

The Relationship Between Visceral Fat Obesity and the Atherogenic Combined Index in Patients with Type 2 Diabetes Mellitus

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Purpose: The presence of abdominal obesity, characterized by an accumulation of visceral fat area (VFA), has been identified as a significant risk factor for the development of type 2 diabetes mellitus (T2DM) and its associated complications. Substantial evidence has proven that it's strongly associated with lipid metabolism. The atherogenic combined index (ACI) is a novel non-traditional lipid index, but there is no clear evidence to explore the relationship with visceral fat obesity (VFO). Our study aimed to interpret this relationship in T2DM.

Methods: In accordance with the research objective, this cross-sectional study retrospectively included 2,323 patients with T2DM from February 2020 to March 2023. The clinical and biochemical data were measured. VFA measurement was conducted at the umbilicus level using a dual bioelectrical impedance analysis. VFO was redefined as $VFA \geq 100 \text{ cm}^2$. The formula of ACI was based on triglyceride, non-high-density lipoprotein cholesterol and high-density lipoprotein cholesterol. Patients were categorized into the VFO group and the non-VFO group, which were then further divided according to gender.

Results: The incidence of VFO was found to be higher among males than females. Among participants of both genders, the level of ACI was found to be significantly increased in the VFO group compared with the non-VFO group (both $p < 0.001$). As the ACI increased, the incidence of VFO increased concomitantly. Univariate correlation analysis revealed a positive correlation between ACI and VFO (correlation coefficient: 0.223, $p < 0.001$ in females; correlation coefficient: 0.302, $p < 0.001$ in males). Logistic regression analysis indicated that ACI was associated with VFO independently (OR: 1.797, $p = 0.029$ in females; OR: 2.501, $p < 0.001$ in males).

Conclusion: The ACI had been found to be independently correlated with VFO in patients with T2DM in both genders. This finding had the potential to facilitate the monitoring and management of VFO in T2DM.

Keywords: atherogenic combined index, type 2 diabetes mellitus, visceral fat obesity, visceral fat area

Introduction

Obesity represents a considerable public health concern, exhibiting a strong correlation with diabetes and its related complications. In particular, abdominal obesity, characterized by an increased visceral fat area (VFA), plays a critical role in the development and progression of diabetes and its complications.¹ The risk of diabetes-related complications is further aggravated in patients with type 2 diabetes mellitus (T2DM), due to excessive visceral fat.²⁻⁵ The International Atherosclerosis Society and the International Chair on Cardiometabolic Risk Working Group on Visceral Obesity provide a synopsis of the extant evidence for visceral adiposity as emerging risk factors for T2DM, atherosclerosis and cardiovascular disease, which suggests that public health messages should emphasize visceral fat in addition to excess weight.⁶ Consequently, ascertaining risk factors associated with increased VFA in patients with T2DM is imperative for enhancing metabolic risk assessment and administration.

It is universally recognized that computed tomography (CT) and magnetic resonance imaging (MRI) are the gold standards for diagnosing VFA,⁷ but CT is costly and involves ionizing radiation, while MRI is time-consuming. Finding easy indices to use to monitor visceral fat obesity (VFO) is critical. Excess visceral adipose tissue releases large amounts



of fatty acids, thereby affecting lipid metabolism.⁸ Traditional and non-traditional lipid markers have been shown to be closely associated with VFA, such as cholesterol (TC), triglyceride (TG), remnant cholesterol (RC), atherogenic index of plasma (AIP) and others.^{9,10} This study introduced a novel lipid index, the atherogenic combined index (ACI), calculated from TG, non-high-density lipoprotein cholesterol (non-HDL-c) and HDL-c levels, which capacity to reflect a more comprehensive lipid profile distinguishes it from other lipid indices and emerging evidence from multiple studies supports its potential utility as a biomarker for coronary artery disease (CAD) and metabolic dysfunction-associated steatotic liver disease (MASLD).^{11,12} Therefore, we speculated that this index may be closely related to VFO. Up to the present, the extant research in this area is limited, and the potential relationships between ACI and VFO have yet to be explored. The objective of this study was to explore the potential correlation between ACI and VFO, with the purpose that ACI may facilitate the early monitoring and management of VFO in patients with T2DM.

However, CT and MRI are not suitable for routine screening, whereas bioelectrical impedance analysis (BIA) represents a more accessible, efficient, and relatively inexpensive approach for VFA assessment and has been recommended as a useful clinical tool for VFA measurement.^{13,14} Additionally, epidemiological and clinical evidence have confirmed distinct gender-related differences in visceral fat distribution, lipid profiles and cardiovascular disease incidence, with males have a higher prevalence of VFO, reproductive-age females exhibit naturally higher HDL-c levels and sex is significantly associated with cardiovascular disease incidence in patients with T2DM.^{15–17} Therefore, this study employed a sex-stratified approach to examine the relationship between ACI and VFO, with VFA assessment by BIA.

Methods

Study Participants

This cross-sectional study retrospectively collected data on patients with T2DM who were hospitalized at Linyi People's Hospital from February 2020 to March 2023. The criteria for inclusion were as follows: (1) A diagnosis of T2DM was made based on the 1999 World Health Organization diagnostic criteria; (2) The age of the subject was 18 years or older. The following exclusion criteria were applied: (1) Type 1 diabetes, acute diabetic conditions, or other particular forms of diabetes; (2) Severe liver dysfunction, defined as a history of liver failure or a current diagnosis, and severe kidney dysfunction; (3) The lack of case data, including patients with missing VFA data and missing data for calculating ACI.

