Original Article

Association between Mean Ocular Perfusion Pressure and Diabetic Retinopathy in a Northeastern Chinese Population*

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Abstract

Objective To evaluate the association between diabetic retinopathy (DR) and mean ocular perfusion pressure (MOPP) in patients with type 2 diabetes mellitus (T2DM).

Methods Patients from the Fushun Diabetic Retinopathy Cohort Study (FS-DIRECT), a community-based prospective cohort study conducted in northeast China, were included in this study. The presence and severity of DR were determined by grading fundus photographs according to the Early Treatment Diabetic Retinopathy Study (ETDRS) retinopathy scale. Systolic and diastolic blood pressure (SBP and DBP) were recorded using an electronic sphygmomanometer. Intraocular pressure (IOP) was measured using an iCare rebound tonometer. MOPP was calculated using the formula MOPP = 2/3 [DBP + 1/3 (SBP − DBP)] − IOP.

Results In total, 1,857 patients who had gradable fundus photography and MOPP data were enrolled in this study. Male patients had a higher MOPP than female patients (52.25 ± 8.75 *vs*. 50.96 ± 8.74 mmHg, $P = 0.002$). Overall, both male and female patients with any type of DR, non-proliferative DR (NPDR), or non-sight-threatening DR (non-STDR) had significantly higher MOPP relative to patients without DR. Increased MOPP (per 1 mmHg) was in turn associated with the presence of any type of DR [odds ratio (*OR*) = 1.03, 95% confidence interval (*CI*) : 1.02–1.04], NPDR (*OR* = 1.03 95% *CI*: 1.02–1.04), and non-STDR (*OR* = 1.03, 95% *CI*: 1.01–1.04) after adjusting for confounders. Increased MOPP (per 1 mmHg) was also associated with an increased likelihood of macular edema (*OR* = 1.02, 95% *CI*: 1.01–1.04).

Conclusions The results suggest that increased MOPP was associated with DR and macular edema in northeastern Chinese patients with T2DM.

Key words: Diabetic retinopathy; Ocular perfusion pressure; Systolic blood pressure; Diastolic blood pressure

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INTRODUCTION

Diabetic retinopathy (DR) is an important global public health issue. Hyperglycemia initiates a number of pathological vascular processes including blood vessel dilation, increased capillary permeability, microaneurysm, and lipid and blood cell exudation. However, the mechanisms underlying these processes remain poorly understood. According to Starling and Laplace's law, reduced retinal blood flow may lead to decreased capillary hydrostatic pressure, resulting in decreased leakage out of compromised retinal capillaries[1,2]. Moreover, studies also showed that increased retinal blood flow was associated with DR progression[3-5]. Because the blood flow through any tissue is generated by perfusion pressure, the mean ocular perfusion pressure (MOPP) is presumably associated with DR.

The association between MOPP and DR has been reported in previous studies[4,6-8]. However, the conclusions drawn about this association have been inconsistent. In both cross-sectional and longitudinal studies, researchers have found that higher MOPP is associated with DR, macular edema, and hard exudation[4,6,7]. However, another cross-sectional epidemiological study did not observe this association[8]. Furthermore, studies examining this association in Asian patients are rare.

MOPP is clinically modifiable because it is the difference between two thirds of the mean arterial pressure (MAP) and the intraocular pressure (IOP) (MOPP = 2⁄3 MAP − IOP). An improved understanding of the association between MOPP, DR, and maculopathy will have potential clinical implications. This study therefore investigated the association between MOPP and DR using information from the Fushun Diabetic Retinopathy Cohort Study (FS-DIRECT), a community-based study, in patients with type 2 diabetes mellitus (T2DM) in northeastern China.

METHODS

The details of the rationale, design, and methodology of the FS-DIRECT study are described elsewhere[9]. Residents of Jiangjun Street, Fushin City, who were aged 30 or older and had T2DM were recruited between July 2012 and May 2013. The Fushun Eye Hospital Ethics Committee approved this study. Written informed consent was obtained from all subjects. The inclusion criteria for this study were that each subject had available data regarding their level of DR and MOPP.

Diabetic Retinopathy and Macular Edema

DM was diagnosed according to the criteria suggested by the American Diabetes Association[10].

