

ORIGINAL RESEARCH

Association of Epicardial Fat Volume With Increased Risk of Obstructive Coronary Artery Disease in Chinese Patients With Suspected Coronary Artery Disease

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BACKGROUND: Epicardial adipose tissue may be associated with the pathogenesis of coronary artery disease (CAD), but its effect on obstructive CAD risk is uncertain. Therefore, we aimed to examine the relationship between epicardial adipose tissue and obstructive CAD in Chinese patients with suspected CAD.

METHODS AND RESULTS: The present study enrolled 194 consecutive inpatients with suspected CAD who underwent both non-contrast computed tomography and coronary angiography. We measured epicardial fat volume (EFV) and evaluated its association with obstructive CAD, which was defined as coronary stenosis severity $\geq 70\%$. Overall, 44.3% patients had obstructive CAD and tend to have higher EFV. Age, body mass index, triglycerides, incidence of hypertension, and hyperlipidemia were higher across tertiles of EFV (P for trend < 0.05). In univariate regression analysis, a per-SD increase in EFV was independently associated with obstructive CAD (odds ratio [OR], 2.31; 95% CI, 1.61–3.32; $P < 0.001$). Consistent with these findings, EFV was still significantly related to obstructive CAD as continuous variable after adjustment for all traditional risk factors and coronary artery calcium (OR per SD, 2.82; 95% CI, 1.68–4.74; $P < 0.001$). Generalized additive model indicated that EFV was linearly associated with risk of obstructive CAD. E -value analysis suggested robustness to unmeasured confounding.

CONCLUSIONS: Our results suggested that in Chinese patients with suspected CAD, EFV was significantly and positively associated with the risk of obstructive CAD, independent of traditional risk factors and coronary artery calcium.

Key Words: coronary artery calcium ■ epicardial fat volume ■ noncontrast computed tomography ■ obstructive coronary artery disease

It is estimated that almost 11 million patients experienced coronary artery disease (CAD) in China. Besides, the incidence and mortality of CAD are still increasing.¹ Obstructive CAD ($\geq 70\%$ stenosis) was a frequent and well-acknowledged cause of myocardial ischemia, and has shown to be a greater discriminator of functionally significant lesions than a 50% stenosis cutoff. The FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study concluded that in patients with obstructive CAD, $> 80\%$ could induce reversible myocardial ischemia,

as established by fractional flow reserve.² Besides, obstructive CAD is more likely to result in major adverse cardiovascular events.³ Therefore, it is essential to recognize modifiable risk markers for reducing its burden. Coronary angiography (CAG) was considered the gold standard for diagnosing CAD. In China, the use of CAG and percutaneous coronary intervention has increased substantially, but the positive rates for CAG were not high, and more than half of patients with suspected CAD undergoing CAG had no obstructive CAD.⁴ Once a diagnosis of obstructive

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CLINICAL PERSPECTIVE

What Is New?

- Epicardial fat volume was significantly and positively associated with risk of obstructive coronary artery disease in Chinese patients with suspected coronary artery disease, independent of traditional risk factors and coronary artery calcium.

What Are the Clinical Implications?

- Epicardial adipose tissue may represent an important imaging biomarker for obstructive coronary artery disease and a potential therapeutic target for primary prevention.

Nonstandard Abbreviations and Acronyms

CACS	coronary artery calcium score
CAG	coronary angiography
DM	diabetes mellitus
EAT	epicardial adipose tissue
EFV	epicardial fat volume
FAME	Fractional Flow Reserve Versus Angiography for Multivessel Evaluation

CAD has been confirmed, the patient's event risk will be determined, and it has a major influence on subsequent therapeutic decisions. Revascularization was recommended for patients with obstructive CAD to effectively eliminate myocardial ischemia and angina symptoms.⁵ Therefore, it is interesting to identify reliable markers of obstructive CAD early to reassess preprocedural risk.

Epicardial adipose tissue (EAT), a metabolic active adipose tissue confined within pericardium, is usually quantified by epicardial fat volume (EFV) from noncontrast computed tomography (CT). Because of the close anatomical association and lack of fibrous fascia separating EAT from myocardium and coronary arteries, inflammatory cytokines secreted by EAT interact with coronary arteries and myocardium through direct paracrine effect and endocrine effect.⁶ In addition, there is growing evidence showing that EFV could alter vascular homeostasis and promote endothelial dysfunction.⁷ It is also reported that statin therapy and intense lifestyle modification could reduce EAT accumulation and affect inflammatory profile simultaneously,⁸ which made EAT a promising marker for primary prevention of obstructive CAD.

