

Chinese Visceral Adipose Index is Associated with Arterial Stiffness in Type 2 Diabetes Patients: A Cross-Sectional Study

Qin Liu¹, Fang Yu¹, Quan Zhou², Haifeng Zhou¹, Huilin Lu¹, Jian Luo¹, Shenglian Gan¹

¹Department of Endocrinology, Changde Hospital, Xiangya School of Medicine, Central South University, Changde, Hunan, People's Republic of China;

²Department of Science and Education, Changde Hospital, Xiangya School of Medicine, Central South University, Changde, Hunan, People's Republic of China

Correspondence: Shenglian Gan, Department of Endocrinology, Changde Hospital, Xiangya School of Medicine, Central South University, 818 Renmin Road, Changde, Hunan, 415000, People's Republic of China, Tel +86 0736 7788026, Email gslghy03@sina.com

Purpose: The purpose of this study is to investigate the association between Chinese Visceral Adipose Index(CVAI) and brachial-ankle pulse wave velocity (baPWV) in type 2 diabetes (T2D) patients, in order to provide scientific evidence for the prevention and treatment of macrovascular complications in T2D.

Patients and Methods: This research adopts the cross-sectional study design. Anthropometric assessment, baPWV assessment and biochemical assessment were performed in 2906 T2D patients. CVAI was calculated from the combination of triglycerides, age, high-density lipoprotein cholesterol, waist circumference, body mass index. Multivariate regression analysis and generalized additive model were used to analyze the association between baPWV and CVAI. Subgroup analysis and interaction analysis were used to analyze the influencing factors.

Results: After adjustment for covariates, baPWV tended to increase in the quartiles of CVAI. In males, As CVAI increases by a unit, baPWV was increased by 0.28 cm/s (95% CI: -0.05, 0.61 P=0.0934). In females, As CVAI increases by a unit, baPWV was increased by 1.60 cm/s (95% CI: 1.07, 2.14). A non-linear connection in males and a linear connection in females between the CVAI and baPWV was revealed. In males, we found that CVAI interacted with baPWV in different duration of diabetes (P interaction = 0.0052), alcohol consumption status (P interaction = 0.0375). In females, CVAI interacted with baPWV in glycated hemoglobin (P interaction = 0.0003), systolic blood pressure (P interaction = 0.0001), diastolic blood pressure (P interaction<0.0001), duration of diabetes (P interaction = 0.0014), the use or non-use of glucose-lowering drugs (P interaction = 0.0006), the use or non-use antihypertensive drugs (P interaction = 0.0004), females' menopausal status (P interaction = 0.0012).

Conclusion: The relationship between CVAI and baPWV in T2D patients is positively non-linear in males and linear in females. In all subjects, this relationship was influenced by diabetes duration. In males, drinking status affected this relationship, and in females, It is influenced by blood pressure, glycemic control, menopausal status, and the use of glucose-lowering and hypotensive drug, highlighting the complex interplay between visceral fat and arterial stiffness in the T2D population.

Keywords: Chinese visceral adipose index, arterial stiffness, type 2 diabetes

Introduction

The global prevalence of type 2 diabetes (T2D) is increasing. It is projected that the worldwide diabetic population will reach 366 million by 2030, up from 171 million in 2000.¹ T2D not only increases the risk of microvascular complications, such as nephropathy and retinopathy, but also increases the risk of macrovascular complications. These complications greatly increase the mortality rate and medical costs of patients.²

The development of cardiovascular complications is strongly influenced by visceral adiposity in T2D patients. First, Insulin resistance (IR) is closely linked to visceral-fat accumulation, which is a key feature of T2D. IR not only affects blood glucose control but may also lead to atherosclerosis and vascular inflammation, which are important risk factors for cardiovascular diseases (CVD).³ Furthermore, visceral fat can directly or indirectly influence the health of the

cardiovascular system by producing various adipocytokines (such as tumor necrosis factor, interleukin-6, etc). These factors can exacerbate inflammatory responses and impair endothelial function, thereby increasing the risk of cardiovascular events.⁴ In addition, the increase in obesity and visceral fat leads to elevated blood lipid levels, which along with insulin resistance, can further exacerbate the hyperglycemic state. This may also alter the networks involved in cholesterol metabolism, potentially representing a molecular characteristic of T2D associated with obesity and CVD.⁵ Therefore, Managing visceral fat accumulation in T2D patients is essential for preventing cardiovascular complications.

The assessment of visceral fat has its advantages and disadvantages. An accurate image can be obtained with computed tomography (CT) or magnetic resonance imaging (MRI), which are helpful in identifying and quantifying visceral fat, but the equipment is expensive and the scanning time is relatively long.⁶ Bioelectrical impedance analysis (BIA) is simple and quick, suitable for large-scale epidemiological studies and clinical applications, but the results may be affected by factors such as hydration.⁷ Our research team published research results suggesting that visceral fat area (VFA) is more strongly correlated with arterial stiffness than abdominal subcutaneous fat area (SFA). In this study, we used the method of BIA, but the method of BIA is not perfect in general hospitals.⁸ Waist circumference (WC) measurement is convenient and practical, but its accuracy as an indicator of visceral fat is limited.⁹ As a measure of excess body fat, body mass index (BMI) does not take into account fat deposition.¹⁰ Therefore, in recent years, we have been looking for reliable indicators that can accurately reflect visceral fat. Our research team also found that in Chinese patients with T2D, lipid accumulation products (LAP) was strongly and positively correlated with baPWV. However, the degree of association between LAP and VFA and SFA was not stated in this study, and LAP did not consider age and gender.¹¹ The Chinese Visceral Adipose Index (CVAI) uses triglycerides (TG), age, high-density lipoprotein cholesterol (HDL-C), WC, and BMI to measure visceral fat area in Chinese adults.¹² In contrast to the CVAI, Visceral Adipose Index (VAI) calculation lacks age, and the VAI was established in Caucasians.¹³ In Chinese population, CVAI is superior to VAI in predicting the risk of carotid plaque.¹⁴ CVAI is a valuable and easily obtainable tool that can effectively reflect the degree of visceral fat. Multiple studies have presented that elevated CVAI is strongly in relation to an increased risk of T2D and its microvascular complications.^{15–18} These studies have mainly focused on microvascular complications in patients with T2D, rather than macrovascular complications. Research has found that in the Chinese population, CVAI has a stronger correlation with hypertension and pre-hypertension, compared to traditional obesity indices, CVAI has demonstrated superior performance in predicting hypertension and prehypertension in the Chinese population.¹⁹ There is a significant increase in CVD risk associated with CVAI.²⁰

The stiffness of the arteries leads to CVD, as well as to the development of T2D complications.^{21,22} Despite the recognized importance of arterial stiffness associated with the development and complications of T2D and various CVD, there is a paucity of research exploring the association between CVAI and arterial stiffness in T2D patient. Consequently, this study examines the association between CVAI and arterial stiffness in individuals with T2D, for the purpose of providing scientific evidence for the further prevention and treatment of macrovascular complications in T2D.