General Conditions and Physical Examinations

The participant's basic information, including age, sex, height, weight, duration of diabetes mellitus, smoking and alcohol habits, and blood pressure data measured with a standard electronic sphygmomanometer, was obtained from medical records. Body mass index (BMI) was calculated based on weight and height, using the formula $BMI = \text{weight (kg)} / \text{height (m)}^2$. VFA measurement was conducted at the umbilicus level using a dual BIA (Omron HDS-2000, Kyoto, Japan).¹⁸ The VFO was defined as $VFA \geq 100 \text{ cm}^2$.

Biochemical Measurements and Indices Calculations

After a full night of fasting, routine blood tests were conducted on patients in the early morning hours, encompassing a comprehensive range of parameters including fasting plasma glucose (FPG), TC, TG, HDL-c, low-density lipoprotein cholesterol (LDL-c), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ -glutamyl transferase (GGT), serum creatinine (Scr), uric acid (UA) and platelets. Hemoglobin (Hb) was measured utilizing biochemical autoanalyzer (Cobas c 702, Roche, Germany), while glycated hemoglobin (HbA1c) levels were determined employing high-performance liquid chromatography. The calculation formulas for the corresponding lipid indices are outlined below. The indicators of lipid metabolism in this study were expressed in mmol/L. When calculating ACI, the relevant variables were converted from mmol/L to mg/dL according to standard conversion ratios. (1) $TG/HDL\text{-}c = TG/HDL\text{-}c$;¹⁹ (2) $\text{Non-HDL-c} = TC - HDL\text{-}c$;²⁰ (3) $AIP = \log_{10} (TG/HDL\text{-}c)$;²¹ (4) $\text{Lipoprotein combine index (LCI)} = TC \times TG \times LDL\text{-}c / HDL\text{-}c$;²² (5) $\text{Platelet/HDL-c ratio (PHR)} = \text{platelet} / HDL\text{-}c$;²³ (6) $\text{Castelli's risk index I (CRI-I)} = TC / HDL\text{-}c$;²⁴ (7) $\text{Castelli's risk index II (CRI-II)} = LDL\text{-}c / HDL\text{-}c$;²⁴ (8) $RC = TC - HDL\text{-}c - LDL\text{-}c$;²⁵ (9) $\text{Atherogenic coefficient (AC)} = (TC - HDL\text{-}c) / HDL\text{-}c$;²⁶ (10) $ACI = \log_{10} (TG \times \text{Non-HDL-c} / HDL\text{-}c)$.¹²

Statistical Analysis

The data were analyzed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Continuous variables that were normally distributed were presented as the mean $\pm$ standard deviation (SD), while those that were abnormally distributed were presented as the median and interquartile range. The independent-samples *t*-test and Mann–Whitney *U*-test were utilized to conduct a comparative analysis of continuous variables that were distributed normally and abnormally, respectively. The chi-square test was utilized for the purpose of conducting comparisons between categorical variables. For the data of the ACI categorical groups, we used the analysis of variance (ANOVA) to perform multiple comparison tests for normally distributed data and the Kruskal–Wallis test to address the issue of abnormally distributed data. Univariate correlation analysis was performed for selecting the variables with statistical significance. Correlation coefficients and variance inflation factors (VIF) were used to assess multicollinearity between lipid indices. The independent variables related to the VFO were analyzed using binary logistic stepwise forward regression. The statistical significance of the observed findings was determined by a two-tailed *P*-value cut off of < 0.05 .

Results

Baseline Clinical and Biochemical Characteristics

Table 1 presents a comprehensive overview of the clinical characteristics exhibited by the participants in this study. In both male and female groups, compared with the non-VFO group, the following variables were significantly higher (all $p < 0.05$):