Previous studies have demonstrated that EFV is clinically associated with atherosclerosis and

presence and severity of CAD, along with an increased incidence of cardiovascular adverse events.^{9,10} Recently, a large Chinese population-based study¹¹ demonstrated that EFV improved prediction of CAD above traditional risk factors and coronary artery calcium score (CACS). Besides, Iwasaki et al¹² found that EFV increased only if CAD with luminal stenosis was $\geq 70\%$. Differently, a multicenter study¹³ failed to find the associations between EFV and CAD. Besides, ethnic differences in EFV have been highlighted previously, and race might be a significant influencing factor when evaluating the relationship between EFV and cardiovascular risk.^{14–16} Most of clinical studies were performed in western population and focused on the relationship between EFV and CAD. The association between EFV and obstructive CAD was only investigated in a limited number of studies, which was still unclear in Chinese population.

Thus, the purpose of the present study was to explore the relationship between EFV and obstructive CAD in Chinese patients with suspected CAD.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

The present study enrolled 194 consecutive inpatients with suspected CAD who underwent noncontrast chest CT and CAG between March 2018 and October 2019 at the Third Affiliated Hospital of Soochow University. CAG was produced within 3 months of noncontrast chest CT in all patients. Patients enrolled had intermediate pretest probability for CAD (pretest probability of CAD, $59.23 \pm 20.92\%$). Traditional CAD risk factors were recorded, including body mass index (BMI), hypertension, hyperlipidemia, diabetes mellitus (DM), active smoking, and symptoms (including angina, dyspnea, atypical chest pain, and dyspnea with angina or atypical chest pain). Height and weight were measured to ascertain BMI. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, or taking antihypertensive medications. Hyperlipidemia was defined as a history of hyperlipidemia, total cholesterol > 5.2 mmol/L, low-density lipoprotein cholesterol > 3.36 mmol/L, or use of lipid-lowering medication. DM was defined by random plasma glucose ≥ 8.0 mmol/L or self-reported history of DM. Active smoking was defined as smoking within past 6 months. Triglycerides, total cholesterol, low-density lipoproteins, and high-density lipoproteins (HDLs) were extracted from patients' records.

The exclusion criteria were as follows: (a) subjects with acute coronary syndrome, (b) subjects with prior percutaneous coronary intervention or coronary artery bypass grafting, (c) subjects with severe arrhythmia, (d) aged <18 years, and (e) pregnancy. Figure 1 shows the flowchart of population selection. The Medical Ethics Committee of our hospital approved this study protocol. The data are anonymous, and the requirement for informed consent was waived because of the observational nature of the study.¹⁷

Measurement of EFV and CACS

A noncontrast CT chest scan was performed (period, 60%–80% RR; tube voltage, 130 kV; tube current, 100 mA; thickness, 3 mm) to acquire CACS and EFV using retrospective electrocardiography-gated technology (Symbia T16; Siemens Medical Systems, Erlangen, Germany). Each scan extended from the plane underneath the tracheal carina to the place 1 to 2 cm below heart diaphragmatic surface, almost 20 cm. EAT was identified as any adipose tissue observed within the pericardial sac with fat voxels (attenuation values between –30 and –190 hounsfield

unit [HU]).¹⁸ The specific method is as follows: First, the upper slice limit, defined by bifurcation of the pulmonary trunk, and the lower slice limit, marked as the last slice containing any portion of the heart, were defined. Then, the reader manually traced the pericardial contour. EFV was calculated by the sum of cross-sectional areas of fat multiplied by slice thickness.¹⁹ The whole process was performed by the software (Syngo Volume; Siemens Medical Solutions). The interobserver reproducibility of EFV was tested among 2 observers in 15 patients (intraclass correlation coefficient, 0.908; 95% CI, 0.750–0.968; $P<0.001$). Coronary artery calcium (CAC) was defined as a dense area in the coronary artery over the threshold of 130 HU. CACS was defined as the sum of calcification score of each coronary artery by using Agatston automatic analysis software.²⁰

Coronary Angiography

CAG was completed by standard techniques via a femoral or radial approach. All coronary angiograms were visually evaluated by an experienced cardiologist.

