SCIENTIFIC RESEARCH

CHARACTERISTICS OF AORTIC VALVE CALCIFICATION AND EPICARDIAL DIPOSE TISSUE ON CARDIAC COMPUTED TOMOGRAPHY ANGIOGRAPHY IN PEOPLE AT HIGH CARDIOVASCULAR RISK

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SUMMARY

Objective: To describe the characteristics of aortic valve calcification (AVC) and epicardial adipose tissue (EAT) on coronary computed tomography (CT) in people at high cardiovascular risk.

Methods: A cross-sectional study was conducted on 102 patients at Bach Mai Hospital from August 2023 to June 2024. Patients were assessed using dual-source CT imaging. AVC was quantified semi-automatically using the Agatston scoring method, like coronary artery calcification scoring, while epicardial fat was measured semi-automatically using Singo software.

Results: Among the 102 patients, 56 (54.9%) had aortic valve calcification and 46 (45.1%) did not. Patients with AVC were significantly older and had higher body mass index (BMI), and greater epicardial fat thickness (EFT) compared to those without AVC. The mean epicardial fat volume (EFV) was 51.8±17.5 cm³, and the epicardial fat volume index (EFVi) was 31.5 ± 10.9 cm³/m². The mean epicardial fat attenuation (mEA) was -85.1±6.1 HU, and it was significantly associated with risk factors such as age, BMI, and diabetes ($p < 0.05$).

Conclusion: CCTA provides valuable insights into the extent of aortic valve calcification and epicardial fat in high-risk cardiovascular patients. Monitoring these indicators can help improve cardiovascular risk management and prediction.

Keywords: *Epicardial fat tissue, aortic valve stenosis calcification, transcatheter aortic valve replacement, coronary Computed Tomography Angiography.*

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I. INTRODUCTION

Aortic stenosis caused by calcification is the most common valvular heart disease and it prevalence is rising globally, impacting both developed and developing countries including Vietnam [1]. This condition poses a significant challenge and burden due to the lack of specific treatments to halt disease progression, with the only definitive solution being aortic valve replacement. Increasing evidence worldwide highlights the critical role of epicardial adipose tissue (EAT) in the development of various cardiovascular diseases and metabolic disorders [2]. Consequently, EAT is considered an independent prognostic factor in atherosclerotic cardiovascular diseases, including aortic valve calcification [3].

Aortic valve and epicardial adipose tissue (EAT) imaging is primarily based on echocardiography, which has several limitations that can be better assessed both qualitatively and quantitatively by computed tomography (CT). This study was conducted with the objective: "To describe the characteristics of aortic valve calcification and epicardial adipose tissue on coronary computed tomography in people at high cardiovascular risk".

II. MATERIALS AND METHODS

2.1. Study Population

Inclusion Criteria:

• Patients with high cardiovascular risk according to the SCORE2 [4] and SCORE2-OP [5] risk assessment models developed by the European Society of Cardiology, were indicated for Coronary Computed Tomography Angiography (CCTA) from August 2023 to June 2024 at Bach Mai Hospital.

• Patients who consented to participate in the study.

Exclusion Criteria:

• Patients with contraindications to intravenous contrast agents (e.g., history of contrast agent allergy).

• Poor image quality on CCTA hampers diagnostic assessment due to image artifacts, blurriness, or segments with undistinguishable vascular structures.

• Patients who have undergone surgery or interventions related to the aortic valve or aorta.

• Patients with a history of rheumatic heart disease.

2.2. Study Design: Cross-sectional study.

2.3. CT imaging protocol:

Patients were scanned using a Dual-Source Somatom Definition Flash CT scanner (Siemens Healthineers, Germany) equipped with an electrocardiogram (ECG) gating system. Intravenous injection of 70 ml of non-ionic contrast agent Iopromide (350 mg/ml) was administered at a rate of 5 ml/second, followed by 40 ml of isotonic saline. Scanning time ranged from 5.7 to 8.4 seconds. The ECG gating system was used to reconstruct data, and imaging was performed at RR intervals of 70-80%.

