

Association Among Abdominal Obesity Induces, Diabetic Retinopathy and Metabolic Syndrome in Community: a Cross-sectional Study

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Research

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Abstract

Background and aims: Obesity often coexists with diabetes has been recognized as a risk factor for diabetic complications. Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes, and the metabolic syndrome (MetS) is one of the most common symptoms of diabetes. The purpose of this study was to explore the relationship between DR and some induces, including NC, CVAI, PWNC and so on; as well as the relationship between DR and MetS.

Methods: From 2018 to 2019, a total of 562 diabetics from the Hulan District of Harbin, Heilongjiang, were selected and completed a questionnaire survey. The questionnaire included basic patient information, anthropometric parameters, blood pressure, biochemical parameters and fundus photography results.

Results: In both men and women, a one standard deviation (SD) increase in NC, CVAI and PWNC was not associated with the prevalence of DR ($P>0.05$). However, in both men and women, a one SD increase in NC, CVAI and PWNC was significantly associated with the prevalence of MetS ($P<0.05$). These association were all adjusted for potential confounding factors. Moreover, DR was not associated with MetS ($P>0.05$).

Conclusions: NC, CVAI and PWNC are associated with the prevalence of MetS. NC in men and CVAI in women had the largest area under the ROC curve compared to the other induces, which may be convenient and valuable anthropometric measurements for early prevention of MetS. However, these induces had no association with DR and there is no relationship between DR and MetS.

Introduction

The global prevalence of diabetes is predicted to increase dramatically in the coming decades as the population grows and ages, in parallel with the rising burden of overweight and obesity, in both developed and developing countries¹. About the epidemiological data, the worldwide prevalence of overweight and obesity has reached 33.3%, which has doubled since 1980².

Moreover, DR is the most common microvascular complication in patients with diabetes and the leading cause of vision loss globally in working middle-aged adults³. And MetS is a cluster of obesity, hypertension, dysglycemia, dyslipidemia, and insulin resistance. Because hyperglycemia, oxidative stress and inflammation are the same processes involved in DR and MetS, several population studies evaluated its association with them. However, the relationship between metabolic syndrome and diabetic microvascular complications is contradictory and needs further study.

In fact, the methods to detect abdominal adiposity include dual-energy X-ray absorptiometry (DEXA), computed tomography (CT), magnetic resonance imaging (MRI) and dual bioelectrical impedance analysis (BIA). However, they are unsuitable for routine clinical practices in a general population on account of the radiation exposure, time requirements and high costs⁴. There are lots of induces to

estimate obesity, such as neck circumference (NC), waist circumference (WC), body mass index (BMI) and the visceral adiposity index (VAI), the lipid accumulation product (LAP), which are calculated using the data of WC, BMI, triglycerides (TG), and high-density lipoprotein (HDL)⁵. Here we must mention two new indicators—Chinese visceral obesity index (CVAI), and the product of WC and NC (PWNC), which are considered to serve as a better predictor of T2DM and MetS in T2DM^{6,7}.

The findings of a cross-sectional study suggest that visceral adiposity is associated with DR in individuals with longstanding T2DM in Asia⁸. However, a study of 2016 found that, in Asian patients with T2DM, a higher BMI appeared to confer a protective effect on DR⁹. Therefore, the association between obesity and DR is equivocal. A new study has found that CVAI was not associated with DR in both men and women⁴. In addition, a study published in 2018 with 1986 type 2 diabetic Asian patients reported a higher prevalence of retinopathy in patients with MetS defined by NCEP-ATP III (37.9% in T2D + MetS vs 28.6% T2D without MetS, $P < 0.001$). And yet, in 2018, Zhou et al published a meta-analysis compiling the results of 12 observational studies which addressed this relationship between MetS and retinopathy in diabetic patients, which reported that no association between MetS and DR in type 1 or type 2 diabetic patients and no correlation between isolated MetS components (BMI, WC, BP, HDL and triglyceride levels) and retinopathy¹⁰.

We aimed to investigate the association between DR and some induces, including WC, NC, WHR, BMI, CVAI, PWNC; as well as the relationship between DR and Mets among people with diabetes in northeast China. Our findings may provide evidence for the early detection, prevention and treatment of MetS and diabetic complications.

Materials And Methods

Subjects

The present study was a cross-sectional study comprising 562 diabetics from the Hulan District of Harbin from 2018 to 2019 (Non-admitted patients), and completed a questionnaire survey. The diagnosis of T2DM in the subjects was consistent with the 1999 WHO diagnostic criteria¹¹. Each subject was examined by a clinical ophthalmologist with the use of an ophthalmoscope. This study was approved by the Ethics Committee of the First Affiliated Hospital of Harbin Medical University and followed the Declaration of Helsinki and STARD guidelines. Written Informed consent was obtained from all participants.

Data collection

The information on sociodemographic characteristics, medical history, family history, and lifestyle factors was accessed by doctors of the First Affiliated Hospital of Harbin Medical University through a face-to-face interview. Anthropometric measurements including weight, height, NC, WC, hip circumference (HC) and blood pressure were conducted by trained staff according to standard protocols.

