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Relationships of pericoronary and epicardial fat measurements in male and female patients with and without coronary artery disease

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ABSTRACT

Introduction: Although pericoronary adipose tissue (PCAT) is a component of the epicardial adipose tissue (EAT) depot, they may have different associations to coronary artery disease (CAD). We explored relationships between pericoronary adipose tissue mean attenuation ($PCAT_{MA}$) and EAT measurements in coronary CT angiography (CCTA) in patients with and without CAD.

Material and Methods: CCTA scans of 185 non-CAD and 81 CAD patients (86.4% >50% stenosis) were included and retrospectively analyzed. $PCAT_{MA}$ and EAT density/volume were measured and analyzed by sex, including associations with age, risk factors and tube voltage using linear regression models.

Results: In non-CAD and CAD, mean $PCAT_{MA}$ and EAT volume were higher in men than in women (non-CAD: -92.5 ± 10.6HU vs -96.2 ± 8.4HU, and 174.4 ± 69.1 cm^3 vs 124.1 ± 57.3 cm^3; CAD: -92.2 ± 9.0HU vs -97.4 ± 9.7HU, and 193.6 ± 62.5 cm^3 vs 148.5 ± 50.5 cm^3 ($p < 0.05$)). EAT density was slightly lower in men than women in non-CAD (-96.4 ± 6.3HU vs -94.4 ± 5.5HU ($p < 0.05$)), and similar in CAD (-98.2 ± 5.2HU vs 98.2 ± 6.4HU). There was strong correlation between $PCAT_{MA}$ and EAT density (non-CAD: $r = 0.725$, $p < 0.001$, CAD: $r = 0.686$, $p < 0.001$) but no correlation between $PCAT_{MA}$ and EAT volume (non-CAD: $r = 0.018$, $p = 0.81$, CAD: $r = -0.055$, $p = 0.63$). A weak inverse association was found between EAT density and EAT volume (non-CAD: $r = -0.244$, $p < 0.001$, CAD: $r = -0.263$, $p = 0.02$). In linear regression models, EAT density was significantly associated with $PCAT_{MA}$ in both non-CAD and CAD patients independent of risk factors and tube voltage.

Conclusion: In CAD and non-CAD patients, EAT density, but not EAT volume, showed significant associations with $PCAT_{MA}$. Compared to women, men had higher $PCAT_{MA}$ and EAT volume independently of disease status, but similar or slightly lower EAT density. Differences in trends and relations of $PCAT_{MA}$ and EAT by sex could indicate that personalized interpretation and thresholding is needed.

1. Introduction

There is increasing interest in pericoronary inflammation as predictor and stratifying factor for coronary artery disease (CAD). Inflammation of coronary arteries is present even before atherosclerotic plaque development[1–3]. Inflammatory biomarkers in CAD may be able to identify patients who benefit from prevention and early treatment[4]. Epicardial adipose tissue (EAT) is the adipose tissue depot

Abbreviations: BMI, Body mass index; CAD, Coronary artery disease; CCTA, Coronary computed tomography angiography; CPR, Curved planar reformation; CVD, Cardiovascular disease; EAT, Epicardial adipose tissue; FAI, Fat attenuation index; kVp, Peak kilovoltage; LAD, Left anterior descending coronary artery; LCx, Left circumflex coronary artery; MACE, Major adverse cardiac events; MI, Myocardial infarction; MPR, MultiPlanar Reconstruction; MRI, Magnetic resonance imaging; $PCAT_{MA}$, Pericoronary adipose tissue mean attenuation; RCA, Right coronary artery; SD, Standard deviation.

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surrounding coronary arteries and myocardium, contained within the pericardium[5]. Higher EAT volume on coronary computed tomography angiography (CCTA) is associated with cardiovascular risk factors, coronary artery calcification and major adverse cardiac events[6]. Moreover, EAT volume can discriminate between patients with and without high-risk coronary plaques, and patients without CAD[7]. EAT volume reflects inflammatory mediators in high-risk CAD patients[8]. Pericoronary adipose tissue (PCAT) refers to the adipose tissue directly surrounding coronary arteries, and is part of the EAT depot [9]. Higher $PCAT_{MA}$ predicts cardiac mortality in patients undergoing CCTA[10]. Other studies have shown the ability of $PCAT_{MA}$ to identify patients with CAD, myocardial infarction (MI)[11] and hemodynamically significant coronary lesions[12]. In a post-hoc analysis of SCOT-HEART trial data, CCTA derived low-attenuation plaque burden and $PCAT_{MA}$ increased the predictive value for 5-year risk of MI[13].

