Research Square

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Visceral Fat Area and Brachial Artery Flow-Mediated Dilation in People With Type 2 Diabetes: A Cross-Sectional Study

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Abstract

Background

Obesity contributes to endothelial dysfunction, but body mass index (BMI) may not capture visceral adiposity. We examined the associations of visceral fat area (VFA) and BMI with brachial artery flow-mediated dilation (FMD) in people with type 2 diabetes mellitus (T2DM).

Methods

This cross-sectional study included 1,683 people with T2DM recruited through the National Metabolic Management Center from April 2021 to August 2023. VFA and BMI tertiles were entered simultaneously in multivariable linear regression models of FMD. Exploratory analyses were stratified by age, sex, and hypertension status.

Results

After multivariable adjustment, the highest VFA tertile was associated with lower FMD compared with the lowest tertile (T3 [≥ 120.0 cm^2] vs T1 [< 84.0 cm^2]: β = -0.395, 95% CI -0.769 to -0.020; P = 0.039). Adjusted BMI-tertile comparisons were not statistically significant. In exploratory stratified analyses, the VFA-FMD association reached statistical significance in women and in people without hypertension; between-stratum interactions were not tested.

Conclusions

Higher VFA was independently associated with lower FMD in people with T2DM, whereas adjusted BMI-tertile comparisons were not statistically significant. Exploratory subgroup results require confirmation with formal interaction testing.

Background

Type 2 diabetes mellitus (T2DM) is characterized by a cluster of metabolic disorders with an increasing global incidence, having risen to among the top 10 causes of death worldwide [1]. People with T2DM face multiorgan complications, and the majority of the health burden is attributable to cardiovascular disease [2]. Accordingly, T2DM development often parallels an elevated risk of diverse cardiovascular conditions [3].

Cardiovascular complications in T2DM are thought to originate partly from impaired vascular endothelial function [4]. Several parameters are recognized as early indicators of vascular injury, including carotid intima-media thickness, brachial-ankle pulse wave velocity, and FMD [5, 6]. FMD reflects endothelium-

dependent vasodilation and is a noninvasive marker of endothelial function [5, 7]. High adiposity, hyperglycemia, and elevated blood pressure are associated with worse endothelial function [8, 9]. Consequently, weight management is a standard component of T2DM care [10].

However, BMI may not accurately capture body fat distribution. A large nationwide survey in China revealed that BMI failed to adequately represent body shape in the Chinese population and could not predict visceral fat accumulation [11]. Moreover, people with T2DM who have a normal BMI have been shown to carry a higher mortality risk than those who are overweight or obese [12], suggesting that adiposity assessed by BMI alone may be misleading. Growing evidence indicates that visceral adipose tissue (VAT) is associated with endothelial dysfunction independently of BMI in young adults and individuals of normal weight [13, 14].

Therefore, this cross-sectional study examined the associations of BMI and VFA with FMD in people with T2DM and explored whether the observed associations were consistent across age, sex, and hypertension strata.

Methods

Study Design and Participants

This cross-sectional study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [15]. Between April 28, 2021, and August 2, 2023, 1,683 individuals with T2DM were consecutively recruited through the National Metabolic Management Center (MMC). Inclusion criteria were: (1) a diagnosis of T2DM based on the 1999 World Health Organization diagnostic criteria; (2) availability of BMI and VFA measurements; and (3) complete clinical data. Exclusion criteria were: (1) missing FMD measurements; (2) end-stage chronic kidney disease; and (3) malignant tumors, pregnancy, or hemodynamic instability.

This study was conducted in accordance with the Declaration of Helsinki (2013 revision) and was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine (lead MMC center; approval number 2017-42). Written informed consent was obtained from all participants.

Data Collection

Demographic characteristics, medication history, and disease history were collected through a standardized questionnaire on the MMC platform. Fasting blood samples were obtained from the antecubital vein after at least 12 hours of overnight fasting. BMI was calculated as body weight (kg) divided by height squared (m^2). VFA was measured at the umbilical level using a dual bioelectrical impedance analysis device (HDS-2000, Omron Co., Ltd., Kyoto, Japan).

Brachial Artery Flow-Mediated Dilation

FMD measurements were performed in accordance with the 2019 expert consensus guidelines using a vascular endothelial function analyzer (Omron UNEX EF, Omron Healthcare Co., Kyoto, Japan) [16]. Participants were instructed to abstain from alcohol and caffeine for 24 hours before assessment. All measurements were obtained in the morning under fasting conditions following a standardized protocol. The ultrasound probe was held in a fixed position throughout, with arterial diameter measurements consistently acquired at the same longitudinal plane. FMD was calculated as the percentage change in post-stimulus vessel diameter relative to baseline [16].