For each subject, six stereoscopic macula images in different fields of color were captured by certified photographers using a 45° nonmydriatic retinal camera (Kowa, VK-2, Tokyo, Japan) after pupil dilation. These fundus photographs were graded in a masked manner according to the modified Airlie House Classification system[11]. The retinopathy level was graded accordingly: (1) no DR (levels 10–20); (2) nonproliferative DR [NPDR, mild (levels 31–37), moderate DR (levels 43–47), or severe DR (level 53)] or (3) proliferative DR (PDR, levels 60–85). Macular edema (ME) was defined as the presence of retinal thickening within 1 disk diameter of the foveal center or as the presence of focal photocoagulation scars in the macular area. Clinically significant ME (CSME) was defined as the presence of either (1) retinal thickening within 500 μm of the macula, or focal photocoagulation scars; (2) hard exudates within 500 μm of the macula with adjacent retinal thickening; (3) retinal thickening of more than one optic disc area within one optic disc diameter of the macula. Mild and moderate NPDR were considered to be non-sight-threatening DR (non-STDR), while severe NPDR, PDR, and CSME were considered to be sight-threatening DR (STDR).

Mean Ocular Perfusion Pressure

Blood pressures were recorded from patients' right arms in the sitting position after at least 5 min of rest using an electronic sphygmomanometer (HEM-8102A; Omron Healthcare, Kyoto, Japan) according to a protocol similar to that used in the Multi-ethnic Study of Atherosclerosis[12]. The patients were advised not to smoke and drink coffee or strong tea half an hour before the measurements. Measurement was performed again 3 min later. The measurement was performed the third time if the two systolic blood pressure (SBP) data were different by more than 10 mmHg or if the diastolic blood pressure (DBP) data were different by more than 5 mmHg. The two closest readings were averaged to calculate the mean SBP and DBP.

IOP was measured using an iCare rebound tonometer (iCare, Helsinki, Finland) from each patient in the sitting position. Six measurements were obtained from the central cornea of each eye, and the data were averaged after excluding the highest and lowest values. Only quality

measurements (indicated by zero to one bar on the device) were accepted.

MOPP was calculated according to the formula MOPP = 2⁄3 [DBP + 1⁄3 (SBP − DBP)] − IOP.

Statistical Analysis

Because DR and IOP levels in the right and left eyes were highly correlated (Pearson correlation coefficient: 0.87 and 0.84, respectively), for simplicity, only data obtained from patients' right eyes were used for further analyses.

Normally distributed parameters are presented as the mean ± standard deviation. *T*-tests or analyses of variance were performed to compare groups relative to either patients with no DR or patients with no ME, respectively. Bonferroni tests were used for pairwise comparisons such as comparing MOPP between patients with no DR and patients with either NPDR or PDR. Chi-square tests were performed to analyze discrete categorical data. Multivariate linear regression was performed (in a stepwise manner) to determine the association between MOPP and factors such as age, sex, refractive error, education level, income level, duration of DM, fasting plasma glucose (FPG), HbA1c, body mass index (BMI), waist-to-hip ratio (WHR), serum creatinine, blood urea nitrogen, blood uric acid, total cholesterol (TC), total triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and urine protein level. Multivariate logistical regressions were performed for the association between presence/stage of DR and risk factors.

Statistical analyses were performed using Statistical Analysis System for Windows, version 9.1.3 (SAS Inc., Cary, NC). A *P* value less than 0.05 was considered to indicate statistical significance.

RESULTS

A total of 1,857 patients (male 768, 41.4%) were enrolled in this study. Mean age of the patients was 61.5 ± 8.7 years and mean DM duration was 7.6 ± 5.9 years. Mean SBP, DBP, and IOP were 147.39 ± 23.32 mmHg, 77.35 ± 11.36 mmHg, and 15.6 ± 3.4 mmHg, respectively. Male patients had lower SBP (146.14 ± 21.70 *vs.* 148.27 ± 24.37 mmHg, *P* = 0.048) and higher DBP (79.28 ± 11.63 *vs.* 75.99 ± 10.96 mmHg, *P* < 0.001) relative to their female counterparts. There was no significant difference in IOP between males and females (15.5 ± 3.4 *vs.* 15.8 ± 3.5 mmHg, *P* = 0.06). A total of 61.9% of patients had mean SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, while 6.4% patients had an IOP ≥ 21 mmHg. Table 1 shows the characteristics of patients with or without DR by sex.