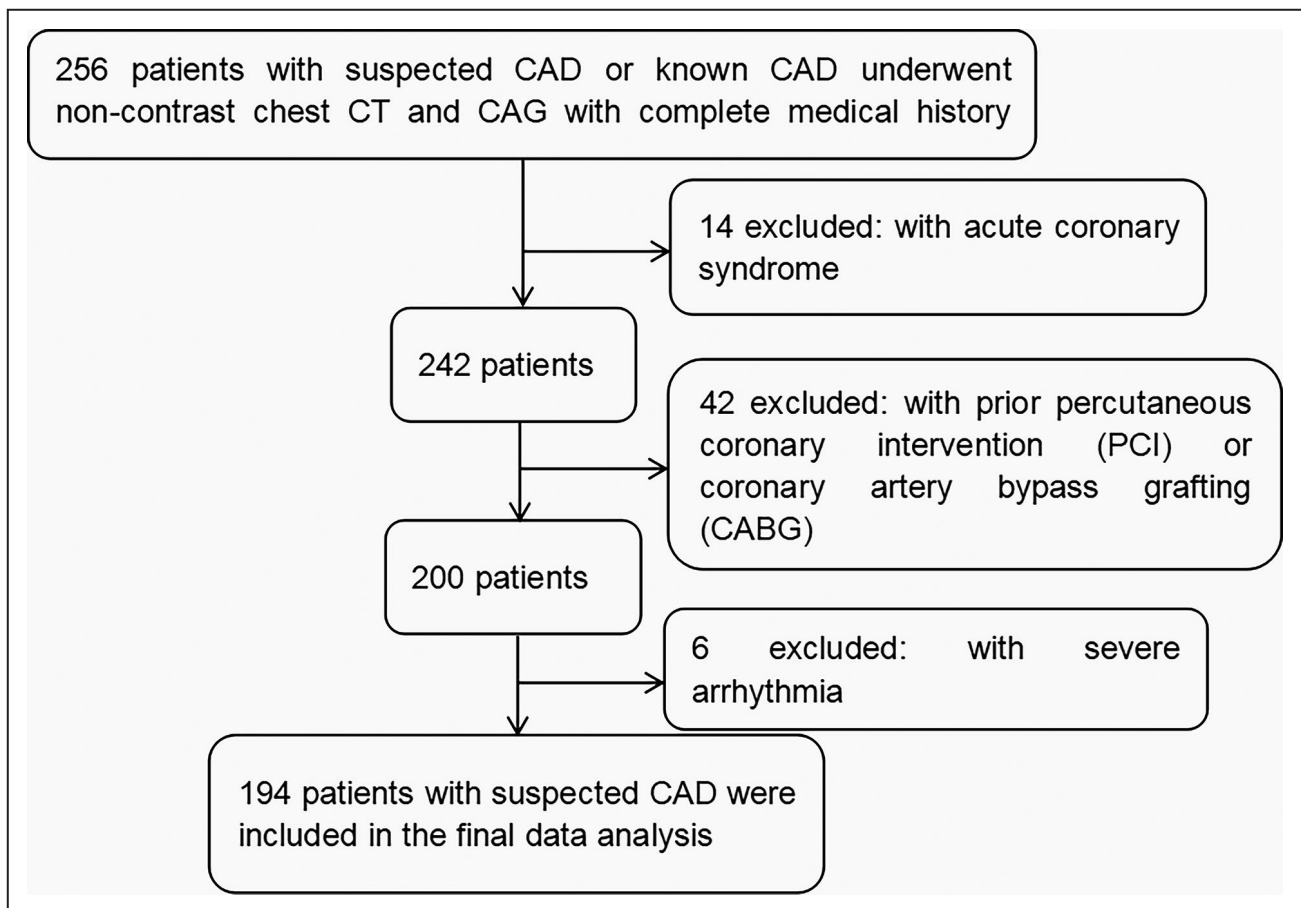


Figure 1. The flowchart of population selection.

CAD indicates coronary artery disease; CAG, coronary angiography; CT, computed tomography; and PCI, percutaneous coronary intervention.

They were blinded of patients' clinical information. Obstructive CAD was defined as $\geq 70\%$ narrowing of the internal diameter of the left anterior descending coronary artery, left circumflex coronary artery, right coronary artery, or their major branches, or $\geq 50\%$ narrowing of the left main coronary artery.²¹

Radiation Exposure

The dose for a noncontrast CT scan to assess CACS and EFV was 1 to 2 mSv.

