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Association of epicardial fat volume with the severity of coronary artery disease: a preliminary study on risk prediction of obstructive coronary heart disease

Hangyi Zhou[1†], Yuxin Pan[2†], Juan Du[1], Fen Liang[2], Xiaojun Ma[2] and Dongling Lv[2*]

Abstract

Background We aimed to explore the correlation between epicardial fat volume (EFV) and the severity of coronary atherosclerotic artery disease (CAD), evaluate the predictive value of EFV for obstructive CAD, and provide prediction for the selection of clinical treatment schemes for CAD.

Methods A total of 203 patients undergoing chest computed tomography (CT) and Coronary Artery Angiography (CAG) were included in this retrospective study. The severity of coronary stenosis and SYNTAX score were evaluated by CAG images. There were 141 patients in obstructive CAD group which was defined as coronary stenosis severity ≥ 70% and 62 patients in non obstructive CAD group.

Results Multivariate logistic regression analysis showed that after adjusting for confounding factors, EFV (OR, 1.008; 95% CI, 1.000-1.016; $p=0.039$) was an independent risk factor for obstructive CAD. Spearman correlation analysis showed a significant positive correlation between EFV and SYNTAX score, as well as the number of coronary lesions ($r=0.157$, $p=0.026$; $r=0.231$, $p=0.002$). The EFV of males was significantly higher than that of females ($p<0.001$). EFV was significantly positively correlated with intrathoracic fat volume (IFV) ($p<0.001$).

Conclusions EFV maybe an independent risk factor for obstructive CAD. Quantitative measurement of EFV by QCT can predict the severity of CAD. EFV was significantly correlated with IFV, but not with BMI.

Clinical trial number Not applicable.

Keywords Epicardial adipose tissue, Obstructive coronary heart disease, SYNTAX score, Stenosis, Quantitative computed tomography, Obesity

†Hangyi Zhou and Yuxin Pan contributed equally to this work.

*Correspondence:
Dongling Lv
lvdongling1226@163.com
[1]Affiliated Hospital of Nanjing University of Chinese Medicine, Jiangsu 210001, China
[2]Changhai Hospital, Naval Medical University, Shanghai 200082, China

Background

Coronary atherosclerotic heart disease (CAD) is a common clinical multiple cardiovascular disease. The morbidity and mortality of CAD are increasing year by year in developing countries. According to the world cardiovascular prevention research, effective primary and secondary prevention in various countries can significantly reduce mortality [1]. Therefore, finding out the relevant risk factors and measurable indicators of CAD is important to identify high-risk groups and carry out early prevention and intervention.

Epicardial adipose tissue (EAT) is the adipose tissue between myocardium and visceral pericardium. It is similar to visceral fat in embryology and morphology which also originates from visceral pleural mesoderm [2]. In recent years, some studies have shown that epicardial fat volume is significantly correlated with coronary artery calcification (CAC), atherosclerotic plaque and coronary artery lesion morphology [3, 4]. The level of metabolic enzymes involved in glycolysis, tricarboxylic acid cycle and fatty acid metabolism in EAT of patients with CAD is low [5]. EAT can not only store energy, but also release a variety of bioactive mediators in the form of paracrine or vascular secretion, induce the imbalance of adipokines and cytokines, damage mitochondrial function, mediate apoptosis, affect the dynamic balance of myocardial physiological function [6], control local and systemic metabolism, cardiac vascular function and vascular tension [7], and promote atherosclerosis and myocardial fibrosis, participate in the occurrence and development of CAD [8].

EFV is a quantitative index of the amount of EAT [9]. Its specific value can be measured by techniques such as QCT. The size of EFV reflects the accumulation degree of EAT, and its changes are closely related to the severity of CAD.

Obstructive CAD (defined as coronary artery stenosis severity ≥ 70%) is a common and recognized cause of myocardial ischemia. It has been proven to be more effective in distinguishing meaningful functional lesions than the 50% stenosis threshold [10], and is more likely to lead to serious adverse cardiovascular events [11]. Studies have found that the average EFV of patients with myocardial ischemia is significantly increased, and after adjusting for coronary artery calcification score (CCS), EFV remains the strongest index to predict myocardial ischemia [12]. EFV increased steeply in patients with significant coronary artery stenosis (defined as percent-diameter stenosis > 50%) and in those with severe CAC [13]. Therefore, identifying modifiable hazard markers can help to improve risk assessment.

Previous studies on the relationship between epicardial fat and CAD mostly focused on patients with coronary artery stenosis ≥ 50%, while there were relatively few studies targeting on patients with coronary artery stenosis ≥ 70%. Therefore, this study measured adipose tissue volume by quantitative computed tomography (QCT) to explore the correlation between EFV and the severity of CAD, in order to identify potential imaging biomarkers for predicting the risk of obstructive CAD, and provide a prediction for the selection of clinical treatment plans for CAD in Chinese population.

In addition, previous studies have mostly concentrated on the relationship between the thickness of EAT and CAD, while the research on EFV as a quantitative index is relatively insufficient. Compared with the thickness index, EFV can more comprehensively reflect the accumulation of epicardial fat and may have a more complex and crucial impact on the pathophysiological process of CAD.

Based on the above background, this study proposes a unique hypothesis: EFV is not only closely related to the occurrence of obstructive CAD but also can predict the severity of the disease. At the same time, there are significant differences in the impact of EFV on CAD among different genders and in patients with comorbidities (such as diabetes), and these differences remain significant after adjusting for traditional risk factors. This hypothesis breaks through the limitations of previous studies and opens up a new path for in-depth understanding of the relationship between EFV and CAD from the perspectives of more precise patient stratification, more comprehensive fat quantification, and multi-factor interaction. It is expected to fill the gaps in existing research and provide new theoretical bases and potential biomarkers for the early diagnosis and personalized prevention and treatment of CAD.

