ORIGINAL RESEARCH

Visceral Fat Area, Not Subcutaneous Fat Area, is Associated with Cardiac Hemodynamics in Type 2 Diabetes

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Background: This study was conducted in patients with type 2 diabetes mellitus (T2DM) to assess the association between visceral fat area (VFA) and cardiac hemodynamics.

Methods: A total of 568 patients with type 2 diabetes (mean age 54±12 years; 40.8% of women) were enrolled. Visceral fat area (VFA, m^2) and subcutaneous fat area (SFA, m^2) were evaluated by a bioelectrical impedance analyzer. Cardiac hemodynamics were measured by echocardiography, and other clinical and laboratory variables were also assessed and recorded. Patients were divided into those with VFA ≤ 100 (n=369) and those with VFA > 100 (n=199).

Results: VFA, SFA, LVMI (left ventricular mass index), left atrial diameter, left ventricular diastolic diameter (LvDd), interventricular septal thickness (IVST), left ventricular systolic diameter (LvSd), and posterior wall thickness (PWT) levels in high-V groups were significantly higher than those in low-V groups. Correlation analysis showed that VFA was positively correlated with LVMI (r=0.120, p=0.004), LVM (r=0.249, p<0.0001), left atrial diameter (r=0.375, p<0.0001), aortic root diameter (r=0.243, p<0.0001), left ventricular systolic diameter (LvSd) (r=0.211, p<0.0001) and negatively correlated with LVEF (r=−0.107, p=0.011). In multivariate linear regression analysis, VFA was the strongest independent determinant of LVMI (β=0.04, p=0.016), LVEF (β=−0.01, p=0.023), and left atrial diameter (β=0.035, p<0.0001), Internal diameter of the aortic root (β=0.014, p<0.0001) and LvSd (β=0.017, p<0.0001). In addition, the VFA also better predicted cardiovascular disease risk with AUC of 0.609 (95% CI:0.563–0.656), compared with SFA, waist–hip ratio (WHR), in a statistically significant manner.

Conclusion: We found a significant correlation between VFA (but not SFA) and cardiac hemodynamic parameters. The VFA has advantages as a predictor of visceral obesity and is significantly associated with the development of cardiovascular risk factors (CVD) in T2DM patients.

Keywords: cardiac hemodynamics, left ventricular mass index, type 2 diabetes mellitus, visceral fat area

Introduction

Nowadays, diabetes mellitus is seriously increasing in the majority of the populations all over the world. The latest epidemiological data on diabetes show the prevalence of diabetes in adults living in China increased from 0.67% using the WHO criteria in 1980 to 12.8% using the ADA criteria in 2017.[1] It has become a major public health problem in developing countries and is associated with the development and progression of high-mortality diseases such as obesity and its subsequent complications. Cardiovascular disease (CVD) is the most common cause of morbidity and mortality

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in patients with diabetes.[2] However, the mechanistic link between diabetes mellitus and CVD is still debated. Besides traditional risk factors including centripetal obesity, insulin resistance and hypertension, novel risk factors such as chronic inflammation, lipid metabolism disorder, atherosclerosis and myocardial steatosis have also been speculated to contribute to the development of abnormal function and structure for CVD in T2DM.[3–7]

Recently, visceral fat has gained attention as one of the possible mechanisms for the link. Visceral fat, mainly found in the abdominal cavity, acts as an extremely active organ that produces several bioactive adipokines and proinflammatory cytokines.[8,9] Excessive visceral fat area is associated with adipocyte dysfunction, increased inflammatory cytokine secretion, and impaired insulin sensitivity, which can increase the risk of atherosclerosis and lead to cardiac and endothelial dysfunction.[10] A few studies reported visceral fat was associated with cardiometabolic risk in the general population,[11,12] in hypertensive patients,[13] in psoriasis patients,[14] in women after menopause[15] and in patients with coronary atherosclerosis.[16] However, the relationship between VFA and cardiac hemodynamics has not been adequately evaluated in comparison with other clinical factors such as blood pressure, age or waist/hip ratio in T2DM.