Table 1 Clinical and Biochemical Characteristics by Presence of VFO

Variables	All	Female			Male		
		Non-VFO Group	VFO Group	p value	Non-VFO Group	VFO Group	p value
Numbers	2323	812	334		527	650	
Sex (Females, n, %)	1146 (49.3%)						
Age (years)	57.3 $\pm$ 12.3	58.7 $\pm$ 10.9	60.6 $\pm$ 13.1	0.013	56.3 $\pm$ 12.3	54.6 $\pm$ 12.9	0.025
Duration of diabetes (years)	7.0 (2.0–12.0)	7.0 (2.0–12.0)	6.00 (1.0–13.0)	0.564	7.0 (1.0–13.0)	6.0 (1.0–12.0)	0.363
Smoking (%)	450 (19.4%)	5 (0.6%)	1 (0.3%)	0.823	163 (30.9%)	281 (43.2%)	< 0.001
Drinking (%)	428 (18.4%)	4 (0.5%)	2 (0.6%)	1.000	166 (31.5%)	256 (39.4%)	0.005
BMI (kg/m ²)	25.62 $\pm$ 3.56	24.01 $\pm$ 2.87	28.63 $\pm$ 3.62	< 0.001	23.78 $\pm$ 2.51	27.58 $\pm$ 2.94	< 0.001
VFA	92.00 (67.00–121.00)	69.00 (52.00–83.00)	120.00 (109.00–138.25)	< 0.001	75.00 (53.00–89.00)	130.00 (116.00–153.00)	< 0.001
SFA	181.00 (139.25–228.00)	158.00 (121.00–200.00)	234.50 (199.75–284.25)	< 0.001	143.00 (114.00–175.00)	215.00 (184.00–253.00)	< 0.001
SBP (mmHg)	130.4 $\pm$ 18.6	129.6 $\pm$ 19.2	136.3 $\pm$ 19.6	< 0.001	125.4 $\pm$ 16.7	132.3 $\pm$ 17.8	< 0.001
DBP (mmHg)	81.1 $\pm$ 11.6	78.5 $\pm$ 10.7	81.6 $\pm$ 12.4	< 0.001	79.9 $\pm$ 10.9	84.9 $\pm$ 11.8	< 0.001
TC (mmol/L)	4.82 $\pm$ 1.22	4.99 $\pm$ 1.23	5.06 $\pm$ 1.23	0.392	4.58 $\pm$ 1.14	4.70 $\pm$ 1.22	0.082
TG (mmol/L)	1.41 (1.02–2.08)	1.30 (0.93–1.83)	1.71 (1.23–2.38)	< 0.001	1.17 (0.83–1.72)	1.64 (1.21–2.57)	< 0.001
HDL-c (mmol/L)	1.16 $\pm$ 0.30	1.27 $\pm$ 0.31	1.17 $\pm$ 0.26	< 0.001	1.15 $\pm$ 0.29	1.02 $\pm$ 0.23	< 0.001
LDL-c (mmol/L)	3.05 $\pm$ 1.03	3.15 $\pm$ 1.04	3.19 $\pm$ 1.07	0.594	2.91 $\pm$ 0.96	2.96 $\pm$ 1.03	0.349
FPG (mmol/L)	8.96 $\pm$ 3.48	8.66 $\pm$ 3.41	9.56 $\pm$ 3.77	< 0.001	8.78 $\pm$ 3.59	9.18 $\pm$ 3.26	0.048
HbA1c (%)	9.36 $\pm$ 2.22	9.32 $\pm$ 2.28	9.53 $\pm$ 2.02	0.147	9.60 $\pm$ 2.50	9.12 $\pm$ 1.97	< 0.001
AST (U/L)	17.30 (14.20–21.70)	16.70 (13.70–21.00)	17.30 (14.20–21.80)	0.052	17.60 (14.10–21.20)	18.00 (15.00–22.63)	0.009
ALT (U/L)	18.30 (13.60–26.00)	16.00 (12.30–22.60)	17.75 (13.00–26.00)	0.004	18.50 (13.90–24.10)	21.65 (15.80–33.00)	< 0.001
GGT (U/L)	21.60 (16.00–31.00)	18.00 (13.00–24.00)	22.00 (16.00–30.13)	< 0.001	21.00 (16.00–30.00)	28.10 (21.00–42.30)	< 0.001
UA (μ mol/L)	287.93 $\pm$ 92.84	250.00 $\pm$ 82.12	288.04 $\pm$ 94.15	< 0.001	296.20 $\pm$ 86.02	328.56 $\pm$ 91.43	< 0.001
Scr (μ mol/L)	65.38 $\pm$ 19.49	56.18 $\pm$ 14.65	58.31 $\pm$ 16.63	0.032	72.50 $\pm$ 19.56	74.75 $\pm$ 19.43	0.049
Hb (g/L)	142.67 $\pm$ 19.26	133.23 $\pm$ 18.88	134.50 $\pm$ 17.07	0.271	149.08 $\pm$ 16.70	153.48 $\pm$ 14.48	< 0.001
Platelet (10^9 /L)	239.87 $\pm$ 63.66	254.70 $\pm$ 68.66	261.71 $\pm$ 60.38	0.089	220.93 $\pm$ 58.44	225.45 $\pm$ 54.28	0.176
TG/HDL-c	1.26 (0.81–2.06)	1.04 (0.68–1.63)	1.48 (1.04–2.22)	< 0.001	1.04 (0.69–1.65)	1.68 (1.12–2.74)	< 0.001
Non-HDL-c	3.67 $\pm$ 1.17	3.72 $\pm$ 1.17	3.89 $\pm$ 1.19	0.025	3.43 $\pm$ 1.11	3.68 $\pm$ 1.19	< 0.001
AIP	0.12 $\pm$ 0.31	0.03 $\pm$ 0.29	0.18 $\pm$ 0.26	< 0.001	0.05 $\pm$ 0.31	0.26 $\pm$ 0.30	< 0.001
LCI	18.13 (9.05–34.34)	15.90 (8.07–29.14)	23.41 (12.71–41.74)	< 0.001	13.86 (6.76–25.76)	22.74 (12.54–42.95)	< 0.001
PHR	220.76 $\pm$ 83.65	214.03 $\pm$ 86.16	236.58 $\pm$ 82.02	< 0.001	204.89 $\pm$ 78.56	234.00 $\pm$ 82.11	< 0.001
CRI-I	4.36 $\pm$ 1.38	4.09 $\pm$ 1.23	4.48 $\pm$ 1.28	< 0.001	4.17 $\pm$ 1.33	4.80 $\pm$ 1.53	< 0.001

(Continued)

Table 1 (Continued).

Variables	All	Female			Male		
		Non-VFO Group	VFO Group	p value	Non-VFO Group	VFO Group	p value
CRI-II	2.75 ± 1.04	2.58 ± 0.96	2.82 ± 1.02	< 0.001	2.65 ± 1.00	3.01 ± 1.12	< 0.001
RC (mmol/L)	0.52 (0.30–0.79)	0.51 (0.30–0.72)	0.63 (0.41–0.93)	< 0.001	0.42 (0.21–0.68)	0.57 (0.35–0.88)	< 0.001
Non-HDL/HDL-c	3.21 (2.38–4.11)	2.95 (2.20–3.77)	3.39 (2.55–4.20)	< 0.001	2.94 (2.22–3.92)	3.64 (2.81–4.53)	< 0.001
LDL-c/HDL-c	2.66 (2.01–3.38)	2.47 (1.89–3.18)	2.78 (2.05–3.47)	< 0.001	2.55 (1.94–3.28)	2.96 (2.29–3.56)	< 0.001
TC/HDL-c	4.21 (3.38–5.11)	3.95 (3.20–4.77)	4.39 (3.55–5.20)	< 0.001	3.94 (3.22–4.92)	4.64 (3.81–5.53)	< 0.001
RC/HDL-c	0.46 (0.25–0.76)	0.41 (0.22–0.63)	0.54 (0.33–0.84)	< 0.001	0.36 (0.17–0.65)	0.59 (0.33–0.94)	< 0.001
AC	3.36 ± 1.38	3.09 ± 1.23	3.48 ± 1.28	< 0.001	3.17 ± 1.33	3.80 ± 1.53	< 0.001
ACI	2.61 ± 0.38	2.53 ± 0.36	2.70 ± 0.33	< 0.001	2.50 ± 0.39	2.75 ± 0.39	< 0.001