Patients and methods

Subjects and study design

This study included 356 patients who underwent CAG and chest CT in the cardiovascular department and other clinical department wards of Affiliated Hospital of Nanjing University of Chinese Medicine from October 2020 to August 2021 (Due to the COVID-19, all patients who were planned to undergo CAG in the research institution underwent CT). Exclusion criteria: (1) Patients with severe arrhythmia; (2) Complicated with acute and subacute cerebrovascular disease, arteriovenous thrombosis, nephrotic syndrome, uremia and other thrombotic diseases; (3) Complicated with hematological diseases such as hemophilia, primary hyperfibrinolysis or serious primary diseases such as malignant tumors; (4) Have a history of infection, fever, trauma or surgery in recent two weeks; Patients with active tuberculosis or rheumatic immune diseases; (5) Patients with severe mental disorders (such as perception disorder and thought disorder); (6) Pregnant and lactating women; (7) incomplete

medical information; Exclude if any of the above conditions are met. Finally, 153 participants were excluded, and a total of 203 participants were enrolled in the current study. There were 141 patients in obstructive CAD group (coronary stenosis severity ≥ 70%) and 62 patients in non obstructive CAD group.

Based on previous literature, the overall detection rate of the disease ranges from 50–70% [1, 14]. To ensure the reliability of the study results, we used the upper limit of the detection rate (70%, $p = 0.70$) for sample size calculation. With a 95% confidence level (Z = 1.96) and a 5% margin of error (δ =0.05), the sample size was calculated using the following formula: $N = Z^{2*}p^{*}(1-p)/\ \delta^2$. Substituting the values, the minimum required sample size was 323. Initially, 356 participants were enrolled in the study. After applying data cleaning and exclusion criteria, 153 participants were excluded, and a total of 203 participants were included in the final analysis. In subsequent analyses, we controlled for potential confounding factors using statistical methods and reported confidence intervals to reflect the uncertainty of the results. Due to the limited sample size and exploratory nature of this study, the results should be interpreted as preliminary. Our findings indicate a tendency that warrants further verification through studies with a higher number of subjects. This study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine.

Data collection

The patients' general clinical data such as gender, age, height, weight, body mass index (BMI), previous history (hypertension, diabetes mellitus (DM)), personal history (smoking history, alcohol history), and family history were collected through electronic medical record review.

All laboratory examinations were conducted based on the first collection of results from patients after admission, with blood lipid and renal function test specimens collected after overnight fasting. Blood lipids: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (ApoA1), apolipoprotein B (APOB), apolipoprotein E (ApoE), lipoprotein (a) (LP (a)); Renal function: Urea, serum creatinine (Scr), uric acid (UA), fasting blood glucose (FBG); glycosylated hemoglobin (HbA1c), troponin I (cTnI), creatine kinase Isozyme (CK-MB), B-type natriuretic peptide (BNP), Hypertensive C Reactive Protein (hs-CRP); Coagulation function: Prothrombin time (PT), activated partial thrombokinase time (APTT), fibrinogen (FIB), D-dimer, ejection fraction (EF) and other information. Hypertension is defined as blood pressure measured three times at rest on different days, with systolic blood pressure ≥ 140mmHg and / or diastolic blood pressure ≥ 90mmHg, or previously diagnosed with hypertension and taking antihypertensive drugs; Diabetes depends on previous history and includes denying previous history but HbA1c ≥ 6.5% or FBG > 7.0mmol/L.

Coronary artery angiography

CAG is crucial in cardiovascular diagnosis and treatment. Its indications include: for patients with ineffective drug treatment for CAD and in need of intervention or bypass surgery; those with recurrent angina after myocardial infarction or a positive exercise test; those with unexplained ischemic ST - T changes or pathological Q - waves on ECG despite no history of angina or myocardial infarction; middle - aged and elderly patients with suspected CAD symptoms but unconfirmed by non - invasive tests.

CAG is the gold standard because it directly shows coronary artery conditions, is superior in evaluating stenosis and lesion characteristics compared to coronary CT, and can clearly display plaque details and stenosis degree, providing a basis for judging disease severity [15]. This lays a solid foundation for exploring the relationship between epicardial fat volume and CAD severity, helping to reveal their intrinsic connection and offering new ideas for diagnosis, treatment, and prognosis assessment.

CAG was performed by digital flat-panel angiography machine (Siemens AG, Wittelsbacherplatz 2,DE 80333 Muenchen, Made in Germany) through femoral or radial approach. Obstructive CAD is defined as left anterior descending artery, left circumflex artery, right coronary artery or its main diameter reduction ≥ 70%, or left main stenosis ≥ 50% [10, 11, 13]. Two experienced interventional cardiologists independently interpreted the contrast images, and gave a SYNTAX score according to the anatomical characteristics such as lesion location, severity, bifurcation and calcification. The final results were the average of both.

Adipose tissue volume measurement

All patients underwent examination on GE Optima 660 spiral CT because of the hospitalization requirements during the COVID-19 epidemic. All CT images were transmitted to QCT Pro workstation (Mindways Software QCT PRO Version 6.1). Thoracic fat volume (TFV), intrathoracic fat volume (IFV), epicardial fat volume (EFV) and subcutaneous fat volume (SFV) were semi-automatically obtained through 2D segmentation using a function called "tissue composition" on QCT Pro workstation. The upper boundary is measured at the bifurcation of the pulmonary artery, and the lower boundary is measured at the apex of left ventricle, with a thickness of 2 mm per layer; The main parameters of the thoracic scan were as follows: 120-kV tube voltage, 100 ~ 400 mA tube current, 500-ms gantry rotation time, 512 × 512

matrix, 0.625-mm slice thickness, 0.5-mm slice interval and a pitch of 0.984. The operator used blind method for the patients' clinical information and lesion results; The adipose tissue volume of all patients was measured by two experienced physicians on the same QCT Pro workstation, and the average value was taken. The inter-rater reliability was assessed using the Intraclass Correlation Coefficient (ICC). The ICC values for TFV, IFV, EFV, and SFV were 0.979 (95% CI: 0.971–0.984), 0.974 (95% CI: 0.964–0.981), 0.864 (95% CI: 0.815–0.900), and 0.984 (95% CI: 0.978–0.988), respectively, all with significant F-test results ($p < 0.001$). These results indicate excellent consistency between the two examiners for all measurements. The measurement chart is shown in Fig. 1.

Statistical analysis

All data were analyzed using IBM SPSS Statistics version 26 (Chicago, IL, USA). Continuous variables were evaluated using Shapiro–Wilk test. Normally distributed data are expressed as mean ± standard deviation, and were assessed using Independent sample t-test or analysis of variance. Non-normally distributed data are expressed as median with interquartile range, and were assessed using Mann Whitney test or Kruskal Wallis test.

