Original Article

Seyed Kianoosh Hosseini (MD) ¹ Ghulam Muhammad Rind Baloch (MD) ² Ali Fathi Jouzdani (MD) ³ Mohammad Ali Seif Rabiei (MD)⁴ Seyed Kamaledin Hadei (MD) ^{2*}

- 1. Department of Cardiology, School of Medicine, Farshchian Cardiovascular Subspecialty Medical Center, Hamadan University of Medical Sciences, Hamadan, Iran
- 2. Department of Radiology, School of Medicine, Farshchian Cardiovascular Subspecialty Medical Center, amadan University of Medical Sciences, Hamadan, Iran
- 3. USERN Office, Hamadan University of Medical Sciences, Hamadan, Iran
- 4. Department of Community Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
- * Correspondence: Seyed Kamaledin Hadei, Department of Radiology, School of Medicine, Farshchian Cardiovascular Subspecialty Medical Center, Hamadan University of Medical Sciences, Hamadan, Iran

E-mail: km.hadei@gmail.com Tel: +98 8138380017

Received: 11 Sep 2024 Revised: 4 Jan 2025 Accepted: 18 Jan 2025 Published: 18 Oct 2025

CT angiography evaluation of epicardial fat volume and its association with coronary artery stenosis: A single-center cross-sectional study

Abstract

Background: The relationship between epicardial fat and coronary stenosis has been a topic of recent discussion. This study aimed to determine the correlation between epicardial fat volume and coronary artery stenosis in patients undergoing CT angiography.

Methods: In this descriptive/cross-sectional study, 240 patients with low to moderate risk of CAD, referred to the CT angiography unit of Farshchian Hospital in Hamadan in 2023, were selected via the Census method. Coronary artery stenosis was assessed using a 128-slice multi-detector CT scan, while epicardial fat volume was measured using CT scan analysis. Statistical analyses were performed using SPSS software Version 21, with a significance level set at 0.05.

Results: The mean age of the patients was 54.69 years, with 52.5% being males. The mean epicardial fat volume was 76.64 ml, and 58.3% of the patients had coronary artery stenosis. The mean epicardial fat volume in patients with coronary stenosis was 82.82 ± 31.41 ml, compared to 65.66 ± 25.79 ml in those without stenosis (p<0.001). There was a significant positive correlation between epicardial fat volume and patients' age, calcium score, vessel score, and LDL levels. Additionally, the mean epicardial fat volume in patients with both obstructive and non-obstructive stenosis in the LAD and LCX was significantly higher than in vessels without stenosis (P < 0.05).

Conclusion: Epicardial fat volume is significantly associated with coronary artery stenosis and calcium score. Therefore, it can be utilized to determine and predict the presence and severity of coronary artery stenosis.

Keywords: Coronary arteries, CT angiography, Epicardial fat, Stenosis.

Citation:

Hosseini SK, Rind Baloch GhM, Fathi Jouzdani A, Seif Rabiei MA, Hadei SK. CT angiography evaluation of epicardial fat volume and its association with coronary artery stenosis: A single-center cross-sectional study. Caspian J Intern Med 2025; 16(4): 767-774.

Cardiovascular diseases, especially coronary artery diseases, have a significant prevalence worldwide. Globally, cardiovascular diseases dominate the death statistics, especially in developed countries. There have been numerous studies on the risk factors of coronary artery disease, such as diabetes, dyslipidemia, smoking, high blood pressure, and family history (1). The association between volume of epicardial fat and coronary artery atherosclerosis raised the possibility that it might be another risk marker (2). Epicardial fat (EF) is a type of visceral fat deposited beneath the pericardium and has the origin of abdominal visceral fat may associated with coronary artery disease (3). EF provides a rich source of free fatty acids and cytokines (3). Abdominal obesity and abdominal adipose tissue are associated with greater epicardial adipose tissue thickness, and epicardial adipose tissue thickness have been related to coronary artery disease (4). Studies have found that epicardial fat tissue increases the production of some cytokines and inflammatory factors. Computerized tomography (CT) scan showed that coronary atherosclerotic and calcified plaques develop more rapidly when epicardial fat tissue is thicker (5).