Definitions

For descriptive purposes, visceral adiposity was defined as VFA ≥ 100 cm^2. BMI categories followed Chinese adult criteria: underweight (< 18.5 kg/m^2), normal weight (18.5–23.9 kg/m^2), and overweight/obesity (≥ 24.0 kg/m^2) [17]. For RCS analyses, endothelial dysfunction was defined as FMD ≤ 6.5% [18].

Statistical Analysis

Continuous variables are reported as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables as counts and percentages. Overall differences across VFA or BMI tertiles were assessed using one-way analysis of variance or the Kruskal-Wallis test for continuous variables and the chi-square test or Fisher exact test for categorical variables, as appropriate.

Pairwise and partial correlation analyses assessed associations between adiposity indices (BMI, VFA, subcutaneous fat area [SFA], and waist circumference) and FMD using Pearson or Spearman coefficients, as appropriate. BMI and VFA were categorized into tertiles and entered simultaneously in linear regression models of FMD. The fully adjusted model included age, sex, hypertension, HbA1c, triglycerides, HDL-C, total cholesterol, smoking, alcohol use, and use of SGLT-2 inhibitors, ACEI/ARB, insulin, and statins. Multivariable logistic RCS models explored nonlinear associations of continuous VFA and BMI with endothelial dysfunction (FMD ≤ 6.5%), using knots at the 5th, 50th, and 95th percentiles. Analyses stratified by age, sex, and hypertension status were exploratory; formal between-stratum interaction tests were not available.

Statistical significance was defined as a two-tailed $P < 0.05$. All analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY) and R version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline Characteristics

The study included 1,683 individuals with T2DM (mean age 56.6 years; 64.5% male). As shown in Table 1, compared with the lowest VFA tertile (< 84 cm^2), the highest tertile (≥ 120 cm^2) showed significantly impaired FMD (3.2 [IQR 1.6–4.9]% vs 4.2 [IQR 2.3–5.9]%; P < 0.001), an adverse metabolic profile (BMI: 28.4 ± 3.3 vs 22.8 ± 2.4 kg/m^2; waist circumference: 97.7 ± 8.3 vs 82.1 ± 7.0 cm; HDL-C: 1.1 ± 0.3 vs 1.3 ± 0.4 mmol/L; all P < 0.001), a higher prevalence of hypertension (53.7% vs 34.5%; P < 0.001), lower estimated glomerular filtration rate (eGFR: 113.5 [IQR 89.8–138.8] vs 118.5 [IQR 96.9–143.6] mL/min/1.73 m^2; P = 0.01), and lower insulin use (20.7% vs 33.0%; P < 0.001).

Table 1
Baseline Characteristics Stratified by VFA Tertile

Variable	Overall (n = 1683)	T1: <84.0 cm² (n = 551)	T2: 84.0–120.0 cm² (n = 568)	T3: ≥120.0 cm² (n = 564)	P value
Sex, male (%)	1086 (64.5)	307 (55.7)	345 (60.7)	434 (77.0)*	< 0.001
Age, years	56.6 (11.0)	56.8 (10.8)	57.1 (10.6)	55.8 (11.5)	0.12
BMI, kg/m²	25.5 (3.6)	22.8 (2.4)	25.3 (2.4)	28.4 (3.3)*	< 0.001
VFA, cm²	100.0 [75.0, 132.0]	62.0 [45.0, 74.0]	100.0 [92.0, 109.0]	145.0 [132.0, 169.0]*	< 0.001
SFA, cm²	166.0 [131.0, 210.0]	127.0 [101.5, 151.0]	167.0 [137.0, 196.0]	212.0 [176.0, 253.0]*	< 0.001
Waist circ., cm	89.7 (9.6)	82.1 (7.0)	89.1 (6.3)	97.7 (8.3)*	< 0.001
FMD, %	3.8 [1.9, 5.5]	4.2 [2.3, 5.9]	4.0 [2.2, 5.7]	3.2 [1.6, 4.9]*	< 0.001
HbA1c, %	7.0 [6.3, 8.2]	7.1 [6.3, 8.3]	6.9 [6.2, 8.1]	7.1 [6.3, 8.3]	0.05
Hypertension (%)	780 (46.4)	190 (34.5)	287 (50.5)	303 (53.7)*	< 0.001
CAD (%)	337 (20.0)	127 (23.1)	98 (17.3)	112 (19.9)	0.053
Stroke (%)	102 (6.1)	34 (6.2)	33 (5.8)	35 (6.2)	0.95
Creatinine, μmol/L	66.0 [55.0, 80.0]	63.0 [52.0, 78.0]	66.0 [56.0, 79.2]	69.0 [58.0, 83.0]*	< 0.001
eGFR, mL/min/1.73 m²	114.0 [93.3, 139.3]	118.5 [96.9, 143.6]	110.5 [93.5, 135.3]	113.5 [89.8, 138.8]*	0.01
HDL-C, mmol/L	1.2 (0.3)	1.3 (0.4)	1.2 (0.3)	1.1 (0.3)*	< 0.001
LDL-C, mmol/L	2.4 (0.9)	2.3 (0.9)	2.3 (0.9)	2.4 (0.9)	0.13
Hemoglobin, g/L	140.5 (18.4)	135.3 (18.2)	141.2 (16.8)	144.9 (18.8)*	< 0.001
Current smoking (%)	505 (30.0)	148 (26.9)	162 (28.5)	195 (34.6)*	0.01
Current drinking (%)	602 (35.8)	144 (26.1)	189 (33.3)	269 (47.7)*	< 0.001
Insulin use (%)	456 (27.1)	182 (33.0)	157 (27.6)	117 (20.7)*	< 0.001
ACEI/ARB use (%)	378 (22.5)	103 (18.7)	136 (23.9)	139 (24.7)	0.03

