

Association Between Metabolic Scores for Visceral Fat and Arterial Stiffness

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Background: This study aimed to investigate the relationship between arterial stiffness and metabolic syndrome-related visceral fat index (METS-VF), a composite formula that inherently includes age, metabolic parameters, and visceral fat.

Methods: A cross-sectional study was conducted between January 2019 and December 2023, enrolling participants from Health Examination Center, and Departments of General Practice and Geriatrics at the First Affiliated Hospital of Fujian Medical University. Arterial stiffness was defined as carotid-femoral pulse wave velocity (cfPWV) of ≥ 10 m/s. METS-VF was calculated based on metabolic score for insulin resistance (METS-IR), waist-to-height ratio (WHtR), age, and gender. Participants were categorized into quartiles (Q1–Q4) according to their METS-VF values. The associations between METS-VF and arterial stiffness were evaluated using linear regression analysis, logistic regression models, stratified analyses, receiver operating characteristic (ROC) curve analysis, and restricted cubic splines (RCS) to identify potential non-linear associations.

Results: A total of 3782 participants, with a mean age of 59.42 ± 11.89 years and 62.96% male, were included in this study. There was a trend of increasing arterial stiffness from lower to higher METS-VF quartile (Q1 to Q4: 19.98%, 28.68%, 37.99%, 49.37%, $\chi^2 = 201.04$, $P < 0.001$). Linear regression analysis showed an independent association between METS-VF with cfPWV ($\beta = 0.19$, 95% CI 0.03 ~ 0.35). In the fully adjusted model, compared with Q1, the participants in Q4 (OR = 1.38, 95% CI 1.06 ~ 1.79, $P = 0.016$) exhibited an increase in arterial stiffness. RCS analysis revealed a non-linear association between METS-VF and arterial stiffness. ROC curve analysis demonstrated that METS-VF had superior discriminative ability for arterial stiffness compared with body mass index (BMI) and WHtR ($P < 0.001$). Similar results were observed in subgroup analyses.

Conclusion: METS-VF is independently and positively associated with arterial stiffness. Its discriminative performance is superior to traditional anthropometric indices, though causality requires further investigation.

Keywords: metabolic syndrome-related visceral fat index, carotid-femoral pulse wave velocity, arterial stiffness, waist-to-height ratio

Introduction

With the continuous increase in population aging, cardiovascular disease (CVD) has become a major public health challenge worldwide.¹ A key contributor to CVD is arterial stiffness, a decline in blood vessel elasticity, which not only raises disease risk, but also serves as a crucial biomarker for predicting adverse cardiovascular events.² Currently, there are various methods for assessing arterial stiffness, but carotid-femoral pulse wave velocity (cfPWV) is still recognized as the “gold standard” due to its measurement stability and clinical relevance.³ From a pathophysiological perspective, the development and progression of arterial stiffness involve multiple interrelated processes, among which chronic

inflammatory responses, oxidative stress imbalance, and metabolic dysregulation are considered core driving mechanism.^{4–6}

Existing studies have indicated that visceral fat accumulation contributes to insulin resistance, which in turn promotes hyperinsulinemia and metabolic disorders, ultimately leading to vascular inflammation and fibrosis, arterial stiffness, and an elevated risk of CVD and adverse cardiovascular events.⁷ Supporting this mechanistic link, prior research by our team has identified several clinical variables including age, sex, waist-to-hip ratio, systolic blood pressure (SBP), diabetes duration, and heart rate—as being associated with cfPWV.⁸ Notably, parameters such as waist-to-hip ratio and diabetes duration further underscore the connection between abdominal obesity, insulin resistance, and arterial stiffness. Consistently, broader evidence indicates that abdominal obesity exhibits a stronger correlation with arterial stiffness than general adiposity measured by body mass index (BMI).⁹ Recently, metabolic syndrome-related visceral fat index (METS-VF) has gained attention as a composite indicator integrating metabolic disorders and visceral fat accumulation.¹⁰ The key advantage of METS-VF lies in its dual capacity to quantify visceral fat accumulation and concurrently capture key features of metabolic syndrome, offering a more comprehensive evaluation of metabolic health.¹¹ Previous studies have established that elevated METS-VF is closely associated with insulin resistance, dyslipidemia, and chronic low-grade inflammation, and these pathological processes has been recognized as key drivers of arterial stiffness.^{12–14} METS-VF has demonstrated clinical predictive value for conditions such as sarcopenia, stroke, and chronic kidney disease, direct evidence regarding its association with arterial stiffness remains limited.^{15–17} This gap in the literature forms the rationale for the present study, which aims to investigate the relationship between METS-VF and arterial stiffness as evaluated by cfPWV.

Methods

Statement of Ethics

This single-center cross-sectional study utilized data from the Fuzhou Study (ChiCTR2000039448; registered 28/10/2020; URL:<http://www.chictr.org.cn>). Conducted in Fuzhou, China, the Fuzhou Study focuses on target organ damage and related risk factors in hypertensive patients. The study adhered to the principles of the Declaration of Helsinki, and written informed consent was obtained from all participants. The protocol received approval from the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No. [2020]306).

Subjects

From January 2019 to December 2023, subjects aged ≥ 18 were recruited from the Health Examination Center, the Departments of General Practice and Geriatrics at the First Affiliated Hospital of Fujian Medical University. The inclusion criteria were: (1) Outpatients: those having regular follow-ups for hypertension or diabetes, or getting screened for related target organ damage. (2) Health Examination Center: adults in routine check-ups who volunteered after being informed of the study aims. (3) Inpatients: the patients who were hospitalized for the stable management of certain chronic conditions including coronary heart disease, Alzheimer's disease, and peptic ulcer disease.

A total of 4675 subjects who underwent cfPWV measurement were initially enrolled. According to the predefined exclusion criteria, 893 subjects were excluded according to the following criteria: (1) History of acute cardiovascular or cerebrovascular events within 6 months, such as acute coronary syndrome, cerebral infarction, cerebral hemorrhage, or transient ischemic attack ($n = 173$); (2) Congestive heart failure, severe arrhythmias, hypertrophic obstructive cardiomyopathy, valvular heart disease, or restrictive cardiomyopathy ($n = 78$); (3) Serum aminotransferase levels $> 3 \times$ upper limit of normal, malignancy, autoimmune diseases, acute infectious diseases, current pregnancy ($n = 219$); (4) Missing data on BMI, fasting plasma glucose (FPG), triglycerides, high-density lipoprotein cholesterol (HDL-C), or waist-to-height ratio (WHtR) ($n = 423$). Consequently, 3782 participants were included in the final analysis (Figure 1).