Publisher: Babol University of Medical Sciences

Study by Aslanabadi et al. (2014) (6) have reported correlations between epicardial fat volume and the severity of coronary artery stenosis, highlighting the potential of epicardial fat as a marker for Coronary Artery Disease (CAD). Additionally, research by Weidlich (2024) (7) and Khurana et al. (2018) (8) has explored the association between epicardial fat volume and cardiac arrhythmias, further emphasizing the multifaceted impact of epicardial fat on cardiovascular health. Moreover, investigations by Robandi et al. (2020) (9) and Xue & Jing (2022) (10) have delved into the relationship between epicardial fat volume and the type of coronary artery plaque, providing insights into the interplay between epicardial fat and atherosclerotic processes. These studies collectively contribute to the growing body of evidence supporting the relevance of epicardial fat evaluation in CAD assessment. Therefore, this single-center cross-sectional study aimed to contribute to this field by evaluating epicardial fat volume through CT angiography and exploring its association with coronary artery stenosis. By building upon existing research, this study seeks to provide further insights into the potential of epicardial fat volume assessment as a non-invasive tool for CAD risk stratification and management.

Methods

Study population: The study protocol complied with the principles of the 2013 Declaration of Helsinki and was approved by the Research and Ethics Committee of Medical Hamadan University of Sciences (IR.UMSHA.REC.1398.171). Written informed consent was obtained from all participants prior to their involvement. This retrospective cross-sectional study, conducted at a single center, included consecutive patients referred for Coronary Computed Tomography Angiography (CCTA) between January 1, 2022, and December 31, 2023. Patients with Glomerular Filtration Rate (GFR) less than 30 cc/min or a history of sensitivity to contrast material or a history of coronary artery bypass surgery and patients with a history of hypothyroidism, chest radiotherapy, and vasculitis were excluded from the study. Two hundred forty patients met the eligibility criteria and were analyzed statistically.

CCTA data acquisition: The patients were administered heart rate-reducing medication, and upon achieving a heart rate of 60 to 65 beats per minute, approximately 70 cubic centimeters (ccs) of isosmolar contrast material (320 milligrams per milliliter (mg/ml) Visipaque) was injected. Following this, a CT scan was performed, and computed tomography angiography (CTA) was conducted using a

multi-detector 128-slice machine (Siemens Somatom Definition AS, Germany). The machine's software semi-automatically calculated the epicardial fat volume in axial sections with a thickness of 3 millimeters (mm) and a threshold range of -250 to 50 Hounsfield units before the injection of the contrast material (figure 1). Post-contrast injection, CTA was performed, followed by coronal and sagittal reconstructions, and the preparation of maximum intensity projection, multiplanar reconstruction (MPR), and volumetric reconstructions. An expert radiologist and cardiologist then examined these images to determine the degree of coronary artery stenosis.

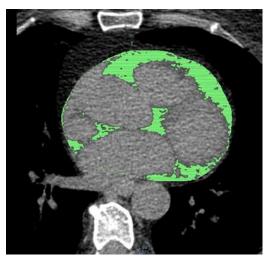


Figure 1. Axial coronary CT angiography images with contrast enhancement illustrating regional thoracic fat depots, including epicardial and paracardial fat. The epicardial fat, outlined in green, represents the adipose tissue situated between the myocardium and the visceral pericardium.

Analysis of coronary atherosclerosis severity: Coronary atherosclerosis severity was assessed using angiography (11, 12). The left anterior descending, left circumflex, and right coronary arteries were each counted as one lesion, whereas the left main coronary artery was counted as two lesions. For secondary branches (e.g., diagonal, obtuse marginal, posterolateral, posterior descending arteries) with stenoses under 50%, a 0.5 lesion score was assigned (13). CT angiography results were used to divide patients into three groups: those without coronary artery stenosis, those with non-obstructive stenosis (less than 50% luminal diameter stenosis), and those with obstructive stenosis (50% or more luminal diameter stenosis). The most severe stenosis was considered when more than one plaque and stenosis were present in a coronary vessel (14) (figure 2).

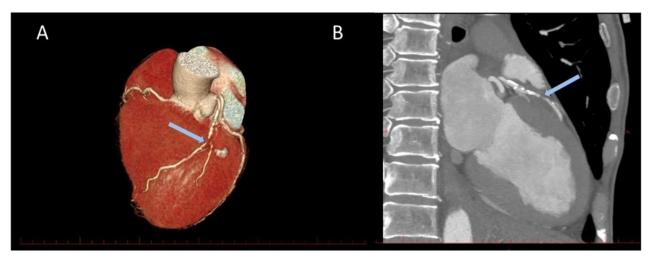


Figure 2. Coronary Artery Imaging Using Computed Tomography Angiography (CTA). (A) A three-dimensional (3D) volume-rendered reconstruction of the heart showing the coronary arteries. The blue arrow indicates a segment of the coronary artery with significant stenosis. (B) A sagittal slice of the computed tomography (CT) scan, illustrating the coronary artery stenosis (highlighted by the blue arrow) in a cross-sectional view. The detailed imaging reveals the extent of the arterial narrowing, critical for evaluating coronary artery disease.