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; FMD, flow-mediated dilation; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; SFA, subcutaneous fat area; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; VFA, visceral fat area.

Variable	Overall (n = 1683)	T1: <84.0 cm² (n = 551)	T2: 84.0–120.0 cm² (n = 568)	T3: ≥120.0 cm² (n = 564)	P value
SGLT-2i use (%)	545 (32.4)	177 (32.1)	188 (33.1)	180 (31.9)	0.90
Statin use (%)	997 (59.2)	303 (55.0)	353 (62.2)	341 (60.5)	0.04

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; FMD, flow-mediated dilation; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; SFA, subcutaneous fat area; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; VFA, visceral fat area.

*Values are mean (SD), median [IQR], or n (%). *Significant difference (P < 0.05) between the highest and lowest VFA tertiles.*

As shown in Table 2, individuals in the highest BMI tertile (≥ 26.7 kg/m²) had a higher prevalence of hypertension (53.6% vs 41.6%–43.7%; P < 0.001), worse endothelial function (FMD: 3.5 [IQR 1.8–5.4]% vs 4.1 [IQR 2.3–5.7]%–3.8 [IQR 1.9–5.5]%; P = 0.01), and a larger waist circumference (98.6 ± 7.8 vs 81.5 ± 6.4–88.9 ± 5.5 cm; P < 0.001) compared with lower BMI tertiles. The highest BMI group also had a lower rate of insulin use (22.9% vs 25.2%–33.2%; P < 0.001) and a higher rate of alcohol consumption (41.1% vs 32.1%–34.0%; P = 0.004).

Table 2
Baseline Characteristics Stratified by BMI Tertile

Variable	Overall (n = 1683)	T1: <23.9 kg/m² (n = 560)	T2: 23.9–26.7 kg/m² (n = 556)	T3: ≥26.7 kg/m² (n = 567)	P value
Sex, male (%)	1086 (64.5)	348 (62.1)	366 (65.8)	372 (65.6)	0.35
Age, years	56.6 (11.0)	57.9 (10.6)	56.9 (10.8)	54.9 (11.3)*	< 0.001
BMI, kg/m²	25.5 (3.6)	21.8 (1.6)	25.3 (0.8)	29.4 (2.5)*	< 0.001
VFA, cm²	100.0 [75.0, 132.0]	71.0 [50.0, 92.0]	99.0 [80.0, 120.0]	135.0 [112.0, 167.0]*	< 0.001
SFA, cm²	166.0 [131.0, 210.0]	122.0 [98.0, 143.0]	168.0 [142.0, 190.0]	222.0 [192.0, 259.0]*	< 0.001
Waist circ., cm	89.7 (9.6)	81.5 (6.4)	88.9 (5.5)	98.6 (7.8)*	< 0.001
FMD, %	3.8 [1.9, 5.5]	4.1 [2.3, 5.7]	3.8 [1.9, 5.5]	3.5 [1.8, 5.4]*	0.01
HbA1c, %	7.0 [6.3, 8.2]	7.2 [6.3, 8.4]	6.9 [6.2, 8.0]	7.0 [6.3, 8.2]	0.01
Hypertension (%)	780 (46.4)	233 (41.6)	243 (43.7)	304 (53.6)*	< 0.001
CAD (%)	337 (20.0)	138 (24.6)	103 (18.5)	96 (16.9)*	0.003
Stroke (%)	102 (6.1)	31 (5.5)	43 (7.7)	28 (4.9)	0.12
Creatinine, μmol/L	66.0 [55.0, 80.0]	64.0 [53.0, 79.0]	68.0 [57.0, 81.0]	67.0 [55.0, 80.5]*	0.02
eGFR, mL/min/1.73 m²	114.0 [93.3, 139.3]	117.6 [94.7, 142.8]	112.1 [93.1, 133.0]	114.2 [91.9, 140.2]*	0.03
HDL-C, mmol/L	1.2 (0.3)	1.3 (0.4)	1.2 (0.3)	1.2 (0.3)*	< 0.001
LDL-C, mmol/L	2.4 (0.9)	2.3 (0.9)	2.4 (0.9)	2.4 (0.9)	0.55
Hemoglobin, g/L	140.5 (18.4)	137.5 (18.9)	141.2 (16.4)	142.8 (19.3)*	< 0.001
Current smoking (%)	505 (30.0)	169 (30.2)	159 (28.6)	177 (31.2)	0.63
Current drinking (%)	602 (35.8)	180 (32.1)	189 (34.0)	233 (41.1)*	0.004
Insulin use (%)	456 (27.1)	186 (33.2)	140 (25.2)	130 (22.9)*	< 0.001
ACEI/ARB use (%)	378 (22.5)	113 (20.2)	123 (22.1)	142 (25.0)	0.14