Note: Data were presented as mean ± SD for normally distributed variables, and median (interquartile ranges) for abnormal distributions. Independent samples *T* test and Mann–Whitney *U*-test were used for comparisons of normally and abnormally distributed continuous variables between non-VFO and VFO groups, respectively. Categorical variables were presented as percentage (%) and were compared by chi-square test. Statistical differences were defined by a *p* value (two-tailed) less than 0.05.

Abbreviations: VFA, visceral fat area; BMI, body mass index; SFA, subcutaneous fat area; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ -Glutamyl transpeptidase; UA, uric acid; Scr, serum creatinine; Hb, hemoglobin; TG/HDL-c, TG/HDL-c ratio; Non-HDL-c, Non-high-density lipoprotein cholesterol; AIP, atherogenic index of plasma; LCI, lipoprotein combine index; PHR, platelet/HDL-ratio; CRI-I, Castelli's risk index I; CRI-II, Castelli's risk index II; RC, remnant cholesterol; AC, Atherogenic Coefficient; ACI, atherogenic combined index.

BMI, VFA, SFA, SBP, DBP, TG, FPG, ALT, GGT, UA, Scr, TG/HDL-c, Non-HDL-c, AIP, LCI, PHR, CRI-I, CRI-II, RC, Non-HDL/HDL-c, LDL-c/HDL-c, TC/HDL-c, RC/HDL-c, AC and ACI. Furthermore, HDL-c levels were significantly lower in the VFO group ($p < 0.001$). No statistically significant differences were observed in duration of diabetes, TC, LDL-c and platelets (all $p > 0.05$). In the male group, the percentage of smoking and drinking, AST and Hb demonstrated a marked increase (all $p < 0.05$), while age and HbA1c levels were lower in the VFO group ($p < 0.05$). In the female group, age revealed a marked increase ($p = 0.013$). Nonetheless, no discernible differences were observed with respect to the percentage of smoking and drinking, HbA1c, AST and Hb in females (all $p > 0.05$). In addition, according to the ACI levels, the participants were divided into four groups: for males, Q1 (1.53–2.36), Q2 (2.36–2.63), Q3 (2.63–2.89) and Q4 (2.89–3.94); for females, Q1 (1.38–2.32), Q2 (2.32–2.59), Q3 (2.59–2.80) and Q4 (2.80–3.73). [Figure 1](#) shows the change in VFO incidence according

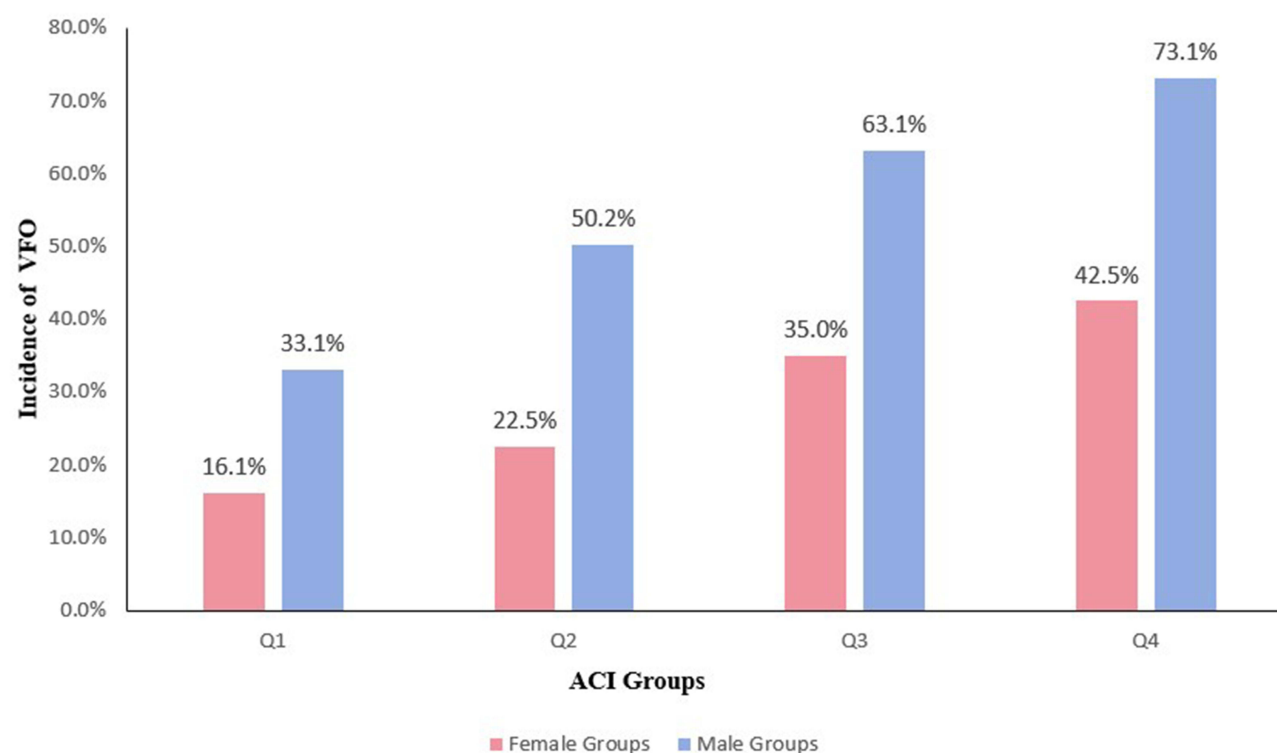


Figure 1 The bar chart shows the prevalence of VFO stratified by ACI quartiles. Blue represents male groups, red represents female groups.