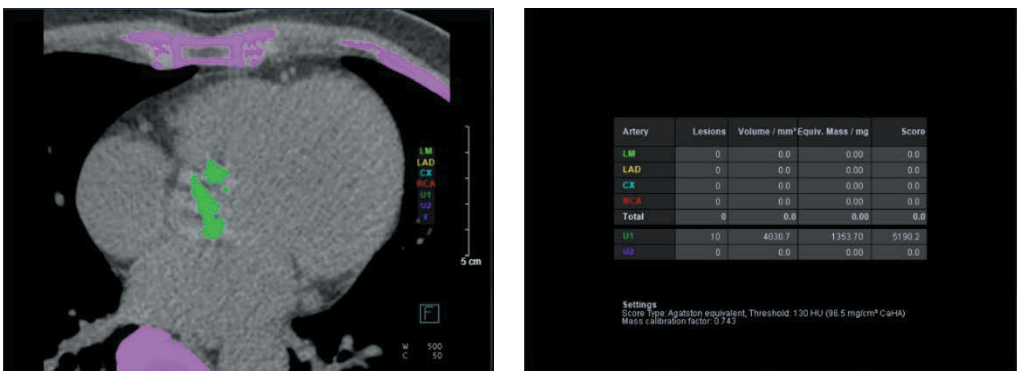

Figure 1. Illustration of a patient with aortic valve calcification measured using the Agatston method

The aortic valve was assessed for thickness, degree of calcification using the Agatston score (with calcification defined as an attenuation threshold >130 HU), and valve area. Severe aortic stenosis was defined by aortic opening area < 1.0 cm² [6].

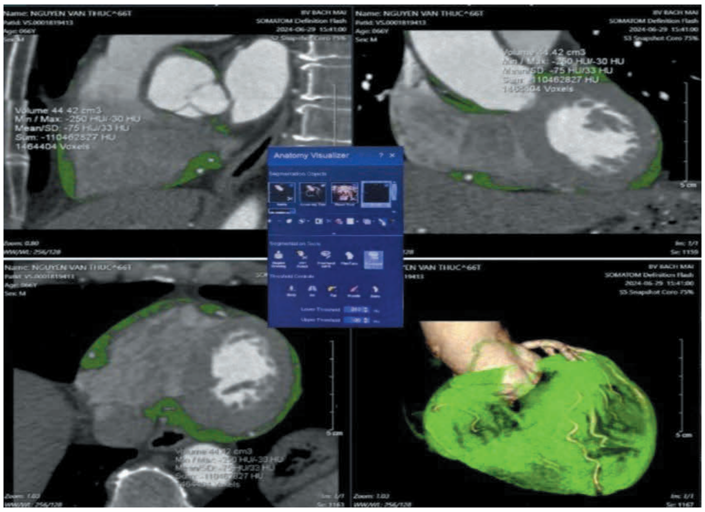

Figure 2. Analysis of epicardial adipose tissue (EAT) on computed tomography images

Epicardial fat, located between the epicardium and myocardium, was identified with attenuation values ranging from -250 to -30 Hounsfield units. Epicardial fat volume (EFV) and mean epicardial fat attenuation (mEA) were measured using the semi-automated Syngo.via software (Siemens Healthineers, Germany). Epicardial fat thickness was measured at the anterior right ventricle. Additionally, concomitant coronary artery lesions were assessed using the Coronary Artery Disease Reporting and Data System (CAD-RADS) [7].

2.4. Statistical Analysis

Data were analyzed using descriptive statistics with IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). The Kruskal-Wallis test was used to compare variables with non-normal distributions, and correlations between two groups were assessed using Spearman's correlation coefficient. Quantitative variables following a normal distribution were compared using the T-test. Qualitative data were compared using the Chi-Square test. A p-value of <0.05 was considered significant. A 95% confidence interval reflects a significance level of 0.05.

2.5. Research Ethics

All patient information was kept confidential and was used solely for research purposes, with no other objectives.

III. RESULTS

A total of 102 patients were divided into two groups: one without aortic valve calcification (46 patients) and one with aortic valve calcification (56 patients). The mean age was 74.4 ± 11.2 years, with 59 (57.8%) males.