At present, the detection of visceral fat mainly includes CT, magnetic resonance imaging (MRI) and dual bioelectrical impedance.[17] Although CT and MRI are the gold standard for quantitative estimation of adipose tissue distribution, these technologies are costly, have radiation issues, and cannot be routinely available. As a non-invasive and relatively accurate method of quantifying visceral fat, dual bioelectrical impedance has other advantages, such as operator independency, and lower costs, when compared to CT and MRI.[18,19] It can be widely used in clinic with a high sensitivity and specificity (0.941 and 0.988, respectively).[20] Besides, recent studies have found that dual bioelectrical impedance analysis can accurately measure the body's various tissue components, including visceral fat and muscle.[21]

Hence, this study intends to measure VFA by dual bioelectrical impedance and investigate its relationship with cardiac hemodynamics in patients with type 2 diabetes.

Methods
Study Design and Patients
A total of 568 consecutive asymptomatic patients with T2DM, who were admitted to our institution (Affiliated Hospital of Jiangsu University, China) for diabetic educational program between June 2019 and February 2020, were enrolled in this study. The diagnosis of T2DM was performed according to the 1999 World Health Organization (WHO) diabetes diagnosis and classification criteria.[22] 43.1% of patients had a previous diagnosis of type 2 diabetes mellitus and hypertension and were in treatment for both conditions. These criteria were chosen to ensure the formation of a high cardiovascular risk cohort. The following conditions should be excluded for all included patients: (1) patients with incomplete clinical and biochemical data; (2) recent use of glucocorticoids or antipsychotics; (3) Patients with type 1 diabetes, special type diabetes and acute severe metabolic disorder of diabetes; (4) patients with coronary atherosclerotic heart disease, congestive heart failure, severe arrhythmia, post-cardiac valve replacement and cardiac pacemaker; (5) Patients with severe liver and kidney dysfunction and abnormal thyroid function; (6) Patients with tumors, autoimmune diseases or diseases of the blood system. This study was approved by the medical ethics committee of the Affiliated Hospital of Jiangsu University in Zhenjiang, China and obtained written informed consent of all subjects.

Physical Examination
All study subjects were examined in the morning after an overnight fast. Height, body weight, waist circumference (WC), hip circumference (HC), heart rate and blood pressure (BP) were measured by trained survey personnel according to standardized methods.

Laboratory Measurement
The participants were asked to collect elbow venous blood after an overnight fast of longer than 8 h. Fasting blood glucose (FBG) was detected by glucose oxidase method, fasting plasma insulin (FIns) and C-peptide (FC-P) were measured by chemiluminescence method, and HbA1c was determined by HPLC. An automatic biochemical analyzer was used to detect aspartate aminotransferase (AST), alanine transaminase (ALT), glutamyl transpeptidase (GT), TC, TG, HDL-C and LDL-C.

Measurement of VFA and Cardiac Hemodynamic Parameters
VFA, along with SFA, was measured at the umbilical level by a dual bioelectrical impedance (DUALSCAN; Omron

Healthcare Co. Ltd, Kyoto, Japan). LVEF was calculated by the Teichholz formula. Left atrial diameter, left ventricular end diastolic, LvDd and LvSd were measured using 2-dimensional echocardiography, according to the guidelines of the American Society of Echocardiography.[23] Left ventricular posterior wall thickness (PWT) and interventricular septal thickness (IVST) were measured at end-diastole.

Data Measurements

The homeostasis model assessment ratio (HOMA-R) index was calculated as fasting plasma glucose × fasting plasma insulin⁄22.5 for assessing insulin resistance.[24] Body mass index (BMI) was calculated from height and weight and the waist–hip ratio (WHR) was calculated from the waist and hip circumference.

LVMI was calculated by this formula:[23]

LV mass = $0.80 \times 1.04 \times \{(IVST + LvDd + PWT)^3 - LvDd^3 + 0.6$ (g)

LVMI = LV mass⁄body surface area (body weight$^{0.425}$ × height$^{0.725}$ × 0.007184).

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (SPSS Inc, Chicago, IL, USA). Data are expressed as mean ± standard deviation (SD) and percentages. Participants were divided into two groups according to the diagnostic criteria of abdominal obesity as follows: Q1 low-VFA (VFA≤100 cm^2), Q2 high-VFA (VFA>100 cm^2). The relationship between variables was assessed using Pearson or Spearman correlation analysis. Linear regression analyses on cardiac functional parameters were performed to identify clinical and laboratory variables that were associated with cardiac functional parameters. The factors related at the $p < 0.05$ level were selected as independent variables for multivariable analysis. The receiver operating characteristic (ROC) curves were generated to identify the optimal value for the prediction of the risk of cardiovascular disease in this population. Optimal cutoffs were derived from maximizing the Yoden index. All tests of significance were 2-tailed, and $p < 0.05$ was considered statistically significant.

