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Research article

Sex-based differences in the associations between abdominal obesity and diabetic retinopathy in diabetic patients with normal weight

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A R T I C L E I N F O

Keywords:
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A B S T R A C T

Purpose: To investigate sex-specific differences in associations of abdominal obesity indexes, systemic factors, and diabetic retinopathy (DR) in type 2 diabetes mellitus (T2DM) subjects with normal body mass index (BMI).
Methods: This cross-sectional study comprised 653 T2DM subjects (402 women and 251 men) with normal BMI (18.5 kg/m^2<BMI<24.0 kg/m^2). All participants completed a standard questionnaire and underwent comprehensive ocular and systemic examinations. Anthropometric parameters were measured and recorded, including weight, height, waist circumference (WC), hip circumference, waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR). Sex-specific associated factors for DR were assessed using logistic regression models.
Results: In the multivariate logistic regressions, the presence of any DR was associated with a longer duration of T2DM (OR = 1.07, p = 0.007) and higher HbA1c (OR = 1.40, p = 0.001) in women, while any DR was associated with younger age at T2DM diagnosis (OR = 0.94, p = 0.020) and higher HbA1c (OR = 1.29, p = 0.011) in men. For women, we identified a positive association between WC (OR = 1.07, p = 0.011), WHR (OR = 1.67, p = 0.002), and WHtR (OR = 1.57, p = 0.004) with any DR after adjusting for confounders, and the third tertiles of WC (OR = 2.29, p = 0.028), WHR (OR = 3.03, p = 0.003), and WHtR (OR = 2.84, p = 0.007) were at high risk of any DR. For men, there were no associations between abdominal obesity indexes and any DR in either continuous variables or categorical variables (all $p > 0.05$).
Main conclusions: There were sex differences in the relationships between WC, WHR, WHtR, and DR in this T2DM population with normal BMI. Our findings provide new insight into a sex-specific mechanism of DR and management of the condition.

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1. Introduction

Diabetic retinopathy (DR) represents a major cause of global vision loss and is a prevalent complication of diabetes mellitus (DM) [1]. The worldwide incidence and impact of DR is expected to increase sharply in the coming decades, rising from approximately 103 million in 2020 to 130 million in 2030 and 161 million in 2045 [2]. In China, which has the largest number of cases of DR globally, it has emerged as a serious public health problem [3], imposing burdens on individuals, families, and society [4]. The personalized identification of risk factors for DR holds significant importance for guiding clinical prevention of the condition.

The association between obesity and DR has been a widely debated public health topic [5–7]. Some findings suggest a positive correlation between obesity and DR [8], while others indicate no link [9] or even a negative correlation [10], especially when using body mass index (BMI), which represents generalized obesity used to define obesity, resulting in the paradox of obesity [11]. These conflicting findings demonstrate the constraints of using BMI as the sole indicator of obesity to stratify the risk of DR. Waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) are commonly used to define abdominal obesity and are proven to have a stronger correlation with DR than BMI [6,10,12,13]. However, previous studies of the relationship between abdominal obesity and DR have not eliminated the interdependence of abdominal obesity and BMI. Individuals with a normal BMI but an elevated WHR reportedly have an increased risk of all-cause and cardiovascular mortality [14]. To date, no studies have investigated the correlation between abdominal obesity and DR in DM subjects with normal weight (that is, normal BMI).

In addition, previous studies have shown that sex differences exist in adipose tissue function and deposition [15] and that women with diabetes or insulin resistance, which are related to abdominal obesity, are more likely to experience an increase in the risk of cardiovascular complications [16–19]. One study from Singapore showed WHR to be positively associated with DR, but only in women [10]. It remains uncertain whether anthropometric parameters due to sex differences result in varying levels of risk for DR in DM patients with normal BMI in Chinese populations.

The purpose of the current study was thus to explore sex-based differences in the associations of abdominal obesity indexes, systemic characteristics, and the presence of DR in diabetic subjects with normal BMI in the Guangzhou Diabetic Eye Study.

2. Methods

2.1. Study design and participants

The participants in the current study were part of the Guangzhou Diabetic Eye Study, a community-based, cohort study of T2DM conducted at the Zhongshan Ophthalmic Center (ZOC), Sun Yat-sen University, China [20]. The present study specifically focused on diabetic participants with normal BMI (18.5 kg/m^2<BMI<24 kg/m^2), as defined by Chinese guidelines [21,22]. Those with an ungradable fundus image caused by an abnormal refractive medium (severe cataract, corneal opacity, etc.) and poor fixation or for whom no WC and hip circumference (HC) data were available were excluded from the current study. The study protocol received approval from the Institutional Ethics Committee of the ZOC and adhered to the guidelines of the Helsinki Declaration (2017KYPJ094). All participants gave their informed written consent before participating in the study.