Height and weight were measured with participants standing without shoes and in lightweight clothes to the nearest 0.1cm and 0.1kg. WC was measured on the midaxillary line between the lowest border of the rib cage and the top of the iliac crest to the nearest 0.1cm. NC was measured below the cricoid cartilage and then at the level of the mid-cervical spine to the nearest 0.1cm. HC was measured at the widest part of the hip at the level of the greater trochanter to the nearest 0.1cm. BMI was calculated as weight in kilograms divided by squared height in meters. WHR was calculated as WC divided by HC. The PWNC was calculated by the product of WC and NC. And the CVAI was calculated as follows:

Males:

$$\text{CVAI} = -267.93 + 0.68 \times \text{age}(y) + 0.03 \times \text{BMI}(\text{kg}/\text{m}^2) + 4.00 \times \text{WC}(\text{cm}) + 22.00 \times \text{Log}_{10} \text{ TG}(\text{mmol}/\text{L}) - 16.32 \times \text{HDL}(\text{mmol}/\text{L})$$

Females:

$$\text{CVAI} = -187.32 + 1.71 \times \text{age}(y) + 4.32 \times \text{BMI}(\text{kg}/\text{m}^2) + 1.12 \times \text{WC}(\text{cm}) + 39.76 \times \text{Log}_{10} \text{ TG}(\text{mmol}/\text{L}) - 11.66 \times \text{HDL}(\text{mmol}/\text{L})$$

Laboratory tests of fasting blood sample were performed using standard bio-chemical analysis methods, which included total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), and uric acid (UA), and using high pressure liquid phase detection method to test glycosylated hemoglobin A1c (HbA1c), and using chemiluminescence method to test fasting C-peptide.

Definition of variables

Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or a self-reported previous diagnosis of hypertension. Dyslipidemia was defined as TC ≥ 6.22 mmol/L(240mg/dl), TG ≥ 2.26 mmol/L(200 mg/dl), LDL-L ≥ 4.14 mmol/L(160 mg/dl), HDL-L < 1.04 mmol/L(40mg/dl).

In accordance with the guidelines for the prevention and treatment of T2DM in China (2020). MetS was defined as the presence of 3 or more of the following features: (1)abdominal obesity (central obesity): WC ≥ 90 cm for males and 85cm for females; (2)hyperglycemia: fasting plasma glucose level (FPG) ≥ 6.1 mmol/l or 2 hours after glucose overload blood glucose ≥ 7.8 mmol/L and/or has been diagnosed as diabetes and treated; (3) hypertension: BP $\geq 130/85$ mmHg (1 mmHg = 0.133 kPa) and (or) have been identified as hypertension and treated; (4)Fasting TG ≥ 1.70 mmol/L; (5)Fasting HDL-L < 1.04 mmol/L.

Participants without DR were defined as having no abnormalities in fundus photographs; participants with DR included individuals with intraretinal microaneurysms, hemorrhages, venous beading, prominent microvascular abnormalities, neovascularization or vitreous/preretinal hemorrhages in accordance with the Global Diabetic Retinopathy Project Group.

Statistical analysis

Data analyses were performed with IBM SPSS Statistics, version 26. Continuous variables were expressed as the mean \pm standard deviation (SD) or the median with an interquartile range (25%, 75%), and categorical variables were presented as percentages (%). The Student's t test and Chi-square test were used for continuous and dichotomous variables, respectively. Logistic regression tests were used to analyze the associations between abdominal obesity indices and DR or MetS. Data were summarized as odds ratios or regression coefficients (95% CI). Chi-square test was used to analyze the relationship between DR and MetS. The receiver operating characteristics (ROC) curve was constructed to evaluate the discrimination of different induces for MetS. The optimal cut-off point was determined by the maximum Youden index. A P-value < 0.05 (two-sided) was regarded as statistically significant.

Results

General characteristics of the diabetic participants

Overall, 202 men and 360 women with diabetes were involved in the basal analyses. Among men, the prevalence of DR was 29.7%, and the prevalence of MetS was 84.2%. In women, the prevalence of DR was 37.8%, and the prevalence of MetS was 83.3%.

Respective characteristics of men and women by DR or MetS.

The clinical and biochemical characteristics of the subjects are shown in Tables 1 and 2. The participants were divided into two groups with or without DR, and with or without MetS. Compared with the men without DR, only CVAI was significantly higher in men with DR ($P < 0.05$). However, no differences in BMI, WC, HC, NC, WHR and PWNC were found between the two groups ($P > 0.05$). And BMI, WC, NC, WHR, CVAI and PWNC were all significantly higher in men with MetS ($P < 0.05$). Compared with the women without DR, only BMI was significantly higher in women with DR ($P < 0.05$). However, no differences in WC, HC, NC, WHR, CVAI and PWNC were found between the two groups ($P > 0.05$). And BMI, WC, HC, NC, WHR, CVAI and PWNC were all significantly higher in women with MetS ($P < 0.05$).

Table 1
General characteristics of all male participants by DR and MetS.

