showed that subjects with presence of hypertension, or with younger age, higher BMI, bigger waist-hip ratio, higher TG, higher LDL-C, and thicker CCT had higher IOP (Supplementary Table S4).

As shown in Table 4, after adjusting for the potential confounders, multivariable analysis showed that significantly higher IOP was found in female, younger age, higher BP, higher LDL-C, lower HDL-C, and thicker CCT. The age- and sex-adjusted mean IOP was not associated with FBG in diabetic participants (mean difference 0.037 [–0.076, 0.151] mm Hg; $P = 0.517$). The model 3 displayed the best fitness (adjusted $R^2 = 0.257$) among the three models.

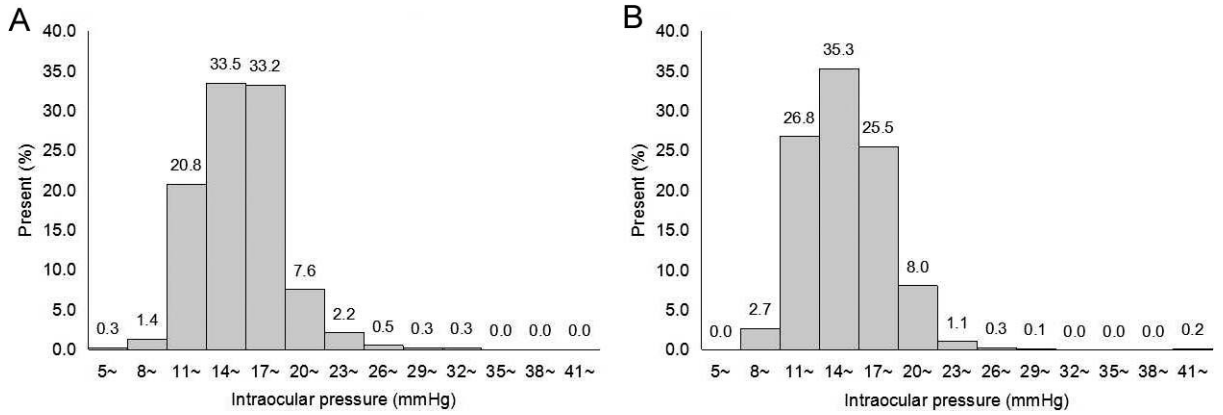

FIGURE 2. Distribution of IOP in diabetic (**A**) and nondiabetic (**B**) participants (right eye). Diabetic participants: skewness is 0.745 (0.127) and kurtosis is 2.225 (0.253); Nondiabetic participants: skewness is 1.234 (0.059) and kurtosis is 6.796 (0.117).

DISCUSSION

Based on larger samples and more comprehensive data, our study found that IOP showed a near normal distribution among general population and right-skewed distribution among diabetes. There was no association between diabetes status and IOP after adjusting for possible confounders. IOP would decrease with older age, greater height, and higher HDL-C, and increase with higher BMI, SBP, DBP, FBG, LDL-C, and thicker CCT in the general population. Risk factors for IOP elevation in diabetic population might be related to female sex, younger age, higher SBP and DBP, higher LDL-C, lower HDL-C, and thicker CCT. The other adjusted ocular biometric parameters, such as AL, ACD, LT, LAF, RLP, pupil diameter, and spherical equivalent, showed to be not related to IOP in both populations.

In our study, the mean IOP is slightly lower than that of the Beijing Eye Study conducted in Northern China (15.58 ± 3.27 mm Hg versus 16.11 ± 3.39 mm Hg), possibly due to lower CCT (0.529 ± 0.030 mm versus 0.556 ± 0.033 mm).[19] In similarly aged groups, the reported IOP in Chinese participants seems to be higher than that of Japanese and Korean participants in which a mean IOP is reported from 11 to 14 mm Hg.[20–23] However, most of the reports in white and black people vary and show a higher[24,25] or similar IOP[26,27] compared with ours. An association study of IOP from 12 population-based studies across Europe showed that mean IOP ranged from 13.6 mm Hg in the Rotterdam Study II to 16.0 mm Hg in the EPIC-Norfolk Eye Study.[28] Difference in ethnics, age, body statures, obesity, CCT, and measurements of IOP may in part explain the difference across studies.