2.2. Measurements of anthropometric parameters

An experienced nurse measured the weight (kg), height (m), WC (cm), and HC (cm) of each DM patient according to standard procedures. Weight was measured on a scale, with participants removing their shoes and any heavy items. Height was measured with a measuring stick while the participant was on the scale. Non-stretchable medical tape was utilized for the measurement of the WC and HC. The WC was measured at the narrowest point between the ribcage and the hip bones at the end of a normal exhalation. The HC was measured at the widest point of the buttocks.

BMI was calculated as weight (kg) divided by height (m^2). According to the Chinese guidelines [22], BMI was categorized as normal, overweight, and obese for scores of 18.5–23.9, 24–27.9, and ≥28.0, respectively. The WHR was calculated as the ratio of WC to HC, while the WHtR was calculated by dividing the WC by the height. Abdominal obesity was defined based on the World Health Organization (WHO) criteria [23,24]: WC ≥ 80 cm for women and ≥94 cm for men; WHR ≥0.85 for women and ≥0.90 for men; or WHtR of ≥0.50. We defined the presence of isolated abdominal obesity as having a normal BMI while meeting one of the three criteria of abdominal obesity.

2.3. Ocular measurements

All participants underwent detailed ocular examinations, including the assessment of best-corrected visual acuity (KR-8800 auto kerato-refractometer; TOPCON Corporation, Tokyo, Japan), intraocular pressure (CT-1 non-contact tonometer; TOPCON Corporation, Tokyo, Japan), axial length (AL; Lenstar LS900; Haag-Streit Group, Koeniz, Switzerland), and standardized seven-field colorful retinal photographs (CR-2; Canon, Tokyo, Japan). The DR was graded by two trained graders using the grading and quality standards of the English National Screening Programme (UK guidelines) [25]. Any DR was defined as the presence of background DR (R1), pre-proliferative DR (R2), or proliferative DR (R3), maculopathy (M1). Vision-threatening DR (VTDR) was considered to be present if M1, R2, or R3 features were found. For individuals with bilateral gradable photographs, the eye with the more severe DR was included. Otherwise, the right eye was chosen for analysis. The presence or absence of DR resulted in the classification of individuals into either the Non DR (NDR) or any DR group, respectively.

2.4. Other measurements

Demographic information and medical histories, including age, gender, smoking and alcohol habits, duration of diabetes, history of systemic and ocular diseases, and medications, were gathered via standardized questionnaires. Systolic blood pressure (SBP; mmHg) and diastolic blood pressure (DBP; mmHg) were measured with a blood pressure monitor after the participant sat quietly for at least 5 min. Fasting (8 h) venous blood samples were collected to test for HbA1c, triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) using standardized procedures from a certified laboratory in China.

2.5. Statistical analysis

Statistical analyses were performed with Stata software (version 17.0, StataCorp, College Station, TX, USA) and the GraphPad Prism 9 (GraphPad Software, CA, USA). The continuous variables were initially evaluated for normality via the Kolmogorov–Smirnov test, and the results were presented as mean ± standard deviation (SD) for normal distribution or the median with an interquartile range (IQR) for abnormal distribution. An independent *t*-test and a Mann–Whitney *U* test were applied if required. A chi-square test or Fisher's exact test were utilized for categorical variables. Univariate and multivariate logistic regression models were employed to investigate the sex-specific relationship between abdominal obesity indexes, systemic characteristics, and DR. The results were recorded as odds ratios (OR), along with 95 % confidence intervals (CI). Statistical significance is indicated by $p < 0.05$.

3. Results

A total of 653 diabetic subjects with normal BMI was enrolled in the current study, comprising 402 women (61.56 %) and 251 men (38.44 %). Compared with men, women had significantly lower levels of BMI, WC, HC, WHR, and AL, whereas they had higher levels of WHtR, SBP, HbA1c, TG, TC, LDL-c, and HDL-c (all $p < 0.05$, as shown in Table 1).