Results

A total of patients with type 2 diabetes (mean age 54 ± 12 years; 40.8% female) were enrolled in the present study. Patients were 54.0 ± 12.0 years-old, systolic and diastolic blood pressure were 127.8 ± 17.6 mmHg and 74.9 ± 10.2 mmHg, and HbA1C was 9.5 ± 2.2%. Among 568 patients, 369 and 199 were classified as low-V and high-V patients. As shown in Table 1, high-V group was significantly younger, has significantly higher LVM and LVMI, higher prevalence of hypertension and hyperlipidemia, and lower LVEF than the low-V group. HbA1c, fasting C-peptide and HOMA-IR level in high-V group were significantly higher than in those with low-V. VFA, SFA, WHR, BMI, TG, LDL-C levels in high-V group were significantly higher than those in low-V group. LVMI, LVM, Left atrial diameter, aortic root diameter, LvDd, LvSd, IVST, PWT were increased, along with the increase of the VFA ($p<0.05$).

In Table 2, VFA was positively correlated with LVMI ($r=0.120$, $p=0.004$), LVM ($r=0.249$, $p<0.0001$), left atrial diameter ($r=0.375$, $p<0.0001$), aortic root diameter ($r=0.243$, $p<0.0001$), LvSd ($r=0.211$, $p<0.0001$), LvDd ($r=0.185$, $p<0.0001$), IVST ($r=0.240$, $p<0.0001$), PWT ($r=0.237$, $p<0.0001$) while negatively correlated with LVEF ($r=-0.107$, $p=0.011$). Among the clinical factors in Table 3, we determined which factors were associated with the cardiac hemodynamics. Besides VFA, these cardiac hemodynamics were mainly correlated with the prevalence of hypertension, SFA, WHR, Cr and SBP ($p<0.05$). Left atrial diameter, Internal diameter of aortic root and LvSd were also correlated with Fasting c-peptide, DBP ($p<0.05$). The LVMI had a significant correlation with VFA ($r=0.120$, $p=0.004$), SFA ($r=0.132$, $p=0.02$), heart rate ($r=-0.106$, $p=0.011$), SBP ($r=0.181$, $p<0.0001$), BMI ($r=0.156$, $p<0.0001$), TC ($r=-0.099$, $p=0.018$), HDL-C ($r=-0.084$, $p=0.046$) and WHR ($r=0.092$, $p=0.028$).

Multivariate linear regression analysis (Table 4) found that with LVMI as the dependent variable, VFA and LVMI were independently correlated after adjusting for gender and age ($p=0.016$). After further correction of TC, HDL-C and LDL-C, VFA and LVMI still showed an independent correlation ($p=0.044$). After HbA1c correction, the correlation between VFA and LVMI remained independent ($p=0.039$). These cardiac hemodynamic parameters were also taken as dependent variables, respectively. Furthermore, VFA was also an independent determinant of these cardiac hemodynamic parameters ($p<0.05$), after correction according to the above model. This indicates that excessive VFA is independently associated with cardiac dysfunction in patients with type 2 diabetes.

We further performed an analysis of the association of clinical characteristics and the risk of cardiovascular disease