Although PCAT is part of the EAT depot, there may be different relations to coronary inflammation. As PCAT is in closer proximity of the coronary artery, its inflammatory effect on the arterial wall could be stronger than for the larger EAT compartment. There is abundant evidence regarding the relationship of EAT to CAD and cardiovascular events[14,15]. However, how PCAT and EAT biomarkers relate to each other is still unclear. If and how we can use either or both measures in clinical practice necessitates knowledge on the relationship between these parameters in non-CAD and CAD patients, and identification of influencing factors. We hypothesized that sex may be an important influencing factor as previous studies showed sex to be significantly associated with CAD and MACE risk[16,17].

This study aimed to evaluate the relationships between CCTA-derived PCAT and EAT measures in patients with and without CAD, and study influencing factors of these parameters, in particular sex.

2. Methods

2.1. Study population

Patients who underwent CCTA for routine indications from January 2015 to November 2017 at the University Medical Center Groningen were identified retrospectively. We selected two groups of patients for the current analysis: a non-CAD group, and a CAD group, to maximize the range of included CAD. For the non-CAD group, the inclusion criteria were: 1) angina indication; 2) no coronary plaque on CCTA. This patient cohort, except for three patients without angina indication, was used in a previous study[18] focusing on the technical aspects of $PCAT_{MA}$. As invasive coronary angiography (with or without fractional flow reserve) is considered the reference standard for assessing the severity of stenosis in the coronary artery, patients with invasive coronary angiography were included. This helped to include patients at both ends of the spectrum (namely: no coronary atherosclerosis at all on CTA vs stenotic disease on reference standard imaging) and maximize the difference in groups that are compared. For the CAD group, the inclusion criteria were 1) angina indication, 2) CAD on CCTA, and 3) invasive coronary angiography (with/without fractional flow reserve) performed. Exclusion criteria for both groups were: 1) objection to data use for scientific research; 2) poor CCTA image quality; 3) anomalous coronary artery origin in which $PCAT_{MA}$ cannot be acquired. The ethical committee of the University Medical Center Groningen approved this retrospective study, and the need for informed consent was waived. The study was compliant with the Declaration of Helsinki. Data was stored and analyzed in a de-identified setting.

2.2. CCTA imaging protocol

A third generation dual-source CT system (Somatom Force; Siemens Healthineers) was used for CCTA imaging following clinical protocol. Nitroglycerin was administered to each patient, unless nitroglycerin use was contra-indicated. Intravenous beta-blocker was administered to patients with high heart rate (>73 beats/minute) and no contra-indications. The tube voltage was 70–120 kilovoltage peak (kVp) according to patient size, determined by CarekV. Depending on heart rate frequency and regularity, a sequential or high-pitch scan mode was used. A dual bolus of contrast media (Iomeron 350; Bracco Altana Pharma) was injected with dose and flow-rate depending on patient characteristics and scan mode. CCTA images were reconstructed with a slice thickness of 0.6 mm.

2.3. CCTA post-processing and quantification

Dedicated software (Aquarius iNtuition, TeraRecon, version 4.4.13) was used. For CCTA post-processing, a three-dimensional model, curved planar reformat images, and multiplanar reformat images were semi-automatically reconstructed. Coronary artery segments with a diameter > 2 mm were analyzed. A radiologist with 8-year experience in CCTA, blinded to patient information, performed all measurements. In case of doubt, a radiologist with 15-year experience was consulted.

$PCAT_{MA}$ was based on right coronary artery (RCA) measurements following prior papers[9,19]. Tissues included in $PCAT_{MA}$ were set to the range from −190HU to −30HU according to the proof-of-concept paper[9]. To prevent artifacts caused by aortic enhancement, measurements started 10 mm from the RCA ostium. The measurement length and width were 40 mm and 3 mm, respectively. A 1 mm gap around the lumen was left to avoid contrast related artifacts. Tissue within a threshold of −190HU to −30HU was included. $PCAT_{MA}$ was defined as the mean CT value of the adipose tissue, see Fig. 1.

EAT was defined as the adipose tissue between epicardium and pericardium[5]. First, a three-dimensional volume-rendering model was reconstructed automatically. Then, unrelated tissues were manually removed. Next, by setting CT range between −190HU to −30HU, the EAT density (HU) and volume (cm^3) were automatically calculated (Fig. 1).