Compared to NDR participants, DR participants tended to be younger at the time of DM diagnosis, have a longer duration of DM and higher SBP and HbA1c levels, and be more likely to have insulin therapy in both men and women (all $p < 0.05$). For women, the levels of WC, WHR, WHtR, TG, and TC were higher in DR than NDR subjects (all $p < 0.05$), but these factors were not significant for DR in men (all $p > 0.05$). The DR group had a shorter AL than NDR participants in men only ($p < 0.05$, as shown in Table 2). The proportion of DR significantly increased with increased WC, WHR, and WHtR in women (all $p < 0.05$), but not in men (all $p > 0.05$) (Fig. 1A and B). In the multivariate regression analyses, the results showed sex differences in risk factors for any DR. For women, a longer duration of

Table 1
Comparison of baseline characteristics between women and men.

Characteristic	women, n = 402	men, n = 251	p-value
Age, years	65.67 (61.00–71.00)	65.21 (61.00–70.00)	0.668[b]
Age of DM diagnosis, years	55.19 (50.00–61.00)	54.43 (49.00–61.00)	0.420[b]
Duration of diabetes, years	10.35 (5.00–15.00)	10.78 (4.00–16.00)	0.560[b]
Use of insulin, n%	12.53	11.06	0.585[c]
Smoking history, n%	0.50	33.87	**<0.001**[c]
Alcohol drinking history, n%	2.74	18.95	**<0.001**[c]
Weight, kg	52.07 (48.00–55.50)	62.04 (58.00–66.00)	**<0.001**[b]
Height, m	1.54 ± 0.06	1.67 ± 0.06	**<0.001**[a]
BMI, kg/m2	21.87 (20.74–23.00)	22.30 (21.46–23.33)	**<0.001**[b]
WC, cm	79.54 ± 5.76	83.73 ± 5.39	**<0.001**[a]
HC, cm	90.10 (87.00–93.00)	92.37 (90.00–95.00)	**<0.001**[b]
WHR	0.88 (0.85–0.92)	0.91 (0.87–0.94)	**<0.001**[b]
WHtR	0.52 (0.49–0.54)	0.50 (0.48–0.52)	**<0.001**[b]
SBP, mmHg	133.54 (121.00–148.00)	130.25 (118.00–141.00)	**0.015**[b]
DBP, mmHg	66.79 ± 9.85	68.13 ± 10.27	0.096[a]
HbA1c, % (mmol/mol)	7.34 (6.40–7.90)	7.21 (6.20–7.80)	**0.044**[b]
TG, mmol/L	2.24 (1.27–2.71)	1.99 (1.10–2.42)	**0.003**[b]
TC, mmol/L	5.19 (4.37–5.96)	4.71 (3.95–5.35)	**<0.001**[b]
LDL-c, mmol/L	3.15 (2.45–3.70)	2.91 (2.18–3.49)	**<0.001**[b]
HDL-c, mmol/L	1.42 (1.11–1.65)	1.30 (1.03–1.48)	**<0.001**[b]
Axial length,mm	23.32 (22.55–23.78)	23.87 (23.11–24.27)	**<0.001**[b]

DM, diabetes mellitus; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist to hip ratio; WHtR, waist to height ratio. SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, haemoglobin A1c; TG, triglycerides; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol.
(mean ± SD) or (median, IQR).
IQR = interquartile range, shown as (25 %, 75 %).
p < 0.05 was considered statistically significant and marked in bold.
[a] Independent-Samples t-test.
[b] Mann-Whitney *U* test.
[c] Chi-square test.

Table 2
Comparison of baseline characteristics between NDR and any DR stratified by sex.