	DR-(n = 142)	DR+(n = 60)	P	MetS-(n = 32)	MetS+(n = 170)	P
Age (years)	54.97 ± 11.28	57.85 ± 8.26	0.076	50.84 ± 14.69	56.76 ± 9.32	0.034
Duration of DM (years)	6 (3,10)	7 (5, 10)	0.017	5.5 (3, 10.75)	6 (4, 10)	0.679
BMI (kg/m ²)	26.81 ± 3.08	27.60 ± 3.35	0.109	25.20 ± 3.40	27.39 ± 3.02	< 0.001
WC (cm)	99.46 ± 8.76	101.78 ± 7.87	0.077	92.78 ± 10.49	101.54 ± 7.39	< 0.001
HC (cm)	100.77 ± 8.11	102.78 ± 11.20	0.155	99.63 ± 7.63	101.70 ± 9.39	0.240
NC (cm)	39.14 ± 5.59	39.82 ± 3.15	0.381	37.53 ± 2.98	39.68 ± 5.22	0.025
WHR	0.99 ± 0.11	0.99 ± 0.10	0.697	0.94 ± 0.12	1.01 ± 0.10	< 0.001
HbA1c (%)	7.82 ± 1.62	8.15 ± 1.80	0.207	8.53 ± 1.72	7.81 ± 1.66	0.025
TG (mmol/L)	1.51 (1.07, 1.95)	1.49 (1.08, 2.05)	0.869	1.14 (0.88, 1.40)	1.59 (1.15, 2.17)	< 0.001
TC (mmol/L)	4.95 ± 1.13	4.63 ± 1.20	0.074	4.55 ± 0.83	4.91 ± 1.20	0.106
LDL(mmol/L)	3.16 ± 0.91	2.60 ± 0.96	0.157	2.84 ± 0.81	3.15 ± 0.94	0.087
HDL(mmol/L)	1.30 ± 0.25	1.38 ± 0.74	0.414	1.32 ± 0.16	1.33 ± 0.50	0.910
SBP (mmHg)	138.84 ± 17.83	143.42 ± 17.89	0.097	124.53 ± 16.28	143.15 ± 16.68	< 0.001
DBP (mmHg)	86.48 ± 11.12	88.67 ± 10.41	0.195	79.06 ± 9.28	88.65 ± 10.57	< 0.001
FPG(mmol/L)	10.91 ± 3.73	11.50 ± 3.87	0.306	11.04 ± 3.85	11.09 ± 3.77	0.939
UA(μmol/L)	282.03 ± 82.78	291.06 ± 93.66	0.497	243.61 ± 51.33	292.44 ± 89.08	< 0.001

Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.

	DR-(n = 142)	DR+(n = 60)	P	MetS-(n = 32)	MetS+(n = 170)	P
CVAI	148.02 ± 50.42	163.12 ± 38.45	0.039	117.60 ± 41.50	159.10 ± 45.88	< 0.001
PWNC (cm ²)	3912 ± 761	4068 ± 577	0.157	3507 ± 638	4043 ± 696	< 0.001
Family history	35(74.5%)	12(25.5%)	0.475	9(19.1%)	38(80.9%)	0.478
Intervention time (years)	5 (2, 9.25)	6 (5, 10)	0.019	5 (2.13, 9.75)	6 (3, 10)	0.531

Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.

Table 2
General characteristics of all female participants by DR and MetS.

	DR-(n = 224)	DR+(n = 136)	P	MetS-(n = 60)	MetS+(n = 300)	P
Age (years)	57.77 ± 10.08	59.71 ± 8.21	0.060	54.07 ± 11.11	59.39 ± 8.84	0.001
Duration of DM (years)	7(4,11)	9(5.25,15)	< 0.001	7(3.25,12)	8(4.25,13)	0.468
BMI (kg/m ²)	26.50 ± 3.84	25.67 ± 2.93	0.026	23.83 ± 2.83	26.63 ± 3.50	< 0.001
WC (cm)	96.46 ± 9.34	96.68 ± 8.59	0.823	88.50 ± 9.58	98.15 ± 8.05	< 0.001
HC (cm)	97.75 ± 8.50	96.85 ± 9.33	0.352	92.58 ± 8.61	98.37 ± 8.55	< 0.001
NC (cm)	0.99 ± 0.11	1.01 ± 0.11	0.249	0.96 ± 0.14	1.00 ± 0.10	0.048
WHR	35.27 ± 2.65	35.11 ± 2.73	0.587	33.48 ± 2.73	35.56 ± 2.53	< 0.001
HbA1c (%)	7.61 ± 1.62	8.18 ± 1.93	0.004	7.80 ± 2.08	7.83 ± 1.70	0.865
TG (mmol/L)	1.58 (1.15, 2.00)	1.57 (1.16, 2.35)	0.930	1.14 (0.92, 1.44)	1.71 (1.29, 2.40)	< 0.001
TC (mmol/L)	4.92 ± 1.12	5.20 ± 1.26	0.029	4.52 ± 1.15	5.12 ± 1.16	< 0.001
LDL(mmol/L)	3.05 ± 0.93	3.22 ± 1.14	0.160	2.78 ± 0.96	3.18 ± 1.02	0.005
HDL(mmol/L)	1.29 ± 0.20	1.31 ± 0.27	0.412	1.34 ± 0.21	1.29 ± 0.23	0.111
SBP (mmHg)	140.49 ± 18.90	142.29 ± 19.27	0.387	124.50 ± 16.67	144.50 ± 17.70	< 0.001
DBP (mmHg)	84.83 ± 12.00	83.90 ± 10.25	0.448	77.25 ± 8.85	85.93 ± 11.27	< 0.001
FPG(mmol/L)	10.90 ± 3.89	12.16 ± 5.11	0.016	11.27 ± 4.97	11.41 ± 4.32	0.820
UA (µmol/L)	240.63 ± 87.27	254.22 ± 74.16	0.131	218.90 ± 43.47	251.14 ± 87.58	< 0.001
CVAI	124.84 ± 36.25	125.27 ± 29.00	0.907	91.51 ± 34.30	131.70 ± 29.30	< 0.001

Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.