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; FMD, flow-mediated dilation; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; SFA, subcutaneous fat area; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; VFA, visceral fat area.

Variable	Overall (n = 1683)	T1: <23.9 kg/m² (n = 560)	T2: 23.9–26.7 kg/m² (n = 556)	T3: ≥26.7 kg/m² (n = 567)	P value
SGLT-2i use (%)	545 (32.4)	181 (32.3)	188 (33.8)	176 (31.0)	0.61
Statin use (%)	997 (59.2)	347 (62.0)	306 (55.0)	344 (60.7)*	0.04

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; FMD, flow-mediated dilation; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; SFA, subcutaneous fat area; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; VFA, visceral fat area.

*Values are mean (SD), median [IQR], or n (%). *Significant difference (P < 0.05) between the highest and lowest BMI tertiles.*

Correlation Between Body Composition Parameters and FMD

Correlation analyses showed that VFA, BMI, SFA, and waist circumference were all inversely associated with FMD (VFA: r = − 0.134, P < 0.001; BMI: r = − 0.089, P < 0.001; SFA: r = − 0.068, P = 0.005; waist: r = − 0.140, P < 0.001; Fig. 1). After partial correlation analysis adjusting for the other fat parameters, VFA (r = − 0.057, P = 0.020) and waist circumference (r = − 0.075, P = 0.002) remained independently associated with FMD, whereas BMI and SFA did not (Table 3).

Table 3
Correlation of FMD with BMI and Body Composition Parameters *Partial correlation analyses were adjusted for all other listed adiposity variables.*

Parameter	r	P value	Partial r	Partial P value
VFA (cm²)	−0.134	< 0.001	−0.057	0.020
BMI (kg/m²)	−0.089	< 0.001	−0.032	0.188
SFA (cm²)	−0.068	0.005	−0.028	0.253
Waist circ. (cm)	−0.140	< 0.001	−0.075	0.002

FMD, flow-mediated dilation; BMI, body mass index; VFA, visceral fat area; SFA, subcutaneous fat area.

Associations of VFA and BMI Tertiles With Endothelial Dysfunction

In the fully adjusted linear regression model, the highest VFA tertile was associated with lower FMD compared with the lowest tertile (T3 [≥ 120 cm²] vs T1 [< 84.0 cm²]: β = -0.395, 95% CI -0.769 to -0.020; P = 0.039). Adjusted BMI-tertile comparisons were not statistically significant (Table 4). RCS analyses did

not show evidence of nonlinearity for VFA or BMI (P for nonlinearity = 0.452 and 0.613, respectively; Fig. 2).

Table 4

Mutually and Fully Adjusted Linear Regression Analysis Both BMI and VFA tertiles were entered simultaneously. The fully adjusted model included age, sex, hypertension, HbA1c, triglycerides (≥ 2.3 mmol/L), HDL-C (< 1.0 mmol/L), total cholesterol (≥ 6.2 mmol/L), smoking, alcohol use, and use of SGLT-2 inhibitors, ACEI/ARB, insulin, and statins.