	Women			Men		
Characteristic	NDR (n = 331)	any DR (n = 71)	p-value	NDR (n = 195)	any DR (n = 56)	p-value
Age, years	65.64 (62.00–70.00)	63.72 (60.50–68.5)	0.396[b]	65.64 (62.00–70.00)	63.72 (60.50–68.50)	0.069[b]
Age of DM diagnosis, years	55.78 ± 8.70	52.45 ± 8.46	**0.004**[a]	55.52 (50.00–62.00)	50.68 (45.00–57.00)	**<0.001**[b]
Duration of diabetes, years	9.58 (4.00–13.00)	13.97 (7.50–21.00)	**<0.001**[b]	10.14 (4.00–15.50)	12.96 (7.00–18.00)	**0.013**[b]
Use of insulin, n%	9.87	24.64	**0.001**[c]	7.14	24.53	**<0.001**[c]
Smoking history, n%	0.60	0	1.000[d]	33.85	33.96	0.987[c]
Alcohol drinking history, n %	2.73	2.82	1.000[d]	17.44	24.53	0.243[c]
Weight, kg	52.16 ± 5.13	51.65 ± 4.83	0.443[a]	62.25 (58.00–66.50)	61.29 (59.00–65.25)	0.714[b]
Height, m	1.54 ± 0.06	1.54 ± 0.05	0.404[a]	1.67 ± 0.06	1.66 ± 0.06	0.323[a]
BMI, kg/m2	21.88 (20.77–23.04)	21.84 (20.68–22.94)	0.737[b]	22.32 (21.51–23.33)	22.22 (21.41–23.34)	0.604[b]
WC, cm	79.19 ± 5.68	81.16 ± 5.87	**0.009**[a]	83.75 ± 5.47	83.63 ± 5.14	0.884[a]
HC, cm	90.27 (87.00–93.00)	89.30 (86.00–92.00)	0.192[b]	92.54 ± 4.06	91.78 ± 3.70	0.207[a]
WHR	0.88 (0.84–0.91)	0.91 (0.88–0.95)	**<0.001**[b]	0.91 ± 0.05	0.91 ± 0.05	0.417[a]
WHtR	0.51 (0.49–0.54)	0.53 (0.50–0.55)	**0.002**[b]	0.50 ± 0.03	0.50 ± 0.03	0.643[a]
SBP, mmHg	132.51 (119.00–147.00)	138.34 (126.00–149.00)	**0.029**[b]	128.78 (117.00–138.00)	135.36 (121.00–147.50)	**0.004**[b]
DBP, mmHg	66.56 ± 9.44	67.83 ± 11.57	0.325[a]	67.93 ± 10.21	68.80 ± 10.54	0.577[a]
HbA1c, % (mmol/mol)	7.13 (6.40–7.60)	8.27 (7.00–8.90)	**<0.001**[b]	7.01 (6.20–7.40)	7.96 (6.40–8.90)	**<0.001**[b]
TG, mmol/L	2.16 (1.23–2.62)	2.61 (1.65–3.28)	**0.023**[b]	1.99 (1.06–2.43)	2.00 (1.14–2.42)	0.984[b]
TC, mmol/L	5.14 ± 1.03	5.43 ± 1.17	**0.035**[a]	4.67 ± 1.00	4.85 ± 1.23	0.255[a]
LDL-c, mmol/L	3.12 ± 0.93	3.33 ± 1.10	0.090[a]	2.86 (2.18–3.44)	3.06 (2.28–3.77)	0.294[b]
HDL-c, mmol/L	1.43 (1.11–1.65)	1.37 (1.08–1.77)	0.287[b]	1.29 (1.03–1.47)	1.32 (1.04–1.55)	0.430[b]
Axial length,mm	23.35 (22.55–23.82)	23.19 (22.47–23.49)	0.162[b]	23.96 (23.25–24.29)	23.55 (22.78–24.16)	**0.017**[b]

NDR, non-diabetic retinopathy; any DR, any diabetic retinopathy; DM, diabetes mellitus; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist to hip ratio; WHtR, waist to height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, haemoglobin A1c; TG, triglycerides; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol.
(mean ± SD) or (median, IQR).
IQR = interquartile range, shown as (25 %, 75 %).
$p < 0.05$ was considered statistically significant and marked in bold.
[a] Independent-Samples t-test.
[b] Mann-Whitney *U* test.
[c] Chi-square test.
[d] Fisher's exact test.

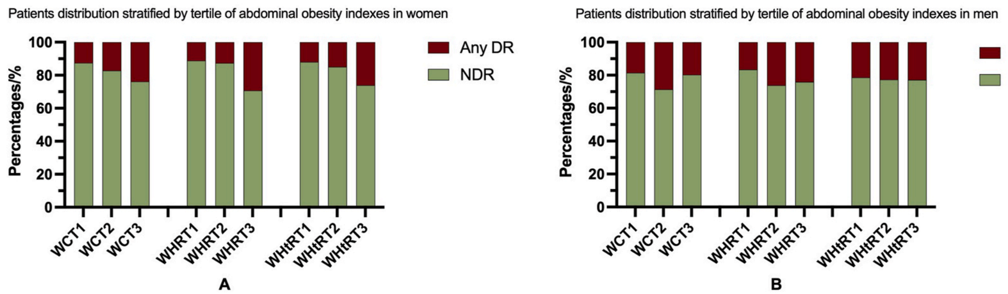

Fig. 1. The proportion of any DR stratified by tertile of abdominal obesity indexes. (A) Women; (B) Men. NDR, non-diabetic retinopathy; any DR, any diabetic retinopathy; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; T, tertile.