	DR-(n = 224)	DR+(n = 136)	P	MetS-(n = 60)	MetS+(n = 300)	P
PWNC (cm ²)	3416 ± 519	3406 ± 489	0.854	2976 ± 501	3500 ± 463	< 0.001
Family history	45(20.1%)	30(22.1%)	0.656	10(16.7%)	65(21.7%)	0.384
Intervention time (years)	6 (4, 11)	8.5 (5, 13)	0.001	6.5 (3.25, 10)	7 (4, 12)	0.175
Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.						

In addition, the participants were also divided into four groups according to the quartiles of NC (Tables 3 and 4). Both in men and women, BMI, NC, WC, HC, CVAI, SBP, DBP, and PWNC were all significant among groups ($P < 0.05$). However, MS was significant ($P < 0.001$) and DR was not significant among groups ($P > 0.05$).

Table 3
General characteristics of male participants divided by quartiles of NC.

	Q1(n = 46)	Q2(n = 45)	Q3(n = 62)	Q4(n = 49)	P
Age (years)	56.76 ± 10.49	55.00 ± 12.58	56.47 ± 10.07	54.90 ± 9.20	0.744
Duration of DM (years)	4.5(3,9)	8(4,12.5)	6(3.88,9)	6(3,10.5)	0.011
BMI (kg/m ²)	24.33 ± 2.78	25.67 ± 2.06	27.79 ± 2.29	29.93 ± 2.52	< 0.001
WC (cm)	92.87 ± 8.78	96.98 ± 6.55	101.85 ± 5.07	107.73 ± 6.29	< 0.001
HC (cm)	96.87 ± 7.38	99.18 ± 11.28	101.60 ± 8.00	107.33 ± 6.44	< 0.001
NC (cm)	35.02 ± 1.54	37.38 ± 0.49	39.92 ± 0.75	44.47 ± 7.25	< 0.001
WHR	0.96 ± 0.12	0.99 ± 0.13	1.01 ± 0.09	1.01 ± 0.06	0.127
HbA1c%	7.91 ± 1.96	8.08 ± 1.82	7.75 ± 1.50	8.00 ± 1.50	0.766
TG (mmol/L)	1.24 (0.94, 1.76)	1.41 (1.07, 1.74)	1.43 (1.00, 2.09)	1.78 (1.39, 2.44)	0.919
TC (mmol/L)	4.85 ± 1.32	4.82 ± 1.17	4.93 ± 1.23	4.81 ± 0.90	0.947
LDL(mmol/L)	3.05 ± 1.12	3.03 ± 0.92	3.10 ± 0.82	3.20 ± 0.87	0.813
HDL(mmol/L)	1.39 ± 0.30	1.33 ± 0.30	1.37 ± 0.70	1.21 ± 0.22	0.199
SBP(mmHg)	138.70 ± 15.18	138.00 ± 14.28	137.98 ± 19.13	146.43 ± 20.62	0.048
DBP(mmHg)	85.43 ± 9.12	84.11 ± 8.07	86.45 ± 11.68	92.35 ± 12.25	0.001
FPG(mmol/L)	11.35 ± 4.67	11.14 ± 3.72	10.99 ± 3.69	10.90 ± 3.00	0.942
UA(μmol/L)	252.47 ± 69.17	262.13 ± 69.64	298.04 ± 93.08	318.84 ± 90.26	< 0.001
CVAI	122.79 ± 35.88	139.83 ± 29.50	155.84 ± 59.18	187.83 ± 27.32	< 0.001
PWNC(cm ²)	3254 ± 345	3625 ± 257	4066 ± 216	4789 ± 775	< 0.001
Family history	12(26.1%)	16(35.6%)	12(19.4%)	7(14.3%)	0.08

Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.

	Q1(n = 46)	Q2(n = 45)	Q3(n = 62)	Q4(n = 49)	P
Intervention time (years)	4 (3, 7)	6 (4, 12.5)	6 (3, 7.25)	6 (3, 10)	0.003
DR	11(23.9%)	13(28.9%)	18(29.0%)	18(36.7%)	0.588
MS	26(56.5%)	38(84.4%)	57(91.9%)	49(100%)	< 0.001
Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.					

Table 4
General characteristics of female participants divided by quartiles of NC.