Variable	β	95% CI	P value
BMI/VFA mutually adjusted model			
VFA tertile 1 [< 84.0 cm²] (ref.)	0	—	—
VFA tertile 2 [84.0–120.0 cm²]	−0.239	−0.557 to 0.080	0.142
VFA tertile 3 [≥ 120.0 cm²]	−0.961	−1.338 to − 0.583	< 0.001
BMI tertile 1 [< 23.9 kg/m²] (ref.)	0	—	—
BMI tertile 2 [23.9–26.7 kg/m²]	0.003	−0.315 to 0.320	0.987
BMI tertile 3 [≥ 26.7 kg/m²]	0.129	−0.246 to 0.504	0.501
Fully adjusted model			
VFA tertile 1 [< 84.0 cm²] (ref.)	0	—	—
VFA tertile 2 [84.0–120.0 cm²]	−0.001	−0.307 to 0.304	0.993
VFA tertile 3 [≥ 120.0 cm²]	−0.395	−0.769 to − 0.020	0.039
BMI tertile 1 [< 23.9 kg/m²] (ref.)	0	—	—
BMI tertile 2 [23.9–26.7 kg/m²]	−0.134	−0.437 to 0.169	0.386
BMI tertile 3 [≥ 26.7 kg/m²]	−0.273	−0.635 to 0.090	0.141

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; FMD, flow-mediated dilation; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; TC, total cholesterol; TG, triglycerides; VFA, visceral fat area.

Figure 2. Restricted cubic spline analyses of adiposity indices and endothelial dysfunction. Solid lines represent multivariable-adjusted odds ratios for endothelial dysfunction (FMD ≤ 6.5%) across (A) VFA and (B) BMI values; shaded areas represent 95% confidence intervals. Knots were placed at the 5th, 50th, and 95th percentiles. P for nonlinearity was 0.452 for VFA and 0.613 for BMI. BMI, body mass index; FMD, flow-mediated dilation; VFA, visceral fat area.

(A) VFA

(B) BMI

Subgroup Analyses

In exploratory stratified analyses, the VFA-FMD association reached statistical significance in women and in people without hypertension but not in men or in people with hypertension (Fig. 3). For BMI, statistically significant estimates were observed in women and in people aged ≥ 60 years. Because formal interaction tests were not performed, differences in statistical significance between strata should not be interpreted as evidence of effect modification.

Figure 3. Stratified associations of adiposity indices with FMD. Estimates are beta coefficients with 95% confidence intervals for the second and third tertiles compared with the first tertile of VFA or BMI within age, sex, and hypertension strata. Formal between-stratum interaction tests were not performed. BMI, body mass index; FMD, flow-mediated dilation; VFA, visceral fat area.

(A) VFA subgroup

(B) BMI subgroup

Discussion

This cross-sectional study showed that higher VFA was independently associated with lower FMD in people with T2DM, whereas adjusted BMI-tertile comparisons were not statistically significant. Stratified results were exploratory because between-stratum interactions were not formally tested.

T2DM confers substantial cardiovascular risk, driving interest in early markers of subclinical vascular disease. Anderson et al demonstrated that FMD predicts cardiovascular events [5], and Lamacchia et al confirmed that baPWV is associated with cardiovascular risk in T2DM [19]. BMI-based weight management is a standard treatment target in T2DM guidelines [20]. Although the present study confirmed a significant crude association between higher BMI and lower FMD, this association was attenuated to non-significance after multivariable adjustment, consistent with prior evidence that BMI may be a suboptimal cardiovascular risk marker. Carnethon et al reported paradoxically higher mortality in normal-weight individuals with incident diabetes compared with those with overweight or obesity [12]; this discrepancy likely reflects confounding by other comorbidities rather than a protective effect of excess weight on cardiovascular outcomes.

By contrast, VFA remained independently associated with lower FMD after multivariable adjustment. A 2021 nationwide Chinese study demonstrated that BMI could not reliably predict visceral fat accumulation [11], and a study in youth with obesity found that visceral fat was associated with arterial stiffness independently of BMI [21]. In Japanese adults with T2DM, higher visceral adiposity was associated with arterial stiffness irrespective of overall obesity status [22]. Mechanistically, visceral fat preferentially accumulates as white adipose tissue, which releases higher levels of adipokines and pro-

inflammatory molecules compared with brown adipose tissue, elevating cardiovascular risk [23]. In addition, greater visceral fat is associated with higher portal free fatty acid flux, promoting hepatic insulin resistance and, ultimately, endothelial dysfunction [24]. Visceral fat accumulation also independently impairs glucose metabolism [25], further worsening vascular endothelial function.

In exploratory sex-stratified analyses, the VFA-FMD association reached statistical significance in women but not in men. This difference in significance does not establish a sex interaction. Xu et al reported an association between VFA and brachial-ankle pulse wave velocity in women with normal-weight T2DM [26]. Estrogen withdrawal after menopause may promote endothelial dysfunction [27]; the mean age of women in our cohort was 59.0 years. Women aged < 50 years had higher FMD and lower VFA than those aged ≥ 50 years (FMD: 4.38 [95% CI 4.07–4.67] vs 3.33 [95% CI 3.17–3.48]%; P < 0.001; VFA: 86.0 [IQR 58.0-107.0] vs 92.0 [IQR 44.5-120.2] cm^2; P = 0.032; see Additional file 1: Table S1). Differences in sex hormone profiles that regulate visceral fat deposition [28] provide one possible explanation, but menopausal status was not available for direct testing.