Methods

Study Population Characteristics

Research was conducted at the Metabolic Management Center (MMC) of Changde Hospital, Xiangya School of Medicine, Central South University, Hunan Province, China. This research adopts the cross-sectional study design. The Metabolic Management Center is a national-level initiative led by academician Ning Guang of the Chinese Academy of Engineering, with the aim of providing comprehensive solutions for the prevention, diagnosis, and management of metabolic disorders across China.²³ Between May 2020 and October 2023, 3201 T2D patients were enrolled. We included people who were 18 years old or older and meeting the 1999 World Health Organization diagnostic criteria for T2D.²⁴ Criteria for exclusion were under 18 years of age (n=8), malignant tumors now or ever (n=19), type 1 diabetes (n=32), pregnancy (n=2), other types of diabetes (n=6), and missing data for BMI (n=44), WC (n=38), TG (n=1), HDL-C (n=37), baPWV (n=101), CVAI ≤ 0 (n=7). After applying the exclusion criteria, 2906 participants with T2D were finally included in the research (Figure 1). This study followed the Declaration of Helsinki. Informed consent was obtained from

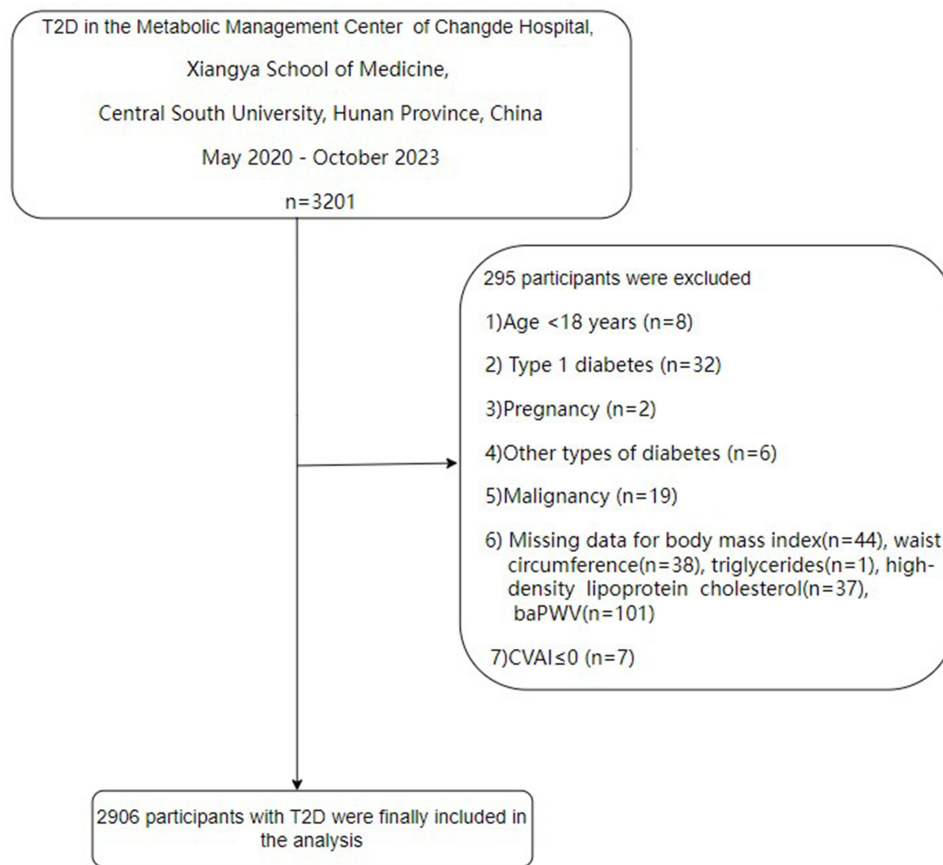


Figure 1 A flow chart.

all participants, and the Institutional Review Board (IRB) of Changde Hospital, Xiangya School of Medicine, Central South University approved the study protocol (number of approval: 2020–061-01).

Clinical Data Collection

Based on standardized questionnaires, we collected data on gender, diabetes duration, age, medical history, the use of antihypertensive, lipid-lowering, and hypoglycemic medication, alcohol consumption, smoking and females menopause status. Smoking status is categorized as never, previous, current. For more than six months, A person who smokes more than one cigarette a day or seven cigarettes a week is considered to be currently smoking. A person who smoked six months ago and not since has been considered to be previous smoking. There are three categories of alcohol consumption status: never, previous, and current. Current alcohol consumption is defined as drinking 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of distilled spirits each week. Previous alcohol consumption means drinking alcohol up to six months ago but not since then. A diabetes course of 0 is defined as the first discovery of elevated blood sugar. As of one year after the cessation of menstruation, the postmenopausal state was defined. The following anthropometric measurements were obtained: systolic blood pressure (SBP), diastolic blood pressure (DBP), height, weight, WC. Following a minimum of five minutes of rest, the blood pressure was measured twice while seated, and the final mean value was calculated. With the participant's shoes removed, the height was measured at the three points of the head (occiput, the ridge between the two shoulder blades, and the sacrum) were in contact with the measurement column. Calculation of BMI was done by dividing weight (kg) by height squared (m²). At the midpoint between the superior and inferior margins of the costal arch, WC was measured using a nonelastic tape. Following fasting for at least 12 hours, using a dual BIA, a physician measured VFA and SFA (HDS-2000 DUALSCAN; Omron Healthcare, Kyoto, Japan).²⁵

Biochemical Data Collection

A blood sample was drawn from each subject after they had fasted for at least eight hours to measure TG, low-density lipoprotein cholesterol (LDL-C), HDL-C, glycated hemoglobin (HbA1c), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), fasting plasma glucose (FPG), white blood cell count (WBC), total cholesterol (TC), uric acid (UA). Equation for calculated estimated glomerular filtration rate (eGFR) with diet improvement in renal disease (MDRD) equation.²⁶ CVAI values were calculated as follows: $CVAI = -267.93 + 0.68 * \text{age} + 0.03 * \text{BMI} + 4.00 * \text{WC} + 22.00 * \log_{10} \text{TG} - 16.32 * \text{HDL}$ (in males); $CVAI = -187.32 + 1.71 * \text{age} + 4.23 * \text{BMI} + 1.12 * \text{WC} + 39.76 * \log_{10} \text{TG} - 11.66 * \text{HDL}$ (in females).¹²

Measurement of baPWV

In order to measure the baPWV, a device that detects atherosclerosis automatically was used (model HBP-8000, Omron Healthcare (China) Co).²⁷ Measuring before, A minimum of five minutes of rest was required for every participant. Wrapping the four cuffs of the automatic recording apparatus bilaterally around the elbows and ankles followed. A 3 cm arm cuff was fastened above the elbow crease, and a 2 cm leg cuff above the medial malleolus. Based on the subject's height, the instrument calculated the distance between the brachium and ankle (La-Lb). Tba is the time difference between the elbow and ankle waveforms. Using the (La-Lb)/Tba formula, we determined the baPWV value. This study evaluated the mean value of baPWV.

Statistical Analysis

Based on CVAI levels, participants were divided into four equal subgroups. Continuous variables with normal distributions were analyzed using the mean $\pm$ SD. With skewed distributions, we used the median (1–3 quartiles). It was used numerical values (percentages) in the case of categorical variables. Continuous variables were analyzed using ANOVA, or the Kruskal–Wallis *H*-test, while categorical data were analyzed using Fisher's exact test, or the chi-square test. In multivariate regression analyses, we calculated the β coefficient and 95% CI (confidence interval) to evaluate CVAI-baPWV relationship. Covariates that resulted in a 10% or greater change in regression coefficients(β) were adjusted, moreover, the screening results for collinearity excluded TC from multivariate regression models ([Supplementary Table 1](#)). CVAI and baPWV dose-response relationships were described using a generalized additive model (GAM) for different sex. The CVAI-baPWV relationship was examined using subgroup analyses and interaction analysis based on potential effect modifiers. For this study, R version 4.2.0 and EmpowerStats version 4.0 were used for statistical analysis.