Categorical variables are presented as numbers (percentage) and were compared by chi-squared test or Fisher exact test. Multivariate logistic regression analysis was performed to construct a predictive model of obstructive CAD, with obstructive CAD as the dependent variable and adjusting for variables significant at $p < 0.2$ in logistic regression analysis. Area Under the Curve (AUC) of Receiver Operating Characteristic (ROC) was conducted to evaluate the ability of EFV to predict obstructive CAD and the severity of CAD; Spearman correlation analysis and linear regression analysis were used to evaluate the correlation between EFV and research indicators. *P* values of < 0.05 were considered statistically significant.

Results

Baseline characteristics

According to the results of CAG, the subjects were divided into 141 cases of obstructive CAD group (coronary stenosis ≥ 70%) and 62 cases of non obstructive CAD group. Table 1 shows the demographic and clinical characteristics of the two groups. The average age of individuals was 68.00 years and men accounted for 64.0%. Obstructive CAD group had a higher proportion of male participants and prevalence of diabetes; higher IFV, EFV, Scr, UA, HbA1c, cTnI, FIB and SYNTAX score levels ($p < 0.05$); and lower TC, HDL-C, APOA1 and APOE levels (all $p < 0.05$).

Multivariate logistic regression analysis of obstructive CAD

Taking obstructive CAD as the dependent variable, variables with significance level $p < 0.2$ in Table 1 were included in the multivariate logistic regression analysis model. Table 2 shows the results that after adjusting for confounding factors, EFV [OR, 1.008; 95% CI, 1.000-1.016; $p = 0.039$] was an independent risk factor for obstructive CAD. In diabetes population and male population, EFV was still an independent risk factor for obstructive CAD ($P = 0.007$; $p = 0.025$) (Table S1, S2).

Roc analyses of EFV and obstructive CAD

The results of the ROC analyses of EFV are sum-marized in Table 3. The area under ROC curve (AUC) of EFV for predicting obstructive CAD is 0.614 (95% CI, 0.532–0.696; $p = 0.010$), and the critical value of EFV of obstructive CAD was 248.75 cm3 (sensitivity, 50.4%; specificity, 69.4%) (Fig. 2; Table 3).

Association between fat volume, SYNTAX score and the number of coronary artery lesions in CAD group

The relationship between BMI, TFV, IFV, EFV, SFV, SYNTAX score and the number of coronary artery lesions was compared in CAD group. The results showed that there were significant differences in IFV between single vessel

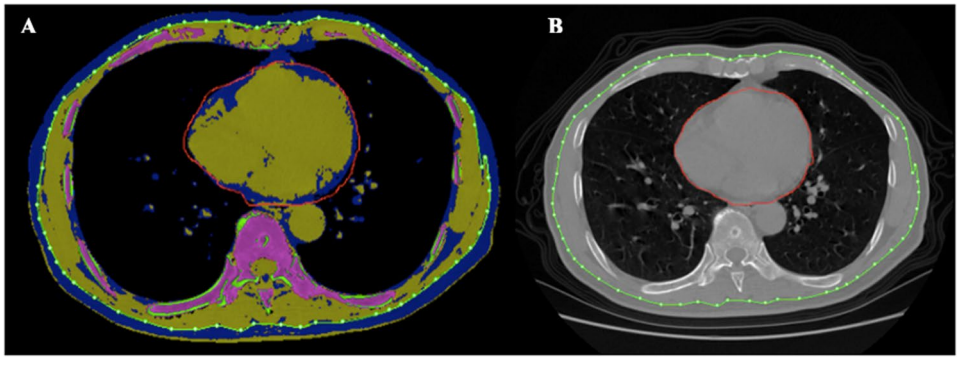

Fig. 1 Adipose tissue measured by QCT. Note: The blue part in figure A represents fat. All the blue parts represent thoracic adipose tissue, the blue part in the green circle represents intrathoracic adipose tissue (IAT), the blue part outside the green circle represents subcutaneous adipose tissue (SAT), and the blue part in the red circle represents epicardial adipose tissue (EAT)

Table 1 Demographic and clinical characteristics of participants between obstructive CAD and Non obstructive CAD group