Table 2 shows the mean MOPP value for male, female, and combined male and female patients. Mean MOPP for all patients was 51.49 ± 8.77 mmHg. Male patients had a higher MOPP than female patients (52.25 ± 8.75 *vs.* 50.96 ± 8.74 mmHg, *P* = 0.002). Both male and female patients (and combined male and female patients) with any type of DR or NPDR had significantly higher MOPP values than patients without DR. Male patients (and combined male and female patients) with ME also had significantly higher MOPP values than did patients without ME.

Table 3 shows the multivariate linear regression results for the factors associated with MOPP. Table 4 shows the association between DR prevalence and the risk factors. In a stepwise multivariate regression model, we found that sex, FPG, BMI, serum creatinine, LDL, HDL, and urine protein levels were significantly associated with MOPP. Furthermore, WHR and blood urea nitrogen were almost significantly associated with MOPP (Table 3). We also found that MOPP, age, refractive error, income level, DM duration, FPG, HbA1c, TG, and urine protein levels were significantly associated with DR after adjusting for MOPP and similar risk factors in a multivariate logistical model. Furthermore, TC was almost significantly associated with DR (Table 4).

In further logistic analyses, after adjusting for factors remaining in the previous multivariate regression model, we found that increased MOPP (per 1 mmHg) was significantly associated with the presence of any type of DR [odds (*OR*) = 1.03, 95% confidence interval (*CI*): 1.02–1.04, *P* < 0.001], NPDR (*OR* = 1.03, 95% *CI*: 1.02–1.04, *P* < 0.001), and non-STDR (*OR* = 1.03, 95% *CI*: 1.01–1.04, *P* < 0.001). Moreover, increased MOPP (per 1 mmHg) was found to be associated with increased ME likelihood (*OR* = 1.02, 95% *CI*: 1.01–1.04, *P* = 0.008). However, no significant association was found between MOPP and PDR, non-STDR and STDR, or non-CSME and CSME (Table 5) relative to NPDR.

DISCUSSION

Previous studies examining the association between MOPP and DR are rare, and to the best of our knowledge, no such studies examined this association in a Chinese population. As MOPP can be measured easily and modified clinically, data concerning MOPP and its association with both DR and maculopathy have clinical significance and

would aid future intervention studies. This study measured MOPP in patients with T2DM living in northeastern China, analyzed factors associated with MOPP, and determined the association between

Table 1. Characteristics of patients with or without diabetic retinopathy by sex

Item	Overall			Men			Women		
	No DR (*n* = 1,151)	DR (*n* = 706)	*P*	No DR (*n* = 491)	DR (*n* = 277)	*P*	No DR (*n* = 660)	DR (*n* = 429)	*P*
Age	61.7 ± 8.7	61.1 ± 8.6	0.16	61.2 ± 9.4	59.6 ± 8.4	0.01	62.0 ± 8.2	62.1 ± 8.5	0.91
Male, *n* (%)	491 (42.7)	277 (39.2)	0.15	–	–		–	–	
Duration of diabetes (years)	5.7 ± 4.8	10.6 ± 6.2	< 0.001	5.2 ± 4.6	10.5 ± 6.2	< 0.001	6.1 ± 4.9	10.6 ± 6.2	< 0.001
FPG (mmol/L)	8.7 ± 2.9	10.4 ± 3.9	< 0.001	8.9 ± 2.9	10.7 ± 4.0	< 0.001	8.6 ± 2.9	10.3 ± 3.9	< 0.001
HbA1c (%)	7.4 ± 1.9	8.3 ± 2.1	< 0.001	7.4 ± 1.9	8.5 ± 2.2	< 0.001	7.4 ± 1.8	8.2 ± 2.1	< 0.001
BMI (kg/m^2)	26.49 ± 3.43	26.23 ± 3.42	0.11	26.44 ± 3.14	25.99 ± 2.96	0.051	26.52 ± 3.63	26.38 ± 3.68	0.054
SBP (mmHg)	144.47 ± 22.80	152.15 ± 23.39	< 0.001	143.71 ± 21.27	150.45 ± 21.82	< 0.001	145.04 ± 23.88	153.25 ± 24.30	< 0.001
DBP (mmHg)	77.08 ± 10.92	77.80 ± 12.03	0.19	78.95 ± 11.06	79.87 ± 12.58	0.31	75.69 ± 10.62	76.46 ± 11.48	0.25
High BP, *n* (%)	654 (56.8)	496 (70.2)	< 0.001	289 (58.9)	191 (69.0)	0.006	365 (55.3)	305 (71.1)	< 0.001
MAP	99.54 ± 12.96	102.58 ± 13.84	< 0.001	100.53 ± 12.64	103.40 ± 13.78	0.004	98.80 ± 13.15	102.06 ± 13.87	< 0.001
IOP	15.63 ± 3.59	15.66 ± 3.16	0.86	15.49 ± 3.53	15.42 ± 3.06	0.79	15.74 ± 3.64	15.81 ± 3.22	0.73
High IOP, *n* (%)	84 (7.3)	34 (4.8)	0.03	37 (7.5)	10 (3.6)	0.03	47 (7.1)	24 (5.6)	0.32
MOPP	50.73 ± 8.43	52.73 ± 9.15	< 0.001	51.54 ± 8.38	53.51 ± 9.25	0.003	50.13 ± 8.43	52.23 ± 9.07	< 0.001