Results

Baseline Characteristics of the Study Population

In our study, 2906 participants were enrolled, 1698 (58.43%) were males and 1208 (41.57%) were females. [Table 1](#) presents the baseline characteristics of the males and females. VFA, DBP, ALT, AST, GGT, UA, WBC, FBG, HbA1C

Table 1 Clinical Characteristics According to Sex in Patients with Type 2 Diabetes

	Male(n=1698)	Female(n=1208)	P value
Age, years	51.18 $\pm$ 10.73	54.86 $\pm$ 10.51	<0.001
VFA, cm ²	90.30 $\pm$ 40.47	75.03 $\pm$ 31.34	<0.001
SFA,cm ²	176.02 $\pm$ 59.20	175.25 $\pm$ 62.31	0.758
SBP, mmHg	134.71 $\pm$ 19.24	138.57 $\pm$ 20.92	<0.001
DBP, mmHg	85.53 $\pm$ 11.47	81.74 $\pm$ 11.36	<0.001

(Continued)

Table I (Continued).

	Male(n=1698)	Female(n=1208)	P value
ALT, U/L	26.00 (18.00–41.00)	21.00 (15.00–33.00)	<0.001
AST, U/L	23.00 (18.00–29.00)	22.00 (18.00–28.00)	0.014
GGT, U/L	31.00 (21.00–53.00)	22.00(16.00–35.00)	<0.001
WBC, 10 ⁹ /L	6.39 ± 1.74	6.18 ± 2.47	0.006
UA,mmol/L)	353.82 ± 87.56	307.41 ± 78.79	<0.001
eGFR,mL/min/1.73m ²	113.15 ± 32.47	120.76 ± 35.73	<0.001
FBG, mmol/L	8.98 ± 3.75	8.47 ± 3.25	<0.001
HbA1c, %	8.67 ± 2.38	8.13 ± 2.07	<0.001
TC, mmol/L	4.91 ± 1.42	5.07 ± 1.10	0.002
LDL-C, mmol/L	2.78 ± 0.89	2.81 ± 0.88	0.294
Duration of diabetes, month	32.00(2.00–86.75)	48.00(8.00–97.00)	<0.001
baPWV,cm/s	1595.47 ± 308.84	1631.57 ± 326.10	0.002
Smoking Never Former Current	891 (52.85%) 142(8.42%) 653 (38.73%)	1177 (97.76%) 9(0.75%) 18 (1.50%)	<0.001
Alcohol Consumption Never Former Current	949 (56.29%) 543(32.21%) 194 (11.51%)	1168 (97.01%) 35 (2.91%) 1 (0.08%)	<0.001
Hypoglycemic Drugs No Yes	422 (25.54%) 1230 (74.46%)	248(20.84%) 942 (79.16%)	0.004
Lipid-lowering Drugs No Yes	1407 (83.55%) 277(16.45%)	1038 (86.28%) 165 (13.72%)	0.044
Antihypertensive Drugs No Yes	1218 (72.24%) 468 (27.76%)	868 (70.02%) 373 (29.98%)	0.192
CVAI	124.69 ± 41.64	104.95 ± 32.79	<0.001
CVAI quartiles Q1 Q2 Q3 Q4	320 (18.85%) 363 (21.38%) 458 (26.97%) 557 (32.80%)	407 (33.69%) 363 (30.05%) 268 (22.19%) 170 (14.07%)	<0.001

Note: Data are expressed as mean ± standard deviation or number (%).

Abbreviations: VFA, Visceral fat area; SFA, subcutaneous fat area; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; WBC, white blood cell count; UA, uric acid; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; baPWV, brachial-ankle pulse wave velocity; CVAI, Chinese visceral adiposity index.

and proportions of smokers and drinkers were higher in males than in females. However, age, eGFR, SBP, TC, duration of diabetes and baPWV were lower in males than in females. More people in the total population were on hypoglycemic drugs, and fewer were on lipid-lowering and antihypertensive drugs. Additionally, males had a higher average CVAI than females (124.69 ± 41.64 vs 104.95 ± 32.79 , P value < 0.001). In contrast with most of the females, most of the males were in the two upper quartiles of CVAI. Therefore, we divided males and females into quartiles based on their CVAI baselines.

CVAI quartiles are presented in [Table 2](#). High CVAI was associated with higher VFA, SFA, SBP, DBP, ALT, GGT, AST, WBC, UA, FBG. High CVAI females were more likely to have diabetes for a longer period of time, while their eGFR was lower and older. There were more women with menopause and fewer women without menopause in the high CVAI group. [Figure 2](#) shows modest increases in BMI, WC, VFA and SFA were observed along with an increase in CVAI.

The Correlations for Body Composition Measures

[Figure 3](#) displays the correlations between anthropometric measurements of body composition (WC, height, weight, BMI, VFA, SFA and CVAI). There was a significant strong positive correlation between the CVAI and weight ($r=0.6051$, $p<0.001$ in females, $r=0.8097$, $p<0.001$ in males), BMI ($r=0.7159$, $p<0.001$ in females, $r=0.8446$, $p<0.001$ in males), WC ($r=0.8094$, $p<0.001$ in females, $r=0.9724$, $p<0.001$ in males), VFA ($r=0.7031$, $p<0.001$ in females, $r=0.8083$, $p<0.001$ in males), SFA ($r=0.6476$, $p<0.001$ in females, $r=0.8263$, $p<0.001$ in males).

Univariate Analysis

As shown in [Supplementary Table 2](#), univariate analysis yielded the following results. It showed that age, VFA, SFA, SBP, DBP, ALT, UA, duration time of T2D, current smoking, current alcohol consumption and the use of antihypertensive, lipid-lowering, hypoglycemic medication were positively correlated with higher baPWV. We also found that AST, GGT, WBC, FBG, TC were not associated with baPWV, whereas eGFR, HbA1c was negatively associated with higher baPWV.

The Association Between CVAI and baPWV

We evaluated the relationship between CVAI and baPWV using multivariate regression models ([Table 3](#)). In males, As CVAI increases by a unit, baPWV was increased by 0.28 cm/s (95% CI: -0.05 , 0.61) in fully adjusted regression model 3. Based on the CVAI quartiles as categorical variables in males, after full adjustment, compared with quartile 1, the β (95% CI) of baPWV was increased by 2.12 (-30.98 , 35.21), 23.93 (-9.99 , 57.86), and 37.62 (1.96 , 73.27) in the quartiles 2, 3, and 4 of CVAI, respectively. In the first to fourth quartiles, baPWV was significantly higher (P for trend $= 0.0212$). In females, As CVAI increases by a unit, baPWV was increased by 1.60 cm/s (95% CI: 1.07 , 2.14) in model 3 fully adjusted. Based on the CVAI quartiles as categorical variables in females, after full adjustment, compared with quartile 1, the β (95% CI) of baPWV was increased by 43.44 (0.18 , 86.70), 58.75 (13.79 , 103.71), and 142.48 (93.86 , 191.11) in the quartiles 2, 3, and 4 of CVAI, respectively. In the first to fourth quartiles, baPWV was significantly higher (P for trend < 0.0001). Additionally, we fitted smoothing curves and weighted generalized additive models to assess their association. After controlling for SBP, DBP, duration of diabetes, smoking, alcohol consumption, hypoglycemic drugs, lipid-lowering drugs, antihypertensive drugs, HbA1c, FBG, LDL-C, ALT, UA, eGFR and increased adjustment for menopausal status in females, a non-linear connection in males and a linear connection in females between the CVAI and baPWV was revealed in [Figure 4](#). CVAI of 78.97, 179.7 are two turning points in the fitting curve in males ([Supplementary Table 3](#)). In males, when CVAI was 78.97–179.7, CVAI was positively correlated with baPWV (β (95% CI): 0.74 (0.24 , 1.24), $P = 0.0037$). We observed no meaningful relationship between CVAI and baPWV when CVAI < 78.97 and CVAI > 179.7 .