2.4. Clinical data

Age, sex, body mass index (BMI) and risk factors of patients were collected from the medical records. Risk factors within three months of the CT scan were defined as present or absent: a) Hypertension; b) Hyperlipidemia; c) Diabetes mellitus; d) Smoking; e) Family history with CAD. When the aforementioned risk factors were not mentioned in the medical records, those were considered as absent.

2.5. Statistical analysis

Continuous variables were evaluated with the Kolmogorov-Smirnov test for normal distribution. Normally distributed data were represented as mean and standard deviation (SD). For the categorical variables, numbers and percentages were reported. Chi-square testing was used to test the differences in risk factors between male and female patients. Independent sample t-tests were used to test differences in $PCAT_{MA}$, EAT density and volume by sex, and in groups with and without risk factors. Pearson's correlation was used to assess correlation between $PCAT_{MA}$ and EAT density/volume. Generalized linear models (GLM) were used to evaluate the relationships between EAT density/volume and $PCAT_{MA}$ in male and female patients (basic GLM). In addition, the GLM model was extended by including age, and risk factors (defined as extended GLM1), and further extended by adding tube voltage (defined as extended GLM2). Akaike information criterion (AIC) was used to evaluate model fit; a smaller AIC value reflects better model fit with higher prediction ability and better fit with the data. P-values < 0.05 were considered significant. Statistical analysis was performed using SPSS version 25 (IBM, Armonk, NY, USA).