to ACI quartiles. Results showed that as the ACI quartile grouping increased, the incidence of VFO in males was 33.1%, 50.2%, 63.1% and 73.1%, while the incidence in females was 16.1%, 22.5%, 35.0% and 42.5%. Additionally, we examined other anthropometric variables, biochemical variables and metabolic indicators, to observe how they changed with increasing ACI quartiles (as shown in [Appendix Table 1](#)).

Univariate Analysis

As demonstrated in [Table 2](#), the association between VFO and each variable was assessed employing Spearman correlation analysis. In two groups, the findings indicated a positive correlation between BMI, SFA, SBP, DBP, TG, FPG, ALT, GGT, UA, Hb, TG/HDL-c, Non-HDL-c, AIP, LCI, PHR, CRI-I, CRI-II, RC, Non-HDL/HDL-c, LDL-c/HDL-c, TC/HDL-c, RC/HDL-c, AC and ACI with VFO (all $p < 0.05$). HDL-c was found to be negatively correlated with VFO (all $p < 0.001$). Duration of diabetes, TC and LDL-c were found to be non-significantly correlated with VFO (all $p > 0.05$). In the male group, the findings revealed a positive correlation between the smoking, drinking, AST and Scr with VFO (all $p < 0.05$). Age and HbA1c levels were found to be negatively correlated with VFO (all $p < 0.05$). No

Table 2 The Correlation Between VFO and Different Variables by Univariate Analysis

Variables	Female		Male	
	Correlation Coefficient	p value	Correlation Coefficient	p value
Age	0.094	0.001	−0.060	0.038
Duration of diabetes	−0.017	0.564	−0.027	0.364
Smoking	−0.020	0.500	0.126	<0.001
Drinking	0.007	0.821	0.082	0.005
BMI	0.548	<0.001	0.605	<0.001
SFA	0.509	<0.001	0.639	<0.001
SBP	0.155	<0.001	0.200	<0.001
DBP	0.116	<0.001	0.214	<0.001
TC	0.036	0.225	0.053	0.071
TG	0.245	<0.001	0.315	<0.001
HDL-c	−0.157	<0.001	−0.241	<0.001
LDL-c	0.024	0.409	0.034	0.237
FPG	0.115	<0.001	0.086	0.003
HbA1c	0.061	0.044	−0.085	0.004
AST	0.057	0.052	0.076	0.009
ALT	0.085	0.004	0.179	<0.001
GGT	0.197	<0.001	0.291	<0.001
UA	0.204	<0.001	0.194	<0.001
Scr	0.058	0.050	0.090	0.002
Hb	0.065	0.028	0.134	<0.001
Platelet	0.061	0.040	0.042	0.151
TG/HDL-c	0.251	<0.001	0.333	<0.001
Non-HDL-c	0.074	0.012	0.117	<0.001
AIP	0.251	<0.001	0.333	<0.001
LCI	0.183	<0.001	0.258	<0.001
PHR	0.146	<0.001	0.197	<0.001
CRI-I	0.146	<0.001	0.228	<0.001
CRI-II	0.114	<0.001	0.173	<0.001
RC	0.166	<0.001	0.221	<0.001
Non-HDL/HDL-c	0.146	<0.001	0.228	<0.001
LDL-c/HDL-c	0.114	<0.001	0.173	<0.001

(Continued)

Table 2 (Continued).

Variables	Female		Male	
	Correlation Coefficient	p value	Correlation Coefficient	p value
TC/HDL-c	0.146	<0.001	0.228	<0.001
RC/HDL-c	0.183	<0.001	0.257	<0.001
AC	0.146	<0.001	0.228	<0.001
ACI	0.223	<0.001	0.302	<0.001

Note: VFO was defined as VFA ≥ 100 cm². Correlation coefficients between VFO and different variables were determined by Spearman correlation analysis.

Abbreviations: BMI, body mass index; SFA, subcutaneous fat area; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ -Glutamyl transpeptidase; UA, uric acid; Scr, serum creatinine; Hb, hemoglobin; TG/HDL-c, TG/HDL-c ratio; Non-HDL-c, Non-high-density lipoprotein cholesterol; AIP, atherogenic index of plasma; LCI, lipoprotein combine index; PHR, platelet/HDL-ratio; CRI-I, Castelli's risk index I; CRI-II, Castelli's risk index II; RC, remnant cholesterol; AC, Atherogenic Coefficient. ACI, atherogenic combined index.

statistically significant differences were observed with respect to the platelets ($p = 0.151$) in males. As shown in [Figure 2A](#), the Spearman correlation coefficients between variables in the male group range from -0.5 to 1.0 , where 1.0 represents a perfect positive correlation and -0.5 represents a moderately negative correlation. The findings revealed a positive correlation between VFO and age, HbA1c and platelets in the female group (all $p < 0.05$). Smoking, drinking, AST and Scr were found to be non-significant correlations of VFO in females (all $p > 0.05$). As demonstrated in [Figure 2B](#), the Spearman correlation coefficients between the variables in the female group range from -0.5 to 1.0 , where 1.0 represents a perfect positive correlation and -0.5 represents a moderately negative correlation.