Subgroup Analyses

[Figures 5](#)(males) and [Figures 6](#)(females) shows the results of subgroup analyses after adjustment of confounding factors. In males, we found that CVAI interacted with baPWV in different duration of diabetes (P interaction = 0.0052), alcohol

Table 2 Clinical Characteristics According to CVAI Quartiles in Patients with Type 2 Diabetes

	Males				P value	Females				P value
	Q1 (≤98.062)	Q2 (98.063~125.918)	Q3 (125.919~151.318)	Q4 (≥151.319)		Q1 (≤81.725)	Q2 (81.726~105.049)	Q3 (105.050~126.833)	Q4(≥126.834)	
Age, years	50.39 ± 10.70	51.41 ± 10.17	52.37 ± 9.92	50.54 ± 11.91	0.026	49.10 ± 9.99	53.56 ± 9.20	55.84 ± 9.50	60.92 ± 9.79	<0.001
VFA, cm2	52.42 ± 26.34	78.71 ± 23.93	98.28 ± 23.31	133.33 ± 35.18	<0.001	50.18 ± 22.37	66.88 ± 21.06	79.12 ± 20.97	104.18 ± 31.00	<0.001
SFA,cm2	118.75 ± 31.47	159.19 ± 27.76	187.18 ± 35.10	241.34 ± 55.12	<0.001	126.79 ± 43.76	158.47 ± 43.69	189.11 ± 50.61	227.22 ± 59.22	<0.001
SBP, mmHg	129.44 ± 18.77	134.47 ± 19.16	136.25 ± 18.88	138.69 ± 18.98	<0.001	130.54 ± 20.17	137.39 ± 19.34	139.92 ± 21.52	146.44 ± 19.50	<0.001
DBP, mmHg	82.00 ± 11.24	85.01 ± 11.39	86.98 ± 11.08	88.12 ± 11.27	<0.001	79.43 ± 10.66	82.23 ± 10.50	82.20 ± 11.92	83.12 ± 12.00	<0.001
ALT, U/L	21.00 (16.00–31.00)	24.50 (17.00–35.00)	28.00 (20.00–43.00)	34.00 (23.00–55.00)	<0.001	18.00 (14.00–25.00)	20.00 (15.00–29.00)	23.50 (16.00–36.75)	25.00 (16.00–41.00)	<0.001
AST, U/L	21.00 (18.00–25.00)	21.00 (17.00–26.00)	23.00 (19.00–30.00)	26.00 (21.00–36.00)	<0.001	20.00 (17.00–25.00)	21.00 (17.00–26.00)	23.00 (19.00–29.00)	24.00 (19.00–34.00)	<0.001
GGT, U/L	22.00 (16.75–33.00)	30.00 (21.00–46.00)	35.00 (22.75–61.00)	46.00 (39.00–71.25)	<0.001	17.00 (13.00–23.00)	21.00 (16.00–30.00)	25.00 (18.00–39.00)	29.00 (20.00–47.00)	<0.001
WBC,10 ⁹ /L	6.11 ± 1.64	6.34 ± 1.70	6.42 ± 1.79	6.71 ± 1.77	<0.001	5.80 ± 2.54	6.06 ± 1.58	6.22 ± 2.41	6.63 ± 3.06	<0.001
UA,mmol/L	330.58 ± 85.44	346.56 ± 86.34	355.30 ± 77.23	383.45 ± 92.58	<0.001	284.66 ± 67.84	294.15 ± 72.66	312.85 ± 81.43	338.19 ± 81.94	<0.001
eGFR,mL/min/1.73m2	115.72 ± 32.77	111.73 ± 32.36	112.47 ± 31.69	112.69 ± 33.04	0.296	129.99 ± 32.96	125.23 ± 33.64	120.27 ± 35.69	107.50 ± 36.70	<0.001
FBG, mmol/L	8.58 ± 3.43	8.86 ± 3.49	9.241 ± 4.05	9.29 ± 3.96	0.022	8.05 ± 3.25	8.55 ± 3.41	8.78 ± 3.24	8.49 ± 3.07	0.048
HbA1c, %	8.60 ± 2.71	8.54 ± 2.27	8.70 ± 2.28	8.82 ± 2.23	0.354	7.18 ± 2.11	8.18 ± 2.15	8.38 ± 2.02	8.17 ± 1.95	0.004
TC, mmol/L	4.85 ± 1.631	4.90 ± 1.22	4.95 ± 1.49	4.94 ± 1.32	0.710	4.95 ± 1.03	5.05 ± 1.08	5.15 ± 1.11	5.11 ± 1.16	0.120
LDL-C, mmol/L	2.71 ± 0.94	2.81 ± 0.91	2.79 ± 0.87	2.81 ± 0.82	0.309	2.69 ± 0.86	2.88 ± 0.94	2.88 ± 0.85	2.80 ± 0.87	0.025
Duration of diabetes, month	35.00 (4.00–85.00)	36.00 (3.00–96.00)	36.00 (1.00–89.00)	24.00 (1.00–72.00)	0.002	40.50 (7.00–81.75)	39.00 (5.00–97.00)	48.00 (10.25–96.00)	67.00 (17.00–120.00)	<0.001
baPWV,cm/s	1540.22 ± 291.15	1595.94 ± 313.37	1624.93 ± 324.68	1620.85 ± 298.82	<0.001	1478.75 ± 257.00	1599.42 ± 298.23	1644.70 ± 282.823	1803.41 ± 370.39	<0.001
Smoking					0.048					0.342
Never	230 (54.50%)	238(56.53%)	221(52.49%)	202 (47.87%)		296 (98.01%)	293 (97.67%)	294(97.67%)	294(97.67%)	
Former	39(9.24%)	25(5.94%)	35(8.31%)	43(10.19%)		4(1.32%)	2(0.67%)	0(0.00%)	3(1.00%)	
Current	153(36.26%)	158(37.53%)	165(39.19%)	177(41.94%)		2(0.66%)	5(1.67%)	7(2.33%)	4(1.33%)	
Alcohol consumption					<0.001					0.071
Never	259 (61.37%)	248(58.91%)	233 (55.34%)	209 (49.53%)		293(97.02%)	285(95.00%)	292 (97.01%)	298(99%)	
Former	129 (30.57%)	139(33.02)	133(31.59%)	142(33.65%)		9(2.98%)	15(5.00%)	8(2.66%)	3(1.00%)	
Current	34 (8.06%)	34(8.08%)	55(13.06%)	71(16.82%)		0(0.00%)	0(0.00%)	1(0.33%)	0(0.00%)	

(Continued)

Table 2 (Continued).