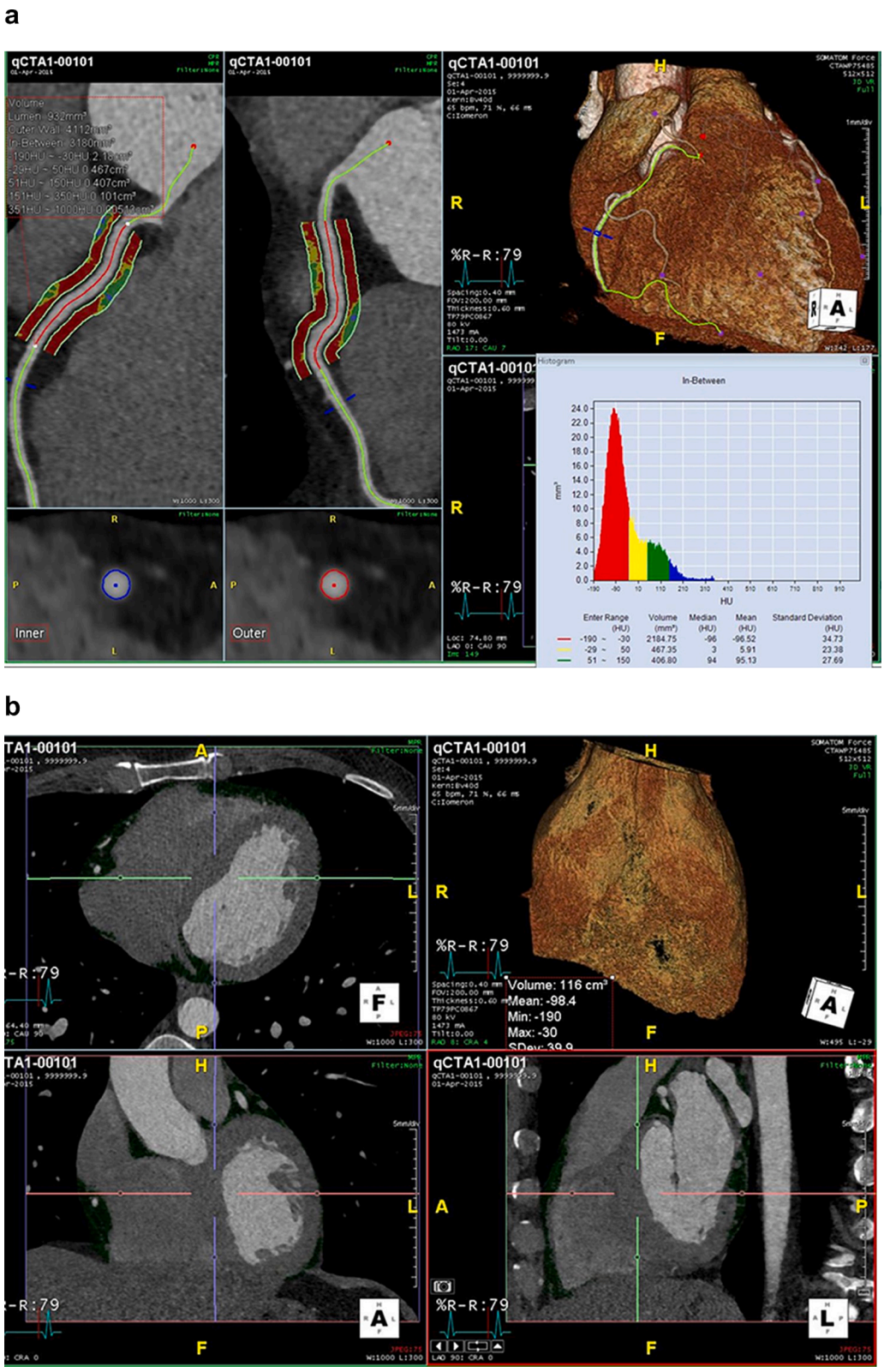

Fig. 1. Schematic overview of $PCAT_{MA}$, EAT volume and EAT density measurements. The images are from a 36-year-old male patient. For the figure, the top row shows the $PCAT_{MA}$ measurements, and the lower figures show the EAT volume and EAT density measurements. In $PCAT_{MA}$ measurement, the red zone is the PCAT. In EAT measurements, the green zone on the MPR images is the EAT.

3. Results

3.1. Patient demographics

In total 185 non-CAD patients and 81 CAD patients were included (mean age of 54.0 ± 12.2 years; 121(45.5%) men). The mean age and sex distribution for non-CAD patients were 50.5 ± 11.6 years, 70 (37.8%) men, and for CAD patients 61.9 ± 9.5 years, 51 (63.0%) men. An overview of patient demographics is displayed in Table 1. There were no significant differences in characteristics between male and female patients except in the non-CAD group where hypertension was more prevalent in women ($p = 0.02$). Tube voltage was used as an indirect measure of patient size.

3.2. PCAT and EAT measurements

Fig. 2 shows an overview of all fat parameters. $PCAT_{MA}$, EAT density and EAT volume for patients with and without risk factors are shown in Table 2. In non-CAD and CAD, mean $PCAT_{MA}$ and EAT volume were higher in men than in women (non-CAD: −92.5 ± 10.6HU vs −96.2 ± 8.4HU, and 174.4 ± 69.1 cm^3 vs 124.1 ± 57.3 cm^3; CAD: −92.2 ± 9.0HU vs −97.4 ± 9.7HU, and 193.6 ± 62.5 cm^3 vs 148.5 ± 50.5 cm^3 ($p < 0.05$)). EAT density was slightly lower in men than women in non-CAD (-96.4 ± 6.3HU vs −94.4 ± 5.5HU ($p < 0.05$)), and similar in CAD (−98.2 ± 5.2HU vs 98.2 ± 6.4HU).

3.3. Relationships between PCAT and EAT measurements

A strong, significant correlation was found between $PCAT_{MA}$ and EAT density in non-CAD ($r = 0.725$, $p < 0.001$) and CAD ($r = 0.686$, $p < 0.001$). There were no relationships between $PCAT_{MA}$ and EAT volume in non-CAD ($r = 0.018$, $p = 0.811$) and CAD ($r = 0.055$, $p = 0.626$). There were weak, significant inverse correlations between EAT density and EAT volume in non-CAD ($r = -0.244$, $p = 0.001$) and CAD ($r = -0.263$, $p = 0.018$). $PCAT_{MA}$, EAT density and EAT volume were correlated to age ($r = -0.172$, $p = 0.019$ for $PCAT_{MA}$, $r = -0.256$, $p < 0.001$ for EAT density, $r = 0.324$, $p < 0.001$ for EAT volume) in non-CAD but not in CAD. Correlations between $PCAT_{MA}$, EAT density and EAT volume by sex in non-CAD and CAD patients are demonstrated in Table 3. There was a weak inverse correlation between EAT density and EAT volume in men while there was no such significant correlation in women. $PCAT_{MA}$ and EAT density were strongly correlated in both men and women.

3.4. Model-based analysis of PCAT and EAT measurements

EAT density was associated with $PCAT_{MA}$ in male and female patients with and without CAD ($p < 0.001$) after adjustment for confounders in all GLM models (Table 4). In the extended GLM2, EAT volume was weakly but significantly (inversely) correlated to $PCAT_{MA}$ in male and female non-CAD patients ($p < 0.001$) while in the CAD group EAT volume was only associated with $PCAT_{MA}$ in male patients. Age was associated with EAT density (inversely) and volume (positively) in non-CAD patients while tube voltage was positively related to EAT density, volume and $PCAT_{MA}$ in non-CAD and CAD. (**Table S1-S3**). According to AIC values, models relating EAT to $PCAT_{MA}$ showed a better fit for CAD vs non-CAD, and for EAT density vs EAT volume. **Figure S1** shows the linear relations between tube voltage and EAT density in non-CAD and CAD patients.