Cardiovascular risk factors and clinical data collection:

In addition to the data obtained from imaging and angiography, which included the presence and severity of coronary artery stenosis, we also collected comprehensive patient histories and clinical data. This included histories of dyslipidemia, triglycerides, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), family history of heart disease, smoking history, diabetes, hypertension (HTN), body mass index (BMI), and coronary artery calcium score (Ca Score) assessed using the Agatston criteria. The data was further categorized based on the location of coronary artery involvement and the number of vessels involved (vessel score).

Statistical analysis: Continuous data were expressed as means±standard deviations or as medians with interquartile ranges, whereas categorical variables were summarized using frequencies and percentages. The Kolmogorov–Smirnov test was conducted to evaluate the normal distribution of continuous variables. To compare continuous variables, the independent t-test and one-way analysis of variance (ANOVA) were employed, with the least significant difference method used for post hoc multiple comparisons.

Results

Study population characteristics: 240 patients were investigated of whom, 126 (52.5%) were men, and 114 (47.5%) were women. The average age of the patients was 54.69±12.04 years, the minimum was 21, and the maximum

was 79 years. 38.8% had a history of hypertension, 35% had dyslipidemia, and 38.8% smoking and 8.6% had a positive family history of premature coronary artery disease (table 1).

Epicardial fat volume, calcium score, age, body mass index and fat profile of patients on coronary artery stenosis: The coronary artery stenosis was not associated with patients' body mass or fat profile. However, significant differences were observed between the groups regarding age, epicardial fat volume, and calcium score. A Tukey's post hoc test revealed that patients with obstructive stenosis had a significantly younger average age than patients with non-obstructive stenosis (p<0.001) and the normal group (p<0.001). Additionally, patients with non-obstructive stenosis had a significantly older average age than those in the normal group (P=0.022). However, the average age difference between patients with obstructive and non-obstructive stenosis was not statistically significant (P=0.119) (table 2).

Calcium scores were significantly higher in the obstructive stenosis group compared to the normal group (p<0.0001) and the non-obstructive stenosis group (p<0.0001). There was no significant difference in calcium scores between the normal and non-obstructive stenosis groups (P=0.715). Epicardial fat volume was significantly higher in patients with obstructive stenosis (P=0.001) and those with non-obstructive stenosis (P=0.002). The average volume of epicardial fat did not differ significantly between patients with obstructive and non-obstructive stenosis (P=0.833). According to the ANOVA test, coronary artery

stenosis and epicardial fat volume differed significantly (figure 3).

Epicardial fat volume in patients with and without coronary artery stenosis in involved arteries: The rates

of obstructive coronary artery stenosis in the Left Main, Left Anterior Descending (LAD), Left Circumflex (LCX), and Right Coronary Artery (RCA) were 0.4%, 15.8%, 9.2%, and 5.8%, respectively (table 3).

Table 1. Demographic profile of subjects

	Without Stenosis	Non-occlusive stenosis (Less than 50%)	Occlusive stenosis (More than 50%)
Number of Cases	117	66	47
Sex (M:F)	59:58	34:32	27:20
Age (Mean±SD)*	51.47±12.23	56.21±11.53	60.57±9.6
Hyperlipidemia	35	23	25
Diabetes	7	9	12
Lipid Drugs	33	16	24
Family History of Coronary Disease	9	4	6
Cigarette	14	16	10
Hypertension	39	26	27

^{*}ANOVA indicated significant difference P-Value (p<0.001) between groups.

Table 2. Epicardial fat volume, calcium score, age, body mass index and fat profile of patients on coronary artery stenosis

	Without Stenosis	Non-occlusive stenosis (Less than 50%)	Occlusive stenosis (More than 50%)	P-value
Epicardial Fat (Mean±SD)	64.85±26.37	79.85±28.75	82.96±32.69	<0/001*
Calcium score (Mean±SD)	16/04±111/11	30/42±64/20	145/38±164/93	<0/001**
BMI (Mean±SD)	27.86±8.33	28.06±7.90	27.13±4.51	0/808*
Triglycerides (Mean±SD)	169.98±78.51	160.82±62.10	175.38±116.57	0/635*
Cholesterol (Mean±SD)	184.99±46.41	188.15±38.48	188.95±44.37	0/837*
HDL (Mean±SD)	47.57±16.01	43.46±15.03	44.51±12.85	0/187*
LDL (Mean±SD)	109.36±33.18	44.51±12.85	112.29±37.04	0/740*