Demographic and Clinical Data

Data on chronological age, biological sex, tobacco use, and alcohol consumption were self-reported by the participants. Height and body weight were measured using calibrated instruments with participants wearing light clothing without

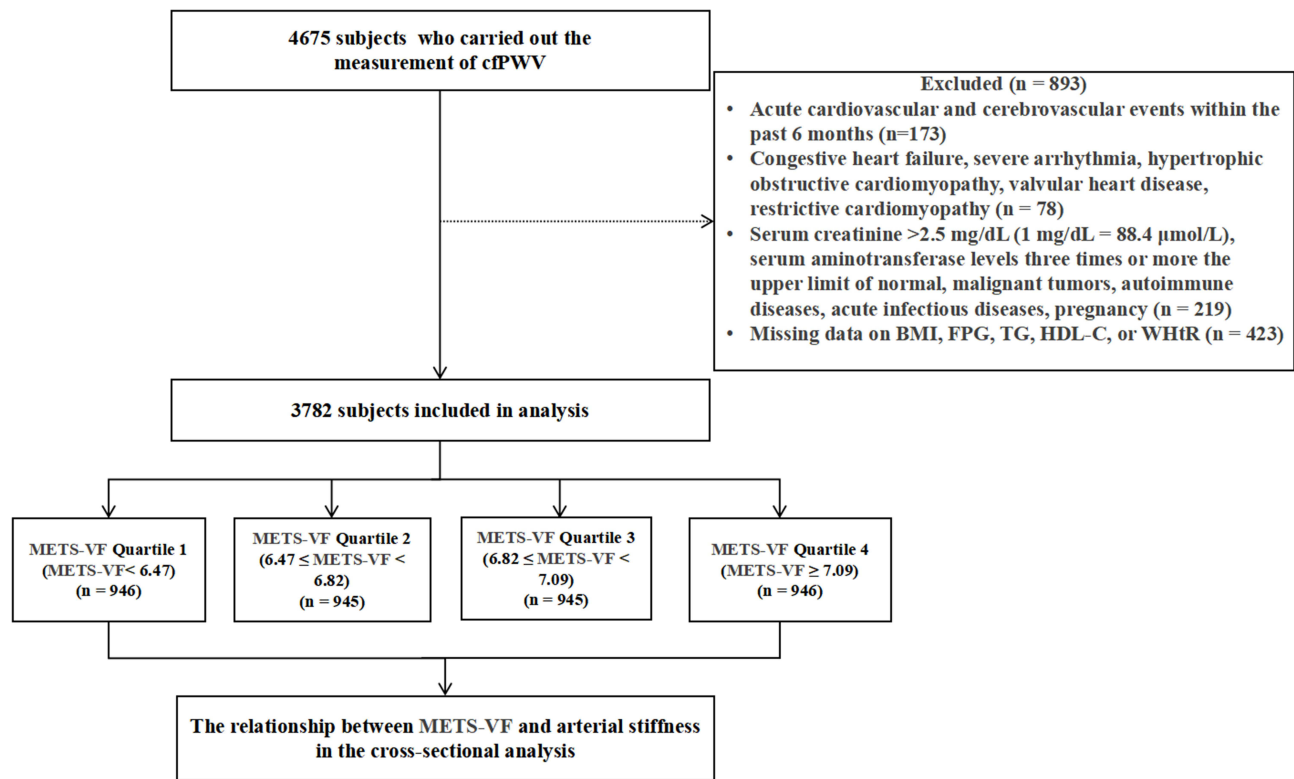


Figure 1 The flow chart of the study.

Abbreviations: cfPWV, carotid-femoral pulse wave velocity; METS-VF, metabolic syndrome-related visceral fat index; BMI, body mass index; FPG, fasting plasma glucose; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; WHtR, waist-to-height ratio.

shoes. Waist circumference (WC) was measured at the horizontal plane located midway between the last rib and the iliac crest, and the measurement was recorded to the nearest 0.5 cm. Smokers were defined as those who had smoked at least 1 cigarette per day for a consecutive period of 12 months or more.¹⁸ Drinkers were defined as those who consumed alcohol on more than one occasion per month.¹⁹ BMI and WHtR were computed using the following formulas: BMI = body weight (kg)/height² (m²) and WHtR=WC (kg)/height (m). Blood pressure was measured three times with an automated oscillometric device (HBP - 1300; Omron Healthcare, Kyoto, Japan) after participants seated and rested for at least 5 minutes. Three consecutive readings were taken and the average was recorded.

Laboratory Measurement

Fasting venous blood samples (≥ 8 hours) were collected, and biochemical parameters—including FPG, total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), triglycerides, and creatinine (CREA)—were measured using an automated analyzer (Siemens ADVIA 2400, USA). Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) formula: estimated GFR (eGFR) [mL/(min·1.73 m²)] = $186 \times [\text{creatinine (mmol/L)} / 88.41]^{-1.154} \times (\text{Age})^{-0.203}$, and the adjustments of the equation were 1 for male and 0.742 for female. Glycosylated hemoglobin A1c (HbA1c) was measured using high-performance liquid chromatography on a Variant™ II system (Bio-Rad Laboratories, Hercules, CA, USA). Urinary creatinine levels were quantified by colorimetric assay (Boehringer Mannheim/Hitachi 717 analyzer), while urinary albumin was assessed via immunoturbidimetry (Roche P800 automated analyzer). The urinary albumin-to-creatinine ratio (UACR) was calculated as the ratio of urinary albumin (mg) to urinary creatinine (g).

Measurement of cfPWV

cfPWV was measured using the Complior Analyzer (Alam Medical, Saint-Quentin-Fallavier, France) with participants in the supine position. After a 10-minute rest period, the distance between the right common carotid artery and the right

common femoral artery was determined using a tape measure. Pulse wave transducers were then positioned over both arteries and carefully adjusted until optimal waveforms were obtained. For each measurement, eight consecutive cardiac cycles were recorded. The procedure was performed twice, and the average value was calculated. cfPWV was calculated using the formula: $\text{cfPWV} = d/t$ (m/s), where d denotes the adjusted distance (measured distance $\times$ 0.8) and t represents the transit time between carotid and femoral pulse waves.²⁰ Arterial stiffness was classified as cfPWV values ≥ 10 m/s.

