Original Article

Association of mean pericoronary adipose tissue attenuation with different demographic factors in a subgroup of patients without coronary artery disease stratified by sex, body mass index, and age

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Background: In patients without coronary artery disease (CAD), few studies have evaluated the association between mean pericoronary adipose tissue attenuation ($PCAT_{MA}$) and patient-based demographic factors, for example, age or sex. Therefore, the purpose of this study is to investigate the association between $PCAT_{MA}$ and various demographic factors in patients without CAD.

Methods: In this case-control study, the 806 patients who underwent coronary computed tomography angiography and were not diagnosed with CAD between July 2020 and July 2022 were retrospectively enrolled. Their $PCAT_{MA}$ values of the proximal right coronary artery were measured automatically. Patients without CAD were stratified according to sex, body mass index (BMI), and age, and the relationship between $PCAT_{MA}$ and different clinical characteristics was explored using Fisher's exact test or Chi-squared test and independent *t*-tests or Wilcoxon Mann-Whitney *U* tests.

Results: Compared to non-smoking women [−88.00 (−95.00, −81.00) HU], women who smoked [−84.00 (−94.00, −78.00) HU, P=0.037] had higher $PCAT_{MA}$ values and a positive correlation with $PCAT_{MA}$ (rs=0.101, P=0.036). Compared to non-hypertensive patients with BMI ≥24.91 kg/m^2 [−87.00 (−95.00, −81.00) HU], hypertensive patients with BMI ≥24.91 kg/m^2 [−84.00 (−92.00, −78.00) HU, P=0.004] had higher $PCAT_{MA}$ values, and a positive correlation with $PCAT_{MA}$ (rs=0.144, P=0.004). In a subgroup of patients without CAD stratified by sex, BMI, and age, $PCAT_{MA}$ values were all higher in patients with dyslipidemia (women, men, BMI ≥24.91 kg/m^2, BMI <24.91 kg/m^2, age ≥55 years, and age <55 years: −82.00, −82.00, −81.50, −82.00, −81.00 and −83.50 HU, respectively) than in those without dyslipidemia (−89.00, −89.00, −89.00, −90.00, −90.00 and −88.00 HU, respectively; all P<0.001) and showed a positive relationship (rs=0.328, 0.339, 0.342, 0.326, 0.367, and 0.298, respectively; all P<0.001).

Conclusions: Higher $PCAT_{MA}$ attenuation values were observed in patients with dyslipidemia, smoking women, and hypertensive patients with BMI ≥24.91 kg/m^2, suggesting that $PCAT_{MA}$ values can be used to detect patients at high risk for future events with CAD even if they do not currently have atherosclerosis.

Keywords: Pericoronary adipose tissue (PCAT); coronary artery disease (CAD); demographic factors

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Introduction

Currently, the study of adipose tissue such as visceral, body surface, and pericardial adipose tissue is attracting increasing attention and has been detected to be associated with the development of numerous diseases (1,2). A prospective study showed that preperitoneal fat thickness or body surface area was related to the development of insulin resistance and diabetes (1). Ishikawa *et al.* (2) demonstrated a significant correlation between epicardial adipose tissue volume and overall longitudinal strain of the left ventricle assessed using speckle echocardiography in patients with preserved left ventricular ejection fraction and no left ventricular regional ventricular wall motion abnormalities. Recent research has found that pericoronary adipose tissue (PCAT) opens a new window for non-invasive assessment of vascular inflammation (3,4).

PCAT is part of the epicardial adipose tissue adjacent to coronary vessels (5). The mean PCAT attenuation ($PCAT_{MA}$) values derived from PCAT can detect biopsy-proven coronary vascular inflammation and correlates with serum levels of atherosclerosis-related inflammatory biomarkers (6,7). In addition, $PCAT_{MA}$ values have been shown to correlate not only with high-risk plaques (8), the degree of plaque stenosis (9), and plaque progression (10), but also with flow reserve fraction (11) and cardiac function (12). This is because PCAT is an endocrine organ with a key role in the regulation of cardiovascular homeostasis and contains both anti-inflammatory and antioxidant substances as well as inflammatory components, and that it can affect localized microvascular function in the coronary arteries, thus making PCAT a new biomarker of coronary inflammation (13-15).

However, a number of previous studies have evaluated $PCAT_{MA}$ values in patients with coronary artery disease (CAD) and acute coronary syndrome, whereas $PCAT_{MA}$ values in populations without CAD are lacking (16,17). Moreover, in patients without CAD, few studies have evaluated the association between $PCAT_{MA}$ and patient-based demographic factors, for example, age or sex. As such, the aim of this study was to stratify patients without CAD by sex, body mass index (BMI), and age to investigate the association between $PCAT_{MA}$ and different demographic factors in patients without CAD. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-951/rc).