	Males				P value	Females				P value
	Q1 (≤98.062)	Q2 (98.063~125.918)	Q3 (125.919 ~151.318)	Q4 (≥151.319)		Q1 (≤81.725)	Q2 (81.726 ~105.049)	Q3 (105.050~126.833)	Q4(≥126.834)	
Hypoglycemic Drugs					0.271					0.021
No	113(27.23%)	109 (26.52%)	107 (25.97%)	93 (22.46%)		68(22.97%)	72 (24.16%)	64 (21.55%)	44 (14.72%)	
Yes	302(72.77%)	302 (73.48%)	305 (74.03%)	321 (77.54%)		228(77.03%)	226 (75.84%)	233 (78.45%)	255 (85.28%)	
Lipid-lowering Drugs					<0.001					0.003
No	382 (90.31%)	360 (85.31%)	344 (81.90%)	321(76.61%)		277 (91.72%)	261 (87.00%)	256 (85.05%)	244(81.33%)	
Yes	41 (9.69%)	62 (14.69%)	76 (18.10%)	98 (23.39%)		25 (8.28%)	39 (13.00%)	45 (14.95%)	56 (18.67%)	
Antihypertensive Drugs					<0.001					<0.001
No	354 (83.69%)	324(76.78%)	280(66.83%)	260(61.61%)		261(86.42%)	227(75.67%)	211(70.10%)	144(47.84%)	
Yes	69 (16.31%)	98 (23.22%)	139(33.17%)	162(38.39%)		41(13.58%)	73(24.33%)	90(29.90%)	157(52.16%)	
Menopausal status (n, %)										<0.001
No						129(43.00%)	82(27.33%)	63(20.93%)	37(12.29%)	
Yes	-	-	-	-		171(57.00%)	218(72.67%)	238(79.0.7%)	264(87.71%)	

Note: Data are expressed as mean ± standard deviation or number (%).
Abbreviations: CVAI, Chinese visceral adiposity index; VFA, Visceral fat area; SFA, subcutaneous fat area; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; WBC, white blood cell count; UA, uric acid; eGFR, Estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; baPWV, brachial-ankle pulse wave velocity.

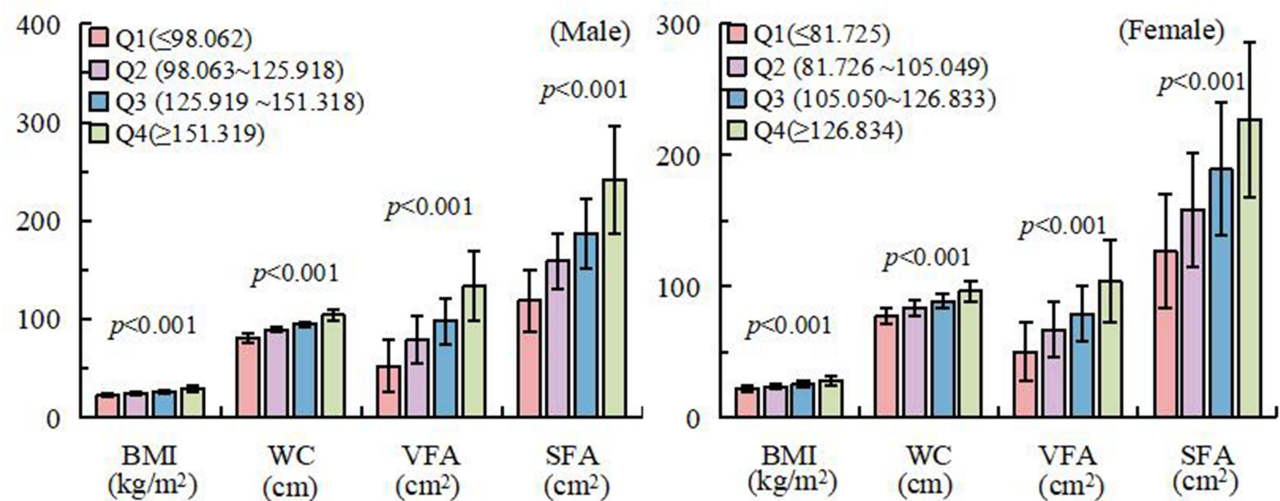


Figure 2 Body mass index (BMI, kg/m²), waist circumference (WC, cm), Visceral fat area (VFA, cm²) and subcutaneous fat area (SFA, cm²) levels according to the quartiles of Chinese Visceral Adipose Index (CVAI) in patients with type 2 diabetes.

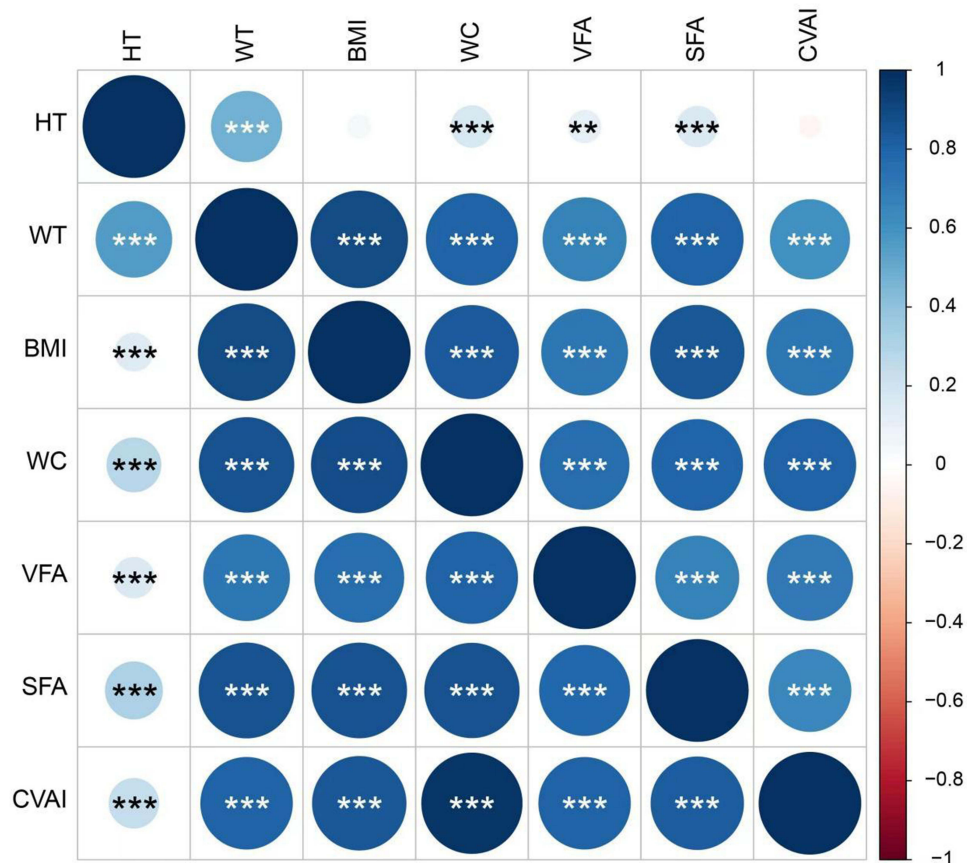


Figure 3 Pearson's correlation between markers for body composition in subjects with type 2 diabetes. Right side (above diagonal) shows correlations of females; left side (below diagonal) shows correlations of males. The size and color of the circles in Figure 2 represent the magnitude of the correlation coefficients. Specifically, ** denotes a highly statistically significant correlation at p < 0.01, and *** denotes a highly statistically significant correlation at p < 0.001.

Abbreviations: HT, height; WT, weight; BMI, kg/m², body mass index; WC, waist; cm, circumference; VFA, cm², Visceral fat area; SFA, cm², subcutaneous fat area; CVAI, Chinese visceral adiposity index.