	Q1(n = 90)	Q2(n = 60)	Q3(n = 148)	Q4(n = 62)	P
Age (years)	57.2 ± 11.43	57.47 ± 9.50	59.24 ± 8.08	59.65 ± 9.20	0.238
Duration of DM (years)	8.5 (5, 12.5)	5 (3,9.75)	8 (5, 13)	7.5 (4,13)	0.046
BMI (kg/m ²)	23.76 ± 2.91	25.88 ± 2.81	26.43 ± 3.25	29.30 ± 3.10	< 0.001
WC (cm)	89.68 ± 7.20	95.30 ± 8.81	97.74 ± 7.55	104.84 ± 7.07	< 0.001
HC (cm)	92.53 ± 9.12	96.95 ± 8.31	98.46 ± 7.82	102.42 ± 7.66	< 0.001
NC (cm)	32.00 ± 1.35	34.01 ± 0.06	35.95 ± 0.79	39.34 ± 1.49	< 0.001
WHR	0.98 ± 0.14	0.99 ± 0.10	1.00 ± 0.10	1.03 ± 0.07	0.05
HbA1c%	7.91 ± 1.88	7.34 ± 1.62	7.84 ± 1.81	8.11 ± 1.57	0.094
TG (mmol/L)	1.59 (1.03, 2.20)	1.38 (1.03, 1.78)	1.62 (1.26, 2.48)	1.58 (1.35, 2.61)	0.018
TC (mmol/L)	5.10 ± 1.10	4.77 ± 1.18	5.00 ± 1.23	5.23 ± 1.15	0.177
LDL(mmol/L)	1.31 ± 0.23	1.28 ± 0.21	1.31 ± 0.24	1.27 ± 0.21	0.522
HDL(mmol/L)	2.94 ± 0.85	2.86 ± 0.80	3.23 ± 1.12	3.32 ± 1.12	0.012
SBP(mmHg)	133.33 ± 18.41	140.72 ± 17.24	144.31 ± 19.50	145.48 ± 17.36	< 0.001
DBP(mmHg)	79.44 ± 9.04	86.00 ± 8.63	86.03 ± 13.12	86.61 ± 10.15	< 0.001
FPG(mmol/L)	12.59 ± 5.12	10.86 ± 4.65	11.13 ± 4.11	10.80 ± 3.56	0.028
UA(μmol/L)	229.03 ± 53.74	241.08 ± 62.71	251.46 ± 106.77	261.00 ± 63.51	0.082
CVAI	105.23 ± 33.10	116.38 ± 33.00	129.81 ± 28.63	150.57 ± 25.77	< 0.001
PWNC(cm ²)	2870 ± 298	3241 ± 301	3514 ± 284	4124 ± 320	< 0.001

Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.

	Q1(n = 90)	Q2(n = 60)	Q3(n = 148)	Q4(n = 62)	P
Family history	16(17.8%)	14(23.3%)	31(20.9%)	14(22.6%)	0.837
Intervention time (years)	8 (5, 12)	5 (2.25, 9)	8 (4, 12)	7 (4,12)	0.019
DR	34(37.8%)	25(41.7%)	56(37.8%)	21(33.9%)	0.852
MS	60(66.7%)	46(76.7%)	134(90.5%)	59(95.2%)	< 0.001
Abbreviations: DR diabetic retinopathy, MetS metabolic syndrome, BMI body mass index, WC waist circumference, HC hip circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC, FPG fasting plasma glucose, HbA1c glycated hemoglobin, HDL high-density lipoprotein, LDL low-density lipoprotein, TG triglycerides, TC total cholesterol, UA uric acid, SBP systolic blood pressure, DBP diastolic blood pressure.					

Associations between abdominal obesity indices and prevalence of DR and MetS.

We found that in increased NC, CVAI, and PWNC were significantly associated with the prevalence of MetS both in men and women (Fig. 1). In men, a one SD increase in NC (OR 1.64; 95%CI 1.34-2.00), CVAI (OR 1.02; 95%CI 0.90-1.05), and PWNC (OR 1.02; 95%CI 0.98-1.06) was significantly associated with a greater prevalence of MetS ($P < 0.05$). In women, a one SD increase in NC (OR 1.39; 95%CI 1.22-1.58), CVAI (OR 1.05; 95%CI 1.00-1.09), and PWNC (OR 1.02; 95%CI 0.98-1.05) was significantly associated with a greater prevalence of MetS ($P < 0.05$). And these association were adjusted for age, duration of diabetes, interventional time, and family history (Fig. 1). Moreover, after adjusting for age, duration of diabetes, interventional time, and family history, in both men and women, a one SD increase in NC, CVAI, and PWNC was not associated with the prevalence of DR (all P for trend > 0.05) (Fig. 2).

Receiver-operating characteristics (ROC) curve analysis.

We found that the diagnostic ability of abdominal obesity indices including BMI, WC, NC, WHR, CVAI and PWNC for MetS among men and women, respectively, analyzed by ROC curve. The differences between the area under the curve of CVAI and that of BMI, WC, NC, WHR, and PWNC for CVD and DKD both in men and women were all significant ($P < 0.05$). However, the differences between the area under the curve of these indices in DR were not significant ($P > 0.05$).

In men, area under ROC curve of BMI, WC, NC, WHR, CVAI and PWNC for MetS was 0.730, 0.746, 0.824, 0.718, 0.717 and 0.816 respectively (all $P < 0.001$). NC had the largest area under the ROC curve compared to the other induces, and the cutoff with the biggest Youden index of NC was 37.50cm with a sensitivity of 71.2% and a specificity of 78.1%. In women, area under ROC curve of BMI, WC, NC, WHR, CVAI and PWNC for MetS was 0.741, 0.786, 0.719, 0.658, 0.828 and 0.800 respectively (all $P < 0.001$). CVAI had the largest area under the ROC curve compared to the other induces, and the cutoff with the biggest Youden index of CVAI was 109.01 with a sensitivity of 80.6% and a specificity of 78.7% (Fig. 3).