Definition

Hypertension was defined as either SBP /diastolic blood pressure (DBP) $\geq 140/90$ mmHg, current use of antihypertensive medications, or a self-reported history of hypertension.²¹ Diabetes was defined as the use of glucose-lowering drugs or a newly confirmed diagnosis.²² The METS-VF index served as our designated exposure variable, with metabolic score for insulin resistance (METS-IR) calculated as $\text{Ln}[(2 \times \text{FPG}) + \text{triglycerides}] \times \text{BMI} / \text{Ln}(\text{HDL-C})$. The formulation for METS-VF was as follows: $\text{METS-VF} = 4.466 + 0.011 \times [\text{Ln}(\text{METS-IR})]^3 + 3.239 \times [\text{Ln}(\text{WHtR})]^3 + 0.319 \times (\text{gender}) + 0.594 \times \text{Ln}(\text{Age})$, where gender was a binary variable with male=1 and female=0.¹¹ The participants were categorized into quartiles based on the METS-VF values: the lowest quartile (Q1) was defined as $\text{METS-VF} < 6.47$, the second quartile (Q2) as $6.47 \leq \text{METS-VF} < 6.82$, the third quartile (Q3) as $6.82 \leq \text{METS-VF} < 7.09$, and the highest quartile (Q4) as $\text{METS-VF} \geq 7.09$.

Statistical Analysis

Normally distributed continuous variables were expressed as mean $\pm$ SD, while non-normally distributed variables were presented as median (IQR). Categorical variables were presented as percentages. Group comparisons employed one-way ANOVA or Kruskal–Wallis tests for continuous variables and Chi-square tests for categorical variables. Linear regression analysis was used to determine the independent variables related to arterial stiffness, while logistic regression was performed to calculate odds ratio (OR) with 95% CI for arterial stiffness. Linear regression included univariate crude analysis and multivariate full adjustment for all potential confounders. Logistic regression used three models including unadjustment, age/gender-adjustment, full adjustment for age, gender, smoking status, SBP, DBP, TC, LDL-C, eGFR, uric acid, HbA1c, UACR. A restricted cubic splines (RCS) model was applied to examine potential non-linear relationships. The receiver operating characteristic (ROC) curve and area under the curve (AUC) analysis was designed to compare the discriminative ability of METS-VF with BMI, WHtR, the traditional anthropometric adiposity indicators, for identifying arterial stiffness, with all indices combined with SBP. The Delong test was employed to compare the differences among the three ROC curves. Stratified analyses were pre-specified to evaluate the consistency of the association between METS-VF and arterial stiffness across subgroups defined by age, gender, BMI, smoking status, hypertension, diabetes, medication use and participant classification. RCS and stratified analyses were adjusted for the same full set of confounders as fully adjusted model in the logistic regression. Statistical analyses were carried out using SPSS (version 22.0, USA) and R software (version 4.3.3, accessible at <http://www.R-project.org>). $P < 0.05$ was considered statistically significant.

Results

Clinical Characteristics

A cross-sectional analysis was conducted on 3782 participants with a mean age of 59.42 ± 11.89 years, including 2381 males (62.96%) and 612 health examinees (16.18%), 1123 outpatients (29.69%), 2047 inpatients (54.12%). Table 1 summarizes the clinical characteristics of the study population categorized by quartiles of METS-VF. The participants in the higher METS-VF quartiles were more likely to be male, smoker and exhibited higher levels of age, SBP, FPG, HbA1c, triglyceride, uric acid, UACR, BMI, higher prevalence of hypertension and diabetes, a greater proportion on lipid-lowering medications, and a higher rate of drinkers, while presented lower levels of TC, HDL-C, LDL-C, eGFR. Notably, a significant trend in increasing arterial stiffness and increasing levels of cfPWV was observed from lower to higher METS-VF quartile (Q1 to Q4: 19.98%, 28.68%, 37.99%, 49.37%, $\chi^2 = 201.04$, $P < 0.001$).

Table 1 Clinical Characteristics of the Participants by METS-VF Quartiles

	Q1 (METS-VF<6.47)	Q2 (6.47 ≤ METS-VF < 6.82)	Q3 (6.82 ≤ METS-VF < 7.09)	Q4 (METS-VF ≥ 7.09)	χ²/F/Z	P
n	946	945	945	946		
Age (years)	53.77 ± 11.86	58.12 ± 10.89	60.68 ± 10.82	65.12 ± 11.02	171.43	<0.001
Gender						
Male (%)	348 (36.8)	569 (60.2)	688 (70.8)	776 (82.0)	467.72	<0.001
Smoker (%)	137 (14.48)	232 (24.55)	267 (28.25)	314 (33.19)	94.79	<0.001
Drinker (%)	65 (6.87)	139 (14.71)	174 (18.41)	190 (20.08)	76.83	<0.001
BMI (kg/m ²)	22.02 (20.40, 23.42)	24.04 (22.69, 25.39)	25.34 (23.94, 26.67)	27.40 (25.89, 29.38)	1786.85	<0.001
Systolic blood pressure (mm Hg)	124.00 (112.00, 139.00)	129.00 (118.00, 141.00)	130.00 (121.00, 143.00)	133.00 (123.00, 146.00)	121.21	<0.001
Diastolic blood pressure (mm Hg)	76.00 (68.00, 85.00)	79.00 (72.00, 87.00)	79.00 (72.00, 87.00)	78.00 (71.00, 86.00)	30.11	<0.001
Hypertension (%)	725 (76.64)	784 (82.96)	830 (87.83)	873 (92.28)	99.84	<0.001
Diabetes (%)	259 (27.38)	414 (43.81)	485 (51.32)	554 (58.56)	204.47	<0.001
Arterial stiffness (%)	189 (19.98)	271 (28.68)	359 (37.99)	467 (49.37)	201.04	<0.001
Fasting plasma glucose (mmol/L)	5.00 (4.60, 5.49)	5.29 (4.83, 6.01)	5.39 (4.89, 6.27)	5.54 (4.92, 6.55)	187.56	<0.001
HbA1c (%)	5.60 (5.30, 6.00)	5.70 (5.40, 6.30)	5.80 (5.50, 6.50)	6.00 (5.60, 6.80)	227.47	<0.001
Triglyceride (mmol/L)	1.06 (0.79, 1.48)	1.36 (0.98, 1.88)	1.38 (1.01, 1.97)	1.49 (1.09, 2.12)	238.39	<0.001
Total cholesterol (mmol/L)	4.78 (4.08, 5.53)	4.72 (3.94, 5.35)	4.52 (3.81, 5.21)	4.34 (3.64, 5.12)	86.00	<0.001
LDL-C (mmol/L)	3.01 (2.44, 3.71)	2.99 (2.31, 3.63)	2.85 (2.20, 3.56)	2.75 (2.11, 3.46)	47.94	<0.001
HDL-C (mmol/L)	1.38 (1.12, 1.65)	1.19 (1.01, 1.43)	1.13 (0.97, 1.33)	1.03 (0.88, 1.23)	494.69	<0.001
Uric acid (mmol/L)	313.55 (267.10, 377.70)	357.00 (303.60, 414.20)	384.00 (320.00, 441.30)	393.15 (333.00, 454.15)	328.84	<0.001
eGFR (mg/min/1.73m ²)	105.78 (94.81, 118.75)	101.00 (91.27, 114.24)	99.12 (86.98, 110.21)	94.09 (83.76, 104.33)	216.67	<0.001
UACR (mg/g)	0.81 (0.72, 0.93)	0.85 (0.74, 0.96)	0.87 (0.77, 0.99)	0.93 (0.81, 1.06)	190.27	<0.001
cfPWV (m/s)	8.84 ± 2.43	9.31 ± 2.27	9.72 ± 2.29	10.37 ± 3.01	63.10	<0.001
Antihypertensive medications (%)	478 (50.53)	480 (50.79)	458 (48.47)	494 (52.22)	2.72	0.437
Antidiabetic medications (%)	142 (15.01)	143 (15.13)	154 (16.30)	169 (17.86)	3.70	0.296
Lipid-lowering medications (%)	230 (24.31)	268 (28.36)	285 (30.16)	354 (37.42)	40.54	<0.001