Logistic Regression Analysis

The potential confounding variables initially included in this study were based on literature reports from previous similar studies and clinically verified factors associated with obesity. As mentioned above, variables with statistical significance in the univariate correlation analysis were included in the regression model. VFO was served as the dependent variable ([Table 3](#)). In the male group, our study adjusting for age, smoking, drinking, BMI, SFA, SBP, DBP, TG, HDL-c, FPG, HbA1c, AST, ALT, GGT, UA, Scr, Hb, TG/HDL-c, Non-HDL-c, AIP, LCI, PHR, CRI-I, CRI-II, RC, Non-HDL/HDL-c, LDL-c/HDL-c, TC/HDL-c, RC/HDL-c, AC and ACI, the results showed that ACI (OR: 2.501; 95% CI: 1.585–3.946), smoking (OR: 1.745; 95% CI: 1.248–2.439), BMI (OR: 1.278; 95% CI: 1.164–1.404), SFA (OR: 1.025; 95% CI: 1.019–1.030), DBP (OR: 1.025; 95% CI: 1.011–1.041), age (OR: 1.023; 95% CI: 1.008–1.039) and GGT (OR: 1.012; 95% CI: 1.002–1.022) were independently associated with VFO. [Figure 3A](#) shows a forest plot of the factors identified by the male group as being independently associated with VFO through logistic regression analysis. In the female group, the following parameters were entered into the logistic regression analysis as independent variables according to the findings of univariate analysis ([Table 3](#)): age, BMI, SFA, SBP, DBP, TG, HDL-c, FPG, HbA1c, ALT, GGT, UA, Hb, platelets, TG/HDL-c, Non-HDL-c, AIP, LCI, PHR, CRI-I, CRI-II, RC, Non-HDL/HDL-c, LDL-c/HDL-c, TC/HDL-c, RC/HDL-c, AC and ACI. The results of the study indicated that ACI (OR: 1.797; 95% CI: 1.061–3.045), BMI (OR: 1.478; 95% CI: 1.356–1.612), FPG (OR: 1.051; 95% CI: 1.000–1.104), age (OR: 1.043; 95% CI: 1.028–1.060), GGT (OR: 1.016; 95% CI: 1.001–1.032) and SFA (OR: 1.005; 95% CI: 1.001–1.009) were independently associated with VFO. [Figure 3B](#) presents a forest plot of the factors identified by the female group through logistic regression analysis that are independently associated with VFO.

Furthermore, it is necessary to point out that due to the similarity of the metrics that comprised the lipid indices, we performed a multicollinearity analysis. We assessed multicollinearity among these variables using correlation coefficients and VIF. The results showed that there was indeed a covariance problem between TG/HDL-c, Non-HDL-c, AIP, LCI, CRI-I, CRI-II, RC, Non-HDL-c/HDL-c, LDL-c/HDL-c, TC/HDL-c, RC/HDL-c, AC and ACI (as