	All Patients (*N* = 203)	Non Obstructive CAD (*N* = 62)	Obstructive CAD (*N* = 141)	t/x2/z	*p*
Men, n(%)	130 (64.0%)	30 (48.4%)	100 (70.9%)	9.496△	0.002*
Age (y)	68.00 (62.00,75.00)	68.00 (62.00,72.25)	69.00 (60.00,75.00)	-0.819	0.413
Smoke, n(%)	75 (36.9%)	18 (29.0%)	57 (40.4%)	2.400△	0.121
Alcohol, n(%)	64 (31.5%)	20 (32.3%)	44 (31.2%)	0.022△	0.882
Family history, n(%)	64 (31.5%)	23 (37.1%)	41 (29.1%)	1.283△	0.257
Hypertension, n(%)	151 (74.4%)	46 (74.2%)	105 (74.5%)	0.002△	0.967
Diabetes, n(%)	78 (38.4%)	16 (25.8%)	62 (44.0%)	6.006△	0.014*
BMI (kg/m2)	24.98 (22.72,26.99)	24.40 (22.13,27.54)	24.98 (23.07,26.66)	-0.398	0.510
TFV (cm3)	2587.49 ± 803.88	2559.02 ± 910.57	2600.01 ± 755.39	-0.334	0.739
IFV (cm3)	1135.64 (920.69,1453.74)	1083.43 (851.79,1286.40)	1155.36 (968.04,1546.91)	-2.342	0.019*
EFV (cm^3)	263.49 (220.80,340.63)	244.75 (207.97,294.48)	274.11 (223.19,351.68)	-2.584	0.010*
SFV (cm^3)	1260.46 (890.14,1824.27)	1286.89 (903.85,1886.41)	1240.30 (887.33,1743.67)	-0.575	0.566
TC (mmol/L)	3.99 (3.24,4.72)	4.27 (3.56,4.65)	3.89 (2.97,4.75)	-2.108	0.035*
TG (mmol/L)	1.42 (1.00,1.87)	1.35 (0.96,1.88)	1.44 (1.01,1.85)	-0.759	0.448
HDL-C (mmol/L)	1.22 (1.06,1.41)	1.40 (1.13,1.58)	1.20 (1.02,1.34)	-3.523	<0.001*
LDL-C (mmol/L)	2.31 (1.75,2.79)	2.37 (1.89,2.76)	2.26 (1.68,2.84)	-0.783	0.433
APOA1 (g/L)	1.31 (1.21,1.41)	1.41 (1.29,1.43)	1.30 (1.19,1.40)	-3.593	< 0.001*
APOB (g/L)	0.75 (0.63,0.86)	0.80 (0.71,0.87)	0.75 (0.60,0.86)	-2.780	0.005
APOE (mg/dL)	3.85 (3.30,4.30)	4.30 (3.60,4.43)	3.85 (3.10,4.10)	-3.543	< 0.001*
LP(a) (mg/L)	166.89 (76.00,236.00)	166.89 (76.00,167.17)	203.81 (71.50,263.00)	-1.601	0.109
UR (mmol/L)	5.92 (5.16,7.20)	5.73 (4.98,6.50)	6.07 (5.17,7.40)	-1.593	0.111
Scr (umol/L)	76.90 (63.90,92.90)	72.15 (58.75,82.95)	81.20 (66.25,96.15)	-2.839	0.005*
FBG (mmol/L)	5.22 (4.61,6.37)	5.03 (4.52,5.75)	5.25 (4.64,6.75)	-1.721	0.085
UA (umol/L)	358.00 (302.00,429.00)	350.40 (265.50,384.25)	368.00 (311.50,441.00)	-2.147	0.032*
HbA1c (%)	6.50 (5.90,6.90)	6.35 (5.90,6.50)	6.50 (6.00,7.20)	-2.039	0.041*
cTnI	0.00 (0.00,0.09)	0.00 (0.00,0.00)	0.00 (0.00,0.81)	-3.677	< 0.001*
CK-MB	13.00 (10.00,20.00)	13.00 (10.00,18.20)	13.00 (10.00,23.50)	-0.505	0.613
PT	13.10 (12.60,13.30)	13.00 (12.60,13.13)	13.10 (12.60,13.45)	-1.026	0.305
APTT	37.50 (34.90,39.70)	37.50 (35.70,39.08)	38.00 (34.80,39.70)	-0.935	0.350
FIB	3.24 (2.88,3.65)	3.16 (2.85,3.36)	3.39 (2.91,3.78)	-2.792	0.005*
D-Dimer	0.43 (0.28,0.93)	0.43 (0.27,0.61)	0.43 (0.28,1.20)	-1.320	0.187
EF (%)	63.90 (60.90,66.90)	64.55 (62.05,67.50)	63.30 (60.10,66.85)	-2.290	0.022
SYNTAX score	14.00 (7.00,22.00)	2.50 (0.00,8.25)	17.00 (12.00,26.50)	-9.368	< 0.001*

△ is the Chi-squared test, is the independent sample T test, and the residual indicators are subject to the rank sum test, *p for trend < 0.05

BMI body mass index, *TFV* thoracic fat volume, *IFV* intrathoracic fat volume, *EFV* epicardial fat volume, *SFV* subcutaneous fat volume, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *APOA1* apolipoprotein A1, *APOB* apolipoprotein B, *APOE* apolipoprotein E, *LP(a)* lipoprotein (a), *UR* urea, *Scr* serum creatinine, *FBG* fasting blood glucose, *UA* uric acid, *HbA1c* glycosylated hemoglobin, *cTnI* troponin I, *CK-MB* creatine kinase Isozyme, *PT* prothrombin time, *APTT* activated partial thrombokinase time, *FIB* fibrinogen, *EF* ejection fraction

lesion group and double vessel lesion group ($p < 0.05$), EFV and IFV between single vessel lesion group and three vessel lesion group ($p < 0.05$), and SYNTAX score among different vessel lesion groups ($p < 0.001$). SYNTAX score, EFV and IFV in three vessel lesion group were higher than those in single vessel lesion group ($p < 0.05$). (Tables 4 and 5).

Roc analyses of EFV and the number of coronary artery lesions in CAD patients

The area under ROC curve (AUC) of EFV for predicting the number of coronary lesions (single and three branches) is 0.681 (95% CI, 0.583–0.778; $p = 0.003$), and the critical value of EFV was 326.87 cm3 (sensitivity, 37.6%; specificity, 96.8%) (Fig. 3; Table S3).

General data of EFV

Spearman correlation analysis showed that EFV was related to age, BMI, TFV, IFV, SFV, SYNTAX score, TG, HDL-C, ApoA1, UR, Scr, FBG, UA, HbA1c and hs CRP ($p < 0.05$) (Fig. 4; Table 6). As shown in Table S4, males had higher IFV and EFV but lower TFV and SFV ($p < 0.001$).

Linear regression analysis of EFV influencing factors

The variables age, BMI, TFV, IFV, SFV, TG, HDLC, ApoA1, UR, Scr, FBG, UA, HbA1c, hs-CRP, SYNTAX score and coronary artery lesion number significantly correlated with EFV ($p < 0.05$) were included in the linear regression analysis. The results showed that EFV was

Table 2 Multivariate logistic regression analysis of obstructive CAD

Variables	B	S.E.	Wald	Sig.	OR	95% CI
Sex	-0.942	0.607	2.409	0.121	0.390	0.119–1.281
Age	0.013	0.021	0.403	0.526	1.013	0.973–1.055
Smoke	0.004	0.511	0.000	0.994	1.004	0.368–2.736
Diabetes	0.857	0.566	2.290	0.130	2.356	0.777–7.147
BMI	0.018	0.067	0.071	0.790	1.018	0.893–1.160
IFV	-0.002	0.001	2.255	0.133	0.998	0.996-1.000
EFV	0.008	0.004	4.263	0.039*	1.008	1.000-1.016
TC	0.577	0.418	1.908	0.167	1.781	0.785–4.039
HDL-C	-1.389	0.958	2.102	0.147	0.249	0.038–1.630
APOA1	-0.121	1.305	0.009	0.926	0.886	0.069–11.429
APOB	-3.221	1.979	2.648	0.104	0.040	0.001–1.931
APOE	-0.084	0.216	0.150	0.698	0.920	0.602–1.405
LP(a)	0.002	0.001	2.181	0.140	1.002	0.999–1.005
UR	-0.198	0.116	2.913	0.088	0.820	0.654–1.030
Scr	0.001	0.008	0.018	0.894	1.001	0.986–1.016
FBG	0.011	0.139	0.007	0.935	1.011	0.770–1.329
UA	0.003	0.002	1.204	0.273	1.003	0.998–1.007
HbA1c	0.068	0.329	0.043	0.836	1.071	0.562–2.039
cTnI	0.065	0.048	1.869	0.172	1.067	0.972–1.172
FIB	0.377	0.252	2.235	0.135	1.458	0.889–2.391
D-Dimer	0.503	0.195	6.693	0.010*	1.654	1.130–2.423
EF (%)	-0.058	0.029	4.019	0.045	0.943	0.891–0.999