Discussion

Obesity due to poor diet and lifestyle habits is a time bomb for diabetes and its complications in the community population. As we all know, obesity frequently coexists with type 2 diabetes mellitus (T2DM), leading to the so-called “diabesity epidemic”¹². However, the relationship between obesity and diabetes complications is ambiguous. A meta-analysis in 2018 (n = 14,575, 13 clinical studies) reported that obesity (assessed by BMI) significantly increased the risk of DR; this effect mainly referred to non-proliferative DR and to patients with T2DM, as shown in subgroup analysis¹³. Moreover, another cross-sectional study (n = 1,414 DM patients) showed that abdominal obesity (assessed by WC) also correlated with DR¹⁴. Also, abdominal obesity (defined by WHR) was positively related to mild-moderate and severe DR in T2DM women⁹. These results suggest that these induce may be associated with DR, however, our findings showed that BMI, WC, NC, CVAI, WHR and PWNC were not associated with the prevalence of DR, which is consistent with the latest research⁴.

Evolving body of evidence suggests that the susceptibility to obesity-associated metabolic disorders is not mediated by the amount of fatness per se, but by the inability for excess energy to be stored appropriately in adipose tissue after reaching an individual’s fat threshold⁸. Adipose tissue plays a pivotal role in storing excess nutrients, sensing nutrient status, and regulating energy mobilization. In the face of long-term excessive nutrition, exhaustion of adipose tissue expandability creates stress on adipocytes and elicits a transition from an adaptive to a maladaptive inflammatory response over time, leading to increased inflammation as characterized by deranged secretion of adipokines and proinflammatory cytokines, abnormal tissue remodeling and fibrosis, and eventually insulin resistance and its manifestations¹⁵. Visceral fat is closely related to inflammation and increased risk for metabolic disorders, whereas subcutaneous adiposity is comparatively less harmful¹⁶.

MetS is a cluster of obesity, hypertension, dysglycemia, dyslipidemia, and insulin resistance, which abdominal obesity and insulin resistance seem to play a central role in promoting the development of MetS^{17,18}. MetS is a risk factor for cardiovascular complications of DM, but the association between MetS and microvascular complications of DM is limited. Moreover, the relationship between the components of metabolic syndrome and DR remains to be studied. NC has been considered a marker of upper body subcutaneous fat deposits and a simple and valuable screening tool for identifying individuals with obesity^{5,19}, which is independently associated with MetS^{19,20}. CVAI is a novel visceral adiposity index developed in Chinese adults that is associated with visceral fat area and insulin resistance^{6,21}. And PWNC is a novel anthropometric index, as an obesity indicator for MetS⁷. In our study, we found NC, CVAI and PWNC were significantly associated with a greater prevalence of MetS. However, they were not associated with DR.

In addition, we also studied the differences among groups grouped by the cervical quartile. We found that NC, CVAI and PWNC are all significant among groups. These induces are all significant with MetS but not significant with DR. Moreover, NC had the largest area under the ROC curve in men, however, CVAI had the

largest area under the ROC curve in women. This may be due to the uneven distribution of body fat between men and women. In men, the cutoff with the biggest Youden index of NC was 37.50cm, which has a higher specificity among these induces. And in women, the cutoff with the biggest Youden index of CVAI was 109.01, but the specificity of PWNC is higher than CVAI.

Hyperglycemia, oxidative stress, and inflammation are processes involved in MetS and DR, so several population studies evaluated its association with DR. A large multicenter clinic-based study from Italy reported an increased risk of type 2 diabetic retinopathy (T2DR) rather than type 1 diabetic retinopathy (T1DR) in patients with MetS²². Indeed, a study showed a 2.7 times higher risk of DR in patients with MetS which comprised of 3 components, while a 4.4 times higher risk of DR in patients with MetS which comprised of 5 components²³. However, neither MetS nor its components are associated with an increased risk of DR based on recent published data²⁴, which is consistent with our findings. This may be due to the fact that most studies are cross-sectional and could not confirm a causal relationship. Moreover, it was associated with differences in race and metabolic markers.

This study has several strengths. Firstly, we investigated for the first time the relationship among abdominal obesity induces and DR and MetS. Secondly, our sample came from a community in northeast China, which the selection of non-admitted patients reduces the selection bias to a certain extent. Thirdly, we investigated for the first time the relationship between PWNC and DR. However, there are also some limitations in our study. First, being a cross-sectional study, causal inference between obesity phenotype indices and diabetic complications cannot be established. Second, the ethnic group investigated was only Han Chinese, thus generalizing the results to other ethnic groups should be done cautiously. Third, the questionnaire of our study did not address whether the patients were taking lipid-lowering drugs or had no history of smoking or alcohol consumption.

Conclusions

The present study demonstrates that NC, CVAI and PWNC are associated with the prevalence of MetS. In men, NC may be a convenient and valuable anthropometric measurement for early prevention of MetS. And in women, CVAI may be more suitable. However, these induces had no association with DR and there is no relationship between DR and MetS. Further prospective studies are necessary to examine our findings in external populations.

Declarations

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Authors' contributions

All the authors contributed significantly to the manuscript. Xin-Li conceived and designed the study, completed statistical analysis and wrote the manuscript. Zi-Wei Yu, Chang-Wei Yang and Ming Hao participated in data collection and collation. Hong-Yu Kuang, Yong Yu and Xu Peng contributed to the preparation of the study and critically reviewed the manuscript. Xin-Yuan Gao gave final approval of the version to be submitted. All authors read and approved the final manuscript.