DM (OR = 1.07, 95 % CI 1.02–1.13, $p = 0.007$) and higher HbA1c (OR = 1.40, 95 % CI 1.15–1.70, $p = 0.001$) were associated with the presence of any DR. For men, we observed that younger age at DM diagnosis (OR = 0.94, 95 % CI 0.90–0.99, $p = 0.020$) and a higher HbA1c (OR = 1.29, 95 % CI 1.06–1.58, $p = 0.011$) were associated with the presence of any DR (Table 3).

There were sex differences in the associations between abdominal obesity indexes and any DR (Table 4 and Fig. 2). For women, when WC and WHtR were assessed as continuous variables, we identified a positive association of WC (OR = 1.07, 95 % CI 1.02–1.13, p = 0.011), WHR (OR = 1.67, 95 % CI 1.21–2.30, p = 0.002), and WHtR (OR = 1.57, 95 % CI 1.16–2.14, p = 0.004) with any DR in the logistic regression adjusted model. After categorization of these abdominal obesity indexes into tertiles, we persistently found that participants in the highest tertiles of WC (OR = 2.29, 95 % CI 1.09–4.81, p = 0.028), WHR (OR = 3.03, 95 % CI 1.44–6.36, p = 0.003), and WHtR (OR = 2.84, 95 % CI 1.33–6.06, p = 0.007) were more likely to have any DR than those in the lowest tertiles after adjusting for confounders(Table 4, Fig. 2A and B). However, we observed an absence of a relationship between the WHO-defined isolated abdominal obesity (all p > 0.05) and any DR in the adjusted model. No associations between abdominal obesity indexes and any DR were observed in men (all p > 0.05) (Table 4, Fig. 2C and D).

Table 3
Logistic regression analysis of related factors for any DR stratified by sex.

Variable	Women				Men			
	Univariable analysis		Multivariable analysis[a]		Univariable analysis		Multivariable analysis[a]	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Age of DM diagnosis (per 1 year increase)	0.96 (0.93–0.99)	**0.005**	1.00 (0.96–1.05)	0.856	0.94 (0.91–0.98)	**0.001**	0.94 (0.90–0.99)	**0.020**
Duration of diabetes (per 1 year increase)	1.09 (1.05–1.13)	**<0.001**	1.07 (1.02–1.13)	**0.007**	1.05 (1.01–1.10)	**0.013**	1.01 (0.95–1.06)	0.862
Use of insulin (unused = 0, used = 1; reference:unused)	2.98 (1.54–5.78)	**0.001**	1.92 (0.91–4.06)	0.089	4.23 (1.82–9.81)	**0.001**	2.30 (0.91–5.83)	0.078
SBP (per 1 mmHg increase)	1.02 (1.00–1.03)	**0.019**	1.01 (0.99–1.03)	0.251	1.02 (1.00–1.04)	**0.013**	1.01 (1.00–1.03)	0.128
DBP (per 1 mmHg increase)	1.01 (0.99–1.04)	0.325			1.01 (0.98–1.04)	0.576		
HbA1c (per 1 % increase)	1.63 (1.37–1.94)	**<0.001**	1.40 (1.15–1.70)	**0.001**	1.41 (1.17–1.69)	**<0.001**	1.29 (1.06–1.58)	**0.011**
TG (per 1 mmol/L increase)	1.21 (1.03–1.42)	**0.019**	1.14 (0.94–1.38)	0.185	1.00 (0.83–1.21)	0.989	/	/
TC (per 1 mmol/L increase)	1.30 (1.02–1.65)	**0.036**	1.21 (0.91–1.61)	0.191	1.18 (0.89–1.56)	0.254	/	/
LDL-c (per 1 mmol/L increase)	1.26 (0.96–1.63)	0.091	/	/	1.23 (0.91–1.68)	0.181	/	/
HDL-c (per 1 mmol/L increase)	0.72 (0.39–1.34)	0.303	/	/	1.25 (0.57–2.70)	0.579	/	/
Axial length,mm	0.89 (0.70–1.12)	0.317	/	/	0.71 (0.52–0.97)	**0.031**	0.77 (0.55–1.06)	0.112

any DR, any diabetic retinopathy; DM, diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, haemoglobin A1c; TG, triglycerides; TC, total cholesterol; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol.
$p < 0.05$ was considered statistically significant and marked in bold.
[a] Variables with $P < 0.05$ in the univariate analysis were included in the multivariate analysis.