Table 1 Clinical Characteristics According to VFA Levels

	VFA		P-value
	Low-V (VFA≤100 cm^2)	High-V (VFA>100 cm^2)	
Age (years)	54.77±11.27	52.88±13.17	0.001
Sex (%male)	54.2	68.3	<0.0001
Hypertension, n%	38.8	51.3	<0.0001
Dyslipidemia, n %	6	6.5	0.853
Metabolic factors			
VFA (cm^2)	67.70±23.38	129.58±25.70	0.011
SFA (cm^2)	155.50±49.23	228.50±62.97	0.006
WHR	0.91±0.06	0.97±0.58	0.143
BMI (kg/m^2)	23.46±2.62	27.62±2.97	<0.0001
SBP (mmHg)	125.10±16.97	132.85±17.83	<0.0001
DBP (mmHg)	73.20±10.19	77.91±9.67	0.072
HbA1c (%)	9.48±2.30	9.53±1.87	0.189
FC-P	2.21±0.97	2.75±1.07	0.436
FBG	10.44±3.40	10.21±3.01	0.209
HOMA-IR	2.74(1.74,4.63)	3.00(1.75,4.61)	0.655
TG (mmol/L)	1.97(1.36,2.88)	1.92(1.38,2.69)	0.505
TC (mmol/L)	4.98±1.16	4.99±1.09	0.023
HDL-C(mmol/L)	1.16±0.38	1.05±0.28	0.156
LDL-C(mmol/L)	2.88±0.90	3.03±2.81	0.130
ALT	21.95 (15.00,36.58)	20.00 (14.00,32.35)	0.166
AST	17.15 (13.90,25.30)	16.20 (12.90,22.88)	0.013
Cr	57.52±17.54	61.45±20.38	0.167
Cardiac hemodynamics			
Heart rate(bpm)	79.61±10.97	80.87±11.58	0.082
LVEF (%)	67.68±4.06	67.30±3.71	0.489
Internal diameter of aortic root (mm)	29.33±2.53	30.31±2.50	<0.0001
Left atrial diameter (mm)	33.80±3.55	36.2-±3.39	<0.0001
LvDd (mm)	44.77±3.59	45.97±3.87	<0.0001
LvSd (mm)	28.26±3.98	29.25±3.53	<0.0001
IVST (mm)	9.7±0.85	10.03±0.73	<0.0001
PWT (mm)	9.87±0.89	10.18±0.79	<0.0001

(*Continued*)

Table 1 (Continued).

	VFA		P-value
	Low-V (VFA≤100 cm^2)	High-V (VFA>100 cm^2)	
LVM (g)	148.51±28.33	161.70±28.51	<0.0001
LVMI (g/m^2)	87.21±15.97	90.33±14.86	<0.0001

Note: Data are given as the mean ± SD, median [interquartile range], or as n (%). **Abbreviations:** ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; Cr, creatinine; DBP, diastolic blood pressure; FC-P, fasting c-peptide; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, high-density lipoprotein cholesterol; IVST, interventricular septum thickness; LDL-C, low-density lipoprotein cholesterol; LvDd, left ventricular diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index; LvSd, left ventricular end systolic diameter; PWT, posterior wall thickness; SBP, systolic blood pressure; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglycerides; VFA, visceral fat area.

(Table 5). According to the prevalence of hypertension, the patients were divided into the hypertensive group and the non-hypertensive group. Compared with the non-hypertensive group, the levels of VFA, SFA, WHR, HOMA-IR in the hypertensive group were significantly increased ($p<0.05$ or $p<0.01$). Compared with patients without hypertension, all cardiac hemodynamic parameters were noticeably increased in patients with hypertension ($p<0.001$), except for LVEF.

Figure 1 shows the performance for predicting the end-point among the markers for cardiovascular disease risk. The AUC of the markers were as follows: VFA 0.61 (95% CI: 0.56–0.66), SFA 0.60 (95% CI: 0.55–0.64) and WHR

Table 2 Correlation Between VFA and Cardiac Hemodynamics

	VFA (cm^2)	
	r	P
LVMI (mm)	0.120	0.004
LVEF (%)	−0.107	0.011
LVM (g)	0.249	<0.0001
LvDd (mm)	0.185	<0.0001
LvSd (mm)	0.211	<0.0001
IVST (mm)	0.240	<0.0001
PWT (mm)	0.237	<0.0001
Left atrial diameter(mm)	0.375	<0.0001
Internal diameter of aortic root(mm)	0.243	<0.0001

Abbreviations: IVST, interventricular septum thickness; LvDd, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMI, left ventricular mass index; LvSd, left ventricular end systolic diameter; PWT, posterior wall thickness; VFA, visceral fat area.