Abbreviations: METS-VF, metabolic syndrome-related visceral fat index; BMI, body mass index; HbA1c, glycosylated hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; UACR, urinary albumin-to-creatinine ratio; cfPWV, carotid-femoral pulse wave velocity.

Univariate and Multivariate Linear Regression Analysis of cfPWV

As shown in Table 2, a linear regression analysis was performed with cfPWV as the dependent variable and age, METS-VF, SBP, DBP, TC, LDL-C, uric acid, eGFR, HbA1c, UACR as the independent variables. In univariate linear regression analysis, METS-VF, SBP, DBP, uric acid, HbA1c, UACR were positively correlated to cfPWV, whereas TC, LDL-C, eGFR were negatively correlated to cfPWV. All the above potential confounders were simultaneously included in the model for full adjustment, to identify independent factors associated with cfPWV after controlling for the mutual interference of covariates. In multivariate linear regression analysis, the following variables were independently associated with cfPWV: age ($\beta = 0.06$, 95% CI 0.05 ~ 0.07, $P < 0.001$), METS-VF ($\beta = 0.19$, 95% CI 0.03 ~ 0.35, $P = 0.018$), SBP ($\beta = 0.04$, 95% CI 0.04 ~ 0.05, $P < 0.001$), DBP ($\beta = -0.01$, 95% CI $-0.02 \sim -0.01$, $P = 0.036$), uric acid ($\beta = 0.01$, 95% CI 0.01 ~ 0.01, $P = 0.017$), eGFR ($\beta = -0.01$, 95% CI $-0.02 \sim -0.01$, $P < 0.001$), HbA1c ($\beta = 0.16$, 95% CI 0.12 ~ 0.21, $P < 0.001$), UACR ($\beta = 0.01$, 95% CI 0.01 ~ 0.01, $P = 0.008$).

Relationship Between METS-VF and Arterial Stiffness

The association between METS-VF and arterial stiffness is presented in Table 3. A positive correlation was observed between METS-VF quartiles and arterial stiffness in the unadjusted Model 1, which remained evident after adjustment

Table 2 Univariate Linear Analysis and Multivariate Linear Analysis of Relative Factors for cfPWV (n=3782)

Variables	Univariate Analysis		Multivariate Analysis	
	β (95% CI)	P	β (95% CI)	P
Age	0.08 (0.07 ~ 0.09)	<0.001	0.06 (0.05 ~ 0.07)	<0.001
METS-VF	1.12 (0.97 ~ 1.27)	<0.001	0.19 (0.03 ~ 0.35)	0.018
Systolic blood pressure	0.05 (0.05 ~ 0.05)	<0.001	0.04 (0.04 ~ 0.05)	<0.001
Diastolic blood pressure	0.01 (0.01 ~ 0.02)	0.005	-0.01 (-0.02 ~ -0.01)	0.036
Total cholesterol	-0.15 (-0.22 ~ -0.07)	<0.001	-0.05 (-0.19 ~ 0.08)	0.427
LDL-C	-0.14 (-0.22 ~ -0.05)	0.003	0.04 (-0.11 ~ 0.19)	0.578
Uric acid	0.01 (0.01 ~ 0.01)	0.009	0.01 (0.01 ~ 0.01)	0.017
eGFR	-0.03 (-0.03, -0.02)	<0.001	-0.01 (-0.02 ~ -0.01)	<0.001
HbA1c	0.25 (0.20 ~ 0.30)	<0.001	0.16 (0.12 ~ 0.21)	<0.001
UACR	0.01 (0.01, 0.01)	<0.001	0.01 (0.01, 0.01)	0.008

Notes: Multivariate linear analysis adjustment for age, systolic blood pressure, diastolic blood pressure, total cholesterol, LDL-C, eGFR, uric acid, HbA1c, UACR.

Abbreviations: METS-VF, metabolic syndrome-related visceral fat index; HbA1c, glycosylated hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; UACR, urinary albumin-to-creatinine ratio; cfPWV, carotid-femoral pulse wave velocity.