Table 3 Association Between CVAI and baPWV in Different Models

	Model 1		Model 2		Model 3	
	β (95% CI)	P value	β(95% CI)	P value	β (95% CI)	P value
Males						
CVAI	0.80 (0.45, 1.15)	<0.0001	0.17 (−0.15, 0.48)	0.2990	0.28(−0.05, 0.61)	0.0934
CVAI quartiles						
Q1	Ref		Ref		Ref	
Q2	33.44(−4.82,71.70)	0.0869	1.97 (−31.01, 34.95)	0.9067	2.12 (−30.98, 35.21)	0.9003
Q3	66.71 (28.32,105.09)	0.0007	24.43 (−9.11, 57.97)	0.1535	23.93 (−9.99,57.86)	0.1670
Q4	79.78 (41.61, 117.95)	<0.0001	24.09(−9.92, 58.09)	0.1653	37.62(1.96 73.27)	0.0388
P for trend	<0.0001		0.0880		0.0212	
Females						
CVAI	3.59 (3.07, 4.11)	<0.0001	1.94 (1.44, 2.44)	<0.0001	1.60 (1.07, 2.14)	<0.0001
CVAI quartiles						
Q1	Ref		Ref		Ref	
Q2	120.66 (72.01, 169.32))	<0.0001	66.51 (22.83,110.19)	0.0029	43.44 (0.18, 86.70)	0.0493
Q3	165.95 (117.29, 214.60)	<0.0001	88.87 (44.66, 133.08)	<0.0001	58.75 (13.79, 103.71)	0.0106
Q4	324.66(276.01, 373.31)	<0.0001	174.18 (127.80,220.55)	<0.0001	142.48 (93.86191.11)	<0.0001
P for trend	<0.0001		<0.0001		<0.0001	

Notes: Model 1 unadjusted; Model 2 adjusted for SBP, DBP,Duration of diabetes, Smoking,Alcohol consumption,Hypoglycemic Drugs, Lipid-lowering Drugs, Antihypertensive Drugs; Model 3 Adjusted for SBP, DBP,Duration of diabetes, Smoking, Alcohol consumption, Hypoglycemic Drugs, Lipid-lowering Drugs, Antihypertensive Drugs, HbA1c, FBG, LDL-C, ALT, UA, eGFR, Increased adjustment for menopausal status in females.

Abbreviations: CVAI, Chinese visceral adiposity index; β , beta coefficient; CI, confidence interval.

consumption status (P interaction = 0.0375). In females, we found that CVAI interacted with baPWV in different levels of glycated hemoglobin (P interaction = 0.0003), SBP (P interaction = 0.0001), DBP (P interaction < 0.0001), duration of diabetes (P interaction = 0.0014), the use or non-use of glucose-lowering drugs (P interaction = 0.0006), the use or non-use antihypertensive drugs (P interaction = 0.0004), females' menopausal status (P interaction = 0.0012).

Discussion

Among Chinese, the CVAI assesses visceral fat dysfunction reliably and effectively. CVAI has specifically considered the age factor and made corrections based on CT values, providing a better reflection of Chinese visceral fat.¹² In addition to being a pathophysiological factor, arterial stiffness is an independent predictor of cardiovascular events.²⁸ The research on the relationship between CVAI and baPWV in T2D patients helps to deepen the understanding of the effects of visceral fat on cardiovascular health in these patients, and provides a basis for clinical prevention and management. This study in a large sample of adult Chinese with T2D demonstrated a significant association between CVAI and arterial stiffness. This relationship remained robust after adjusting for various confounding factors, suggesting that CVAI may be a valuable marker for evaluating cardiovascular risk in T2D patients. Importantly, Characteristics of CVAI and the relationship between CVAI and baPWV were significantly different in different genders. When CVAI was 78.97–179.7, a positive correlation was found between CVAI and baPWV in males. In females, there was a positive linear relationship between CAVI and baPWV. This indicates that the impact of visceral adiposity on arterial health may differ between genders and highlights the need for sex-specific risk assessment and management strategies.

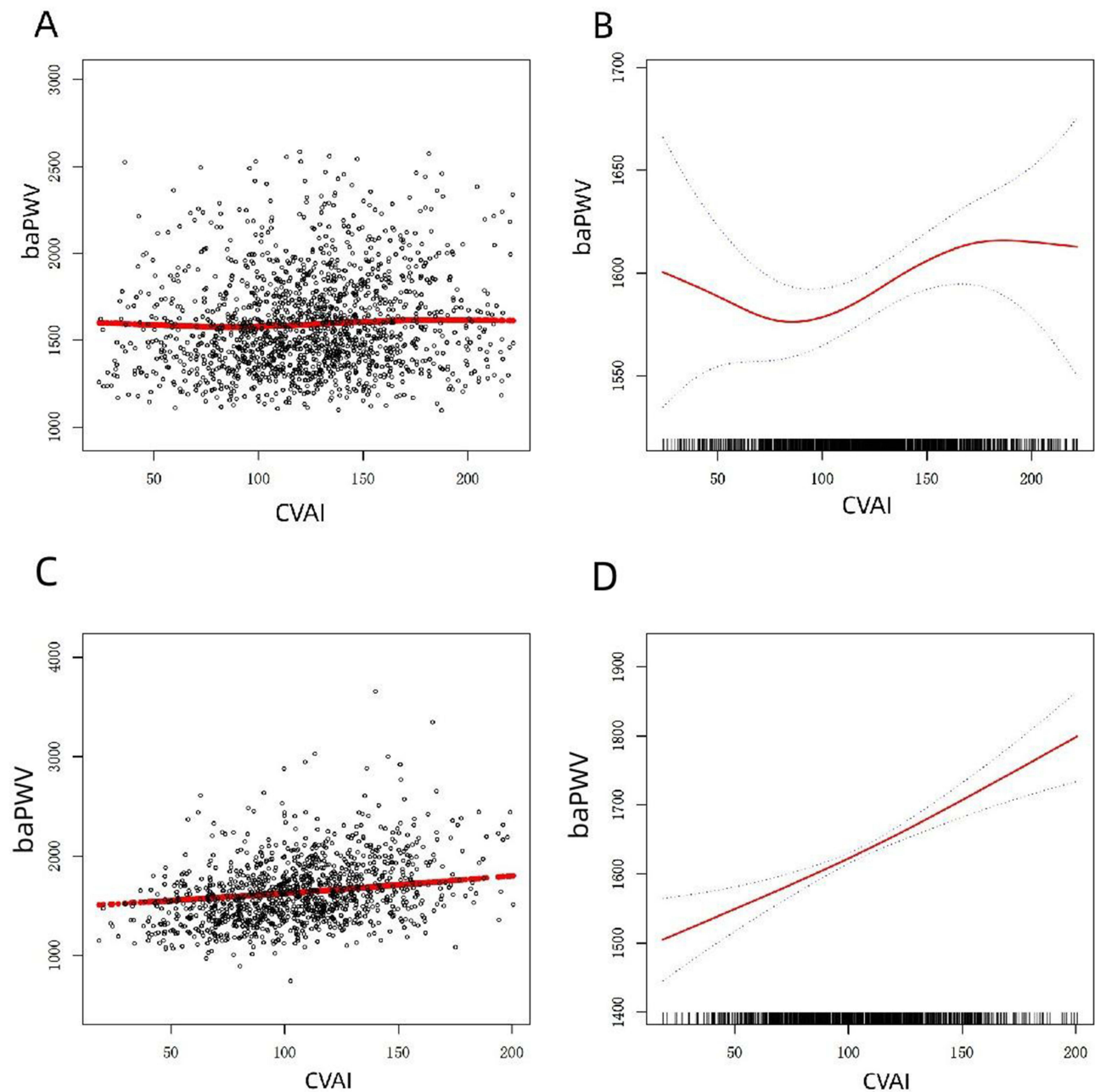


Figure 4 The linear relationship between CVAI and baPWV in males (**A** and **B**) and in females (**C** and **D**). We adjusted for SBP, DBP, duration of diabetes, smoking, alcohol consumption, hypoglycemic drugs, lipid-lowering drugs, antihypertensive drugs, HbA1c, FBG, LDL-C, ALT, UA, eGFR. Increased adjustment for menopausal status in females.