Table 3 Pearson's Correlation Between Cardiac Hemodynamics and Clinical Data

	LVMI		LVEF		LVM		Left Atrial Diameter		Internal Diameter of Aortic Root		LvSd	
	r	p	r	p	r	p	r	p	r	p	r	p
Hypertension (n %)	0.203	<0.0001	−0.049	n.s.	0.292	<0.0001	0.213	<0.0001	0.144	<0.0001	0.242	<0.0001
Dyslipidemia (n%)	−0.41	n.s.	−0.038	n.s.	−0.003	n.s.	0.022	n.s.	−0.04	n.s.	0.055	n.s.
SFA (cm^2)	0.132	0.02	−0.81	n.s.	0.23	<0.0001	0.372	<0.0001	0.16	<0.0001	0.164	<0.0001
WHR	0.092	0.028	−0.067	n.s.	0.221	<0.0001	0.337	<0.0001	0.23	<0.0001	0.123	0.003
BMI (kg/m^2)	0.156	<0.0001	−0.064	n.s.	0.34	<0.0001	0.476	<0.0001	0.238	<0.0001	0.25	<0.0001
SBP (mmHg)	0.181	<0.0001	−0.01	n.s.	0.209	<0.0001	0.218	<0.0001	0.177	<0.0001	0.106	0.012
DBP (mmHg)	0.061	n.s.	−0.06	n.s.	0.119	0.004	0.106	0.011	0.222	<0.0001	0.1	0.017
Heart rate(bpm)	−0.106	0.011	−0.025	n.s.	−0.122	0.004	−0.149	<0.0001	−0.054	n.s.	−0.084	0.041
HbA1c (%)	−0.01	n.s.	0.026	n.s.	0.018	n.s.	−0.024	n.s.	0.077	n.s.	−0.027	n.s.
FC-P	0.03	n.s.	−0.033	n.s.	0.139	0.001	0.191	<0.0001	0.105	0.012	0.098	0.019
FBG	0.037	n.s.	0.05	n.s.	0.059	n.s.	−0.027	n.s.	0.077	n.s.	−0.004	n.s.
HOMA-IR	0.069	n.s.	−0.045	n.s.	0.111	0.008	0.185	<0.0001	0.1	0.017	0.054	n.s.
TG (mmol/L)	−0.025	n.s.	−0.017	n.s.	0.006	n.s.	0.065	n.s.	0.037	n.s.	0.017	n.s.
TC (mmol/L)	−0.099	0.018	0.011	n.s.	−0.107	0.11	−0.02	n.s.	−0.081	n.s.	−0.052	n.s.
HDL-C (mmol/L)	−0.084	0.046	0.018	n.s.	−0.074	n.s.	−0.073	n.s.	−0.109	0.009	−0.037	n.s.
LDL-C (mmol/L)	−0.054	n.s.	−0.001	n.s.	−0.109	0.009	−0.05	n.s.	−0.069	n.s.	−0.071	n.s.
ALT	−0.05	n.s.	−0.113	0.007	0.062	n.s.	0.073	n.s.	0.044	n.s.	0.09	0.032
AST	−0.036	n.s.	−0.146	<0.0001	0.015	n.s.	0.073	n.s.	0.023	n.s.	0.079	n.s.
Cr	0.11	0.009	−0.181	<0.0001	0.198	<0.0001	0.08	n.s.	0.223	<0.0001	0.185	<0.0001

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; Cr, creatinine; DBP, diastolic blood pressure; FC-P, fasting c-peptide; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, high-density lipoprotein cholesterol; IVST, interventricular septum thickness; LDL-C, low-density lipoprotein cholesterol; LvDd, left ventricular diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index; LvSd, left ventricular end systolic diameter; PWT, posterior wall thickness; SBP, systolic blood pressure; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglycerides; VFA, visceral fat area.

Table 4 Multivariate Linear Regression Analysis Between Cardiac Hemodynamics and VFA

	LVMI		LVEF		Left Atrial Diameter		Internal Diameter of Aortic Root		LvSd	
	β	p	β	p	β	p	β	p	β	p
Model 1	0.04	0.016	−0.01	0.023	0.035	<0.0001	0.014	<0.0001	0.017	<0.0001
Model 2	0.035	0.044	−0.011	0.012	0.035	<0.0001	0.013	<0.0001	0.018	<0.0001
Model 3	0.036	0.039	−0.011	0.014	0.036	<0.0001	0.013	<0.0001	0.018	<0.0001

Notes: Model 1 was adjusted for sex and age. Model 2 was adjusted for sex, age, TC, HDL-C, LDL-C. Model 3 was adjusted for sex, age, TC, HDL-C, LDL-C, HbA1c.
Abbreviations: LVMI, left ventricular mass index; LvSd, left ventricular end systolic diameter; VFA, visceral fat area.