The distribution of IOP in the Southern Chinese people aged 40 years or older is similar to that found in other Asian people, with a negative age-IOP relationship in cross-sectional analysis.[5,20–22,29,30] There is no consensus on the direction of association between IOP and age in the literature, with studies reporting increasing IOP,[31,32] decreasing IOP, no association of IOP[26] with older age, or an inverted U-shaped relationship.[28] Possible reasons for this inconsistency are differential associations by population, or a nonmonotonic relationship between age and IOP such that different studies of different aged participants yield different results.[28] Although hormonal difference may play a role in sex difference of IOP, and several studies found that female participants had higher IOP than male participants,[2,5,29] our study only observed the similar result in the diabetic population, while there was no sex difference in IOP distribution in the general population.

Most risk factors for IOP in our study are consistent with the literature. Higher BMI has been consistently reported as a risk factor for higher IOP, through its effect on blood viscosity and episcleral venous pressure.[20,21,33–35] A significant decrease in IOP with greater height after adjustment for possible confounders was found in our general population, which was consistent with a meta-analysis of pan-European study.[28] The mechanism underlying lower IOP in taller people is not clear, but may be related to the distance between the eye and the heart.[28] As shown in our study, BP is the most commonly reported risk factor for high IOP as higher BP could lead to an increase in ocular ultrafiltration and decrease in aqueous liquid outflow.[8,20–22,29,30,34–40] Contrary to the results that higher IOP is significantly correlated with history of diabetes mellitus in other reports,[20,29,34,35,41–43] our study found that IOP is not related to diabetes status in general population or to FBG in diabetic population, which suggested that diabetes mellitus or higher glucose might be not a risk factor for high IOP or glaucoma. We also identified that IOP was positively correlated with LDL-C and negatively correlated with HDL-C, while Yokomichi et al.[8] found that IOP was positively correlated with HDL-C and TG levels in a Japanese population. Although increased osmotic gradient and fibronectin accumulation related with diabetes and obesity have been suggested to play a role in IOP variation, the real association and underlying mechanism need further study. It is worth noting that, as our findings show, dyslipidemia is often closely related to abnormal BMI, BP, and blood sugar. Thus, these factors should be considered together when the relationship between blood lipids and IOP is analyzed, which can provide clues for screening of elevated IOP and related disease.

CCT has been demonstrated to be an important ocular contributor to IOP elevation, and the correlation between CCT and IOP in this study is similar to that for other populations.[4,20,33,35,40] It has been reported that the mean IOP increased by approximately 2.3 mm Hg for every 100-μm increment in CCT by ultrasound pachymetry,[4] while IOP increased 0.7 mm Hg per 20-μm thicker CCT (2.1 mm Hg/100 μm) in our general population. With respect to ophthalmic parameter, corneal curvature was another cornea-related factor influencing the IOP readings besides CCT. Our result shows that the larger the corneal curvature radius (R1), the lower are the IOP readings, suggesting that a relatively flat cornea as compared to a relatively steep cornea needs less force to be flattened to an area of a defined size.[44] In addition, other biometric factors possibly associated with glaucoma, such as AL, ACD, LT, LAF, RLP, pupil diameter, were not associated with high IOP in our both general population and diabetic subgroup.

Given the ever-increasing prevalence of diabetes and the higher risk of glaucoma in diabetic population, risk factor

Table 4. Multiple Linear Regression Models of IOP in the Right Eye of Diabetic Persons Among Participants of the Current Study