*p for trend < 0.05. Abbreviations as in Table 1

Table 3 ROC curve analyses for each index as predictors of obstructive CAD

Variables	AUC (95%CI)	Sensitivity	Specificity	Youden's index	p
EFV	0.614 (0.532,0.696)	0.504	0.694	0.198	0.010*
EFV D-Dimer	0.672 (0.595,0.749)	0.574	0.726	0.300	< 0.001*
Sex Diabetes EFV D-Dimer	0.728 (0.658,0.798)	0.674	0.710	0.384	< 0.001*

*p for trend < 0.05. Abbreviations as in Table 1

significantly positively correlated with IFV ($p < 0.001$) (Fig. 5; Table 7).

Discussion

In this study, EFV was measured quantitatively by QCT to explore the influencing factors of EFV and its relationship with the severity of coronary artery disease, and to evaluate the predictive value of EFV in obstructive CAD. We found that EFV was positively correlated with SYNTAX score and the number of coronary artery lesions, and EFV was an independent risk factor for obstructive CAD, which could predict the severity of coronary artery lesions. In addition, EFV was significantly correlated with gender and IFV, but not with BMI, TFV and SFV.

Previous studies have shown that EAT is related to coronary plaque and high-risk coronary lesion morphology [3]. Even after adjusting for cardiovascular disease (CVD) risk factors and CCS, EFV can also predict CAD events [3, 16, 17]. SYNTAX score is an integral system for risk stratification according to the anatomical characteristics of coronary artery lesions which quantitatively evaluates the complexity of coronary artery lesions according to the anatomical characteristics such as lesion location, severity, bifurcation and calcification. Most studies on the relationship between EAT and SYNTAX score mainly focus on EAT thickness [18–20]. Our study showed a positive correlation and linear relationship between EAT volume and SYNTAX score. SYNTAX score is an independent predictor of major adverse cardiovascular and cerebrovascular events in the PCI treatment group of CAD patients, and can be used to predict clinical prognosis [21].A meta-analysis found that patients with high SYNTAX score were more likely to have myocardial infarction, major adverse cardiac event (MACE), revascularization and stent thrombosis, with a significantly higher mortality rate than patients with lower SYNTAX score [22], which was consistent with our study results. We also found that EFV of three vessels lesion group was significantly higher than that of single vessel lesion group, which was consistent with the study of SUN [23]. Meanwhile, we observed that IFV of the three vessels lesion group was significantly higher than that of the single vessel lesion group. The AUC of EFV for predicting the number of coronary lesions (single and three branches) was 0.681 (95% CI, 0.583–0.778; $p = 0.003$), and the critical value of EFV was 326.87 cm3 (sensitivity, 37.6%;

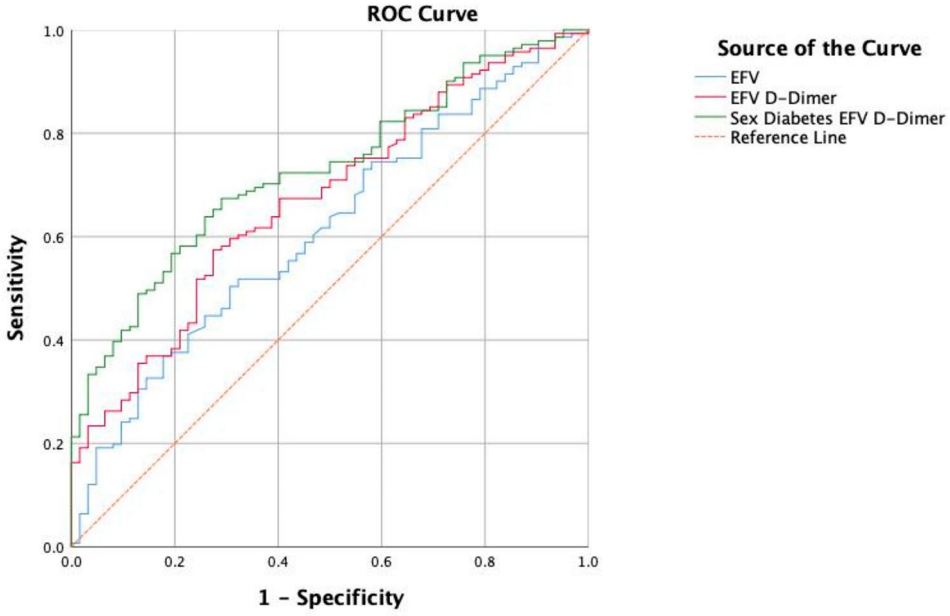

Fig. 2 ROC curve analyses for each index as predictors of obstructive CAD

Table 4 Association between fat volume, SYNTAX score and the number of coronary artery lesions

Variables	Single Vessel (*N* = 31)	Double Vessels (*N* = 48)	Three Vessels (*N* = 93)	F/H (K)	*p*
BMI (kg/m^2)	24.90 ± 3.70	25.39 ± 3.15	24.76 ± 2.93	0.433	0.730
TFV (cm^3)	2470.11 ± 866.99	2573.60 ± 747.54	2632.01 ± 796.69	0.317	0.813
IFV (cm^3)	1047.02 (786.89,1237.92)	1163.17 (959.48,1577.14)	1160.56 (1005.20,1625.89)	8.844	0.012*
EFV (cm^3)	240.20 (199.57,295.12)	276.92 (213.17,324.11)	277.14 (230.45,360.24)	8.857	0.012*
SFV (cm^3)	1304.23 (724.81,1980.07)	1129.04 (908.26,1845.83)	1260.46 (869.89,1709.21)	0.332	0.847
SYNTAX score	7.00 (3.50,12.00)	11.25 (9.00,16.00)	22.00 (16.00,32.50)	86.325	< 0.001*

BMI and TFV were compared using analysis of variance, while EFV, IFV, SFV, and SYNTAX scores were compared using rank sum tests, * *p* for trend < 0.05. Abbreviations as in Table 1

Table 5 Pairwise comparison between CAD groups with different number of coronary artery lesions

Variables (*P*)	Single VS Double	Double VS Three	Single VS Three
BMI	0.528	0.238	0.830
TFV	0.574	0.674	0.340
IFV	0.033*	0.426	0.003*
EFV	0.101	0.250	0.003*
SFV	0.537	0.993	0.634
SYNTAX score	< 0.001*	< 0.001*	< 0.001*

BMI and TFV were compared using analysis of variance, while EFV, IFV, SFV, and SYNTAX scores were compared using rank sum tests, * *p* for trend < 0.05. Abbreviations as in Table 1

specificity, 96.8%); It showed that quantitative calculation of EFV can predict the severity of coronary artery disease.