Statistical Analysis

Continuous variables are expressed as mean \pm SD when normally distributed and median (25th–75th percentile) when nonnormally distributed. Normality was assessed for each variable by the Kolmogorov-Smirnov test. We compared baseline characteristics between patients with or without obstructive CAD. Mann-Whitney *U* test, independent-sample *t*-test, and χ^2 test were performed, as appropriate. The influence of factors related to tertiles of EFV was evaluated by trend test. Multivariable logistic regression models were produced to assess the association between EFV and obstructive CAD; 4 models were generated: (1) a univariable model with EFV as a predictor; (2) multivariable model 1, adjusted for age and sex; (3) multivariable model 2 (confounder model): we assessed the confounding effect of covariates by examining the association of EFV with obstructive CAD before and after adding the covariate. If the scale of the β coefficient changed by $>10\%$, we concluded that the covariate was a confounder. Besides, any variable that was significantly different between obstructive CAD and nonobstructive CAD group ($P < 0.10$) was also retained as confounder. (4) Multivariable model 3 was constructed on the basis of our team's interpretation of a broad review of the literature, and adjusted for age, sex, BMI, hypertension, DM, hyperlipidemia, active smoking, and CAC. From the models, we present odds ratios (ORs) and 95% CIs. Collinearity between significant independent variables was assessed, and only variables with correlation coefficients $B < 0.25$ or variance inflation factors < 5 were contained. General additive model and cubic spline smoothing technique were performed to evaluate the association between EFV and the incidence of obstructive CAD. We explored the potential for unmeasured confounding by calculating *E* values.²² The *E* value quantifies the required magnitude of an unmeasured confounder that could negate the observed association between EFV and obstructive CAD. Interaction and stratified analyses were conducted according to sex. All tests were performed 2 sided with R3.4.3 (<http://www.R-project.org>; software packages: glmnet, pROC, rms, and dca. R) and Prism 7 (GraphPad Software, San Diego, CA). $P < 0.05$ indicated statistical significance.

RESULTS

Patient Characteristics

Baseline characteristics of all patients are shown in Table 1, and 86 (44.3%) patients had obstructive CAD. Overall, the mean age was 61.38 ± 9.64 years, 136 (70.1%) were men, and mean BMI was 24.86 ± 2.94 kg/m². Mean EFV was 119.47 ± 36.56 cm³ (range, 37.30–246.49 cm³). Compared with patients without obstructive CAD, patients with obstructive CAD tend to have higher value of EFV (133.87 ± 36.59 cm³ versus 108.00 ± 32.37 cm³; $P < 0.001$), as well as a higher proportion of DM and CAC and lower value of HDL. Table 2 demonstrated the influence factors of EFV. Age, BMI, triglycerides, and incidence of hypertension and hyperlipidemia were higher across tertiles of EFV (P for trend < 0.05).

Univariable Logistic Regression Analysis Between EFV and Obstructive CAD

The relationship between EFV and obstructive CAD was presented in Table 3. According to the results of unadjusted logistic regression analysis, a per-SD increase in EFV was independently associated with obstructive CAD (OR, 2.31; 95% CI, 1.61–3.32; $P < 0.001$), and the OR for obstructive CAD was 5.59 (95% CI, 2.62–11.95; $P < 0.001$) in patients with EFV of top tertile compared with those in the bottom tertile.

Multivariable Logistic Regression Analysis Between EFV and Obstructive CAD

The multivariable logistic regression analysis also demonstrated a significant association between EFV and obstructive CAD. In multivariable-adjusted model 1 (adjusted for age and sex), the OR for obstructive CAD progressively increased across tertiles of EFV (P for trend < 0.001), and for a per-SD increase in EFV, the OR was 2.24 (95% CI, 1.55–3.23; $P < 0.001$). Adjustment for confounders in multivariable-adjusted model 2 (age, sex, BMI, hypertension, DM, HDL, and CAC) also did not significantly alter the results. After adjustment for all traditional risk factors and CAC in multivariable-adjusted model 3 with the bottom tertile (tertile 1) as reference, the OR was 3.34 for middle tertile (tertile 2) (95% CI, 1.37–8.15; $P = 0.008$) and 9.28 for top tertile (tertile 3) (95% CI, 3.14–27.41; $P < 0.001$). Consistent with these findings, multivariate analysis demonstrated that EFV as continuous variable was still significantly related to obstructive CAD (OR for per SD, 2.82; 95% CI, 1.68–4.74; $P < 0.001$). Figure 2 shows the forest plot presenting the multivariable-adjusted ORs from multivariable-adjusted model 3. When stratifying the population by sex, the OR between EFV (per SD) and obstructive CAD was similar after adjustment for