Methods

Study population

This retrospective study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Lanzhou University Second Hospital approved the study (No. 2021A-165), and the requirement for informed consent was waived due to the retrospective nature of the study. In this case-control study, patients who underwent coronary computed tomography angiography (CCTA) for chest pain or discomfort, etc., within 3 days of admission were reviewed, and patients without CAD were retrospectively enrolled between July 2020 and July 2022. Patients without CAD were defined as no coronary plaques visible to the naked eye on CCTA images examined by two radiologists with 10 years of cardiovascular diagnostic experience. If the two radiologists did not agree on the diagnosis, a senior chief radiologist made the final decision. The exclusion criteria were as follows: (I) coronary artery malformation, prosthetic valves, or pacemakers; (II) history of myocardial infarction, myocarditis, or vasculitis; (III) incomplete clinical information; and (IV) poor image quality for imaging assessment. *Figure 1* illustrates the specific screening process for the patients.

Demographic factors collection

We used the hospital information system to collect clinical information about the patients, including age, gender, BMI, smoking, hypertension, dyslipidemia, and hyperglycaemia. Hypertension was defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg. Patients with total cholesterol ≥5.2 mmol/L or triglycerides ≥1.7 mmol/L or low-density lipoprotein cholesterol

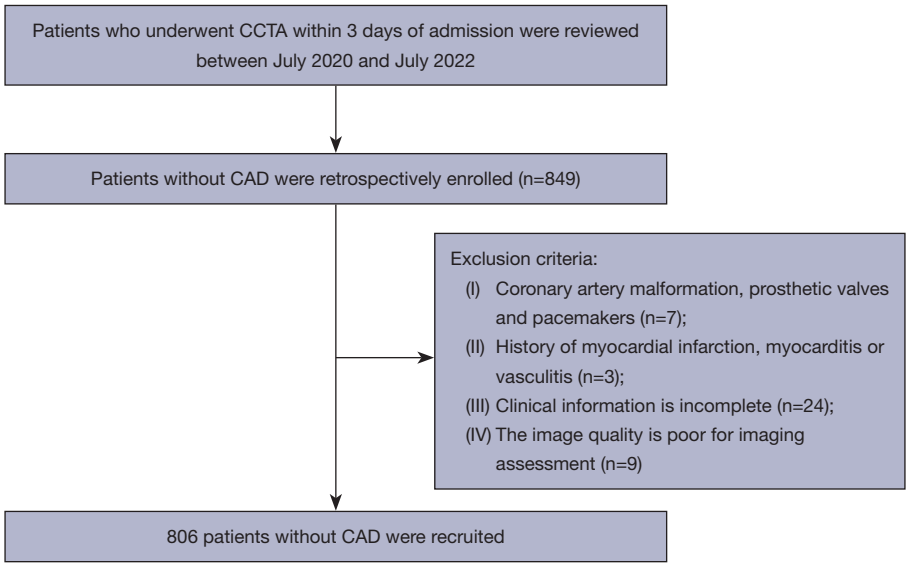

Figure 1 Flow chart of patient screening. CCTA, coronary computed tomography angiography; CAD, coronary artery disease.

≥3.4 mmol/L or high-density lipoprotein cholesterol <1.0 mmol/L were diagnosed as dyslipidemia based on fasting venous serum test indices. Patients treated with oral hypoglycemic agents, insulin or with a fasting blood glucose of 7.0 mmol/L were defined as hyperglycaemia.

CCTA examination

The patient examinations were all performed using a 256-row widescope CT scanner (Revolution CT, GE Healthcare; Milwaukee, WI, USA). CCTA acquisition included all levels from 1 cm below the tracheal bifurcation to the bottom of the heart, and was triggered via smart tracking, with the region of interest placed in the ascending aorta. The contrast agent iopromide (370 mg/mL) was injected 0.9 mL/kg into the median cubital vein at a rate of 5.0–5.5 mL/s, followed by a 40 mL normal saline rinse at the same rate. CCTA was acquired with prospective electrocardiographic gating, and set up as follows: tube voltage =100 kvp, tube current =400–700 mA, scanning field of view =36 cm, display field of view =24 cm, matrix =512×512, rotation time =0.28 s, slice thickness =0.625 mm. The reconstruction parameters were smooth kernel (STANDARD) and 60% of adaptive statistical iterative reconstruction Veo.