In exploratory analyses, the VFA-FMD association did not reach statistical significance in people with hypertension. This finding does not establish an interaction with hypertension. One possible explanation is that blood pressure-related endothelial injury or earlier lifestyle modification could reduce the apparent incremental association of visceral adiposity, but this hypothesis requires prospective evaluation [29].

Several limitations should be noted. First, the cross-sectional design precludes causal inference; prospective multicenter studies are needed to confirm temporality. Second, FMD is operator-dependent, although use of an automated analyzer and a standardized protocol may reduce measurement variability. Third, formal interaction tests were not available, so subgroup findings are exploratory. Fourth, menopausal status was incompletely recorded, limiting assessment of estrogen withdrawal. Finally, residual confounding from unmeasured factors cannot be excluded.

Conclusions

In conclusion, higher VFA, independent of BMI, was associated with lower FMD in people with T2DM. Exploratory stratified associations require confirmation with formal interaction testing. Visceral fat assessment may complement BMI, although prospective studies are needed to establish its clinical value.

Abbreviations

ACEI
angiotensin-converting enzyme inhibitor
ARB
angiotensin receptor blocker
BMI
body mass index

CAD
coronary artery disease
CI
confidence interval
eGFR
estimated glomerular filtration rate
FMD
flow-mediated dilation
HbA1c
glycated hemoglobin A1c
HDL-C
high-density lipoprotein cholesterol
IQR
interquartile range
LDL-C
low-density lipoprotein cholesterol
MMC
National Metabolic Management Center
RCS
restricted cubic spline
SD
standard deviation
SFA
subcutaneous fat area
SGLT-2i
sodium-glucose cotransporter-2 inhibitor
T2DM
type 2 diabetes mellitus
VFA
visceral fat area.

Declarations

Ethics approval and consent to participate: This study was conducted in accordance with the Declaration of Helsinki (2013 revision). The research protocol was approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine (approval No. 2017-42, dated May 2, 2017). Written informed consent was obtained from all participants.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Figures