^{*}One-way analysis of variance, **Kruskal-Wallis test. BMI: body mass index; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Table 3. Frequency distribution of coronary artery stenosis in subjects based on coronary artery stenosis

Main vessels	Without Stenosis	Non-occlusive stenosis (less than 50%)	Occlusive stenosis (More than 50%)		
Left Main	224 (93/3)	15 (6/2)	1 (0/4)		
LAD	139 (57/9)	63 (26/2)	38 (15/8)		
LCX	184 (76/7)	34 (14/2)	22 (9/2)		
RCA	188 (78/3)	38 (15/8)	14 (5/8)		

LAD: left anterior descending (coronary artery); LCX: left circumflex (coronary artery); RCA: right coronary artery.

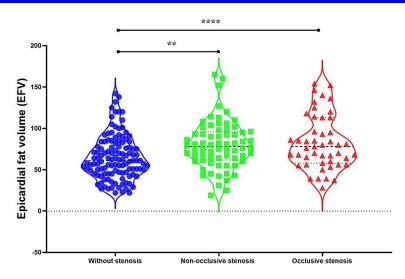


Figure 3. Distribution of mean epicardial fat volume according to the degree of vascular stenosis.

***: p-value <0.001

Relationship between epicardial fat volume and demographic and clinical characteristics: The analysis of the correlation between epicardial fat volume and various clinical parameters in patients with coronary artery stenosis revealed several significant findings. Epicardial fat volume showed a significant positive correlation with age (r = 0.229, P = 0.001), calcium score (r = 0.292, p < 0.001), vessel score (r = 0.192, P = 0.003), and LDL levels (r = 0.159, P = 0.021).

However, no significant correlation was found between epicardial fat volume and BMI (r = 0.037, P = 0.585),

systolic blood pressure (r=0.130, P=0.056), diastolic blood pressure (r=0.087, P=0.204), triglyceride levels (r=-0.027, P=0.692), cholesterol levels (r=0.110, P=0.106), HDL levels (r=0.044, P=0.523), or fasting blood sugar (r=0.004, P=0.949). These findings suggest that age, calcium score, vessel score, and LDL levels are significantly associated with epicardial fat volume in patients with coronary artery stenosis, while other parameters such as BMI, blood pressure, triglycerides, cholesterol, HDL, and fasting blood sugar do not show a significant correlation (table 4).

Table 4. Correlation between epicardial fat volume and coronary artery stenosis in patients under investigation according to age and sex, BMI and sugar and lipid profile

		Age	BMI	Calcium score	Vessel score	Systolic blood pressure	Diastolic blood pressure	Triglyceride	Cholesterol	HDL	LDL
	r	0.229	0.037	0.292	0.192	0.130	0.087	-0.027	0.110	0.044	0.159
	P-value	0/001	0/585	< 0/001	0.003	0.056	0.204	0.692	0.106	0.523	0.021

BMI: body mass index; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Discussion

Epicardial fat volume in the present study averaged 76.64 ml. An Italian study by Milanese et al. revealed 90.52 ml in 1344 patients undergoing angiography (15). On the other hand, in the study by Iwasaki et al. in Japan on 527 patients, this amount was 99.4 mL (16). In the study by Aslanabadi et al. in 2014 in Iran, it was 72.09±35.50 ml. (17). This may be because our country is at the beginning of a cardiovascular disease epidemic. Nevertheless,

cardiovascular diseases are more prevalent in developed countries such as Japan and Italy. There is a strong correlation between epicardial fat thickness measured by echocardiography and early coronary artery disease (18). There is evidence that epicardial fat can reflect visceral fat and contribute to the severity of coronary heart disease (19). In our study, out of 240 examined patients, 100 (58.3%) had coronary artery stenosis. One hundred (58.3%) of the 240 patients examined in our study had coronary arterial

stenosis. There was a significant increase in epicardial fat volume in patients with coronary stenosis. Additionally, epicardial fat was significantly correlated with the severity of stenosis in LAD and LCX coronary arteries. Coronary plaques and vascular stenosis increase in individuals with high epicardial fat volumes, especially in the RCA and LAD (20). According to the study's results on the relationship between epicardial tissue coronary flow reduction and EFT thickness, the groups with and without CSFP had significantly different mean EFT thicknesses (21).