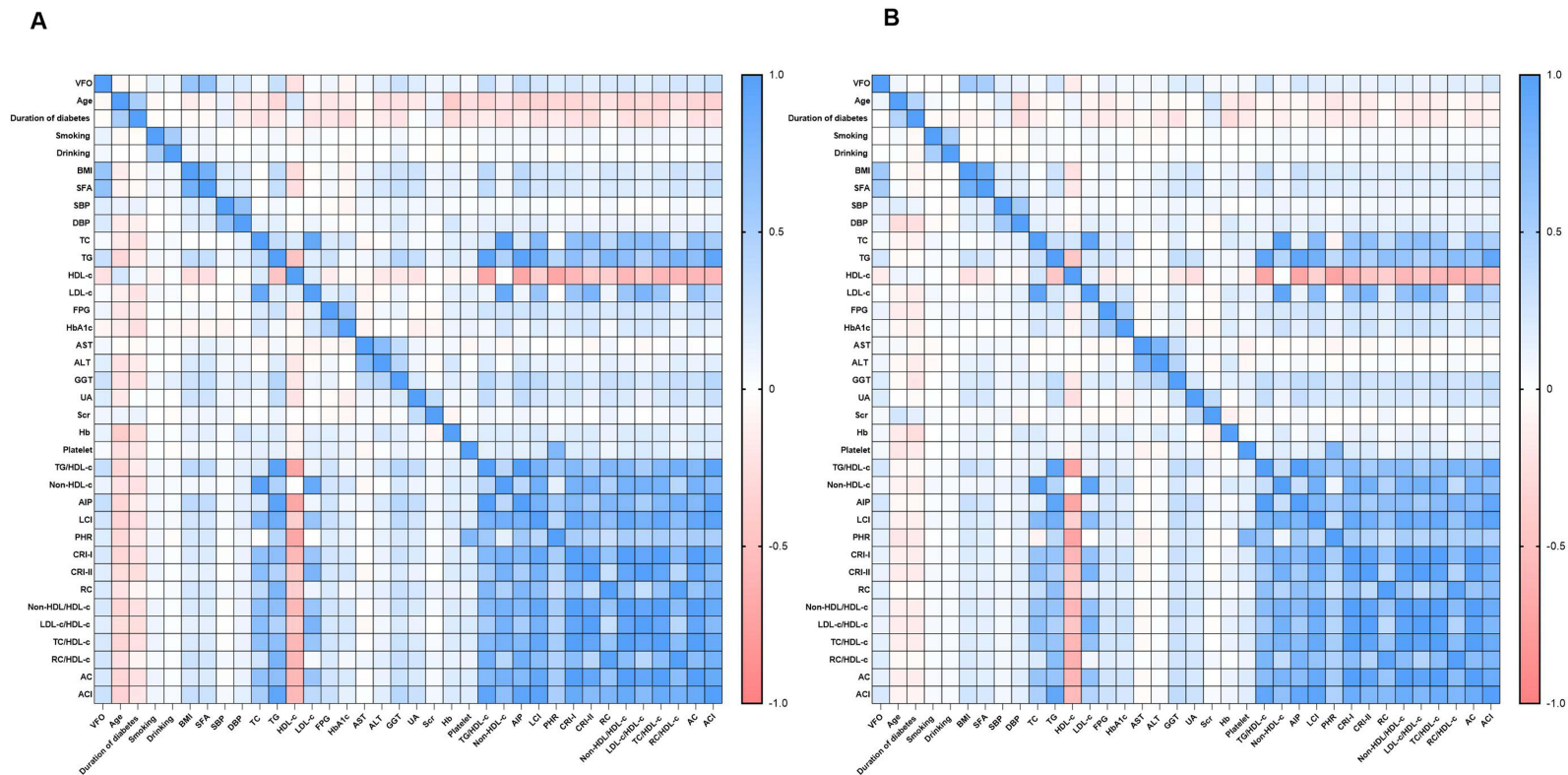


Figure 2 The heatmap shows the Spearman correlation coefficients among variables. **(A)** male groups; **(B)** female groups. Blue represents a strong positive correlation (close to +1), red represents a strong negative correlation (close to -1), and white indicates a weak or no correlation (close to 0).

Table 3 The Independent Variables for VFO

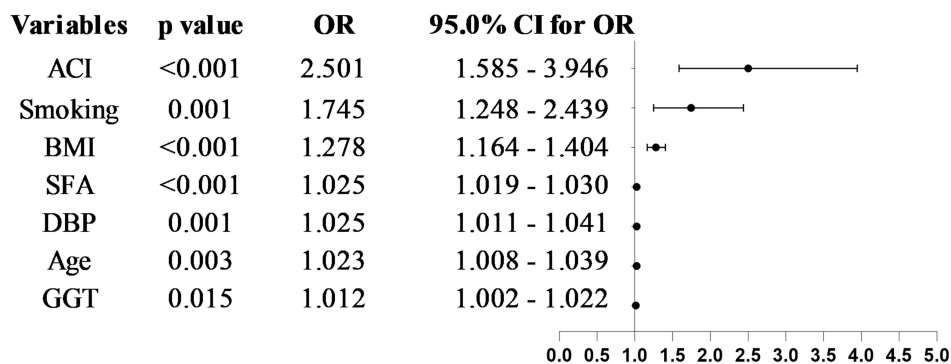
Variables	B	SE	Wald	p value	OR	95.0% CI for OR
In Females						
ACI	0.586	0.269	4.748	0.029	1.797	1.061–3.045
BMI	0.391	0.044	78.294	<0.001	1.478	1.356–1.612
FPG	0.049	0.025	3.830	0.050	1.051	1.000–1.104
Age	0.042	0.008	29.522	<0.001	1.043	1.028–1.060
GGT	0.016	0.008	4.315	0.038	1.016	1.001–1.032
SFA	0.005	0.002	6.859	0.009	1.005	1.001–1.009
In Males						
ACI	0.917	0.233	15.523	<0.001	2.501	1.585–3.946
Smoking	0.556	0.171	10.582	0.001	1.745	1.248–2.439
BMI	0.246	0.048	26.511	<0.001	1.278	1.164–1.404
SFA	0.024	0.003	82.387	<0.001	1.025	1.019–1.030
DBP	0.025	0.007	11.346	0.001	1.025	1.011–1.041
Age	0.023	0.008	8.791	0.003	1.023	1.008–1.039
GGT	0.012	0.005	5.964	0.015	1.012	1.002–1.022

Note: VFO was defined as VFA ≥ 100 cm². The independent variables for VFO were assessed by logistic regression analysis.

Abbreviations: ACI, atherogenic combined index; BMI, body mass index; FPG, fasting plasma glucose; SFA, subcutaneous fat area; DBP, diastolic blood pressure; GGT, γ -Glutamyl transpeptidase.

shown in [Appendix Tables 2–4](#)). Therefore, after adjusting for common confounders, we further analyzed the correlation between each of the above lipid indices and VFO separately, and the results still showed that OR, p-value, Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) of ACI are superior to other

A



B

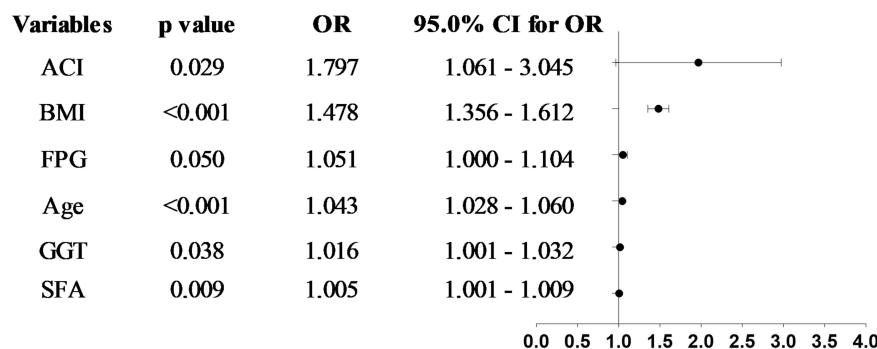


Figure 3 Forest plot of factors independently associated with VFO. (A) male groups; (B) female groups.

variables (shown in [Appendix Tables 5](#) in males and [Appendix Tables 6](#) in females), which further confirmed the significant correlation between ACI and VFO.