Table 5 Clinical Characteristics According to the Prevalence of Hypertension

|	Hypertension		P-value
	N-Hypertensive (n=323)	Hypertensive (n=245)	
Age (years)	53.72±11.50	54.46±12.73	n.s.
Sex (%male)	53.9	66.1	0.003
Metabolic factors			
VFA (cm²)	83.38±37.65	97.24±37.33	<0.0001
SFA (cm²)	172.84±63.49	192.99±65.66	<0.0001
WHR	0.93±0.06	0.94±0.07	0.008
BMI(kg/m²)	24.34±3.34	25.70±3.29	<0.0001
SBP(mmHg)	126.84±17.57	129.16±17.65	n.s.
DBP(mmHg)	74.64±10.33	75.20±10.11	n.s.
HbA1c(%)	9.56±2.21	9.45±2.09	n.s.
FC-P	2.37±1.04	2.44±1.02	n.s.
FBG	10.47±3.27	10.25±3.26	n.s.
HOMA-IR	2.74(1.67,4.36)	3.00(1.93,5.28)	0.03
TG (mmol/L)	1.94(1.35,2.86)	1.95(1.38,2.73)	n.s.
TC (mmol/L)	5.03±1.15	4.92±1.11	n.s.
HDL-C(mmol/L)	1.14±0.37	1.11±0.32	n.s.
LDL-C(mmol/L)	2.93±0.89	2.93±2.57	n.s.
ALT	20.20(14.60,32.30)	22.60 (14.50,36.80)	n.s.
AST	16.30(13.10,23.00)	17.10 (13.25,25.20)	n.s.
Cr	57.83±19.27	60.20±17.73	n.s.
Cardiac hemodynamics			
Heart rate(bpm)	80.83±10.96	79.13±11.49	n.s.
Internal diameter of aortic root (mm)	29.36±2.49	30.07±2.60	0.001
Left atrial diameter (mm)	33.96±3.40	35.54±3.81	<0.0001
LvDd (mm)	44.39±3.38	46.22±3.92	<0.0001
LvSd (mm)	27.99±3.76	29.40±3.81	<0.0001
IVST (mm)	9.83±0.85	10.17±0.85	<0.0001
PWT (mm)	9.70±0.82	9.96±0.82	<0.0001
LVM (g)	145.78±25.77	162.56±30.37	<0.0001
LVMI (g/m²)	85.49±14.31	91.90±16.53	<0.0001
LVEF (%)	67.72±3.88	67.33±4.01	n.s.

Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; Cr, creatinine; DBP, diastolic blood pressure; FC-P, fasting c-peptide; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, high-density lipoprotein cholesterol; IVST, interventricular septum thickness; LDL-C, low-density lipoprotein cholesterol; LvDd, left ventricular diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index; LvSd, left ventricular end systolic diameter; PWT, posterior wall thickness; SBP, systolic blood pressure; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglycerides; VFA, visceral fat area.

0.57 (95% CI: 0.52–0.62). The results showed that the area under ROC curve predicted by VFA was larger than that of SFA and WHR, and the difference was considered statistically significant ($p<0.01$). When the VFA was 89.6 cm², the maximum Youden index was 0.174, so 89.6 was the best cut-off value, with a sensitivity of 58% and a specificity of 59.4% (Table 6).

Discussion

Obesity is a major risk factor for type 2 diabetes. Long-term and persistent obesity significantly increases the incidence of diabetes, compared to the general population.[1] What is more, people with abdominal obesity have a much greater risk of diabetes than those with buttock obesity.[25] After the occurrence of diabetes, the glucose and lipid metabolism of the human body is further disturbed, resulting in the increase of blood glucose, blood lipid and fat redistribution, which will to a certain extent aggravate the degree of obesity. Thus, obesity and diabetes form a vicious circle of mutual cause and effect. The risk of cardiovascular disease is increased in diabetics, who account for 65% of all deaths in diabetics.[26] Compared with non-diabetics, T2DM patients have earlier onset, more severe and more extensive cardiovascular disease. The risk of cardiovascular disease in diabetic patients is related to obesity, dyslipidemia, abnormal distribution of fat, IR, etc.[27]