The average epicardial fat was significantly extra between people with and without coronary artery stenosis in the present study. Furthermore, patients without calcification had significantly lower epicardial fat than patients with obstructive and non-obstructive calcifications. As our study shows, the mean epicardial fat of normal subjects was considerably lower than obstructive or nonobstructive in LAD and LCX. It has been found that epicardial fat volume is associated with coronary atherosclerosis, according to Iwasaki et al. Patients with severe coronary artery stenosis and those with severe coronary artery calcification have increased epicardial fat levels steeply (16). In the context of determining the relationship between epicardial fat and the severity of coronary artery involvement, a significant association was observed between the greater thickness of epicardial fat and the severity of coronary disease (22). Our study also confirms this in line with other studies. Our study's relationship between epicardial fat volume and vessel score was positive and significant. As epicardial overweight thickness increases, coronary artery stenosis severity increases as well. In line with our results, Aslanabadi et al. concluded that epicardial fat volume is related to coronary artery disease severity and that epicardial fat volume is a reliable predictor of CAD. A positive and significant correlation was found between epicardial fat volume and calcium score (r=0.292, p<0.001) (17).

It was found that epicardial fat volume correlated positively and significantly with serum LDL and age but not with sex or BMI. The amount of epicardial fat in the heart is related to age, weight, and BMI and is known as a risk factor for coronary artery disease (8). The study by Manno et al. found that epicardial fat is associated with systolic and diastolic blood pressure, BMI, and waist circumference (23). In our study, the relationship between epicardial fat volume, serum LDL, and the patient's age was consistent. However, contrary to the results of the mentioned study, in our study, no significant relationship was observed between epicardial fat volume and blood pressure, and BMI, which may be the reason for the difference in the results due to the

difference in the research sample group. A higher risk of coronary heart disease is associated with metabolic syndrome, which was the study group in line with this study. Regarding the relationship between obesity and epicardial fat volume, some researchers believe that epicardial fat reflects visceral fat and plays a role in the severity of coronary disease (24). On the other hand, some others have reported that the fatty acid composition of subcutaneous and epicardial fat is different (16, 25). This study was conducted at a single medical center, which limits the generalizability of the results to other populations. Larger, multicenter studies are needed to validate these findings across different demographics and clinical settings. As a cross-sectional study, it does not establish causality between epicardial fat volume (EFV) and coronary artery stenosis. Longitudinal studies are required to determine the predictive role of EFV in CAD progression over time. Future research should focus on longitudinal studies to establish the temporal relationship between EFV and the progression of coronary artery stenosis. This would help clarify the role of EFV as a predictive marker for CAD. Conducting multicenter studies involving diverse populations from different geographical and clinical settings could improve the generalizability of the findings and confirm the association between EFV and CAD across different ethnicities and age groups.

Future studies could incorporate advanced imaging modalities and analyses, such as cardiac MRI, PET scans, and quantitative analysis like radiomics, to provide more comprehensive evaluations of epicardial fat and its metabolic activity, thereby improving the accuracy of CAD risk assessment. Epicardial fat volume and coronary artery stenosis severity is significantly related in people with medium and low risk of coronary artery disease. Coronary artery stenosis and severity can be determined and predicted with an epicardial fat volume marker. Coronary artery stenosis and severity may be predicted by measuring epicardial fat volume in people with medium and low risk of coronary artery disease. It would be useful to investigate the relationship between epicardial fat volume and coronary artery stenosis in a more comprehensive study.

Acknowledgments

We sincerely thank the patients and medical staff of Farshchian Cardiovascular Hospital for their valuable contributions to this study.

Funding: Financial support for this research was provided by the Vice-Chancellor for Research and Technology of Hamadan University of Medical Sciences, Hamadan, Iran (Grant No. 32121).

Ethics approval: The study protocol adhered to the 2013 Helsinki Declaration, and the study received approval from the research and Ethics Committee at Hamadan University of Medical Sciences (IR.UMSHA.REC.1398.171). All participants gave written informed consent before participating in the study.

Conflict of interests: The authors declare that they have no conflicts of interest.

Authors' contribution: S.K.H.: Conceptualization, supervision, resources, writing-review & editing; G.M.R.B.: Investigation, data curation; A.F.J.: Methodology, formal analysis, software, validation, writing-original draft, writing-review & editing; M.A.S.R.: Study design, methodology, statistical analysis, validation; S.K.Ha.: Data curation, investigation, administration, visualization, writing-review & editing.

Data sharing: The datasets utilized and analyzed in this study can be obtained from the corresponding author upon reasonable request.

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