4. Discussion

In patients with and without CAD, we showed a strong association between $PCAT_{MA}$ and EAT density, but no correlation between $PCAT_{MA}$ and EAT volume. EAT density and EAT volume showed a weak inverse relationship. Men had higher $PCAT_{MA}$ and EAT volume than women, while EAT density showed the opposite trend. The differences in $PCAT_{MA}$ (around 4HU) and in EAT volume (50 cm^3) between male and female patients were small but significant. GLM results showed that EAT density was significantly related to $PCAT_{MA}$ in all patients after correcting for risk factors.

The relationship between EAT volume and EAT density has been studied before. In 456 individuals, lower EAT density and higher EAT volume on non-contrast cardiac CT were associated with coronary calcification, serum levels of plaque inflammatory biomarkers and major adverse cardiac events[20]. A second study reported an inverse association between EAT density and volume in a non-CAD cohort[21]. Furthermore, a meta-analysis concluded an inverse relationship between EAT density and volume in CAD and non-CAD patients[22]. Our study shows that this inverse relationship between EAT density and EAT volume is consistent in male and female patients. The inverse association is likely related to the fact that larger EAT volume implies larger

Table 1
Characteristics of the cohort.

	Non-CAD patients (n = 185)				CAD patients (n = 81)			
	Male patients N = 70 (37.8%)		Female patients N = 115 (62.2%)		Male patients N = 51 (63.0%)		Female patients N = 30 (37.0%)	
Patients' demographics								
Age(years)		50.0 ± 10.7		51.4 ± 12.1		60.0 ± 8.8		65.2 ± 9.8
BMI*		26.0 ± 3.7		26.7 ± 5.9		27.9 ± 4.5		28.2 ± 5.3
Clinical risk factors								
Smoking	30	42.9%	43	37.4%	32	62.7%	20	66.7%
Hypertension	11	15.7%	36	31.3%	34	66.7%	18	60.0%
Diabetes Mellitus	3	4.3%	9	7.8%	12	23.5%	5	16.7%
Family history	23	32.9%	43	37.4%	25	49.0%	10	33.3%
Hyperlipidemia	15	21.4%	20	17.4%	23	45.1%	13	43.3%
Maximal stenosis degree at ICA								
<50%					4	4.9%	7	8.6%
50%~70%					11	13.6%	11	13.6%
>70%					36	44.4 %	12	14.8%
CCTA tube voltage (kVp)								
70	21	30.0%	47	40.9%	17	33.3%	13	43.3%
80	22	31.4%	29	25.2%	16	31.4%	7	23.3%
90	20	28.6%	19	16.5%	15	29.4%	4	13.3%
100–120	7	10.0%	20	17.4%	3	5.9%	6	20.0%

CAD coronary artery disease; BMI body mass index; CCTA coronary CT angiography; EAT Epicardial adipose tissues; ICA Invasive coronary angiography; $PCAT_{MA}$ Pericoronary adipose tissues mean attenuation. *BMI information was available in 105 patients of the 185 patients in healthy group and 69 patients of the 81 patients in CAD group.