3.1. Baseline Participant Characteristics

Table 1. Patients'characteristics

Characteristics	All Participants (n = 102)	No Aortic Valve Calcification (n = 46 ~ 45.1%)	Aortic Valve Calcification (n = 56 ~ 54.9%)	p
Age (years)	74.4 ± 11.2	69.8 ± 12.1	78.3 ± 8.7	0.000
Male (%)	59 (57.8%)	29 (63%)	30 (53.6%)	0.335
Female (%)	43 (42.2%)	17 (37%)	26 (46.4%)	
BMI (kg/m2)	22.3 ± 1.3	21.7 ± 0.8	22.8 ± 1.4	0.000
Hypertension (%)	57 (55.9%)	24 (52.2%)	33 (58.9%)	0.494

Diabetes (%)	14 (13.7%)	6 (13%)	8 (14.3%)	0.856
Hyperlipidemia (%)	41 (40.2%)	14 (30.4%)	27 (48.2%)	0.068
Smoking (%)	27 (26.5%)	13 (28.3%)	14 (25%)	0.710
Coronary artery stenosis >50%	23 (22.5%)	3 (6.5%)	20 (35.7%)	0.000

The group with aortic valve calcification (AVC) had a significantly higher mean age compared to the group without AVC ($p < 0.001$). There was no significant difference in gender distribution between the two groups ($p = 0.575$). The average body mass index (BMI) was higher in the AVC group compared to the non-AVC group (22.8 ± 1.4 vs. 21.7 ± 0.8, $p < 0.001$). There were no significant differences in hypertension, diabetes and smoking between the two groups ($p > 0.05$). Dyslipidemia was more prevalent in the AVC group (48.2% vs. 30.4%, $p = 0.068$), though it did not reach statistical significance. Coronary artery stenosis > 50% was significantly higher in the AVC group ($p < 0.001$).

3.2. Imaging Characteristics of the Aortic Valve and Epicardial Fat Tissue on CCTA

Table 2. Aortic valve imaging parameters

Parameter	All Participants (n = 102)	No Aortic Valve Calcification (n = 46)		Aortic Valve Calcification (n = 56)		
		No Stenosis (n = 46)	Stenosis (n = 0)	No Stenosis (n = 48)	Stenosis (n = 8)	p
AVCS (HU)	430.3 ± 1491.8	0	0	99.1 ± 137.9	4891.7 ± 2695.8	0.000
AVCi (HU/m^2)	255.8 ± 899.9	0	0	58.1 ± 78.1	2912.6 ± 1696.8	0.000
AVT (mm)	1.6 ± 0.7	1.2 ± 0.3	0	1.6 ± 0.4	3.7 ± 0.7	0000

(AVCS, aortic valve calcification score; AVCi, aortic valve calcification index; AVT, aortic valve thickness)

All 102 patients in our study had trileaflet aortic valves, with no cases of valve leaflet abnormalities. In the group without aortic valve calcification, none of the patients had aortic stenosis, with an average valve thickness of 1.2 ± 0.3 mm. In the group with aortic valve calcification, 8 patients had aortic stenosis, with significantly higher aortic valve calcification scores, indexed aortic valve calcification scores (AVCi), and valve thickness compared to the group without stenosis ($p < 0.001$).

Table 3. Results of EAT parameters and their association with characteristics of patients

Parameter	EFT(mm) 5.6 ± 1.3	EFV(cm^3) 51.8 ± 17.5	EFVi(cm^3/m^2) 31.5 ± 10.9	mEA(HU) - 85.1 ± 6.1
Age (years)	p = 0.462 r = - 0.074	p = 0.89 r= - 0.014	p = 0.984 r = - 0.002	p = 0.039 r = 0.205
Sex	p = 0.564	p = 0.177	p = 0.002	p = 0.121
BMI (kg/m^2)	p = 0.000 r = 0.346	p = 0.805 r = 0.025	p = 0.5 r= - 0.068	p = 0.02 r = 0.231