Table 1. Characteristics of Studied Patients

Characteristics	All Patients (N=194)	Obstructive CAD (N=86)	No Obstructive CAD (N=108)	P Value
Age, y	61.38±9.64	62.84±10.14	60.22±9.01	0.02*
Men, n (%)	136 (70.1)	66 (76.7)	70 (64.8)	0.07
BMI, kg/m ²	24.86±2.94	25.09±2.85	24.68±3.01	0.27
Active smoking, n (%)	74 (38.1)	37 (43.0)	37 (34.3)	0.21
Hypertension, n (%)	139 (71.2)	67 (77.9)	72 (66.7)	0.08
Diabetes mellitus, n (%)	59 (30.1)	34 (39.5)	25 (23.1)	0.014*
Hyperlipidemia, n (%)	61 (31.4)	28 (32.6)	33 (54.1)	0.75
TC, mmol/L	3.90±0.91	3.82±0.83	3.96±0.95	0.24
Triglycerides, mmol/L	1.78±0.95	1.75±0.97	1.80±0.93	0.70
HDL, mmol/L	1.06±0.26	1.00±0.23	1.11±0.27	0.01*
LDL, mmol/L	2.02±0.69	2.02±0.64	2.03±0.73	0.88
Symptom, n (%)	128 (66.0)	58 (67.4)	70 (64.8)	0.70
CAC prevalence, n (%)	105 (54.1)	64 (74.4)	41 (38.0)	<0.001*
EFV, cm ³	119.47±36.56	133.87±36.59	108.00±32.37	<0.001*

Data are given as mean±SD, unless otherwise indicated. Symptom includes angina, dyspnea, atypical chest pain, and dyspnea with angina or atypical chest pain. BMI indicates body mass index; CAC, coronary artery calcium; CAD, coronary artery disease; EFV, epicardial fat volume; HDL, high-density lipoprotein; LDL, low-density lipoprotein; and TC, total cholesterol.

**P*<0.05.

traditional risk factors and CAC (men: OR, 2.52 [95% CI, 1.44–4.38]; women: OR, 4.17 [95% CI, 1.54–11.33]; *P* interaction=0.34).

Generalized additive model (Figure 3) was performed to visually assess association between EFV and risk of obstructive CAD after adjusting for age,

sex, BMI, presence of hypertension, hyperlipidemia, DM, active smoking, and CAC. It turned out that EFV tended to be linearly associated with obstructive CAD.

We generated an *E* value to assess the sensitivity to unmeasured confounding. The primary findings were

Table 2. Baseline Characteristics Stratified by Tertiles of EFV

Characteristics	Bottom Tertile	Middle Tertile	Top Tertile	P Value for Trend
EFV, minimum–maximum, cm ³	37.30–107.36	107.36–128.49	128.49–246.49	
EFV, mean (SD), cm ³	83.34 (18.69)	117.06 (6.60)	157.97 (28.31)	
EFV, median (IQR), cm ³	87.14 (30.85)	116.61 (11.23)	147.2 (34.24)	
Age, y	58.22±9.87	62.25±8.80	63.69±9.49	0.003*
Men, n (%)	45 (69.23)	44 (68.75)	47 (72.31)	0.70
BMI, kg/m ²	23.17±2.70	24.76±2.31	26.64±2.73	<0.001*
Symptom, n (%)	39 (60.00)	42 (65.62)	47 (72.31)	0.14
Active smoking, n (%)	24 (36.92)	20 (31.25)	30 (46.15)	0.28
Hypertension, n (%)	40 (61.54)	44 (68.75)	55 (84.62)	0.003*
Diabetes mellitus, n (%)	18 (27.69)	16 (25.00)	25 (38.46)	0.18
Hyperlipidemia, n (%)	16 (24.62)	16 (25.00)	29 (44.62)	0.020*
TC, mmol/L	3.98±0.87	3.78±0.85	3.93±0.98	0.42
Triglycerides, mmol/L	1.62±0.99	1.71±0.76	2.01±1.04	0.044*
HDL, mmol/L	1.11±0.31	1.06±0.22	1.03±0.23	0.19
LDL, mmol/L	2.10±0.77	1.93±0.57	2.04±0.71	0.37
CAC prevalence, n (%)	31 (47.69)	34 (53.12)	40 (61.54)	0.11
Obstructive CAD, n (%)	16 (24.6)	28 (43.8)	42 (64.6)	<0.001*

Data are given as mean±SD, unless otherwise indicated. Symptom includes angina, dyspnea, atypical chest pain, and dyspnea with angina or atypical chest pain. BMI indicates body mass index; CAC, coronary artery calcium; CAD, coronary artery disease; EFV, epicardial fat volume; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; and TC, total cholesterol.