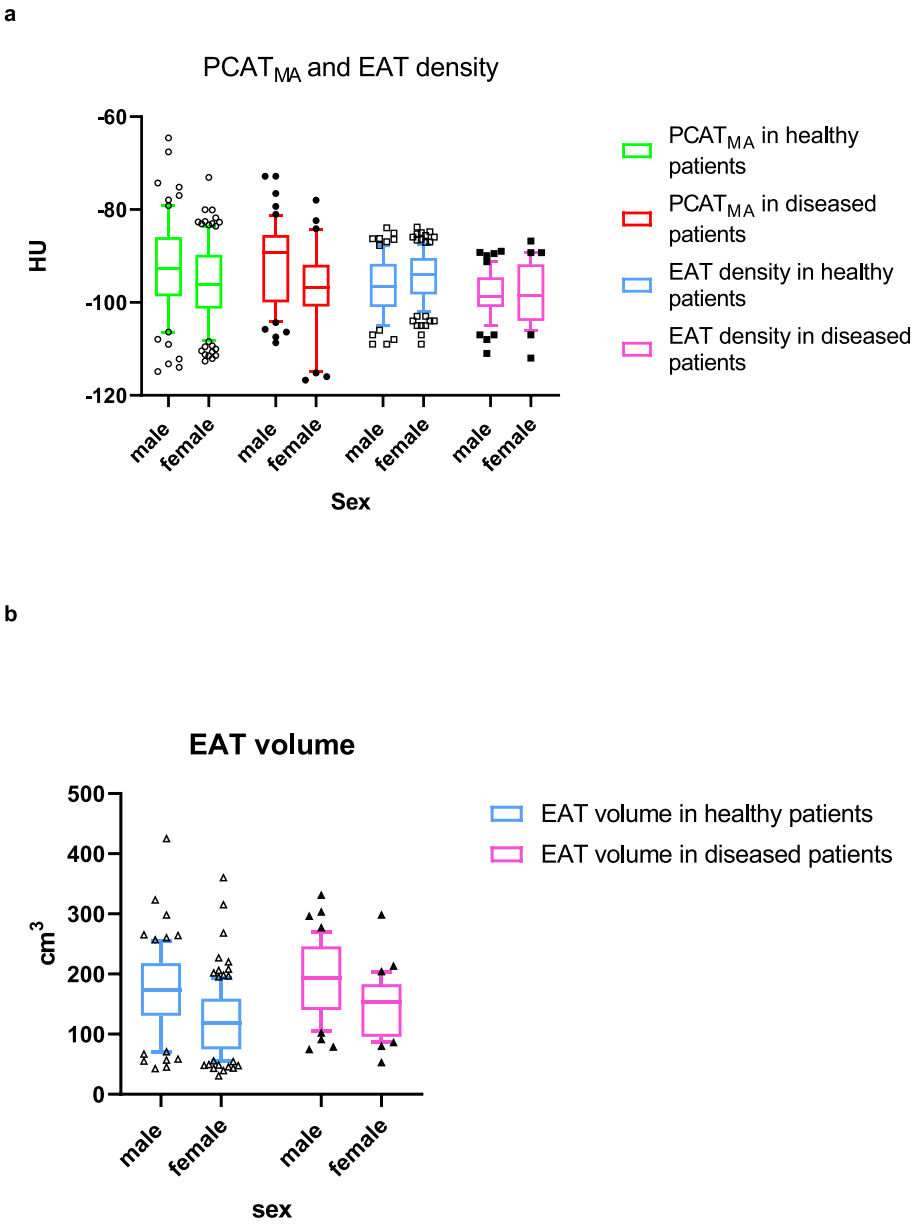

Fig. 2. PCAT$_{MA}$ and EAT density (a) and EAT volume (b) measurements in male and female patients with and without CAD. The error bars indicate the median and interquartile range. The lower error bar represents the 10th percentile, and the upper error bar represents the 90th percentile.

Table 2
Mean values of PCAT$_{MA}$, EAT volume and EAT density by presence of risk factors.

	DM Mean ± SD	**No DM** Mean ± SD	**P value**	**Hyperlipidemia** Mean ± SD	**No Hyperlipidemia** Mean ± SD	**P value**	**Hypertension** Mean ± SD	**No Hypertension** Mean ± SD	**P value**
Non-CAD patients									
	N = 12	N = 173		N = 35	N = 150		N = 47	N = 138	
PCAT$_{MA}$(HU)	-91 ± 10	-95 ± 9	0.20	-98 ± 10	-94 ± 9	0.06	-94 ± 11	-95 ± 9	0.59
EAT density (HU)	-94 ± 7	-95 ± 6	0.38	-97 ± 5	-95 ± 6	0.02	-95 ± 6	-95 ± 6	0.73
EAT volume(cm^3)	154 ± 59	142 ± 67	0.55	166 ± 70	138 ± 65	0.02	161 ± 68	137 ± 65	0.04
CAD patients									
	N = 17	N = 64		N = 36	N = 45		N = 52	N = 29	
PCAT$_{MA}$(HU)	-93 ± 8	-94 ± 10	0.75	-94 ± 9	-94 ± 10	0.93	-93 ± 8	-96 ± 11	0.15
EAT density (HU)	-98 ± 6	-98 ± 5	0.82	-98 ± 6	-98 ± 5	0.73	-98 ± 5	-99 ± 6	0.53
EAT volume(cm^3)	206 ± 45	169 ± 64	0.03	191 ± 58	166 ± 63	0.07	191 ± 59	151 ± 59	0.01

DM Diabetes mellitus; EAT Epicardial adipose tissue; PCAT$_{MA}$ Pericoronary adipose tissue mean attenuation; SD standard deviation.