VFA is a commonly used index to evaluate abdominal obesity. Visceral fat, as an important functional organ, is important for cardiometabolic complications. Visceral adipose tissue secretes many bioactive adipocytokines, such as leptin, adiponectin, leptin, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-8, and MCP-1.[8] These adipocytokines are thought to contribute to changes in heart structure and function.[28–30] This study was grouped according to the classification criteria of abdominal obesity, and the analysis showed that SFA, LVMI, LVEF, left atrial diameter, LvDd, IVST, LvSd, PWT levels in high-V groups were higher than those in low-V groups. These findings are similar to those studied in the general population study.[11] For further study, with multiple linear regression analysis of LVMI as a dependent variable, the correlation between VFA and LVMI was significant ($p<0.05$). After adjusting for many factors, the correlation remained. Furthermore, VFA was also an independent determinant of LVEF, left atrial diameter, Internal diameter of aortic root, LvSd ($p<0.05$), after correction according to
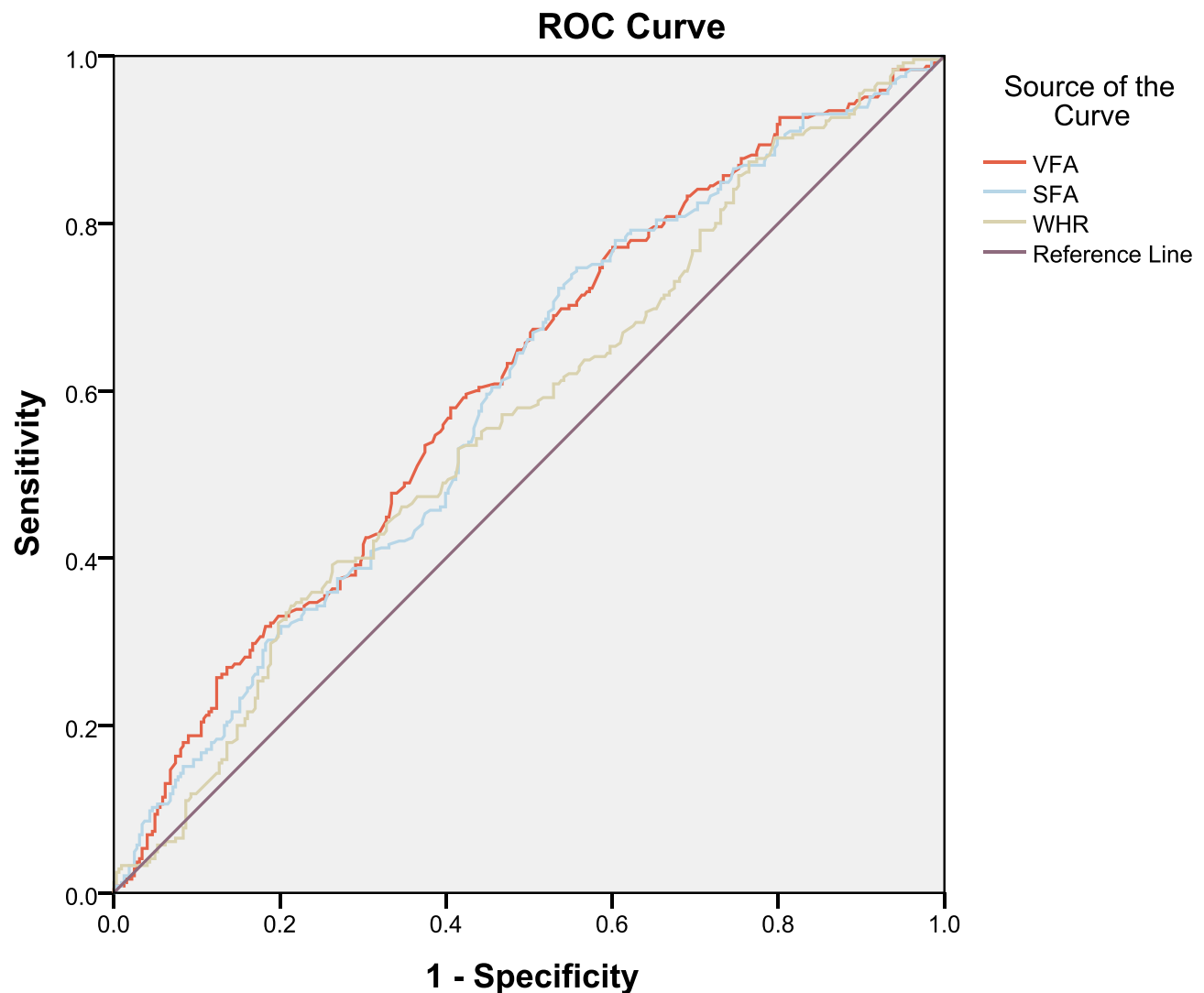
ROC Curve

Diagonal segments are produced by ties.