	Unadjusted Difference in IOP		Adjusted Difference in IOP					
			Model 1		Model 2		Model 3	
	β (95% CI), mm Hg	*P*	β (95% CI), mm Hg	*P*	β (95% CI), mm Hg	*P*	β (95% CI), mm Hg	*P*
Sex, male vs. female	−0.147 (−0.831 to 0.537)	0.673	−0.680 (−1.475 to 0.115)	0.093	−0.358 (−1.284 to 0.569)	0.447	−0.775 (−1.530 to −0.020)	0.044
Age, per 10 y	−0.857 (−1.181 to −0.534)	<0.001	−0.823 (−1.166 to −0.480)	<0.001	−1.001 (−1.468 to −0.535)	<0.001	−0.809 (−1.138 to −0.480)	<0.001
BMI, per 5 kg/m^2	0.720 (0.273 to 1.168)	0.002	0.271 (−0.156 to 0.699)	0.213	-	-	0.283 (−0.125 to 0.690)	0.173
Height, per 10 cm	0.167 (−0.230 to 0.563)	0.409	−0.032 (−0.497 to 0.432)	0.892	-	-	−0.244 (−0.690 to 0.201)	0.281
SBP, per 10 mm Hg	0.452 (0.271 to 0.633)	<0.001	0.378 (0.162 to 0.594)	0.001	-	-	0.321 (0.114 to 0.529)	0.003
DBP, per 10 mm Hg	1.013 (0.682 to 1.343)	<0.001	0.400 (−0.008 to 0.807)	0.054	-	-	0.429 (0.036 to 0.822)	0.032
FBG, mmol/L	0.053 (−0.063 to 0.169)	0.371	0.054 (−0.052 to 0.161)	0.314	-	-	0.061 (−0.041 to 0.164)	0.238
LDL-C, mmol/L	0.572 (0.245 to 0.899)	0.001	0.478 (0.171 to 0.785)	0.002	-	-	0.430 (0.138 to 0.722)	0.004
HDL-C, mmol/L	−1.363 (−2.258 to −0.468)	0.003	−1.358 (−2.224 to −0.492)	0.002	-	-	−1.166 (−1.994 to −0.339)	0.006
CCT, per 20 μm	0.585 (0.373 to 0.796)	<0.001	-	-	0.310 (−0.359 to 0.980)	0.362	0.545 (0.347 to 0.743)	<0.001
R1	−0.518 (−1.783 to 0.747)	0.421	-	-	−2.081(−4.501 to 0.339)	0.092	-	-
AL, mm	0.103 (−0.286 to 0.491)	0.603	-	-	1.369 (−4.790 to 7.527)	0.662	-	-
ACD, mm	0.646 (−0.254 to 1.546)	0.159	-	-	−8.300 (−39.537 to 22.936)	0.601	-	-
LT, mm	−0.337 (−0.981 to 0.306)	0.303	-	-	1.999 (−12.133 to 16.131)	0.781	-	-
LAF	−0.717 (−2.077 to 0.643)	0.300	-	-	−13.618 (−39.459 to 12.222)	0.300	-	-
RLP	1.676 (0.281 to 3.071)	0.019	-	-	18.856 (−54.130 to 91.843)	0.611	-	-
Pupil diameter, mm	0.165 (−0.362 to 0.692)	0.538	-	-	0.077 (−0.558 to 0.713)	0.810	-	-
Spherical equivalent, D	−0.003 (−0.226 to 0.220)	0.978	-	-	0.159 (−0.132 to 0.451)	0.282	-	-
Adjusted R^2	-		0.194		0.126		0.257	

Unadjusted, results are from univariable regression models. Model 1, results from multivariable regression models adjusted for sex, age, BMI, height, SBP, DBP, FBG, HDL-C, and LDL-C. Model 2, results from multivariable regression models adjusted for sex, age, CCT, R1, AL, ACD, LT, LAF, RLP, pupil diameter, and spherical equivalent. Model 3, results from multivariable regression models adjusted for sex, age, BMI, height, SBP, DBP, FBG, HDL-C, LDL-C, and CCT. SBP, systolic BP; DBP, diastolic BP.