There are gender differences in the characteristics of CVAI in the participants. Several researches have suggested that males have higher CVAI than females and the proportion of males with higher CVAI level is higher than that of females.^{12,18,29} In our study, the results consistent with previous studies. The differences can be attributed to a multifaceted interplay of factors, including anatomical variations, hormonal influences, metabolic processes, and lifestyle disparities. First of all, some research has demonstrated that males tend to accumulate more fat in the abdominal region, while females typically exhibit a higher degree of fat deposition in the gluteal and thigh areas,³⁰ and It is likely related to sex hormone levels, such as testosterone (a male sex hormone) which may promote the accumulation of abdominal fat.³¹ In addition, from a metabolic perspective, there are also distinctions between males and females in the

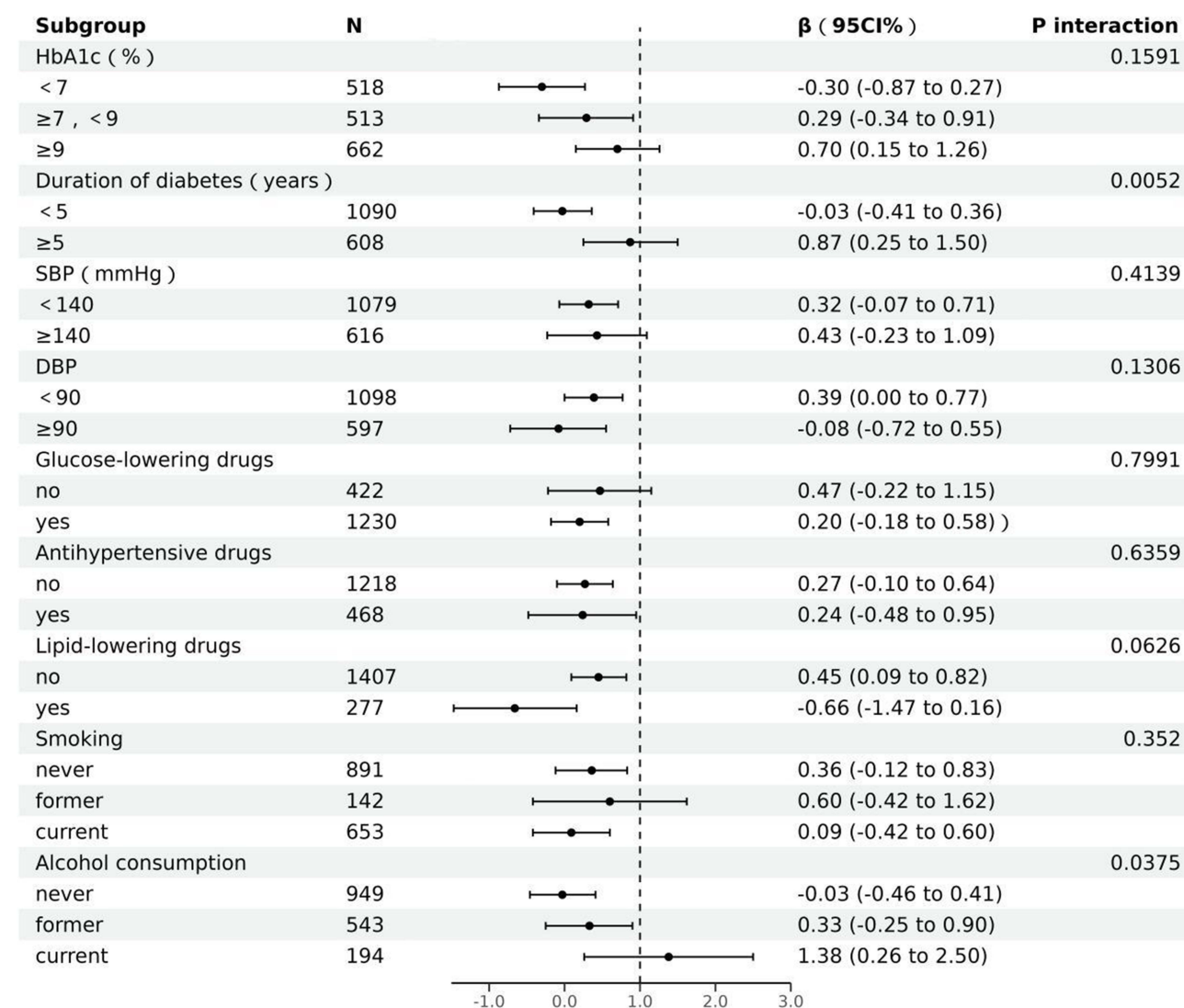


Figure 5 Subgroup analyses for the association between CVAI and baPWV in males were adjusted for SBP, DBP, duration of diabetes, smoking, alcohol consumption, hypoglycemic drugs, lipid-lowering drugs, antihypertensive drugs, HbA1c, FBG, LDL-C, ALT, UA, eGFR.

enzyme activities of fatty acid oxidation, lipolysis, and lipid synthesis. For example, research has found that men have higher hepatic lipase activity, which is associated with their higher visceral fat mass.³² The gender differences may be related to the unique biological and behavioral characteristics. For example, men may be more inclined towards a sedentary lifestyle, while women may be more physically active.³³ These factors collectively contribute to the distinct patterns of fat distribution observed between genders. Given these fundamental differences, the CVAI is calculated separately for males and females, as this approach better captures the gender-specific characteristics. Therefore, we recommend conducting CVAI-related analyses in a sex-stratified manner to ensure the validity.

In this study, the relationship between CVAI and visceral fat was strongly correlated. The positive correlation between CVAI and baPWV suggests that the accumulation of visceral fat in T2D patients increases cardiovascular risk. Previous studies have found similar results. Previous study found that cardiovascular events were more likely to occur among individuals with T2D who had a higher proportion of visceral fat.³⁴ The Chinese multicenter study found that normal-weight visceral obesity poses a higher 10-year atherosclerotic CVD risk to T2D patients.³⁵

Subgroup analyses provided further insights into the complex interplay between CVAI, glycemic control, and other cardiometabolic factors. In our study, The degree of baPWV increase increased with every 1 unit increase in CVAI was