We further analyzed the associations of abdominal obesity indexes and VTDR by sex (Supplemental Figs. 1A–1D). We found that higher WHR was significantly associated with VTDR (OR = 1.97, 95 % CI 1.08–3.61, p = 0.027) in women after adjusting for confounders. Patients in the third tertiles of WHR were at higher risk of VTDR occurrence (OR = 3.75, 95 % CI 1.01–13.96, p = 0.048). No associations were observed between abdominal obesity indexes and VTDR in men (all $p > 0.05$).

4. Discussion

To the best of our knowledge, the current study is the first to evaluate sex-specific clinical characteristics and associated factors for DR in DM subjects with normal BMI. Higher HbA1c and longer duration of DM were associated with any DR in women, while higher HbA1c and younger age at diagnosis of DM were associated with the presence of any DR in men. Additionally, only among the women was there a significant association between abdominal obesity as measured by WC, WHR, WHtR, and any DR in both continuous and categorical variables. However, additional analysis found no relationship between the WHO-defined isolated abdominal obesity and any DR in women.

A higher HbA1c level was a strong risk factor for DR regardless of sex, which is consistent with previous studies [26–28]. Kawasaki et al. [8] suggested that the risks of onset and progression of DR increased linearly by 36 % and 66 %, respectively, for every 1 % (10.9 mmol/mol) increase in HbA1c. Some studies have indicated that long-term adequate glycemic control could significantly reduce the presence of DR or other microvascular complications of DM [3,29]. In addition, a longer duration of DM in women and a younger age at DM diagnosis in men were related to DR, possibly because the relatively longer duration of hyperglycemia (inadequate glycemic control) in these individuals renders them more likely to develop microvascular damage [30].

Only one study from Singapore has investigated the sex difference in abdominal obesity and DR. The study's results showed that in women, a higher WHR was associated with DR. However, the participants of that study represented a mixed Asian population, and the interdependence of BMI with WHR was not excluded. In addition, no abdominal obesity index other than WHR was analyzed in the Singapore study.

In the current study, we first proved that the association between isolated abdominal obesity indexes and any DR exhibited sex differences. Moreover, we found that WC, WHR, and WHtR had significant positive associations with any DR in women only. Further, we showed that higher abdominal obesity indexes are associated with insulin resistance [31–33]. Insulin resistance without obvious hyperglycemia potentially acts as an early driver of DR [34]. This sex-specific susceptibility of abdominal obesity to any DR may be partly due to isolated abdominal obesity being more commonly observed in women than in men [12]. A previous study proposed that the presence of abdominal obesity is a more accurate marker of obesity-related metabolic risk in women than in men and leads to an increased probability of DR [35]. This difference may be related to the influence of sex hormones on adipose tissue function and deposition [15,36]. However, we should interpret the our results of sex differences with caution due to the relatively small numbers of

Table 4
The relationship between indicators of abdominal obesity and any DR stratified by sex.