There are multiple reasons for the low AUC value of EFV in predicting obstructive CAD. Firstly, this study compared patients with a degree of coronary stenosis ≥ 70% with patients with a degree of coronary stenosis < 70%. Patients with a degree of coronary stenosis < 70% may have higher EFV than those with a degree of coronary stenosis < 50%, thereby reducing the intergroup differences. In addition, the pathogenesis of obstructive CAD is complex, involving the interaction of multiple factors, and a single EFV indicator cannot comprehensively cover the occurrence and development process of the disease. To improve the predictive efficacy of EFV, we considered constructing a combined prediction model by integrating other biomarkers, which is expected to construct a more comprehensive and accurate combined prediction model and improve the ability to predict obstructive CAD.

Previous studies have shown that Pericardial fat and visceral abdominal adipose tissue (VAT), but not intrathoracic fat, are associated with CVD independent of traditional measures of obesity but not after further adjustment for traditional risk factor [19, 24]. EAT thickness is related to SYNTAX score, while intra-abdominal fat thickness and clinical indicators related to obesity do not show any association with CAD complexity [19], which support our study results. Other studies have shown that EFV is closely related to atherosclerotic

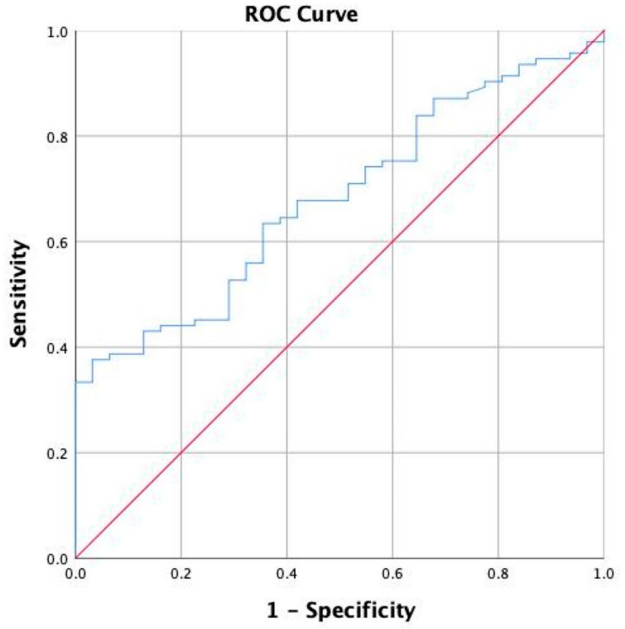

Fig. 3 ROC analyses of EFV predicting the number of coronary artery lesions in CAD patients

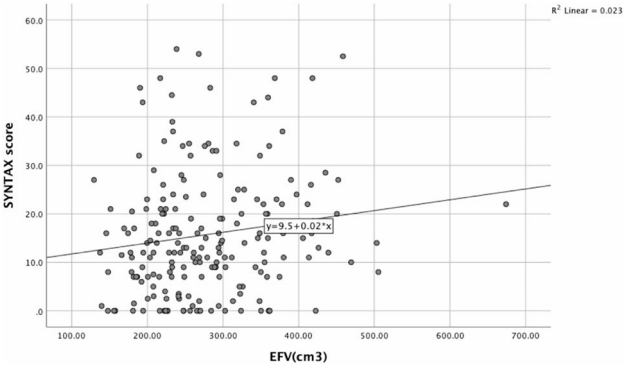

Fig. 4 Scatter plot and fitting linear model of the relationship between EFV and SYNTAX score

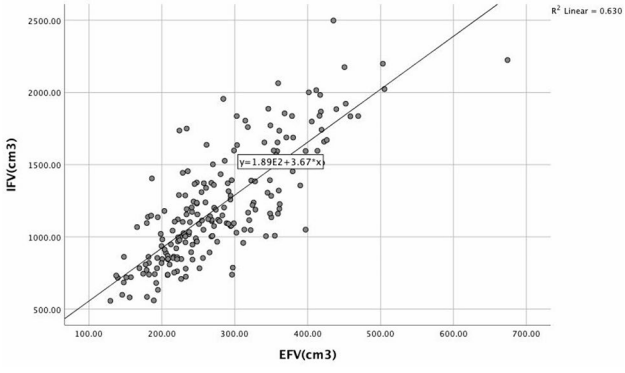

Fig. 5 Scatter plot and fitting linear model of the relationship between EFV and IFV

Table 6 Spearman correlation analysis between EFV and general clinical data

Variables	*R*	*p*
Age	0.149	0.033*
BMI	0.387	< 0.001**
TFV	0.489	< 0.001**
IFV	0.770	< 0.001**
SFV	0.184	0.009**
SYNTAX score	0.157	0.026*
TC	-0.035	0.615
TG	0.199	0.004**
HDL-C	-0.280	< 0.001**
LDL-C	0.038	0.586
APOA1	-0.150	0.033*
APOB	0.040	0.570
APOE	0.009	0.896
LP(a)	-0.124	0.077
UR	0.187	0.007**
Scr	0.195	0.005**
FBG	0.248	< 0.001**
UA	0.153	0.029*
HbA1c	0.176	0.012*
cTnI	0.059	0.405
CKMB	-0.085	0.228
BNP	0.076	0.419
hs-CRP	0.281	0.004**
PT	0.068	0.337
APPT	0.063	0.374
FIB	0.125	0.075
D-Dimer	0.087	0.216