**P* for trend <0.05.

Table 3. Multivariate Regression Analysis for Effect of EFV on Obstructive CAD

Variable	Crude Model		Multivariable-Adjusted Model 1		Multivariable-Adjusted Model 2		Multivariable-Adjusted Model 3	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
EFV (continuous) per SD	2.31 (1.61–3.32)	<0.001	2.24 (1.55–3.23)	<0.001	2.73 (1.63–4.57)	<0.001	2.82 (1.68–4.74)	<0.001
Tertiles								
Bottom tertile (events/ N=16/65)	1		1		1		1	
Middle tertile (events/ N=28/64)	2.38 (1.13–5.04)	0.02	2.26 (1.05–4.85)	0.04	3.23 (1.31–7.99)	0.011	3.34 (1.37–8.15)	0.008
Top tertile (events/ N=42/65)*	5.59 (2.62–11.95)	<0.001	5.15 (2.36–11.25)	<0.001	8.84 (3.03–25.83)	<0.001	9.28 (3.14–27.41)	<0.001

Multivariable model 1 was adjusted for age and sex; multivariable model 2 (confounder model) was adjusted for age, sex, body mass index, hypertension, diabetes mellitus, high-density lipoprotein, and coronary artery calcium prevalence; and multivariable model 3 was adjusted for age, sex, body mass index, hypertension, diabetes mellitus, active smoking, hyperlipidemia, and coronary artery calcium prevalence. CAD indicates coronary artery disease; EFV, epicardial fat volume; and OR, odd ratio.

*For trend, $P < 0.001$.

robust. For unmeasured confounding to change our results that EFV was significantly related to obstructive CAD would be unlikely (E value, 2.75).

DISCUSSION

The main findings of the study were as follows. (1) Compared with patients without obstructive CAD, individuals with obstructive CAD had a higher value of

EFV, as well as a higher proportion of DM and CAC, and lower value of HDL. (2) Age, BMI, triglycerides, and prevalence of hypertension and hyperlipidemia increased with tertiles of EFV. (3) In multivariable logistic regression analysis, EFV was significantly and positively associated with obstructive CAD, independent of traditional risk factors and CAC. Generalized additive model indicated that EFV was linearly associated with risk of obstructive CAD.