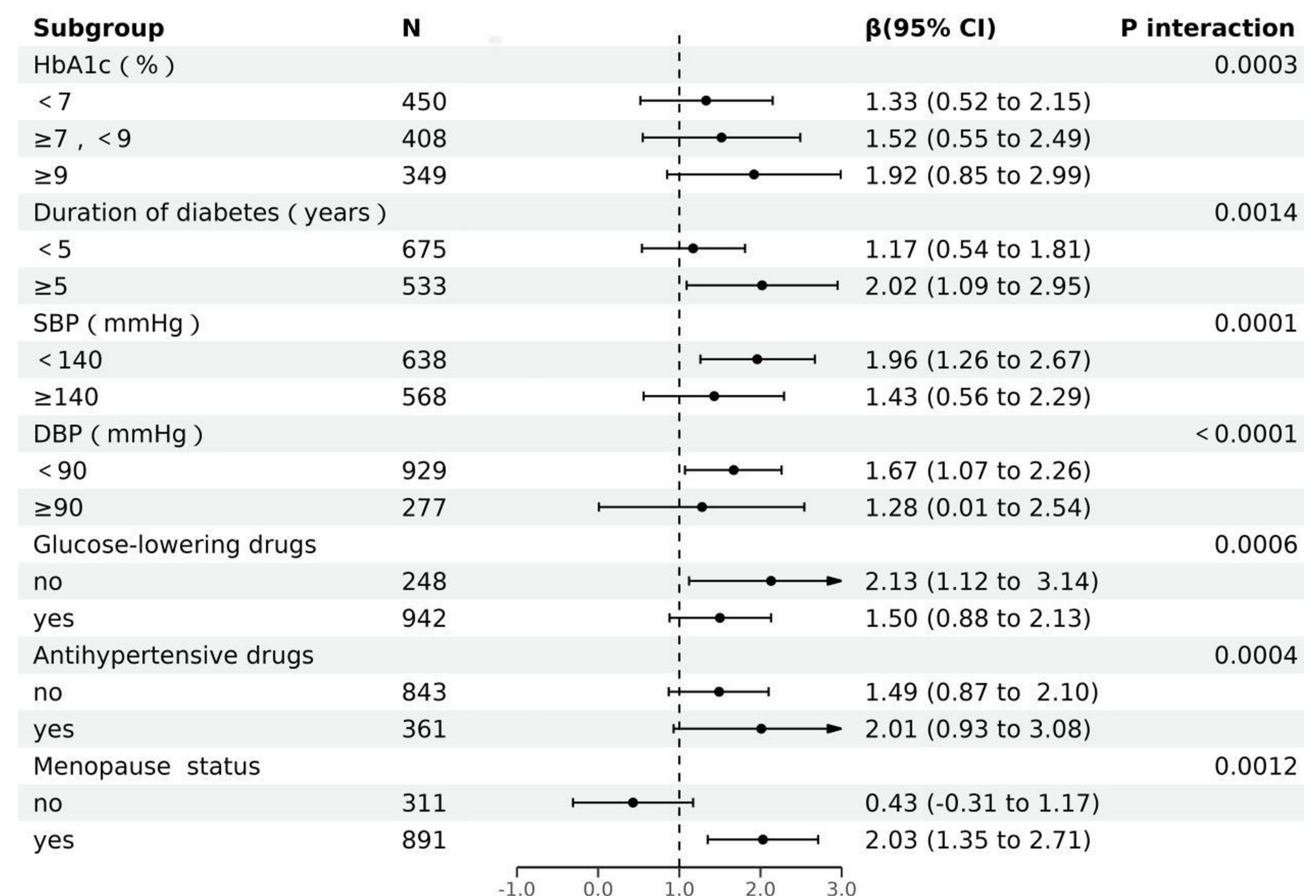


Figure 6 Subgroup analyses for the association between CVAI and baPWV in females were adjusted for SBP, DBP, duration of diabetes, smoking, alcohol consumption, hypoglycemic drugs, lipid-lowering drugs, antihypertensive drugs, HbA1c, FBG, LDL-C, ALT, UA, eGFR, menopausal status.

more significant in patients with a long course of diabetes. This may be because prolonged hyperglycemia can lead to endothelial dysfunction. It leads to atherosclerosis and reduced arterial elasticity.³⁶ In addition, alcohol consumption among males also interacted with the relationship between CVAI and baPWV. Researchers have found that overdrinkers are more likely to develop atherosclerosis.³⁷ Unfortunately, our researchers' classification of drinking status was not specific to the amount of alcohol consumed by each patient. The modifying roles of HbA1c, blood pressure, use of glucose-lowering or antihypertensive medications and menopausal state underscores the multifaceted pathways through which visceral fat can influence vascular health in T2D in females. High blood pressure condition of visceral fat and the relationship between arterial stiffness effect value to reduce may have the following reason: patients with high blood pressure vessels itself already exists a certain degree of hardening and rigid.³⁸ Thus, as visceral fat accumulates further, vessel stiffness increases by a relatively small amount. The blood vessels of normal blood pressure people are more elastic, and the increase of visceral fat will significantly increase the stiffness of blood vessels. However, patients taking antihypertensive drugs for a long time had a relatively higher increase in arterial stiffness affected by visceral fat. The use of antidiabetic drugs increased the effect size between CVAI and arterial stiffness. Because the type and dose of glucose-lowering drugs taken by the patients were not recorded, the specific effect of glucose-lowering drugs cannot be discussed in depth. Estrogen, through its multiple mechanisms of regulating lipid metabolism, suppressing inflammatory response, and improving vascular function, has a protective effect against atherosclerosis and coronary artery disease,^{39–41} which can particularly explain the more significant increase in arterial stiffness with the rise of visceral fat in postmenopausal women compared to premenopausal women in our study.

By using robust statistical methods, this study comprehensively evaluated the relationship between CVAI and arterial stiffness in T2D patients, providing valuable insights into about visceral fat in the occurrence of macrovascular complications in this high-risk population. Included are multiple regression analyses and generalized additive models that allow elucidations of the nature of the CVAI-baPWV relationship and identification of potential influence modulators, as well as sex-stratified analyses that can examine potential sex-specific association differences, an important consideration given known differences in body fat distribution and cardiovascular risk between males and females. The main limitations of our study are: (1) As a result of the study's cross-sectional design, causal relationships between CVAI and arterial stiffness cannot be established. (2) The study population was restricted to individuals with T2D, which may limit the generalizability of the findings. (3) The potential influence of confounding factors, such as dietary habits, physical activity levels, and the use of specific medications, were not comprehensively evaluated, and incorporating these variables in future research may help elucidate the complex interplay between visceral adiposity, glycemic control, and cardiovascular risk in the T2D population. (4) We could not do the subanalyses by in females by smoking, status of drinking, and use of lipid-lowering drugs to investigate the association of CVAI with baPWV because too few women in our study population smoked, drank alcohol, and took lipid-lowering medications.

As a conclusion, this study provides compelling evidence that the CVAI is associated with arterial stiffness in individuals with T2D. Routine assessment of CVAI may help identify high-risk individuals and guide targeted interventions to mitigate the burden of cardiovascular complications in this vulnerable population.

Conclusion

The relationship between CVAI and baPWV in patients with T2D was positively non-linear in males and linear in females. In all subjects, this relationship was influenced by diabetes duration. In males, drinking status affected the relationship. And in females, It was influenced by blood pressure, glycemic control, menopausal status, and the use of glucose-lowering and hypotensive drug, highlighting the complex interplay between visceral fat and arterial stiffness in the T2D population. Our findings shed light on the association between CVAI and arterial stiffness as well as the factors influencing this association and gender differences, which may provide a basis for how to control visceral adiposity to reduce CVD in T2D patients. This study provides a new basis for the clinical application value of CVAI in cardiovascular diseases. Gender differences and complex influencing factors should be paid attention to when CVAI is used in other populations.

Abbreviations

T2D, Type 2 diabetes; CVAI, Chinese Visceral Adiposity Index; baPWV, Brachial-ankle pulse wave velocity; IR, Insulin resistance; CVD, Cardiovascular diseases; CT, Computed tomography; MRI, Magnetic resonance imaging; BIA, Bioelectrical impedance analysis; WC, Waist circumference; BMI, Body mass index; TG, Triglycerides; HDL-C, High-density lipoprotein cholesterol; VAI, Visceral Adipose Index; MMC, Metabolic Management Center; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; VFA, Visceral fat area; SFA, Subcutaneous fat area; LDL-C, Low-density lipoprotein cholesterol; HbA1c, Glycated hemoglobin; ALT, Alanine aminotransferase; GGT, Gamma-glutamyl transferase; AST, Aspartate aminotransferase; FBG, Fasting plasma glucose; WBC, White blood cell count; TC, Total cholesterol; UA, Uric acid; eGFR, Estimated glomerular filtration rate.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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