Note. FPG: fasting plasma glucose; HbA1c: glycosylated hemoglobin A1c; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; IOP: intraocular pressure; MOPP: mean ocular perfusion pressure; DR: diabetic retinopathy. High BP is defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg; high IOP is defined as IOP ≥ 21 mmHg.

Table 2. MOPP values by sex in the study population

Item	Overall			Male			Female		
	n	Mean ± SD	*P*	*n*	Mean ± SD	*P*	*n*	Mean ± SD	*P*
Overall	1,857	51.49 ± 8.77	–	768	52.25 ± 8.75	–	1,089	50.96 ± 8.74	–
Retinopathy									
No DR	1,151	50.73 ± 8.43	Ref	491	51.54 ± 8.38	Ref	660	50.13 ± 8.43	Ref
Any DR	706	52.73 ± 9.15	< 0.001	277	53.51 ± 9.25	0.003	429	52.23 ± 9.07	< 0.001
NPDR	639	52.74 ± 9.23	Sig	251	53.32 ± 9.30	Sig	388	52.37 ± 9.18	Sig
PDR	67	52.62 ± 8.40	NS	26	55.33 ± 8.71	NS	41	50.89 ± 7.82	NS
Non-STDR	516	52.72 ± 9.44	Sig	205	53.19 ± 9.68	NS	311	52.40 ± 9.28	Sig
STDR	190	52.76 ± 8.34	Sig	72	54.41 ± 7.88	Sig	118	51.76 ± 8.48	NS
Maculopathy									
No ME	1,548	51.17 ± 8.64	Ref	656	51.86 ± 8.72	Ref	892	50.67 ± 8.56	Ref
ME	250	53.01 ± 9.26	0.002	89	54.78 ± 8.75	0.003	161	52.03 ± 9.41	0.070
Non-CSME	120	53.58 ± 10.08	Sig	42	55.80 ± 9.35	Sig	78	52.39 ± 10.31	NS
CSME	130	52.47 ± 8.43	NS	47	53.87 ± 8.17	NS	83	51.69 ± 8.52	NS

Note. MOPP: mean ocular perfusion pressure; DR: diabetic retinopathy; NPDR: non-proliferative DR; PDR: proliferative DR; STDR: sight-threatening DR; ME: macular edema; CSME: clinically significant ME; SD: standard deviation; Ref: reference group; Sig: significant; NS: not significant.

MOPP and DR. In this study, we found that male patients with T2DM had higher MOPP and DBP values than their female counterparts. Furthermore, sex was significantly associated with MOPP after adjusting for confounders such as fasting blood glucose[13] and body mass index (BMI)[8]. This finding was consistent with that reported in a previous population-based study that examined patients with open-angle glaucoma in a Malay population. The authors found that men had higher MOPP and DBP values than women[14]. However, in an Indian population-based study, Raman et al.[8] reported that female patients with T2DM had higher MOPP and SBP values than male patients. This discrepancy may due to the higher BMI and the reduced health seeking behavior of women on the Indian subcontinent. In addition to sex and BMI, we found that urine protein levels and serum creatinine levels were also associated with MOPP and had relatively high standardized β coefficients, highlighting the association between nephropathy and MOPP. This association was also reported by Raman et al.[8]

In this study, male and female (and combined male and female) patients with any type of DR, NPDR, and non-STDR had higher MOPP values than patients without DR. MOPP was also higher in male and combined male and female patients with ME than in patients without ME. These results were consistent with those reported in previous studies[4,8]. In an Indian population-based study, Raman et al.[8] reported that combined male and female patients with any DR, male patients with STDR or CSME, and female patients with any DR or non-STDR had higher MOPP values.