		Women				Men			
		Univariable analysis		Adjusted[a]		Univariable analysis		Adjusted[b]	
Variable		OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
WC categories									
WC ≥ 80 cm for females or ≥94 cm for males	NO	Ref.		Ref.		Ref.		Ref.	
	YES	1.77 (1.05–2.98)	**0.033**	1.75 (0.96–3.18)	0.066	0.43 (0.05–3.47)	0.425	1.07 (0.11–10.59)	0.951
Tertile 1		Ref.		Ref.		Ref.		Ref.	
Tertile 2		1.45 (0.74–2.85)	0.278	1.59 (0.74–3.42)	0.239	1.75 (0.85–3.60)	0.128	1.72 (0.73–4.04)	0.213
Tertile 3		2.19 (1.16–4.15)	**0.016**	2.29 (1.09–4.81)	**0.028**	1.08 (0.50–2.33)	0.851	1.44 (0.60–3.47)	0.410
WC per 1 cm increase		1.06 (1.01–1.11)	**0.009**	1.07 (1.02–1.13)	**0.011**	1.00 (0.94–1.05)	0.884	1.02 (0.96–1.09)	0.490
WHR categories									
WHR≥0.85 for females or ≥0.90 for males	NO	Ref.		Ref.		Ref.		Ref.	
	YES	1.55 (0.83–2.87)	0.165	1.28 (0.64–2.55)	0.482	1.85 (0.99–3.46)	0.055	1.96 (0.96–4.01)	0.064
Tertile 1		Ref.		Ref.		Ref.		Ref.	
Tertile 2		1.14 (0.55–2.39)	0.723	1.07 (0.47–2.42)	0.872	1.77 (0.84–3.76)	0.135	1.40 (0.60–3.31)	0.439
Tertile 3		3.29 (1.71–6.33)	**<0.001**	3.03 (1.44–6.36)	**0.003**	1.59 (0.74–3.40)	0.235	1.70 (0.72–4.01)	0.225
WHR per 1-SD increase		1.68 (1.27–2.23)	**<0.001**	1.67 (1.21–2.30)	**0.002**	1.13 (0.84–1.53)	0.415	1.19 (0.83–1.72)	0.346
WHtR categories									
WHtR ≥0.50	NO	Ref.		Ref.		Ref.		Ref.	
	YES	1.83 (1.02–3.30)	**0.044**	1.84 (0.93–3.64)	0.082	1.13 (0.62–2.05)	0.687	1.70 (0.83–3.48)	0.143
Tertile 1		Ref.		Ref.		Ref.		Ref.	
Tertile 2		1.29 (0.64–2.62)	0.474	1.05 (0.47–2.34)	0.911	1.07 (0.52–2.22)	0.852	1.35 (0.56–3.25)	0.504
Tertile 3		2.61 (1.36–4.99)	**0.004**	2.84 (1.33–6.06)	**0.007**	1.09 (0.52–2.26)	0.820	1.87 (0.78–4.52)	0.163
WHtR per 1-SD increase		1.46 (1.13–1.89)	**0.004**	1.57 (1.16–2.14)	**0.004**	1.07 (0.80–1.45)	0.642	1.24 (0.86–1.78)	0.243

any DR, any diabetic retinopathy; WC, waist circumference; WHR, waist to hip ratio; WHtR, waist to height ratio.
$p < 0.05$ was bolded to indicate statistical significance.
[a] Adjusted for age of T2DM diagnosis, duration of diabetes, use of insulin, SBP, HbA1c, total cholesterol, and triglycerides.
[b] Adjusted for age of T2DM diagnosis, duration of diabetes, use of insulin, SBP, HbA1c and axial length.

male participants with DM and isolated abdominal obesity and the cross-sectional design. Thus, further longitudinal studies with larger samples are required to verify this relationship.

Interestingly, we found that although both continuous variables and higher tertiles of abdominal obesity indexes were significantly associated with any DR in women, the WHO-defined criteria for abdominal obesity were not related to any DR. The results revealed that a single abdominal obesity criterion for all BMI categories is inadequate to identify individuals at risk of DR. BMI category-specific thresholds for abdominal obesity may be used to enhance the detection of those at high risk of any DR in the future [37]. The WHO criteria are not suitable for detecting any DR risk in Chinese populations because these criteria were set based on mixed Asian populations, not Chinese ones, and there are differences in how body fat is distributed in individuals of Chinese and other ethnicities [23]. Other research has further confirmed our hypothesis that there is no predictive performance of the WHO criteria for cardiovascular disease or diabetes [38,39]. The ethnic differences in body size and distribution of body fat [40] highlight the need to establish population-specific abdominal obesity for Chinese populations. However, further longitudinal studies with larger sample sizes are required to confirm our findings.

The strengths of the current study lie in the detailed ocular and systemic examinations carried out using standard protocols. Additionally, we included only participants with normal BMI to eliminate the interdependence of generalized obesity and abdominal obesity. However, there are several limitations. First, we cannot evaluate the causal relationships between abdominal obesity and DR in this cross-sectional study. Second, the study sample was relatively small, and we included only 38.44 % men with normal BMI, which may induce bias. Third, our study focused on a population from a single community in southern China. Differences in diet and lifestyle among different areas may affect the generalizability of the results. In conclusion, our study found that sex differences exist between the WC, WHR, WHtR, and DR of DM subjects with normal BMI, and these abdominal obesity indexes were only associated with DR in women, not in men. Further longitudinal studies with larger sample sizes are required to confirm the sex difference and causal relationship between WC, WHR, WHtR, and DR in DM subjects with normal BMI. Additionally, besides WC, WHR, and WHtR,