Table 3 The Quartile of METS-VF Associated with Arterial Stiffness (n=3782)

	Model 1		Model 2		Model 3	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
METS-VF_per_IQR	2.00 (1.81 ~ 2.20)	<0.001	2.03 (1.72 ~ 2.39)	0.010	1.20 (1.06 ~ 1.35)	0.004
METS-VF quartiles						
Q1 (METS-VF<6.47)	Ref		Ref		Ref	
Q2 (6.47≤ METS-VF < 6.82)	1.09 (1.05 ~ 1.15)	<0.001	1.04 (1.00 ~ 1.09)	0.039	1.07 (0.84 ~ 1.36)	0.598
Q3 (6.82 ≤ METS-VF < 7.09)	1.13 (1.09 ~ 1.19)	<0.001	1.06 (1.02 ~ 1.11)	0.002	1.28 (1.00 ~ 1.63)	0.053
Q4 (METS-VF≥ 7.09)	1.25 (1.19 ~ 1.30)	<0.001	1.13 (1.09 ~ 1.18)	<0.001	1.38 (1.06 ~ 1.79)	0.016
P for trend	<0.001		<0.001		<0.001	

Notes: Model 1: unadjusted model; Model 2: adjustment for age, gender; Model 3 adjustment for age, gender, smoking status, systolic blood pressure, diastolic blood pressure, total cholesterol, low-density lipoprotein cholesterol, estimated glomerular filtration rate, uric acid, glycosylated hemoglobin A1c, urinary albumin-to-creatinine ratio.

Abbreviation: METS-VF, metabolic syndrome-related visceral fat index.

for age and gender (Model 2) and persisted further in the full adjustment for age, gender, smoking status, SBP, DBP, TC, LDL-C, eGFR, HbA1c, and UACR (Model 3). Specifically, the OR for each increase in quartile was 2.00 (95% CI 1.81 ~ 2.20, $P < 0.001$) in Model 1, 2.03 (95% CI 1.72 ~ 2.39, $P = 0.010$) in Model 2, 1.20 (95% CI 1.06 ~ 1.35, $P = 0.004$) in Model 3. In the unadjusted model (Table 3, Model 1), compared with participants in Q1 for arterial stiffness, the ORs for Q2, Q3, and Q4 were 1.09 (95% CI 1.05 ~ 1.15, $P < 0.001$), 1.13 (95% CI 1.09 ~ 1.19, $P < 0.001$), and 1.25 (95% CI 1.19 ~ 1.30, $P < 0.001$), respectively. After adjusting for age and gender (Model 2), participants in Q2, Q3, and Q4 had progressively higher odds of arterial stiffness compared with those in Q1, with ORs of 1.04 (95% CI 1.00 ~ 1.09, $P = 0.039$), 1.06 (95% CI 1.02 ~ 1.11, $P = 0.002$), and 1.13 (95% CI 1.09 ~ 1.18, $P < 0.001$), respectively. After adjusting for age, gender, smoking status, SBP, DBP, TC, LDL-C, eGFR, uric acid, HbA1c, UACR (Model 3), Q4 had an OR of 1.38 (95% CI 1.06 ~ 1.79, $P = 0.016$) compared to Q1. These data underscored the independent association between METS-VF and arterial stiffness.

A significant non-linear relationship was observed between METS-VF and arterial stiffness in the RCS model, which adjusted for age, gender, smoking status, SBP, DBP, TC, LDL-C, eGFR, uric acid, HbA1c, UACR (P for non-linearity = 0.025, Figure 2). Specifically, when METS-VF exceeded the inflection point of 6.81, the association changed markedly, and beyond this threshold, the risk of arterial stiffness increased sharply and in an accelerated manner.

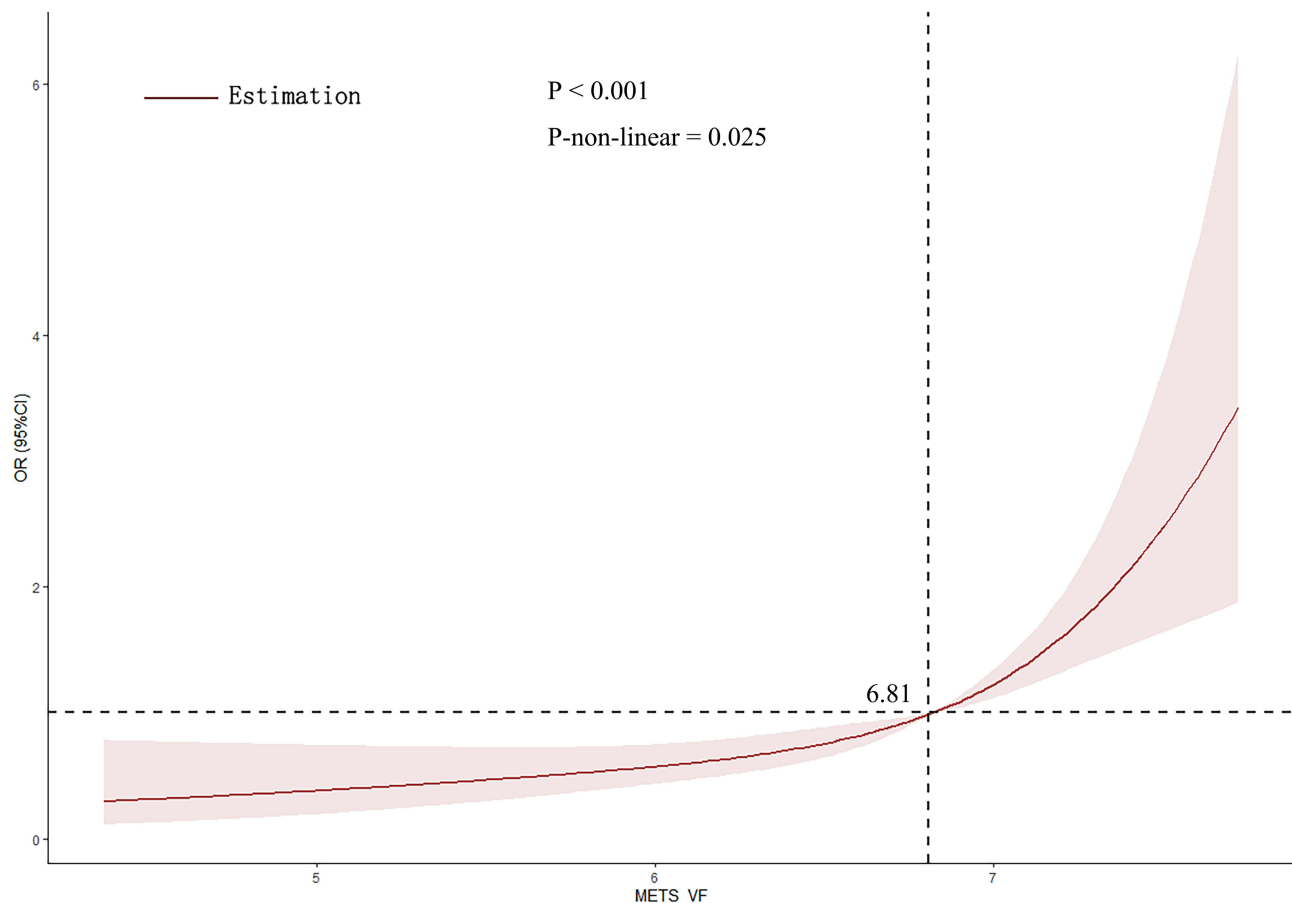


Figure 2 Restricted cubic spline for the relationship between METS-VF and arterial stiffness.