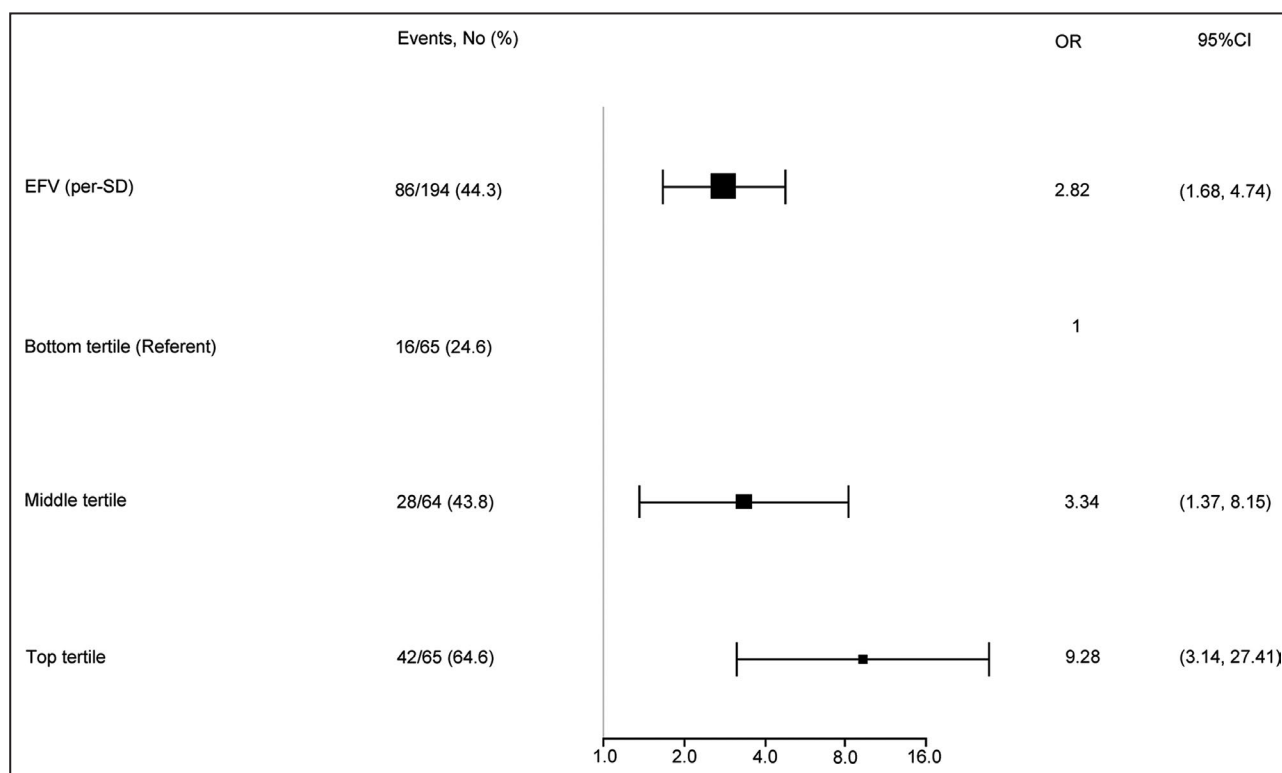


Figure 2. Forest plot presenting the multivariable-adjusted odds ratios (ORs) from multivariable-adjusted model 3. EFV indicates epicardial fat volume.

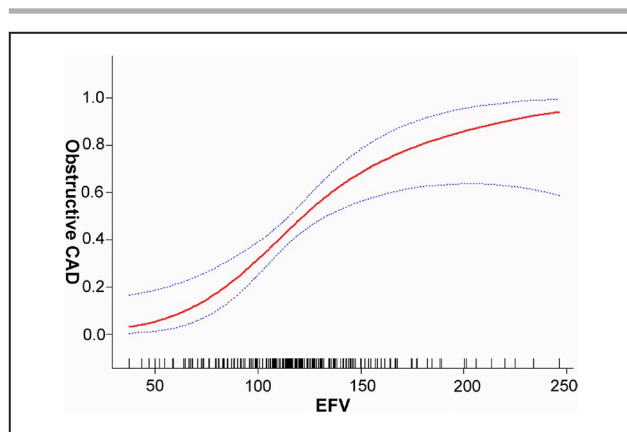


Figure 3. General additive model demonstrated the relationship between epicardial fat volume (EFV) and the risk of obstructive coronary artery disease (CAD) after adjusting for age, sex, body mass index, presence of hypertension, hyperlipidemia, diabetes mellitus, active smoking, and coronary artery calcium.

In the figure, the solid line indicates the estimated risk of obstructive CAD, and the dotted lines represent pointwise 95% CI.

EAT locates close to the coronary arteries, accounts for 15% to 20% of cardiac volume, and covers ~80% of cardiac surface. Its unique anatomical proximity to the myocardium and the coronary arteries led to the hypothesis that EAT played a pivotal role in the pathogenesis of CAD, but the exact pathophysiologic mechanism was still unclear. It was speculated that EAT could secrete many inflammatory cytokines, including interleukin-1B, interleukin-6, MCP (monocyte chemoattractant protein), and tumor necrosis factor; then, these proinflammatory signals act toward atherogenesis through endocrine effect and direct paracrine effect.⁶ EFV was reported to be associated with vulnerable plaques, such as “soft” and “mixed” plaques, which could result in negative outcomes.²³ Besides, oxidative stress, coronary blood flow impairment, and endothelial damage were also speculated to account for the association observed between EFV and CAD in some studies.⁷

It was demonstrated in the present study that EFV was related to cardiovascular risk factors, such as age, BMI, hypertension, and hyperlipidemia, in Chinese patients with suspected CAD. Similarly, Jang et al²⁴ showed significant association of EAT with fasting blood glucose, triglyceride, HDL, and blood pressure in healthy adults aged <60 years. We extended the results by confirming them in patients with suspected CAD. Besides, there are significant racial differences in EFV and its relationship with cardiovascular risk factors. Moharram et al¹⁴ concluded that EAT thickness was significantly associated with BMI in New Zealand European patients, but not in Māori/Pacific patients, which demonstrated that the same level of BMI