Figure 1 ROC curve analysis of VFA, SFA and WHR prediction of cardiovascular disease risk. Red, VFA; blue, SFA; brown, WHR.

the above model. The ROC curve also shows that the predictive value of VFA for cardiovascular disease risk is 0.609. Thus, we had observed a significant association between visceral fat and cardiac hemodynamic parameters in all participants.

As obesity, hypertension is also a common cardiovascular risk factor with high prevalence in the world.[31,32] Chronic hypertension causes endothelial dysfunction and inflammation, accelerates lipid deposition, and leads to the occurrence and progression of atherosclerosis and

Table 6 ROC Curve Analysis of VFA in Predicting Cardiovascular Disease Risk

Variables	AUC	95% CI	Sensitivity (%)	Specificity (%)	Cut-Off value	Youden Index
VFA	0.609	0.563–0.656	0.580	0.594	89.60	0.174
SFA	0.595	0.548–0.641	0.747	0.443	153.85	0.190
WHR	0.568	0.520–0.615	0.392	0.737	0.959	0.129

Abbreviations: CI, confidence interval; SFA, subcutaneous fat area; VFA, visceral fat area.

ventricular hypertrophy.[3,33] In this study, 43% of patients had hypertension. Patients were divided into two groups according to the prevalence of hypertension. The level of cardiac hemodynamic parameters was generally higher in patients with hypertension than in those without hypertension, the difference between the groups was statistically significant ($P \leq 0.001$). Patients in the hypertension group had higher VFA than SFA, and both levels were higher than those in the non-hypertension group, consistent with previous studies.[34,35] Although the activation of renin-angiotensin system in diabetic patients is itself associated with oxidative damage and increased apoptotic necrosis of myocardial cells in diabetic heart, the dysfunction of adipose tissue is caused by visceral fat accumulation also produces angiotensin, thus inducing systemic hypertension.[36] The pathogenesis of obesity and hypertension is complex and sometimes interdependent. The main role, other than endothelium and adipokines, is attributed to the genetic, to the environmental factors, to the sympathetic nervous system, to renal and adrenal function, and to the insulin resistance.[37]

WHR is also a common indicator of abdominal obesity. WHR was more efficient than WC and BMI to identify cardiometabolic risk factors in non-obese Chinese.[31] On this basis, we found that VFA has a better predictive value than SFA and WHR. In line with other findings,[38,39] our data showed that HbA1c, HOMA-IR, fasting C-peptide and Hb in the High-VFA group were higher than those in the Low-VFA group. Sogabe[40] suggested that there was a correlation between VFA and liver enzyme spectrum, inconsistent with the results of this study. Nevertheless, data resulting from human studies are conflicting, these inconsistencies most likely result from variations in studied subjects: genetic background, sex and age, sample size and assay methods used.

Several limitations of the present study should be considered. First, our study population is only limited to primarily Han Chinese, the conclusions drawn from the data are not generally representative. Second, due to the cross-sectional nature of the study, we cannot draw a causal relationship between VFA and cardiac hemodynamics. Further longitudinal follow-up studies are needed to verify if visceral fat could be a therapeutic target for preventing the progression of CVD in T2DM.

Conclusion

The above results together confirm that excess visceral fat was significantly correlated with cardiac hemodynamic

parameters and hypertension in T2DM. The VFA has advantages as a predictor of visceral obesity and is significantly associated with the development of CVD in T2DM.

Compliance with Ethical Standards

The study was approved by the Biomedical Research Ethics Committee of the Affiliated Hospital of Jiangsu University, Zhenjiang, China, and performed in accordance with the Declaration of Helsinki. All participants had informed consent to the purpose of the study.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest.

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