Notes: The red solid line presents the fitted OR curve. The light red shaded area denotes 95% CI of the estimated OR. The horizontal black dashed line indicates the reference line (OR = 1). The vertical black dashed line marks the inflection point at METS-VF = 6.81. Adjustment for age, gender, systolic blood pressure, diastolic blood pressure, low-density lipoprotein cholesterol, estimated glomerular filtration rate, glycosylated hemoglobin A1c, urinary albumin-to-creatinine ratio. $n=3782$.

Abbreviations: METS-VF, metabolic syndrome-related visceral fat index; OR, odds ratio; CI, confidence interval.

Table 4 Discriminative Performance of METS-VF, BMI, and WHtR Combined with SBP for Identifying Arterial Stiffness (n=3782)

Test	AUC (95% CI)	Cut-off	Specificity	Sensitivity	P value	P value (DeLong Test) Comparing AUC of METS-VF+SBP with Other Markers+SBP
METS-VF	0.648 (0.629 ~ 0.666)	6.834	0.586	0.632	<0.001	–
METS-VF+SBP	0.723 (0.710 ~ 0.744)	0.344	0.672	0.661	<0.001	Reference
BMI+SBP	0.700 (0.682 ~ 0.717)	0.340	0.674	0.619	<0.001	<0.001
WHtR+SBP	0.708 (0.691 ~ 0.725)	0.299	0.572	0.733	<0.001	<0.001

Abbreviations: AUC, area under the curve; METS-VF, metabolic syndrome-related visceral fat index; SBP, systolic blood pressure; BMI, body mass index; WHtR, waist-to-height-ratio.

ROC Curves of METS-VF, BMI, WHtR for Discrimination of Arterial Stiffness

Based on the results from Table 4 and Figure 3, the METS-VF index combined with SBP demonstrated the highest discriminative ability for arterial stiffness, with an AUC of 0.723 (95% CI 0.710 ~ 0.744, $P < 0.001$). This was significantly superior to both BMI combined with SBP (AUC = 0.700, 95% CI 0.682 ~ 0.717, $P < 0.001$) and WHtR combined with SBP (AUC = 0.708, 95% CI 0.691 ~ 0.725, $P < 0.001$), as confirmed by the DeLong test (all $P < 0.001$). Additionally, the standalone METS-VF index also exhibited acceptable discriminative performance (AUC = 0.648, 95% CI 0.629 ~ 0.666, $P < 0.001$), further supporting its clinical utility as a screening marker for arterial stiffness.

Stratified Analyses

Stratified analyses are presented in Figure 4, which was adjusted for the same full set of confounders as Model 3 in the logistic regression including age, gender, smoking status, SBP, DBP, TC, LDL - C, eGFR, uric acid, HbA1c, and UACR

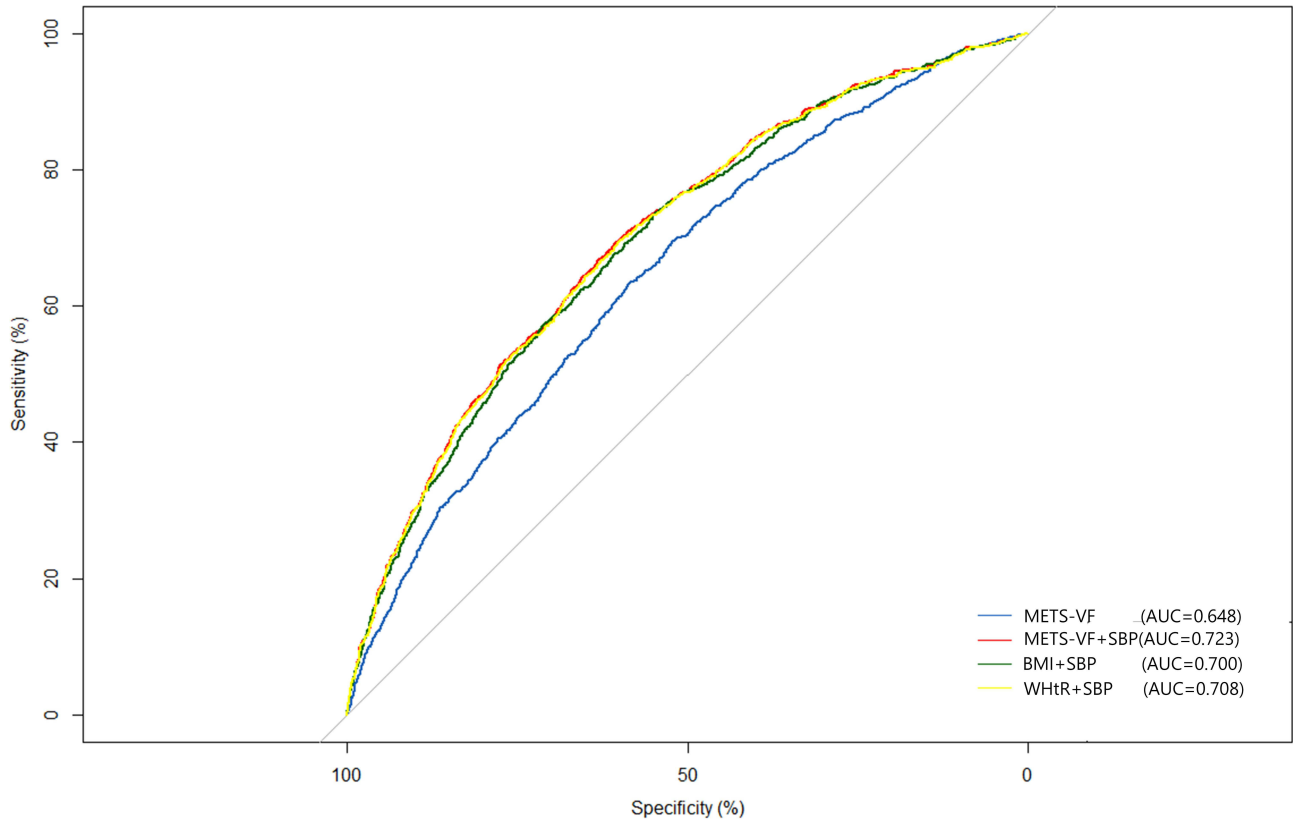


Figure 3 ROC curves of METS-VF, BMI, WHtR combined with SBP for discrimination of arterial stiffness.