Discussion

This study was designed to explore the relationship between the ACI and VFO in T2DM patients, the core findings perfectly address and achieve this objective. We not only confirmed a significant positive correlation between ACI and VFO, but also identified that ACI had an independent relationship with VFO in both genders, filling the research gap regarding the unclear relationship between this novel non-traditional lipid index and VFO in patients with T2DM.

Visceral fat accumulation is a well-recognized key driver of T2DM progression and its cardiometabolic complications.²⁷ This finding established a novel bridge between lipid atherogenicity and visceral fat metabolism in T2DM. Existing studies have confirmed the value of traditional and non-traditional lipid indices such as TC, TG, RC and AIP and others in predicting VFO.^{9,10} These results further demonstrated that ACI had a more robust association with VFO, which retained significance in the regression model after adjusting for other lipid indices, enriching the panel of lipid indices for VFO in T2DM. In addition, our previous study illustrated that ACI had independently associated with MASLD in T2DM,¹¹ the current findings form a complementary evidence base for ACI's clinical value in evaluating metabolic comorbidities (VFO and MASLD) in T2DM.

The present study revealed the association between ACI and VFO previously unobserved. Nevertheless, the potential mechanisms underlying the correlation between the two remain unproven. The ACI was initially proposed as a potential novel index, which synthesizes a more comprehensive lipid profile compared to other indices, including TG, non-HDL-c and HDL-c levels.¹² The typical lipid changes observed in obese individuals with VFO are characterized by atherogenic dyslipidaemia, including increased TG and non-HDL-c levels and decreased HDL-c levels.²⁸ Adipocyte dysfunction leads to an influx of lipids into the liver, which in turn causes hypertriglyceridemia by increasing very low-density lipoprotein (VLDL-c) synthesis.²⁹ The non-HDL-c incorporates all plasma lipoproteins, including LDL-c, triglyceride-rich lipoproteins (TRL), TRL remnants, and lipoprotein [Lp(a)].³⁰ Studies have identified a strong correlation between metabolic syndrome, such as obesity and non-HDL-c.³¹ Obesity triggers a relative deficiency of lipoprotein lipase, a leptin imbalance, and increased hepatic lipase and endothelial lipase activity, which together lead to decreased levels of HDL-c.³² The above rationale supports the correlation between ACI and VFO.

Furthermore, the results of this study demonstrated a strong correlation between obesity indicators (BMI and SFA), age, GGT and VFO in both male and female subjects. Obesity may increase the biological age of certain tissues and cell types, which may be a potential mechanism for the link between age and VFO.³³ GGT is a vital indicator of MASLD,³⁴ VFO is closely associated with MASLD,³⁵ this further validated the correlation of GGT in VFO. In the female group, FPG demonstrated a positive correlation with VFO. Chronically elevated lipid levels have been found to disrupt glucose homeostasis, whereas exposure to high glucose has been shown to trigger synergistic glucolipotoxic effects.³⁶ This indicates that heightened blood glucose levels may result in lipid metabolism disorders, which consequently influence visceral fat metabolism. In the male group, smoking and DBP demonstrated a positive correlation with VFO. Study has confirmed that smoking onset and continued smoking may causally increase abdominal adiposity.³⁷ VFO may play a crucial role in activating the sympathetic nervous system and the renin-angiotensin-aldosterone system, resulting in an increased risk of developing hypertension.³⁸ The complex and interrelated nature of VFO's determinants may underlie this observation.

Limitations

However, it is crucial to acknowledge the limitations of this study. Firstly, due to the intrinsic limitations of cross-sectional studies, it was difficult to determine whether there was a causal relationship between ACI and VFO. Secondly, the collected data were the measurement results for the major patients after administration of glucose-lowering and lipid-lowering drugs, determined by treatment needs and risk assessment. It was not feasible to eliminate the bias caused by these factors. Thirdly, studies have confirmed that the measurement accuracy of BIA is lower than that of CT and MRI.³⁹ And its reliability may be affected by conditions that influence the body's hydration status, including diabetes.⁴⁰

Therefore, further gold standard methods are required for verification in the future. Finally, although waist circumference is a very important indicator of abdominal obesity, it was not included in our database. Instead, we included VFA and SFA, which the study indicated were strongly associated with VFO.⁴¹ In the future, multicenter, large-scale, longitudinal or interventional studies should be conducted to investigate the relationship between ACI and VFO in T2DM in depth and further explore the cut-off values or risk thresholds.

Conclusion

In summary, among the various lipid parameters, the unconventional lipid parameter ACI was independently associated with the occurrence of VFO in patients with T2DM. In view of the crucial function of VFO in the development of T2DM and CAD, the independent association of ACI may render it a prospective target for early intervention and management.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the corresponding author, without undue reservation.

Ethics Approval and Consent to Participate

The study was undertaken in accordance with the Declaration of Helsinki and was ratified by the Ethics Committee of Linyi People's Hospital (approval number: 202404-H-018, approval date: April 2024). The studies were undertaken in compliance with the local legislation and institutional requirements. All participants provided written informed consent prior to enrolment.

Author Contributions

YL: Conceptualization, Formal analysis, Writing— original draft, Data curation. XM: Writing— original draft, Formal analysis. XZ: Writing— original draft, Methodology. YP: Writing— review & editing, Resource, Conceptualization, Software. WD: Writing – review & editing, Conceptualization, Software. GG: Writing – review & editing, Formal Analysis, Supervision. BJ: Writing – review & editing, Visualization, Resources, Project administration, Validation, Funding acquisition, Supervision.

All authors 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 declare no competing interests in this study.

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