analysis for IOP among this subgroup is of important public health significance. Unfortunately, rare data are available for the Chinese population to date, and whether risk factors for IOP among diabetes are different from the nondiabetic population is largely unknown. Different from a nearly normal distribution in the nondiabetic population, IOP shows a right-skewed distribution in our diabetic population. SBP, DBP, and LDL-C, rather than FBG, were more positively correlated with higher IOP in the diabetic population, which mechanism might be related to metabolic syndrome in general.[38] Although diabetes was generally considered to be associated with higher IOP and thicker CCT, CCT contributed a small proportion of mediating effect to the total effect of diabetes on IOP.[10] It is considered that diabetes-related autonomic dysfunction and corneal stiffening caused by glycation-induced corneal collagen cross-links in diabetes may contribute to increase IOP.[45]

Strengths of the current study include a population-based design, a large sample size, and the availability of multiple potential risk factors (systemic and ocular parameters) for IOP. However, some limitations need to be noted. First, the cross-sectional design is subject to cohort effect, and our conclusion still needs further validation from longitudinal cohorts. Second, inclusion method and exclusion criteria in this study might lead to selection bias. Third, IOP was measured by NCT instead of Goldmann tonometer (Gold standard), but NCT had been reported to have a good reliability within the normal IOP range.[46] Forth, our results can only represent IOP during the measuring period, and may not be able to reflect the circadian IOP fluctuations.[47]

In conclusion, the distribution of IOP in our study is similar to that in the majority of Asian population-based reports. In the general population aged 40 years or older from Southern China, higher IOP was significantly correlated with younger age, lower height, and HDL-C, and higher BMI, BP, FBG, LDL-C, and CCT. Female sex, thicker CCT, and higher BMI, BP, HDL-C, and LDL-C may be more likely to have higher IOP in diabetic population. By identifying specific characteristics associated with IOP, those results have implications for detecting persons most likely to have higher IOP. Because high IOP is a major risk factor for glaucoma, it would be reasonable to speculate that similar associations would be found for both conditions. Of cause, the real association between these IOP-related risk factors and glaucoma still need further investigation.

Acknowledgments

The authors appreciate the great support offered by the government of Hengli Town for this study. We thank the staff of Hengli Hospital for their work relating to the survey.

Supported by the National Natural Science Foundation, Beijing, China (81371031), Guangdong Natural Science Foundation (2017A030313609), Project of Guangdong Medical Science and Technology Research Foundation, Guangzhou, China (A2018401), Guangzhou Science and Technology Project, Guangzhou, China (Z032012245, 201704020048). The funding organizations had no role in the design or conduct of this research.

Disclosure: **Y. Cui**, None; **X. Yang**, None; **G. Zhang**, None; **H. Guo**, None; **M. Zhang**, None; **L. Zhang**, None; **J. Zeng**, None; **Q. Liu**, None; **L. Zhang**, None; **Q. Meng**, None