Notes: Solid line: the reference line (AUC = 0.5), n=3782.

Abbreviations: AUC, area under the curve; ROC, receiver operating characteristic curve; METS-VF, metabolic syndrome-related visceral fat index; BMI, body mass index; WHtR, waist-to-height ratio; SBP, systolic blood pressure; CI, confidence interval.

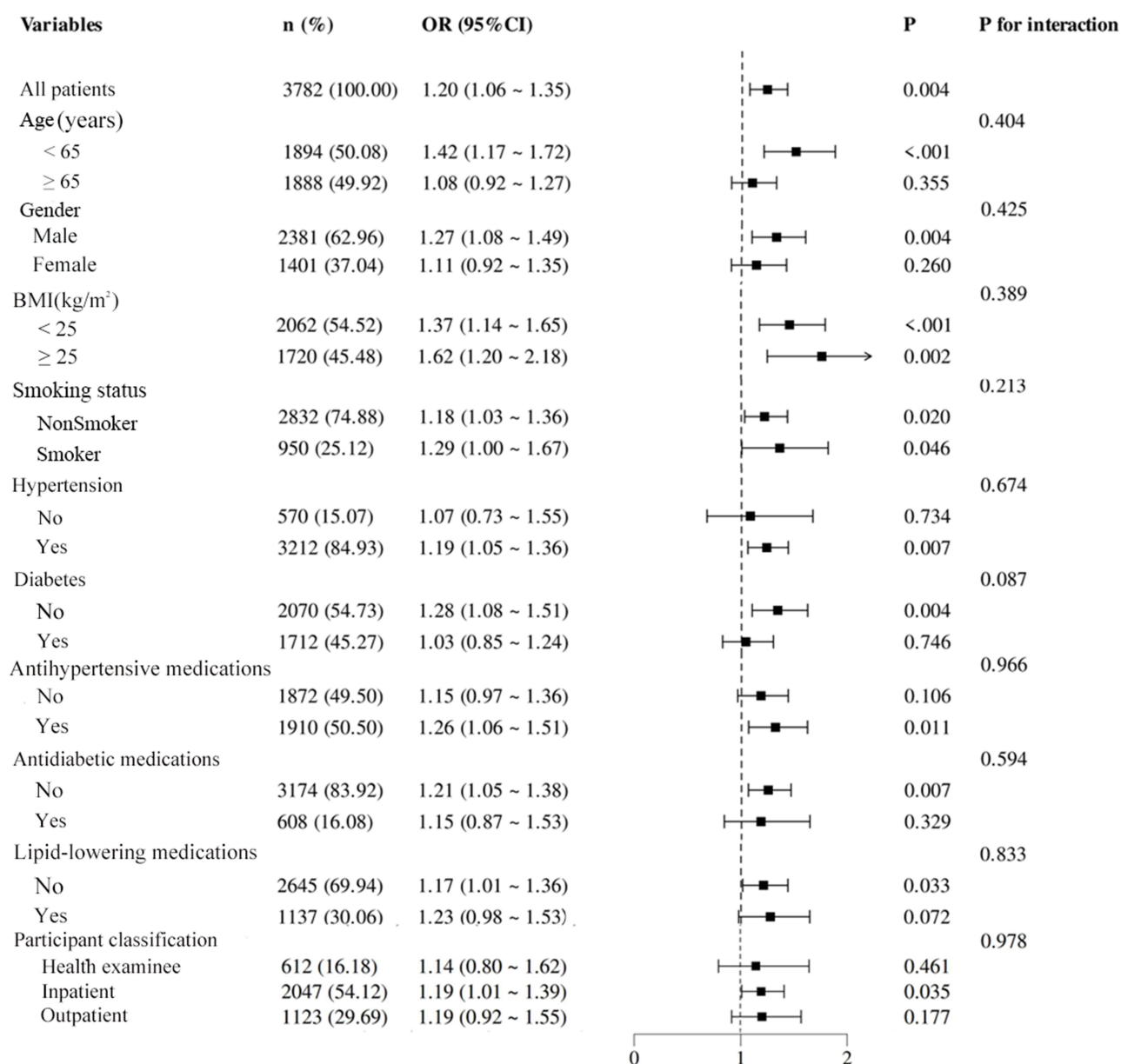


Figure 4 Stratified analysis for the association of METS-VF with arterial stiffness.

Notes: Adjustment for age, gender, smoking status, systolic blood pressure, diastolic blood pressure, total cholesterol, low-density lipoprotein cholesterol, estimated glomerular filtration rate, uric acid, glycosylated hemoglobin A1c, urinary albumin-to-creatinine ratio. n=3782.

Abbreviations: METS-VF, metabolic syndrome-related visceral fat index; BMI, body mass index; OR, odds ratio; CI, confidence interval.

A significant association was observed in patients aged <65 years (OR = 1.42, 95% CI 1.17 ~ 1.72, $P < 0.001$) not in those aged ≥65 years (OR = 1.08, 95% CI 0.92 ~ 1.27, $P = 0.335$) but the P for interaction was 0.404, indicating the modifying effect of age was not statistically significant. Gender stratification revealed an association between METS-VF and arterial stiffness in male (OR = 1.27, 95% CI 1.08 ~ 1.49, $P = 0.004$), whereas no association was observed in female (OR = 1.11, 95% CI 0.92 ~ 1.35, $P = 0.260$). Similarly, the sex interaction was non-significant (P for interaction = 0.425). In addition, the same situation lies in the subgroups regarding whether the participants have diabetes or not and whether they are using antidiabetic medications. Significant associations were observed across BMI categories (BMI <25 kg/m²: OR = 1.37, 95% CI 1.14 ~ 1.65, $P < 0.001$; BMI ≥25 kg/m²: OR = 1.62, 95% CI 1.20 ~ 2.18, $P = 0.002$) with a non-significant BMI interaction (P for interaction = 0.213). Furthermore, analogous patterns were observed in subgroups stratified by hypertension status, antihypertensive/lipid-lowering medication use, and participant recruitment source.