Notably, the differences in MOPP between this study and Raman et al.[8] were small (< 6 mmHg). In another clinical study, Patel et al.[4] reported that MOPP values were higher in patients with DR than in non-diabetes control subjects and higher in patients with PDR than in patients with diabetes but without retinopathy. In contrast, Langham et al.[15] found that choroidal blood flow decreases with the severity of DR. Although they did not study retinal perfusion directly, they speculated that this phenomenon was due to increased choroidal vascular resistance and decreased choroidal perfusion pressure. It should be mentioned that their speculation was based on indirect evidence of choroidal pulsatile blood flow using a relatively small sample size (n = 52).

The association between MOPP and the prevalence/severity of DR was further supported by the multivariate logistic analyses performed in this study. We found that a higher MOPP increased the risk of DR, NPDR, and ME. In a 4 year longitudinal population-based study, Moss et al.[6] reported that the multivariate odds ratio of DR after a 10 mmHg increase in ocular perfusion pressure was 2.13 in young-onset patients (95% *CI*, 1.30–3.50). Roy and Klein[7] reported that patients with type 1 diabetes and high MOPP were approximately twice as likely to have macular edema (*OR*, 95% *CI*: 2.16, 1.20–3.88) and severe hard exudates (*OR*, 95% *CI*: 2.08, 1.11–3.88) relative to patients with type 1 diabetes and low MOPP, even after adjusting for the diabetes duration. However, in an Indian population-based study, Raman et al.[8] found no association between MOPP and DR in either male or female (or combined male and female) patients after sequentially adjusting for risk factors.

Although studies directly examining the association between MOPP and DR are rare, many studies have assessed the relationship between

Table 3. Factors associated with MOPP in the study population

Factors	β coefficient	95% *CI*	Standardized β coefficient	*P* value	VIF
Sex (male, female)	−0.90	−1.78, −0.03	−0.05	0.04	1.23
Fasting plasma glucose (mmol/L)	0.13	0.02, 0.25	0.05	0.03	1.04
Body mass index (kg/m^2)	0.40	0.28, 0.51	0.15	< 0.001	1.05
Waist/hip ratio	5.91	−0.20, 12.02	0.04	0.06	1.04
Serum creatinine (μmmol/L)	0.03	0.01, 0.06	0.08	0.002	1.21
Blood urea nitrogen (mmol/L)	−0.12	−0.24, 0.01	−0.04	0.06	1.06
Low-density lipoprotein (mmol/L)	0.58	0.15, 1.00	0.06	0.01	1.07
High-density lipoprotein (mmol/L)	−1.26	−2.34, −0.17	−0.05	0.02	1.09
Urine protein level (5 levels)	0.71	0.43, 0.99	0.11	< 0.001	1.03

Note. *CI*: confidence interval; MOPP: mean ocular perfusion pressure; VIF: variance inflation factor.

retinal blood flow and DR[3-5,16-18]. A series of studies have reported that increased retinal blood flow is associated with background DR[3-5], preproliferative DR, and PDR[4]. Konno et al.[16] reported a transition from low to high retinal blood flow and increased retinopathy in patients with an increasingly longer duration of type 1 diabetes, suggesting that abnormal retinal blood flow (either high or low) is harmful to the retina. Using the non-invasive Heidelberg Retinal Flowmeter, Cuypers et al.[17] reported a stable trend of increasing retinal capillary flow in response to increasingly severe DR (from diabetes patients without DR to patients with severe non-proliferative DR). However, Man et al.[18] denied that this association exists in patients with either type 1 or type 2 diabetes.