Hypertension	p = 0.067	p = 0.644	p = 0.99	p = 0.779
Diabetes	p = 0.668	p = 0.239	p = 0.205	p = 0.047
Dyslipidemia	p = 0.003	p = 0.992	p = 0.898	p = 0.766
Smoking	p = 0.259	p = 0.359	p = 0.064	p = 0.086
Coronary artery stenosis >50%	p = 0.262	p = 0.599	p = 0.322	p = 0.258

(EFT, epicardial fat thickness; EFV, Epicardial fat volume; EFVi, epicardial fat volume index; mEA, epicardial fat attenuation)

The results indicate that EFT is moderately correlated with body mass index (BMI) and dyslipidemia ($p < 0.05$). Epicardial fat volume (EFV) does not show a significant association with cardiovascular risk factors. However, when adjusted for body surface area (BSA), the EFVi shows a statistically significant difference by gender, with females (35.6 ± 9.5 cm^3/m^2) tending to have higher values than males (28.8 ± 11.2 cm^3/m^2). The mean epicardial fat attenuation (mEA) is also associated with age, BMI, and diabetes ($p < 0.05$). Other factors such as hypertension, smoking, and coronary artery stenosis do not show any significant correlation with EAT parameters.

Table 4. Comparison of EAT Parameters Between Patients With and Without AVC

Parameter	All Participants (n = 102)	No Aortic Valve Calcification (n = 46 ~ 45.1%)	Aortic Valve Calcification (n = 56 ~ 54.9%)	p
EFT (mm)	5.6 ± 1.3	5.2 ± 1.1	6.1 ± 1.4	**0.002**
EFV (cm^3)	51.8 ± 17.5	53.4 ± 16	50.5 ± 18.7	0.414
EFVi (cm^3/m^2)	31.5 ± 10.9	32.7 ± 10.0	30.7 ± 11.8	0.365
mEA (HU)	- 85.1 ± 6.1	- 84.7 ± 7.4	- 85.4 ± 4.8	0.465

The average epicardial fat thickness (EFT) for the entire study population was 5.6 ± 1.3 mm. The group with aortic valve calcification had a significantly higher EFT compared to the group without calcification ($p = 0.002$). However, there were no statistically significant differences in other EAT parameters between the two groups.

Table 5. Correlation between EAT and Aortic Valve Calcification

Parameter	AVCS(HU)		AVCi (HU/m^2)	
	r	p	r	p
EFT (mm)	**0.483**	**0.000**	**0.483**	**0.000**
EFV (cm^3)	- 0.156	0.118	- 0.156	0.118
EFVi (cm^3/m^2)	- 0.192	0.054	- 0.188	0.058
mEA (HU)	0.079	0.432	0.081	0.418

Results of the analysis indicate that the epicardial fat thickness (EFT) shows a moderately significant linear correlation with aortic valve calcification (AVCS and AVCi), with a p-value < 0.001. In contrast, the parameters related to volume and mean attenuation (EFV, EFVi, and mEA) did not demonstrate a statistically significant correlation with aortic valve calcification, with p-values > 0.05.

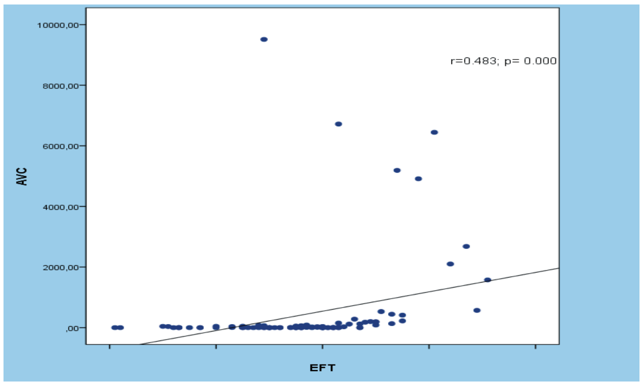

Figure 3. Correlation between EFT and AVC

IV. DISCUSSION

Aortic valve calcification (AVC) and epicardial adipose tissue (EAT) are receiving increasing attention in biomedical research due to their roles in inflammatory processes and metabolic disorders associated with atherosclerotic cardiovascular diseases [8]. Our study analyzed imaging parameters of AVC and EAT, and their associations with general cardiovascular risk factors.