* *p* for trend < 0.05, ** P for trend < 0.001

BMI body mass index, *TFV* thoracic fat volume, *IFV* intrathoracic fat volume, *EFV* epicardial fat volume, *SFV* subcutaneous fat volume, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *APOA1* apolipoprotein A1, *APOB* apolipoprotein B, *APOE* apolipoprotein E, *LP(a)* lipoprotein (a), *UR* urea, *Scr* serum creatinine, *FBG* fasting blood glucose, *UA* uric acid, *HbA1c* glycosylated hemoglobin, *cTnI* troponin I, *CK-MB* creatine kinase Isozyme, *BNP* B-type natriuretic peptide; *hs-CRP* hypertensive C reactive protein; *PT* prothrombin time, *APTT* activated partial thrombokinase time, *FIB* fibrinogen

plaque and plaque load, but not to obstructive CAD (stenosis > 70%) [4]. We found that obstructive CAD with coronary stenosis ≥ 70% is closely related to the increase of EFV and IFV, but not to BMI, TFV and SFV. It may be that visceral fat (such as EFV and IFV) participates in inflammatory response, leading to a number of metabolic alterations, which has a stronger impact on CAD than systemic fat and other ectopic fat (such as SFV and TFV), and can better predict metabolic abnormalities and atherosclerosis [16, 25–27]. Multivariate logistic regression analysis showed that EFV was an independent risk factor for obstructive CAD, which was independent and stronger than IFV. It was still established in diabetes population and male population. Our results was consistent with previous studies that showed EFV was significantly positively associated with the risk of obstructive CAD in

Table 7 Linear regression analysis of EFV influencing factors

Variables	B	Std. Error	Beta	t	*p*
(Constant)	-70.055	88.472		-0.792	0.431
Sex	31.185	18.087	0.154	1.724	0.088
Age	0.817	0.566	0.085	1.445	0.152
BMI	-0.214	2.017	-0.007	-0.106	0.916
lesion number	10.747	7.502	0.114	1.432	0.156
SYNTAX score	0.179	0.615	0.023	0.291	0.771
TG	-6.502	6.436	-0.066	-1.010	0.315
HDL-C	-36.564	27.550	-0.138	-1.327	0.188
APOA1	54.480	38.239	0.139	1.425	0.158
UR	0.065	3.501	0.002	0.019	0.985
Scr	-0.136	0.160	-0.081	-0.849	0.398
FBG	0.886	3.273	0.021	0.271	0.787
UA	-0.009	0.055	-0.013	-0.169	0.866
HbA1c	-0.355	7.969	-0.004	-0.044	0.965
hs-CRP	-0.462	0.492	-0.065	-0.939	0.351
IFV	0.210	0.020	0.939	10.433	< 0.001*
SFV	-0.015	0.012	-0.098	-1.188	0.238

* *p* for trend < 0.05. Abbreviations as in Table 1

patients suspected of CAD, but not with traditional risk factors and CAC [10]. The volume of adipocytes in EAT is smaller than that of adipose tissue in other parts, and there is no anatomical barrier with myocardium. They participate in inflammatory response, oxidative stress, endothelial dysfunction, myocardial fat filtration, vasoconstriction and local proliferation of vascular smooth muscle cells by secreting inflammatory cytokines, adipokines, inorganic molecules, reactive oxygen species, microRNA and microbubbles [28], inducing pathological tissue remodeling and myocardial fibrosis, accelerate the process of atherosclerosis and promote the occurrence and development of CAD [29–31]. Based on the above findings, we used EFV to predict obstructive CAD, the AUC was 0.614 (95% CI, 0.532–0.696; $p = 0.010$), and the critical value of EFV of obstructive CAD was 248.75 cm3 (sensitivity, 50.4%; specificity, 69.4%). Therefore, EFV, an independent risk factor, can be considered as a potential predictor of obstructive CAD in clinical application. We also found that using EFV combined with D-Dimer to predict obstructive CAD resulted in an AUC of 0.672 (95% CI, 0.595–0.749; $p < 0.001$), possibly due to that higher levels of D-Dimer in plasma are one of the most useful biomarkers for acute myocardial infarction [32]. Recent studies have also shown that elevated D-Dimer levels are associated with the severity of CAD in patients with ST elevation myocardial infarction and the incidence of coronary microvascular dysfunctionn [32, 33]. The baseline D-Dimer level may have important prognostic value in patients with CAD [34]. Although there is currently no literature directly studying the relationship between D-dimer and epicardial fat volume, their potential connection can be inferred from their common mechanisms of action. From the perspective of potential mechanisms, there are mainly the following points: First, in terms of the inflammatory response, the epicardial adipose tissue can secrete various inflammatory factors. These factors may activate the coagulation system, causing the D - dimer level to rise [35]. Second, regarding metabolic disorders, an increase in epicardial fat volume may trigger metabolic disorders such as insulin resistance and abnormal lipid metabolism, and then activate the coagulation system. Third, in terms of the correlation with CAD, previous studies have found that in patients with CAD, the D - dimer/fibrinogen ratio (D/F) is positively correlated with the epicardial adipose tissue thickness (EAT), indicating that the two may affect the occurrence and development of cardiovascular diseases through common inflammatory and metabolic pathways.In summary, both D - dimer and epicardial fat volume are closely related to the occurrence and development of cardiovascular diseases. The two are likely to interact through inflammatory responses and metabolic disorders, jointly influencing the pathophysiological processes of cardiovascular diseases. Future research needs to further explore the causal relationship between them and their specific mechanisms of action in cardiovascular diseases, so as to provide more powerful theoretical and practical support for the diagnosis, treatment, and prognosis evaluation of cardiovascular diseases.

Gender is also one of the factors affecting the correlation between EAT and CAD. Previous studies have shown that EFV, degree of CAC and percentage of significant coronary lumen stenosis are significantly higher in men than in women [16, 36]. Korean genomic epidemiological study found that men may have more EAT and higher cardiac metabolic index, including blood pressure, blood glucose and cholesterol levels [37]. Similarly, a study showed that there were gender differences in the distribution of ectopic fat in Chinese patients, with higher visceral fat volume (VFV) and periaortic fat volume (PAFV) in men and higher abdominal subcutaneous fat volume (SFV) in women, and PAFV was significantly associated with coronary atherosclerosis [38]. Among patients with suspected and confirmed CAD, women had lower IFV and EFV. Quantification of IFV provides incremental predictive value for MACE in women, beyond that provided by traditional risk factors and imaging findings [39]. Our research showed that males had higher IFV/BMI and EFV/BMI but lower TFV/BMI and SFV/BMI ($p < 0.001$), and males were more likely to suffer from obstructive CAD, which was consistent with Previous studies. BMI is a crude marker of total adiposity. However, the research results on the correlation between EAT and BMI were not consistent [23, 40]. Our study found that EFV was significantly positively correlated with BMI, TFV, IFV and SFV. After incorporating variables

significantly correlated with EFV into linear regression analysis, it was found that there was no significant correlation between EFV and gender, BMI, etc. IFV was the only significant variable related to EFV ($p < 0.001$). Many studies have demonstrated the importance of VAT as a risk factor for CVD and cardiac structure and function [3]. Although our study showed that IFV of obstructive CAD group is significantly higher than that of non obstructive CAD group, the correlation is not significant after multivariate logistic regression analysis, indicating that EAT is more closely related to obstructive CAD than IAT.