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Availability of data and materials

The data are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no potential conflicts of interest regarding the publication of this paper.

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Figures

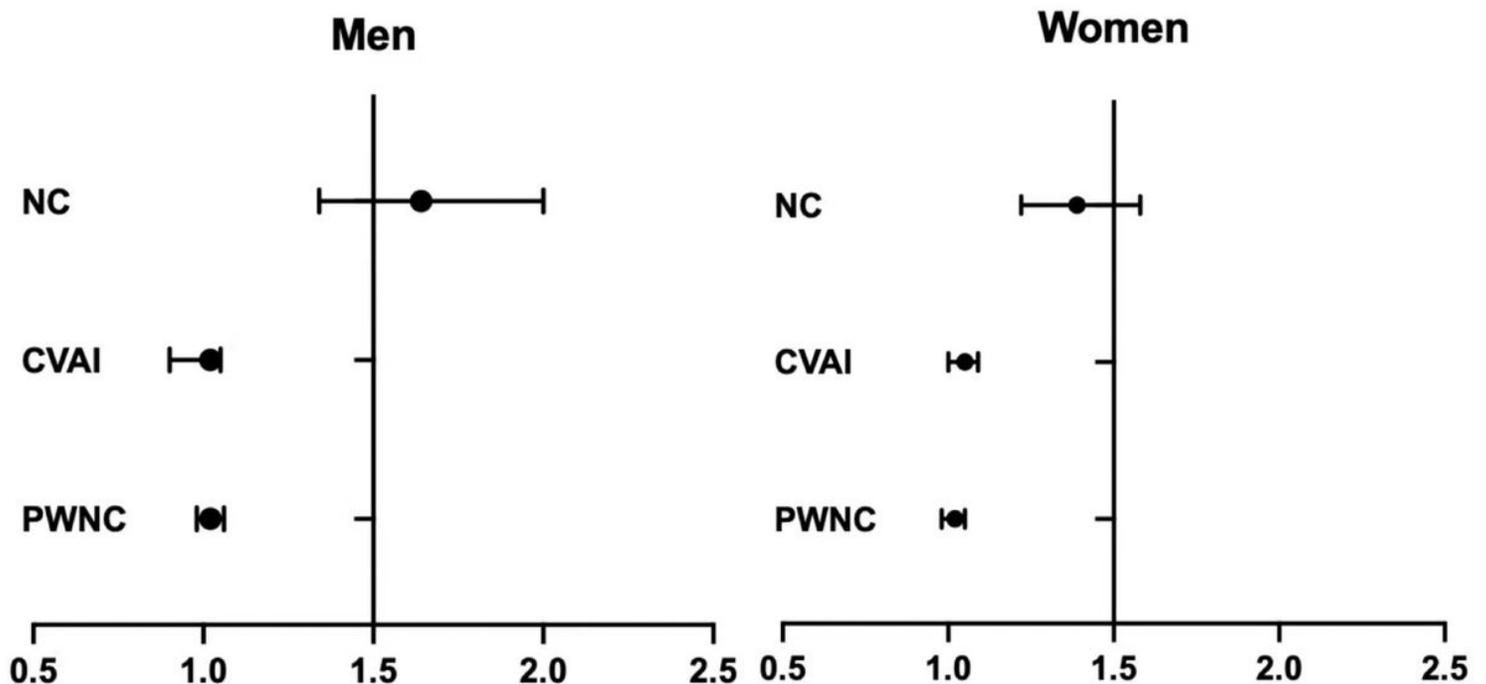


Figure 1

Associations between abdominal obesity indices and the prevalence of MetS. Logistic regression analyses were used for abdominal obesity index and the association between the abdominal obesity index and the prevalence of MetS. The model was adjusted for age, duration of diabetes, interventional time, family history, intensity of motion and treatment.