The results indicate that patients with AVC had significantly higher average age and BMI compared to those without calcification, consistent with findings from previous studies such as Ferreira-González (2013) [9], Milanese et al (2019) [10]. Additionally, the prevalence of coronary artery stenosis >50% was also higher in the group with AVC, consistent with the findings of Thien Vu (2021) [11] and Son Bui et al (2022) [12] which indicate that patients with severe aortic valve calcification and thickening often have more extensive coronary artery involvement compared to those with mild calcification. However, factors such as hypertension, smoking, and dyslipidemia did not show significant differences. This may be attributed to the study sample primarily being in the early stages of aortic valve damage, with only 8 (7.8%) patients in the advanced stage exhibiting moderate to severe aortic stenosis. In terms of CCTA imaging characteristics, patients with aortic stenosis had significantly higher levels of valve thickening and calcification compared to those without stenosis, consistent with the findings of Pawade (2019) [13] and Doris (2020) [14], highlighting that AVC is a crucial marker for predicting valve stenosis and disease progression.

Regarding EAT, we found that the thickness of EAT was significantly correlated with BMI and dyslipidemia ($p < 0.05$), while other factors did not show a notable correlation. This result aligns with and differs from the findings of Çetin (2013) [15], who also identified associations with age, male gender, and obesity through BMI but did not observe relationships with dyslipidemia, blood glucose, or smoking. Currently, studies worldwide have not reached a consensus on the relationship between epicardial adipose tissue and gender. Our findings indicate that after adjusting for body surface area (BSA), the EFVi index was significantly higher in females compared to males, which is consistent with Shim's results [16] but differs from Mazzocco's study [17]. This discrepancy may be attributed to variations in fat distribution between genders, particularly in postmenopausal women, as well as differences in demographic characteristics across countries. Additionally, we found that the mean epicardial adipose tissue density (mEA) was significantly related to age, BMI, and diabetes ($p < 0.05$), in agreement with Jie Liu's study (2023) [18]. Other factors did not show statistically significant differences with EAT parameters, which may be due to sample selection or the study sample size not being large enough or representative of the general Vietnamese population.

The pathophysiology of aortic valve thickening and calcification has been shown to significantly involve inflammatory factors [19]. EAT has the potential to secrete inflammatory mediators that contribute to the progression of cardiovascular disease, including aortic valve calcification [3]. In our study, the thickness of epicardial adipose tissue (EFT) was significantly higher in patients with aortic valve calcification compared to those without calcification, with a moderate linear correlation between EFT and aortic valve calcification (AVC) showing a p-value < 0.001 and $r = 0.483$, consistent with the findings of Alnabelsi (2016) [20] However, epicardial adipose tissue volume (EFV) and the indexed EFVi did not show significant differences between the two groups ($p > 0.05$). Similarly, Eberhard (2019) [21] did not find a correlation between EFV and AVC ($p = 0.429$). Nevertheless, other studies have indicated that EFV not only has prognostic value for cardiovascular events in asymptomatic aortic stenosis patients [22] but also independently correlates with all-cause mortality following transcatheter aortic valve replacement [21]. Nabati et al. (2018) concluded that EAT was a factor that has driven the progression of AVC [23].

Overall, our study provides additional insights into the characteristics of aortic valve calcification, epicardial adipose tissue, and their associations with cardiovascular risk factors. Compared with international studies, our findings align with key relationships but also reveal some discrepancies. These findings underscore the need for further research projects to gain a deeper understanding of contemporary cardiovascular risk factors.

V. CONCLUSION

Coronary Computed Tomography imaging reveals that both aortic valve calcification (AVC) and epicardial adipose tissue (EAT) are correlated with cardiovascular risk factors in patients at high risk for cardiovascular disease. AVC is closely related to age, body mass index (BMI), and coronary artery disease severity, while the thickness and average density of EAT are collerated with BMI, dyslipidemia, and diabetes. The linear correlation between EAT thickness and AVC suggests that EAT may contribute to the progression of this calcification process.

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