References

1. Chan EW, Li X, Tham YC, et al. Glaucoma in Asia: regional prevalence variations and future projections. *Br J Ophthalmol*. 2016;100:78–85.
2. Astrom S, Stenlund H, Linden C. Intraocular pressure changes over 21 years - a longitudinal age-cohort study in northern Sweden. *Acta Ophthalmol*. 2014;92:417–420.
3. Preussner PR, Grossmann A, Ngounou F, et al. Glaucoma screening in Western Cameroon. *Graefes Arch Clin Exp Ophthalmol*. 2009;247:1671–1675.
4. Wang D, Huang W, Li Y, et al. Intraocular pressure, central corneal thickness, and glaucoma in Chinese adults: the Liwan Eye Study. *Am J Ophthalmol*. 2011;152:454–462.e1.
5. Han X, Niu Y, Guo X, et al. Age-related changes of intraocular pressure in elderly people in Southern China: Lingtou Eye Cohort Study. *PLoS One*. 2016;11:e0151766.
6. Zhao D, Kim MH, Pastor-Barriuso R, et al. A longitudinal study of age-related changes in intraocular pressure: the Kangbuk Samsung Health Study. *Invest Ophthalmol Vis Sci*. 2014;55:6244–6250.
7. Wang YX, Xu L, Zhang XH, et al. Five-year change in intraocular pressure associated with changes in arterial blood pressure and body mass index. The Beijing Eye Study. *PLoS One*. 2013;8:e77180.
8. Yokomichi H, Kashiwagi K, Kitamura K, et al. Evaluation of the associations between changes in intraocular pressure and metabolic syndrome parameters: a retrospective cohort study in Japan. *BMJ Open*. 2016;6:e010360.
9. Zhao D, Cho J, Kim MH, et al. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis. *Ophthalmology*. 2015;122:72–78.
10. Luo XY, Tan NYQ, Chee ML, et al. Direct and indirect associations between diabetes and intraocular pressure: The Singapore Epidemiology of Eye Diseases Study. *Invest Ophthalmol Vis Sci*. 2018;59:2205–2211.
11. Cho NH, Shaw JE, Karuranga S, et al. IDF diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract*. 2018;138:271–281.
12. Zhao YX, Chen XW. Diabetes and risk of glaucoma: systematic review and a meta-analysis of prospective cohort studies. *Int J Ophthalmol*. 2017;10:1430–1435
13. Meng Q, Cui Y, Zhang M, et al. Design and baseline characteristics of a population-based study of eye disease in southern Chinese people: the Dongguan Eye Study. *Clin Exp Ophthalmol*. 2016;44:170–180.
14. Cui Y, Zhang L, Zhang M, et al. Prevalence and causes of low vision and blindness in a Chinese population with type 2 diabetes: the Dongguan Eye Study. *Sci Rep*. 2017;7:11195.
15. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33:S62–S69.
16. Jiang X, Varma R, Wu S, et al. Baseline risk factors that predict the development of open-angle glaucoma in a population: the Los Angeles Latino Eye Study. *Ophthalmology*. 2012;119:2245–2253.
17. Moghimi S, Vahedian Z, Fakhraie G, et al. Ocular biometry in the subtypes of angle closure: an anterior segment optical coherence tomography study. *Am J Ophthalmol*. 2013;155:664–673.
18. Chen YY, Chen YY, Sheu SJ, Chou P. The biometric study in different stages of primary angle-closure glaucoma. *Eye (Lond)*. 2013;27:1070–1076.
19. Xu L, Li J, Zheng Y, et al. Intraocular pressure in northern China in an urban and rural population: the Beijing Eye Study. *Am J Ophthalmol*. 2005;140:913–915.
20. Kawase K, Tomidokoro A, Araie M, et al. Ocular and systemic factors related to intraocular pressure in Japanese adults: the Tajimi Study. *Br J Ophthalmol*. 2008;92:1175–1179.
21. Nomura H, Shimokata H, Ando F, et al. Age-related changes in intraocular pressure in a large Japanese population: a cross-sectional and longitudinal study. *Ophthalmology*. 1999;106:2016–2022.
22. Baek SU, Kee C, Suh W. Longitudinal analysis of age-related changes in intraocular pressure in South Korea. *Eye (Lond)*. 2015;29:625–629.