Invasive coronary angiography (ICA) is the gold standard for the diagnosis of CAD and can further complete coronary revascularization during the examination. However, elective ICA is associated with the risk of complications [41], and only 38 – 50% of patients receiving ICA are diagnosed with CAD [42]. DISCHARGE study [43] found that among patients with stable chest pain, who had a moderate probability of CAD and had the opportunity to receive further CAG, the risk of major cardiovascular adverse events was similar in the preferred CT and ICA groups, and the preferred CT strategy could reduce the incidence of major surgery related complications. Therefore, our study reassessed the risk of obstructive CAD by measuring EAT and other ectopic fat volumes through body composition analysis of QCT. EFV measured by QCT may be a marker for predicting obstructive CAD, which can assist in identifying patients with coronary artery stenosis ≥ 70% and conducting early intervention treatment. Accordingly, it may be used as one of the auxiliary examinations for the diagnosis of coronary artery disease severity and provide prediction for the selection of clinical treatment scheme for CAD.

Interventions such as lifestyle changes (such as Mediterranean diet [44]), Bariatric surgery and drug treatment (such as HMG CoA reductase inhibitor, GLP-1 receptor agonist and SGLT2 inhibitor [45, 46]) may change EFV and its relationship with cardiac structure and function [5, 6, 47], so as to make the potential of targeted drugs to regulate EAT volume and genetic characteristics, and open up a new way for the treatment of cardiovascular diseases.

There are several limitations to our study. Through a comprehensive and systematic review and in-depth analysis of relevant literature, and a rigorous comparison with the sample sizes of similar studies [48–50], the sample size of this research has already complied with statistical requirements and has sufficient research power. During the research process, we carefully formulated strict inclusion and exclusion criteria, widely collected multi-dimensional information of patients, and skillfully applied methods such as multivariate logistic regression analysis and linear analysis to effectively reduce biases and significantly enhance the credibility of the conclusions. To further strengthen the reliability and persuasiveness of the research results, we plan to conduct a broader study in the future, including non obstructive CAD patients and healthy individuals without CAD, to deeply validate the relevant results and ensure the robustness and universality of the research conclusions. Secondly, this retrospective study identifies correlations between the observed indices and target variables but cannot establish causation. Thirdly, no analysis has been conducted regarding whether the study participants have utilized or are currently employing lipid-lowering medications, which might exert a certain influence on EFV. Hence, subsequent research endeavors should be dedicated to further dissecting this correlation. Future large-scale multi-center prospective studies are imperative to further corroborate the relationship between EFV and other cardiac diseases, as well as its impact on clinical prognosis. Fourthly, CAC data were not collected in this study. In the future, it will be feasible to re-measure the CAC index by reviewing the patients' CT imaging data and employ ROC curve analysis to compare the individual and combined predictive capabilities of EFV and CAC for obstructive CAD. Fifthly, Non-gated CT has limitations in the measurement of epicardial adipose tissue. It cannot synchronize with the cardiac cycle precisely, easily resulting in motion artifacts that affect the accurate determination of the boundary and volume of epicardial adipose tissue. Moreover, the reproducibility in clinical applications is also poor. In this study, due to the COVID-19 pandemic, non-gated CT was adopted as a routine examination before patients' hospitalization instead of gated CT. However, the study used QCT for quantitative measurement of non-gated CT images, which had minimal interference from cardiac motion and relatively high accuracy [51]. Nevertheless, the inherent defects of non-gated CT itself cannot be ignored, and future research needs to explore improvement methods to enhance its measurement level in this regard.

Conclusions

EFV maybe an independent risk factor for obstructive CAD, and quantitative measurement of EFV by QCT can predict the severity of coronary artery disease. EFV is significantly correlated with IFV, but not with BMI, TFV and SFV.

Abbreviations

APOA1	Apolipoprotein A1
APOB	Apolipoprotein B
APOE	Apolipoprotein E
APTT	Activated Partial Thromboplastin Time
BMI	Body Mass Index
BNP	B-type Natriuretic Peptide
CAC	Coronary Artery Calcification
CCS	coronary artery calcification score

CAD	Coronary Atherosclerotic Heart Disease
CAG	Coronary Artery Angiography
CK	MB-Creatine Kinase-MB
CVD	Cardiovascular Disease
cTnI	Sensitivity Troponin I
EAT	Epicardial Adipose Tissue
EFV	Epicardial Fat Volume
FBG	Fasting Blood Glucose
FIB	Fibrinogen
HbA1c	Hemoglobin A1c
HDL	C-High-Density Lipoprotein Cholesterol
hs	CRP-Hypertensive C Reactive Protein
IAT	Intrathoracic Adipose Tissue
ICA	Invasive Coronary Angiography
IFV	Intrathoracic Fat Volume
LDL	C-Low-Density Lipoprotein Cholesterol
LP(a)	Lipoprotein(a)
MACE	Major Adverse Cardiac Event
PCI	Percutaneous Coronary Intervention
PT	Prothrombin Time
QCT	Quantitative Computer Tomography
Scr	Serum Creatinine
SFV	Subcutaneous Fat Volume
TC	Total Cholesterol
TG	Triglyceride
UA	Uric Acid
UR	Urea

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04743-3.

Supplementary Material 1

Supplementary Material 2

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Not applicable.

Author contributions
DL, HZ, YP designed the study and drafted the manuscript. HZ and JD analysed the data and generated the figures. HZ, FL and XM collected data. All authors have read and approved the final version of the manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This retrospective study was approved by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine. Informed consent was waived by the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine because of the retrospective design. The Declaration of Helsinki was followed throughout the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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