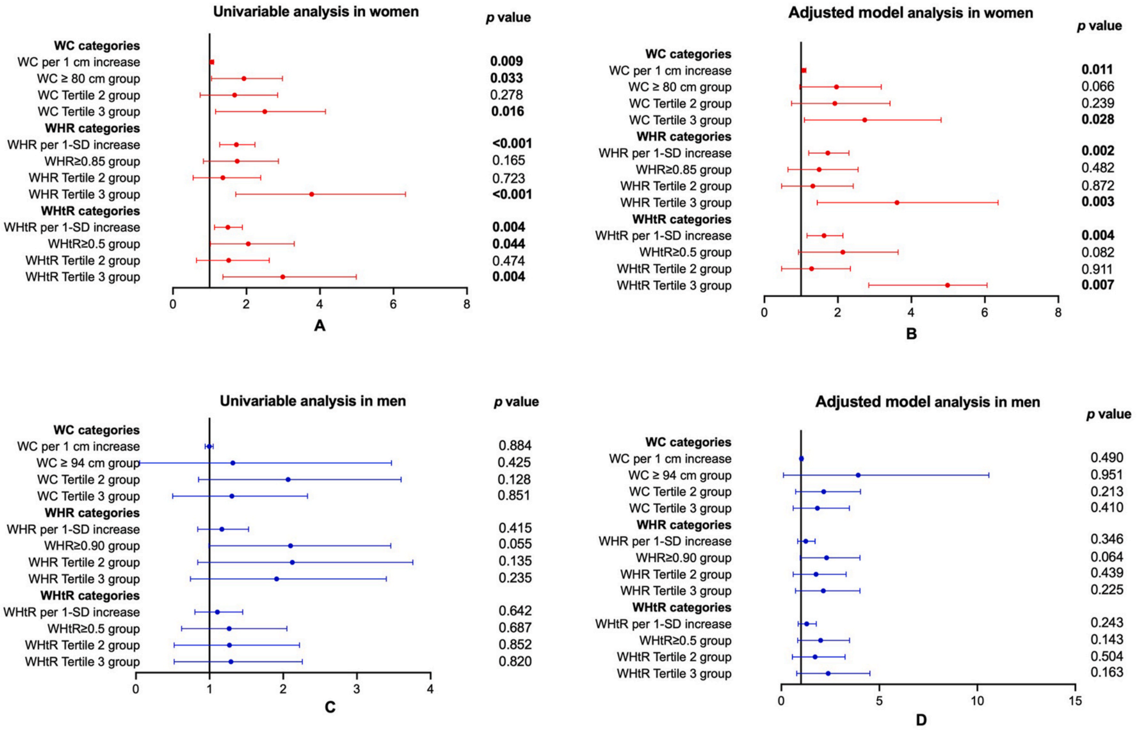

Fig. 2. The relationships between indicators of abdominal obesity and any diabetic retinopathy stratified by sex. (A) Univariate analysis in women; (B) Multivariate analysis in women; (C) Univariate analysis in men; (D) Multivariate analysis in men. WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.

which represent traditional abdominal obesity, other newly established indexes for central or abdominal obesity exist, such as the visceral adiposity index, lipid accumulation product, body shape index, body adiposity index, and Chinese visceral adiposity index [41,42]. Future research should focus on exploring the relationship between these enriched obesity indicators and DR by sex in DM subjects with normal BMI.

Declarations: The authors have no financial or other conflicts of interest concerning this study.

Ethical approval statement: The study protocol received approval from the Institutional Ethics Committee of ZOC and adhered to the guidelines of the Helsinki Declaration (2017KYPJ094). All participants gave their informed written consent before participating in the study.

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Data availability statement

Data are not available for ethical reasons. Further enquiries can be directed to the corresponding author.

CRediT authorship contribution statement

Yuan Liu: Writing – original draft, Methodology, Conceptualization. **Kaiqun Liu:** Writing – original draft, Methodology, Conceptualization. **Liqiong Xie:** Formal analysis, Data curation. **Chengguo Zuo:** Writing – review & editing, Funding acquisition. **Lanhua Wang:** Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Conceptualization. **Wenyong Huang:** Writing – review & editing, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e36683.

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