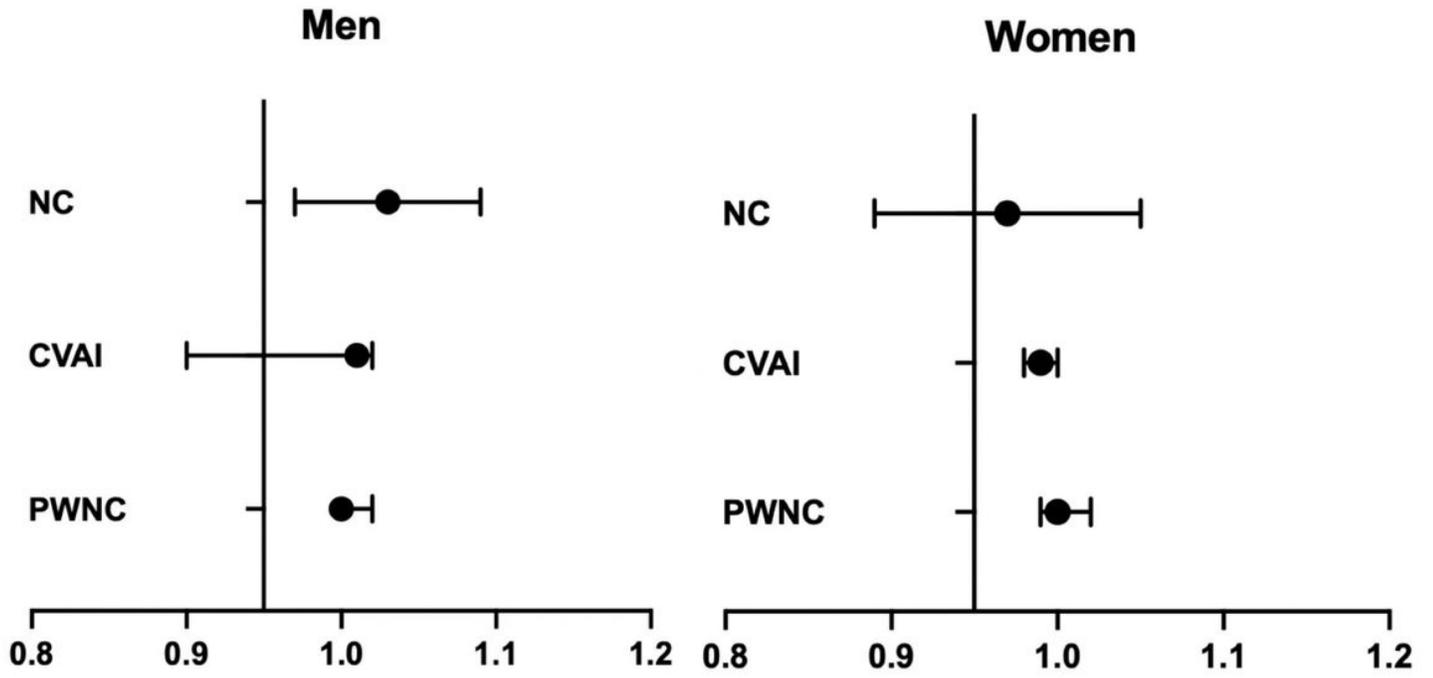


Figure 2

Associations between abdominal obesity indices and the prevalence of DR. Logistic regression analyses were used for abdominal obesity index and the association between the abdominal obesity index and the prevalence of DR. The model was adjusted for age, duration of diabetes, interventional time, family history, intensity of motion and treatment.

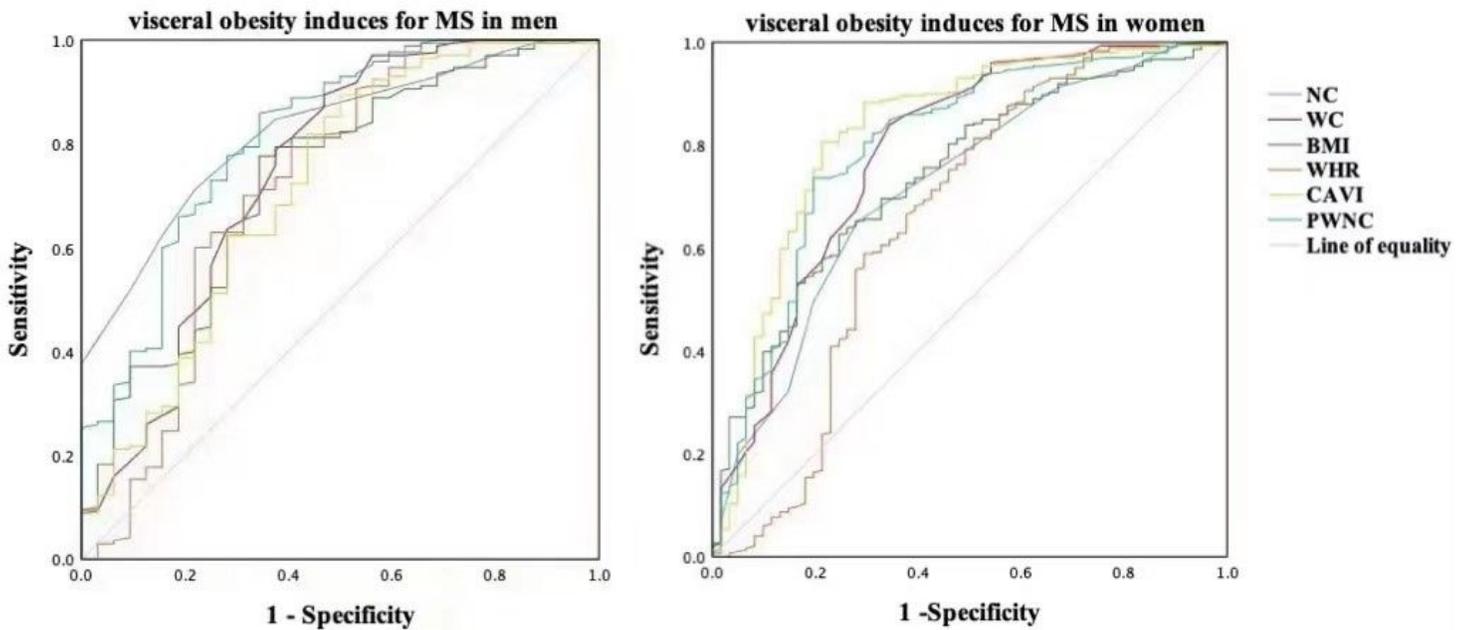


Figure 3

The ROC curve of abdominal obesity indices for diagnosing MetS in men and women. BMI body mass index, WC waist circumference, NC neck circumference, CVAI Chinese visceral adiposity index, WHR waist-to-hip ratio, PWNC product of WC and NC.