23. Choi JA, Han K, Park YM, Park CK. Age-related association of refractive error with intraocular pressure in the Korea National Health and Nutrition Examination Survey. *PLoS One*. 2014;9:e111879.
24. Sommer A, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans. The Baltimore Eye Survey. *Arch Ophthalmol*. 1991;109:1090–1095.
25. Nemesure B, Wu SY, Hennis A, et al. Corneal thickness and intraocular pressure in the Barbados eye studies. *Arch Ophthalmol*. 2003;121:240–244.
26. Klein BE, Klein R, Linton KL. Intraocular pressure in an American community. The Beaver Dam Eye Study. *Invest Ophthalmol Vis Sci*. 1992;33:2224–2228.
27. Bonomi L, Marchini G, Marraffa M, et al. The relationship between intraocular pressure and glaucoma in a defined population. Data from the Egna-Neumarkt Glaucoma Study. *Ophthalmologica*. 2001;215:34–38.
28. Khawaja AP, Springelkamp H, Creuzot-Garcher C, et al. Associations with intraocular pressure across Europe: The European Eye Epidemiology (E3) Consortium. *Eur J Epidemiol*. 2016;31:1101–1111
29. Lin HY, Hsu WM, Chou P, et al. Intraocular pressure measured with a noncontact tonometer in an elderly Chinese population: the Shihpai Eye Study. *Arch Ophthalmol*. 2005;123:381–386.
30. Lee MK, Cho SI, Kim H, et al. Epidemiologic characteristics of intraocular pressure in the Korean and Mongolian populations: the Healthy Twin and the GENDISCAN Study. *Ophthalmology*. 2012;119:450–457.
31. Wu SY, Leske MC. Associations with intraocular pressure in the Barbados Eye Study. *Arch Ophthalmol*. 1997;115:1572–1576.
32. Memarzadeh F, Ying-Lai M, Azen SP, Varma R; Los Angeles Latino Eye Study Group. Associations with intraocular pressure in Latinos: the Los Angeles Latino Eye Study. *Am J Ophthalmol*. 2008;146:69–76.
33. Zhao D, Kim MH, Pastor-Barriuso R, et al. A longitudinal study of association between adiposity markers and intraocular pressure: The Kangbuk Samsung Health Study. *PLoS One*. 2016;11:e0146057.
34. Zhou Q, Liang YB, Wong TY, et al. Intraocular pressure and its relationship to ocular and systemic factors in a healthy Chinese rural population: the Handan Eye Study. *Ophthalmic Epidemiol*. 2012;19:278–284.
35. Tomoyose E, Higa A, Sakai H, et al. Intraocular pressure and related systemic and ocular biometric factors in a population-based study in Japan: the Kumejima study. *Am J Ophthalmol*. 2010;150:279–286.
36. Mitchell P, Lee AJ, Wang JJ, et al. Intraocular pressure over the clinical range of blood pressure: Blue Mountains Eye Study findings. *Am J Ophthalmol*. 2005;140:131–132.
37. Klein BE, Klein R, Knudtson MD. Intraocular pressure and systemic blood pressure: longitudinal perspective: the Beaver Dam Eye Study. *Br J Ophthalmol*. 2005;89:284–287.
38. Xu L, Wang H, Wang Y, et al. Intraocular pressure correlated with arterial blood pressure. The Beijing Eye Study. *Am J Ophthalmol*. 2007;144:461–462.
39. Memarzadeh F, Ying-Lai M, Chung J, et al. Blood pressure, perfusion pressure, and open-angle glaucoma: the Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci*. 2010;51:2872–2877.
40. Wong TT, Wong TY, Foster PJ, et al. The relationship of intraocular pressure with age, systolic blood pressure, and central corneal thickness in an Asian population. *Invest Ophthalmol Vis Sci*. 2009;50:4097–4102.
41. Klein BE, Klein R, Moss SE. Intraocular pressure in diabetic persons. *Ophthalmology*. 1984;91:1356–1360.
42. Chopra V, Varma R, Francis BA, Wu J, Torres M, Azen SP; Los Angeles Latino Eye Study Group. Type 2 diabetes mellitus and the risk of open-angle glaucoma the Los Angeles Latino Eye Study. *Ophthalmology*. 2008;115:227–232.
43. Tan GS, Wong TY, Fong CW, Aung T; Singapore Malay Eye Study. Diabetes, metabolic abnormalities, and glaucoma. *Arch Ophthalmol*. 2009;127:1354–1361.
44. Wang YX, Xu L, Wei WB, Jonas JB. Intraocular pressure and its normal range adjusted for ocular and systemic parameters. The Beijing Eye Study 2011. *PLoS One*. 2018;13:e0196926.
45. Krueger RR, Ramos-Esteban JC. How might corneal elasticity help us understand diabetes and intraocular pressure? *J Refract Surg*. 2007;23:85–88.
46. Carbonaro F, Andrew T, Mackey DA, et al. Comparison of three methods of intraocular pressure measurement and their relation to central corneal thickness. *Eye (Lond)*. 2010;24:1165–1170.
47. Fogagnolo P, Orzalesi N, Ferreras A, Rossetti L. The circadian curve of intraocular pressure: can we estimate its characteristics during office hours? *Invest Ophthalmol Vis Sci*. 2009;50:2209–2215.

Investigative Ophthalmology & Visual Science