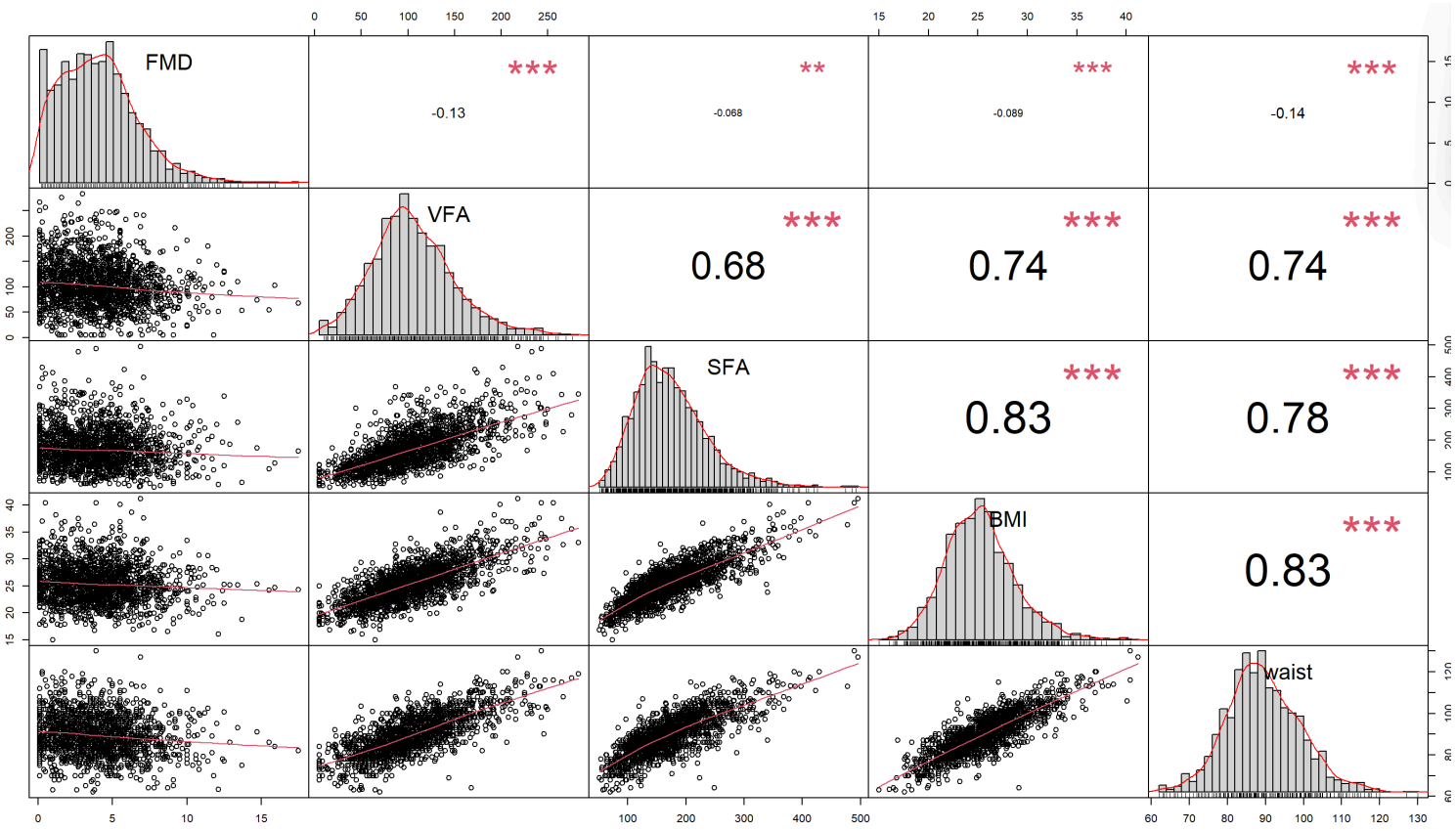


Figure 1

Correlations of adiposity indices with FMD. Correlation coefficients and significance levels are displayed for VFA, SFA, BMI, waist circumference, and FMD; Pearson or Spearman coefficients were used as appropriate. BMI, body mass index; FMD, flow-mediated dilation; SFA, subcutaneous fat area; VFA, visceral fat area.