Table 3
Correlations between $PCAT_{MA}$, EAT density and EAT volume by sex in non– CAD and CAD patients.

Correlations between $PCAT_{MA}$, EAT density and EAT volume		
non-CAD patients	**Men**	**Women**
$PCAT_{MA}$ vs EAT density	r = 0.777, p < 0.001	r = 0.788, p < 0.001
$PCAT_{MA}$ vs EAT volume	r = −0.176, p = 0.146	r = 0.054, p = 0.568
EAT density vs EAT volume	r = −0.326, p = 0.006	r = −0.093, p = 0.324
CAD patients	**men**	**women**
$PCAT_{MA}$ vs EAT density	r = 0.705, p < 0.001	r = 0.723, p < 0.001
$PCAT_{MA}$ vs EAT volume	r = −0.275, p = 0.051	r = 0.048, p = 0.802
EAT density vs EAT volume	r = −0.355, p = 0.011	r = −0.172, p = 0.365

CAD coronary artery disease; EAT Epicardial adipose tissue; $PCAT_{MA}$ Pericoronary adipose tissue mean attenuation.

Table 4
Generalized linear model results for association between $PCAT_{MA}$ and EAT density/volume in non-CAD and CAD patients.

	$PCAT_{MA}$					
	Effect size	P value	AIC	Effect size	P value	AIC
Non-CAD group	**Male patients (n = 70)**			**Female patients (n = 115)**		
Basic GLM						
EAT density	1.310	<0.001	469.1	1.202	<0.001	709.5
EAT volume	−0.027	0.14	531.6	0.008	0.56	820.6
Extended GLM1						
EAT density	1.281	<0.001	475.8	1.237	<0.001	709.1
EAT volume	−0.008	0.65	528.9	0.017	0.27	825.5
Extended GLM2						
EAT density	1.091	<0.001	476.5	1.057	<0.001	703.9
EAT volume	−0.059	<0.001	498.6	−0.069	<0.001	762.9
CAD group	**Male patients (n = 51)**			**Female patients (n = 30)**		
Basic GLM						
EAT density	1.222	<0.001	338.6	1.100	<0.001	204.6
EAT volume	−0.040	0.04	369.6	0.009	0.79	226.7
Extended GLM1						
EAT density	1.157	<0.001	336.6	0.915	<0.001	208.1
EAT volume	−0.041	0.04	366.8	−0.032	0.32	223.0
Extended GLM2						
EAT density	1.034	<0.001	340.2	1.196	<0.001	203.7
EAT volume	−0.086	<0.001	337.4	−0.049	0.10	223.3

AIC Akaike's Information Criterion; CAD coronary artery disease; EAT Epicardial adipose tissue; GLM Generalized linear model; kVp Kilo voltage peak; $PCAT_{MA}$ Pericoronary adipose tissue mean attenuation. Age and risk factors were included in the extended GLM1. Age, risk factors and kVp were included in the extended GLM2.

adipocytes, resulting in lower EAT density, hence CAD processes affect the two measurements differently.

The relationship between PCAT and EAT is unresolved; they are both adipose tissues located in the pericardium, but they have different fat composition and adipocytes. Our results show that $PCAT_{MA}$ was not directly correlated to EAT volume in non-CAD and CAD patients. In the model corrected results, EAT volume was inversely associated with $PCAT_{MA}$ in patients with and without CAD, but only very weakly. It is likely due to the fact that larger fat volume implies larger adipocytes, resulting in lower fat density. In a recent study by Hoshino et al. $PCAT_{MA}$ and EAT volume were also inversely correlated in CAD patients (r = −0.367, p < 0.001)[23]; however, the inverse associations in our study were much weaker.