Recent studies that have used optical coherence tomography angiography (OCTA) to examine retinal capillary density or the retinal nonperfusion area have consistently reported a stable decrease of capillary perfusion density in patients with increasingly advanced DR. This finding appears paradoxical in light of our current results[19-24]. For example, Agemy et al. found that capillary perfusion density values were significantly lower in nearly all layers of all study groups than in controls[19]. Ishibazawa et al.[21] found a greater nonperfusion area in patients with PDR than in those with moderate NPDR. Notably, because MOPP was calculated from brachial blood pressure and IOP, MOPP does not represent retinal blood flow, retinal capillary density, or nonperfusion area directly. Furthermore, structural and hemodynamic changes in retinal blood vessels are complex pathological events that are not yet fully understood, warranting further study.

The medications used to manage systemic blood pressure and IOP should also be considered as confounders because MOPP was calculated from systemic blood pressure and IOP. However, one limitation of this study is that detailed information regarding patients' antihypertensive therapies was unavailable. Because only 15 patients (0.8%) reported taking antiglaucoma medication (by questionnaire) and because excluding these patients from the analysis did not affect our results (e.g., *OR*, 95% *CI* for no DR *vs*. NPDR: 1.03, 1.02–1.04), we believe that the influence of antiglaucoma medication on our results was negligible.

This study had several limitations. First, although we found an association between MOPP and DR, our cross-sectional data cannot make causal determinations. Second, IOP was not measured using the standard Goldmann applanation tonometer method. However, because the inter-device agreement and consistency between the Goldmann applanation tonometer and the iCare rebound tonometer are good (intraclass correlation coefficient 0.77, mean difference 0.44 mmHg)[25], we

Table 4. PLEASE SEE the table of the supplement word file in reply email, since it was changed much

Risk factors	*OR* (95% *CI*)	*P* value
MOPP (mmHg)	1.03 (1.02, 1.04)	< 0.001
Age (years)	0.98 (0.97, 0.99)	0.002
Refractive error (diopter)	1.07 (1.02, 1.11)	0.002
Income level (3 levels)	0.76 (0.62, 0.92)	0.006
Duration of DM (years)	1.17 (1.15, 1.20)	< 0.001
Fasting plasma glucose (mmol/L)	1.07 (1.02, 1.11)	0.003
HbA1c (%)	1.12 (1.05, 1.20)	0.001
Total cholesterol (mmol/L)	1.09 (1.00, 1.20)	0.056
Total triglycerides (mmol/L)	0.90 (0.84, 0.97)	0.005
Urine protein level (5 levels)	1.17 (1.08, 1.26)	< 0.001

Note. *OR*: odds ratio; *CI*: confidence interval; MOPP: mean ocular perfusion pressure; DM: diabetes mellitus; HbA1c: glycosylated hemoglobin A1c.

Table 5. Multivariate logistic regression analysis of MOPP (per 1 mmHg) for the prevalence/severity of DR and ME

Item	*OR* (95% *CI*)	*P* value
No DR *vs*. Any DR	1.03 (1.02, 1.04)	< 0.001
No DR *vs*. NPDR	1.03 (1.02, 1.04)	< 0.001
NPDR *vs*. PDR	0.99 (0.96, 1.03)	0.660
No DR *vs*. non-STDR	1.03 (1.01, 1.04)	< 0.001
non-STDR *vs*. STDR	1.00 (0.98, 1.02)	0.750
No ME *vs*. ME	1.02 (1.01, 1.04)	0.008
Non-CSME *vs*. CSME	0.99 (0.96, 1.02)	0.350

Note. MOPP: mean ocular perfusion pressure; DR: diabetic retinopathy; ME: macular edema; NPDR: non-proliferative DR; PDR: proliferative DR; CSME: clinically significant ME; *OR*: odds ratio; *CI*: confidence interval; STDR: sight-threatening DR. The multivariate logistic regression models adjusted for MOPP, age, refractive error, income level, duration of diabetes mellitus, fasting blood glucose, HbA1c, total cholesterol, total triglycerides, and urine protein level.

believe our MOPP calculations are accurate. Third, as mentioned above, the potential confounders regarding antihypertensive therapy were not adjusted for in our multivariate analyses.

In conclusion, this study examined the factors associated with MOPP in patients with T2DM in a northeastern Chinese population. The factors assessed were sex, FPG, BMI, serum creatinine, and urine protein levels. More importantly, a higher MOPP was associated with NPDR, non-STDR, and macular edema.

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DECLARATION OF INTEREST

The authors declare that there are no conflicts of interest. This manuscript has not been published previously, and it is not simultaneously being considered for publication elsewhere.

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