indicated different risk in different ethnic groups. Sun et al¹⁶ demonstrated that indigenous individuals had significantly higher EFV than nonindigenous individuals in Australia and supported the possibility that EAT may result in the greater burden of cardiovascular disease in indigenous populations. We are in agreement with those studies and extend the results in Chinese Han population. Because our results were obtained in a homogeneous population of Chinese Han, the findings cannot be extrapolated to other ethnic populations. Further studies are needed to demonstrate whether the results are generalizable to different ethnic populations. In addition, EAT can be modified to improve cardiovascular risk, which might provide a new method for primary prevention of CAD. Kim et al²⁵ found that EAT was significantly reduced by aerobic exercise training, and the percentage change of EAT was twice higher than those of waist circumference and BMI. Colonetti et al⁸ indicated that no matter what type of exercise could significantly reduce EAT.

Our results indicated that EFV was significantly and positively associated with obstructive CAD, and after adjustment for traditional risk factors and CAC, the risk for obstructive CAD went up by 1.82 times for each SD increase in EFV. Different from BMI, EFV represents visceral adiposity rather than general obesity, and the quantitative determination of EFV may offer additional information on cardiovascular risk. Because obstructive CAD is highly related to myocardial ischemia and major adverse cardiovascular events and may benefit more from revascularization, this simple measurement of EFV may help select certain patients for high-dose statin therapy, intense lifestyle modification, and revascularization, if needed. There has been limited research considering the relationship between EFV and obstructive CAD based on western population. Sinha et al²⁶ found that EAT thickness, measured by echocardiography, was significantly associated with obstructive CAD by CAG. Different from this study, we quantified EAT by CT, which is also proved to be a repeatable and robust method to evaluate adipose tissue accumulation because of high spatial resolution.²⁷ Besides, Rajani et al²⁸ also concluded that, in patients with noncalcified or partially calcified disease, EFV is significantly associated with coronary stenosis severity $\geq 70\%$, assessed by coronary CT angiography. In the present study, CAD was evaluated by CAG, which is considered as gold standard. In contrast, some studies came to opposite conclusion, and it is still unclear whether EAT could provide significant clinical value as an imaging biomarker of cardiovascular risk. The CORE320 (Coronary Artery Evaluation using 320-row Multidetector Computed Tomography Angiography and Myocardial Perfusion) Multicenter Study¹³ did not find association between EFV and

CAD. The categorical threshold in this study was $\geq 50\%$ diameter stenosis by CAG, which may not account for the presence of plaque instability.

EFV can be routinely acquired by noncontrast CT used for CACS, avoiding the need for dedicated diagnostic testing, which enhanced its attraction for clinical application. Cardiovascular risk assessment depends on traditional risk factors and has a limited performance, and 20% coronary events were reported to appear in patients without traditional risk factors, so the search for innovative and reproducible cardiovascular risk marker, such as EFV, seems promising. El Khoudary et al²⁹ demonstrated that oral conjugated equine estrogens may slow EAT accumulation in recently menopausal women. Because the risk of CAD could be lowered by interventions to decrease EFV, EFV may serve as a potential therapeutic target more than a cardiovascular risk factor. Last, EFV was identified as an independent predictor of future major adverse cardiovascular events beyond traditional risk factors in the general population.³⁰ As prognosis is more important than the presence of CAD, further prospective studies are necessary to evaluate the potential significance of EFV for clinical management.

Limitations

There are several limitations of our study. First, considering the retrospectively cross-sectional design of our study, we could not infer causality. Second, because no event follow-up was done, our study cannot verify prognostic implications. Third, anthropometric measures, such as waist circumference, were not measured in the study. Instead, we investigated traditional risk factors, including BMI, which is also an indicator of high cardiovascular risk and widely accepted as a parameter reflecting systemic body fat in clinical studies. Besides, we used the *E*-value analysis to quantify the potential implications of unmeasured confounders and found that an unmeasured confounder will not change the direction of our results. Besides, we focused on the relationship between EAT volume and obstructive CAD ($\geq 70\%$ stenosis) in Chinese population. More subjects should be included to further investigate the association between EFV and CAD in nonobstructive CAD group. Last, EFV measurement is still a time-consuming procedure without standardization; automatic software needs to be designed to make EFV a clinically useful imaging biomarker.

CONCLUSIONS

In Chinese patients with suspected CAD, EFV was significantly and positively associated with risk of obstructive CAD, independent of traditional risk factors

and CAC. Further studies are needed to identify longitudinal changes in EFV.

ARTICLE INFORMATION

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Disclosures

None.

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