The relationship of EAT density and $PCAT_{MA}$ has been scarcely explored as $PCAT_{MA}$ is a relatively new biomarker and the role of EAT density as a potential imaging biomarker is still debated[20,24]. The strong correlation shown in the current study is confirmed in one other study, investigating 177 patients with intermediate (30–80%) LAD stenosis on CCTA [23]. This relationship may be explained by the fact that PCAT is part of, and located in, the EAT depot, and both concern measures of CT attenuation. The differential correlations of EAT density and $PCAT_{MA}$ with EAT volume suggest that EAT density and $PCAT_{MA}$ reflect different aspects of the adipose tissue related inflammatory process. However, it is imperative that further study is conducted to investigate whether prognostic value for major adverse cardiovascular events differs for EAT and $PCAT_{MA}$. PCAT and EAT measures differed by sex. Sex is an important influencing factor in CAD patients that affects risk, treatment, and outcomes[25–27]. In our study, male patients without CAD had higher $PCAT_{MA}$, lower EAT density, and higher EAT volume compared to female patients without CAD. Similar trends were found in CAD patients except for EAT density. The sex difference may be explained by the fact that male patients have different sex hormones affecting adipose tissues differently. Recent results from the Omic-scale study show that there are sex-related differences in adipogenesis-related genes and in expression during adipogenesis[25]. A prior study showed that $PCAT_{MA}$ and EAT volume were significantly higher in male than in female patients, while EAT density showed the opposite trend[28]. Our results showed similar trends for $PCAT_{MA}$ and EAT volume, although $PCAT_{MA}$ values were lower due to the fact that scanning was performed at lower kVp. Our study provides evidence that the sex difference in $PCAT_{MA}$ is independent of kVp level, which is important since CCTA is increasingly performed at low tube voltage. In CAD patients, the difference of EAT density between men and women was negligible (<0.1HU); possibly the influence of plaque or stenosis on EAT density overrides the sex difference.

Age is also a known risk factor for CAD and a factor that affects adipose tissue throughout the body. Several studies found that increasing age is independently associated with (higher) EAT volume, potentially by mediating EAT adipokines [29,30]. Our study showed that age was only significantly associated with fat measures in non-CAD patients. Possibly, the presence of CAD affects the local fat compartment more strongly than age.

This study shows that patient-based risk factors such as hyperlipidemia and hypertension were significantly related to EAT volume, rather than EAT density and $PCAT_{MA}$. This suggests that EAT volume is a patient-based biomarker while $PCAT_{MA}$ is more reflective of the local (coronary) inflammatory status[9].

Our study reveals a linear trend between kVp and EAT density/volume and $PCAT_{MA}$ in non-CAD and CAD patients, extending the prior finding in a non-CAD population that tube voltage significantly affects EAT volume and $PCAT_{MA}$[18]. Mohamed *et al* found that EAT volume was overestimated in 100 kVp non-contrast CT scans compared to 120 kVp scans (175 ± 85 ml vs. 159 ± 76 ml) [31]. Thus, tube voltage may also affect EAT volume and even density measurements. After adjustment for influencing factors including kVp, EAT density still showed a significant association with $PCAT_{MA}$.

4.1. Limitations

This is a retrospective, single-center study of patients with clinically indicated CCTA, and no follow-up information is available. CCTA scans were made at a range of kVp levels depending on patient BMI; however, GLM models were used to correct for the influence of kVp, and thereby the effect of BMI, on the adipose tissue biomarkers. BMI and kVp showed a strong linear correlation, and therefore kVp was used as an indirect measure for BMI influence in case of missing BMI value. All measurements were done on contract enhanced CT scans to enable optimal comparison of EAT and $PCAT_{MA}$ measurements without confounding effects of image protocol settings. In this study, we made a deliberate decision not to subtract PCAT voxels from EAT. Our rationale behind this choice was to ensure the utilization of the most widely used and standardized methods for assessing PCAT and EAT. Moreover, we aimed to enhance the generalizability of our findings to other studies in the field.

5. Conclusion

In patients with and without CAD, $PCAT_{MA}$ and EAT density were strongly correlated while EAT volume only showed weak or no correlations with EAT density and $PCAT_{MA}$. Compared to women, men had higher $PCAT_{MA}$ and EAT volume independently of disease status, but similar or lower EAT density. The different trends of these measurements should be considered when using cardiac fat measures as part of CAD risk assessment and clinical decision-making.

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Statistics and Biometry

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Informed Consent

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Ethical Approval

Institutional Review Board approval was obtained.

CRediT authorship contribution statement

Runlei Ma: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Marly van Assen:** Writing – review & editing, Supervision. **Grigory Sidorenkov:** Methodology, Formal analysis. **Daan Ties:** Data curation, Writing – review & editing. **Arthur Stillman:** Writing – review & editing. **Carlo de Cecco:** Writing – review & editing. **Pim van der Harst:** Writing – review & editing, Supervision, Resources. **Rozemarijn Vliegenthart:** Supervision, Project administration, Conceptualization, Methodology, Resources, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejrad.2023.111154.

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