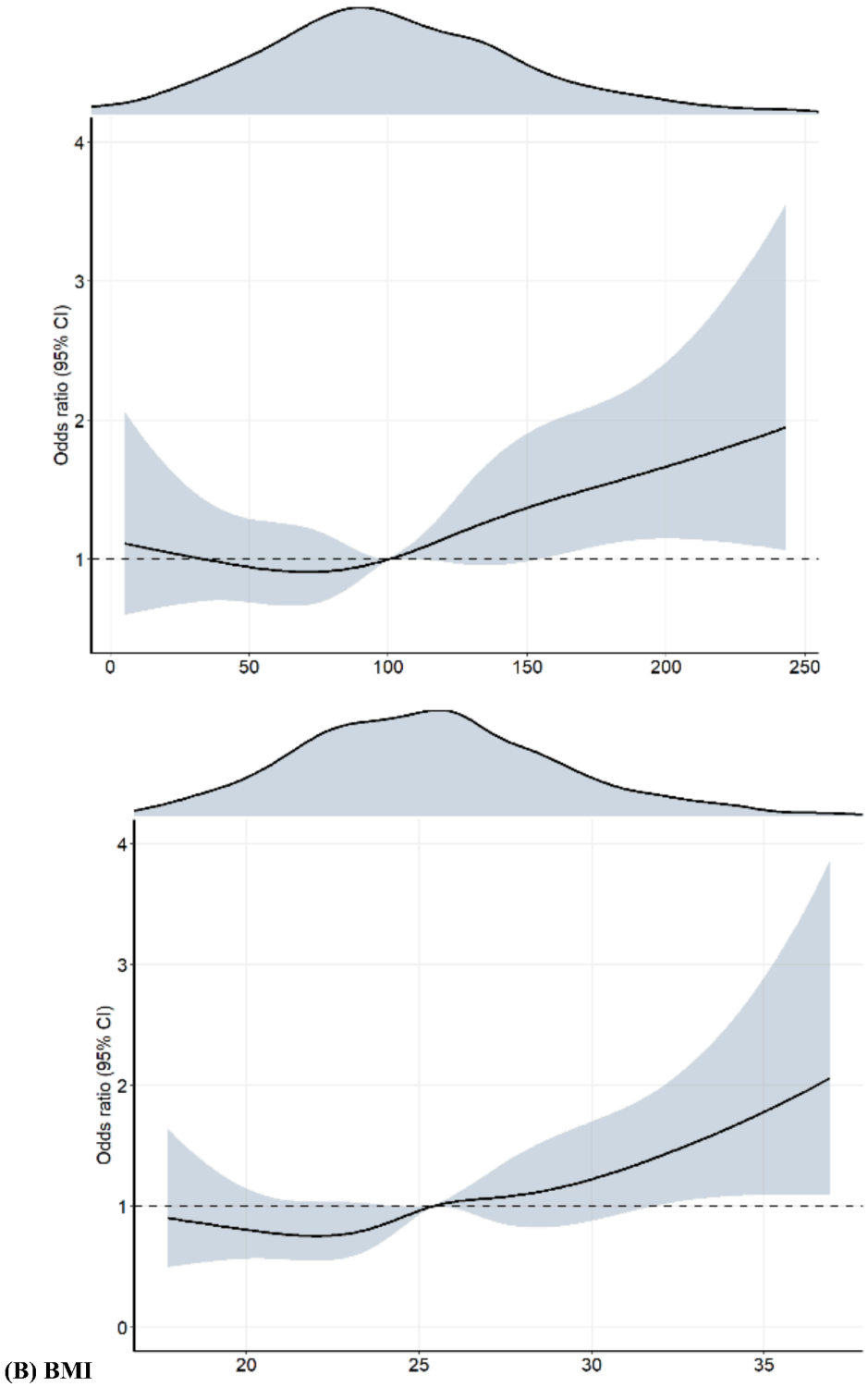


Figure 2

Restricted cubic spline analyses of adiposity indices and endothelial dysfunction. Solid lines represent multivariable-adjusted odds ratios for endothelial dysfunction (FMD ≤6.5%) across (A) VFA and (B) BMI values; shaded areas represent 95% confidence intervals. Knots were placed at the 5th, 50th, and 95th percentiles. P for nonlinearity was 0.452 for VFA and 0.613 for BMI. BMI, body mass index; FMD, flow-mediated dilation; VFA, visceral fat area.

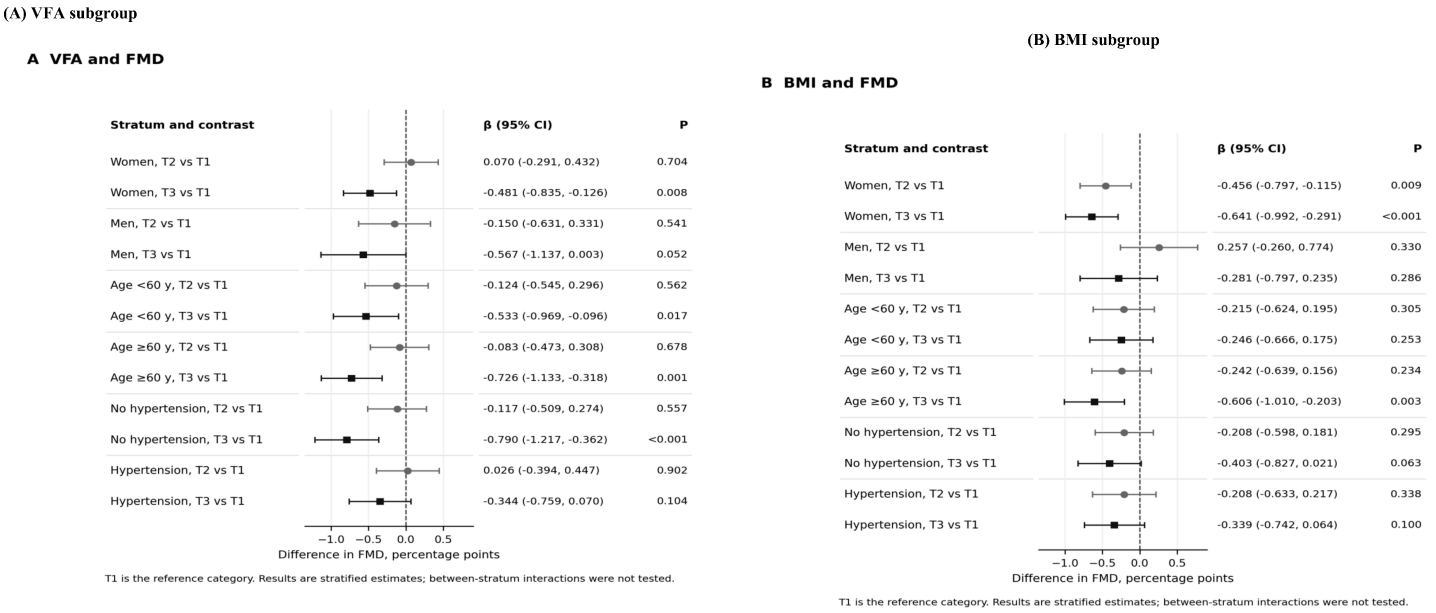


Figure 3

Stratified associations of adiposity indices with FMD. Estimates are beta coefficients with 95% confidence intervals for the second and third tertiles compared with the first tertile of VFA or BMI within age, sex, and hypertension strata. Formal between-stratum interaction tests were not performed. BMI, body mass index; FMD, flow-mediated dilation; VFA, visceral fat area.

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