Discussion

This study systematically investigated the association between the METS-VF index and arterial stiffness in a cohort of 3782 participants. The cross-sectional analyses revealed a significant positive association between METS-VF and arterial stiffness, and the association was not entirely linear. METS-VF combined with SBP had superior discriminative ability for arterial stiffness compared with traditional indicators such as BMI or WHtR combined with SBP. Stratified analyses across different subgroups further confirmed the robustness and consistency of this relationship. These findings provide new evidence for the potential role of abdominal obesity and insulin resistance in the pathogenesis of arterial stiffness.

Obesity is a well-established risk factor for arterial stiffness.²³ While BMI is commonly used to assess overall adiposity, it cannot differentiate fat distribution or specifically quantify visceral adipose tissue.²⁴ In contrast, measures focusing on visceral fat have shown a stronger and more consistent correlation with arterial stiffness.²⁵ Strasser et al demonstrated that abdominal obesity and visceral fat are positively correlated with arterial stiffness.²⁶ Similarly, Huayu Sun et al conducted a retrospective study on 14,877 individuals and found that the Chinese visceral adiposity index has a closer relationship with the risk of arterial stiffness, and its predictive ability for arterial stiffness is superior to that of BMI and WC.²⁷ However, gold-standard imaging techniques for abdominal obesity such as magnetic resonance imaging and computed tomography are limited by high cost, technical demands, and potential radiation exposure, restricting their use in large-scale studies.^{28,29} The METS-VF index offers a practical, non-invasive alternative by integrating four parameters: METS-IR, WHtR, age, and gender. This composite design makes METS-VF not merely an anthropometric measure but a comprehensive surrogate of metabolically harmful adiposity.³⁰ Previous studies have shown that METS-IR can effectively predict fat distribution, supporting the use of METS-VF as a superior and simpler tool compared to traditional anthropometric measures.^{11,31} In a retrospective study of 6827 participants, Zhu et al demonstrated that METS-VF was associated with an increased risk of CVD and all-cause mortality.³² In this study, multivariable-adjusted logistic regression analyses showed that METS-VF remained independently associated with arterial stiffness. Our data have confirmed a positive association between METS-VF and arterial stiffness, highlighting the role of abdominal obesity, insulin resistance, and aging in arterial stiffness.

The relationship between METS-VF and arterial stiffness may be mediated through interconnected pathways, and visceral adipose tissue functions as an active endocrine organ, secreting adipokines such as leptin, adiponectin, and tumor necrosis factor- α (TNF- α), which promote chronic low-grade inflammation and endothelial dysfunction.³³ This inflammatory state drives vascular fibrosis and reduces arterial compliance, culminating in the progression of arterial stiffness.³⁴ Furthermore, high METS-VF commonly linked to metabolic disturbances including hyperglycemia and dyslipidemia, which enhance oxidative stress via overproduction of reactive oxygen species (ROS).^{35,36} Consequently, ROS leads to structural damage of elastin and collagen in the vascular wall.³⁷ ROS also impairs endothelial function by reducing nitric oxide bioavailability, limiting vasodilation and promoting stiffness. Additionally, insulin resistance, as the pathological core of abdominal obesity, activates the renin-angiotensin-aldosterone system, stimulating vascular smooth muscle cell proliferation, vasoconstriction, and extracellular matrix remodeling, all contributing to increased arterial stiffness.³⁸ Consistent with this pathophysiological framework, our results demonstrate a significant association between METS-VF and arterial stiffness, and METS-VF combined with SBP demonstrated superior discriminative performance for arterial stiffness over traditional indicators in ROC curve analysis, as indicated by a larger AUC. This is not difficult to understand, because METS-VF is a composite indicator integrating metabolic dysregulation, insulin resistance, visceral adiposity and aging. This association underscores the potential clinical value of METS-VF in identifying individuals at elevated risk of arterial stiffness. More importantly, aside from age and gender, the other parameters used to calculate METS-VF are modifiable, underscoring the importance of lifestyle changes and pharmacological interventions.

Several limitations must be acknowledged. Firstly, the observational, cross-sectional, and single-center design precludes causal inference. Secondly, participants were recruited exclusively from southern China, which may limit generalizability to other geographic or ethnic populations. Finally, although METS-VF is a validated surrogate for visceral fat, it does not capture precise anatomical fat distribution. Nevertheless, it provides a more feasible and cost-effective tool for visceral adiposity assessment in clinical practice. Further investigations are warranted to establish causality between METS-VF and vascular health. Additionally, our observation of an inverse association between METS-VF and conventional LDL-C diverges from conventional findings. A potential resolution to this discrepancy

lies in the confounding factor of lipid -lowering medication, which is likely more prevalent in the high METS-VF cohort due to their greater burden of cardiovascular metabolic conditions. This study also makes three distinct contributions. Firstly, through direct comparison, we demonstrate the superior discriminatory power of METS-VF over traditional anthropometric indices such as BMI and WHtR. Secondly, the discovery of a non - linear relationship between METS-VF and arterial stiffness, analyzed via RCS. Thirdly, extensive subgroup analyses confirm the robustness of this association across key demographic and clinical strata.

Conclusion

METS-VF is significantly and independently associated with arterial stiffness, as evaluated by elevated cfPWV, in a large-sample clinical cohort. A clear relationship was observed, underscoring the role of abdominal obesity, as a modifiable risk factor, in promoting arterial stiffness through inflammatory and metabolic pathways.

Abbreviations

AUC, area under the curve; BMI, body mass index; CVD, cardiovascular disease; cfPWV, carotid-femoral pulse wave velocity; DBP, diastolic blood pressure; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; METS-VF, metabolic syndrome-related visceral fat index; OR, odds ratio; RCS, restricted cubic splines; ROC, receiver operating characteristic; ROS, reactive oxygen species; SBP, systolic blood pressure; TC, total cholesterol; TNF- α , tumor necrosis factor- α ; UACR, urinary albumin-to-creatinine ratio; WC, waist circumference; WHtR, waist-to-height ratio.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author (Tingjun Wang) on reasonable request.

Ethics Approval

The study protocol adhered to the Helsinki declaration and all participants signed the informed consent. The protocol received approval from the Ethics Committee of the First Affiliated Hospital of Fujian Medical University (Approval No. [2020]306).

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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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