PCAT attenuation measurement

The PCAT attenuation measurement software (Shukun Technology Co., Ltd., Shanghai, China, version 1.11.5) was employed by a radiologist with more than 10 years of cardiovascular diagnostic experience and without knowledge of the clinical data for quantification. As noted previously (6), the proximal 10–50 mm segment of the right coronary artery (RCA), with a width of radial distance from the outer wall of the vessel equal to the diameter of the coronary artery, was tracked fully automatically by the software. The lumen and internal and external vessel wall boundaries within the aforementioned area were automatically divided. Subsequently, the average CT attenuation values for all voxels between –190 and –30 HU in the foregoing region, which are PCAT attenuation values, were calculated automatically by the software. In this study, we used $PCAT_{MA}$ of the proximal segment of the RCA for follow-up analysis. *Figure 2* shows the measurement of $PCAT_{MA}$ in the proximal RCA segment.

Statistical analysis

All data were calculated with SPSS 26.0 (IBM, Armonk, NY, USA) and GraphPad Prism 9.0.0 (GraphPad Software, San Diego, CA, USA). Categorical data were expressed as frequency (percentage) and differences between the two groups were compared using Fisher's exact test or Chi-squared test. For continuous data normality, tests were administered using the Kolmogorov-Smirnov test, conforming to a normal distribution denoted as mean ± standard deviation and a non-normal distribution denoted

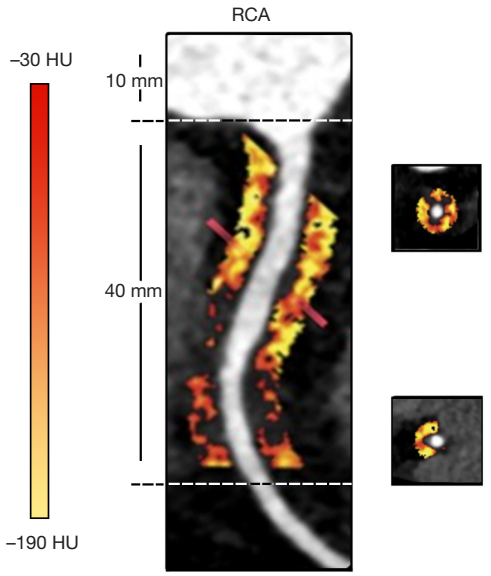

Figure 2 The measurement of $PCAT_{MA}$ in the RCA proximal segment. $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; RCA, right coronary artery; HU, Hounsfield unit.

Table 1 Patients' demographic factors

Characteristics	All (n=806)
Age (years), medians (interquartile range)	55.00 (45.00, 66.00)
Gender, n (%)	
Men	374 (46.4)
Women	432 (53.6)
BMI (kg/m^2), median (interquartile range)	24.91 (22.17, 27.79)
Smoking, n (%)	
Yes	264 (32.8)
No	542 (67.2)
Hypertension, n (%)	
Yes	313 (38.8)
No	493 (61.2)
Hyperglycaemia, n (%)	
Yes	253 (31.4)
No	553 (68.6)
Dyslipidemia, n (%)	
Yes	254 (31.5)
No	552 (68.5)
$PCAT_{MA}$ (HU), median (interquartile range)	–87.00 (–94.00, –80.00)

BMI, body mass index; $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; HU, Hounsfield unit.

as medians (interquartile range). Comparisons of continuous data between the two groups were implemented using independent *t*-tests or Wilcoxon Mann-Whitney *U* tests. Between-group correlations were evaluated using Pearson or Spearman correlation analysis, as appropriate. P<0.05 (bilateral) was regarded as statistically significant.

Results

Patient demographics

An overview of patients' baseline characteristics is presented in *Table 1*. In total, 806 patients without CAD were recruited, including 374 males and 432 females, with a mean age, BMI, and $PCAT_{MA}$ of 55.00 (45.00, 66.00) years, 24.91 (22.17, 27.79) kg/m^2, and –87.00 (–94.00, –80.00) HU, respectively. Of these patients, 264 were smokers, 313 were hypertensive, 253 were hyperglycemic, and 254 were dyslipidemic.

Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by sex

In women without CAD, we found that smoking patients had a higher $PCAT_{MA}$ of –84.00 (–94.00, –78.00) HU than non-smoking patients [–88.00 (–95.00, –81.00) HU, P=0.037], and patients diagnosed with dyslipidemia [–82.00 (–89.00, –77.00) HU] also had a higher $PCAT_{MA}$ than patients with non-dyslipidemia [–89.00 (–97.00, –82.00) HU, P<0.001]. In addition, men without CAD who were dyslipidemic [–82.00 (–88.00, –77.00) *vs.* –89.00 (–97.00, –81.75) HU, P<0.001; *Table 2*, *Figure 3*] had higher $PCAT_{MA}$. Correlation analysis demonstrated that $PCAT_{MA}$ levels were positively correlated with smoking (rs=0.101, P=0.036) and dyslipidemia (rs=0.328, P<0.001; Table S1) in women without CAD, and $PCAT_{MA}$ levels were positively correlated with dyslipidemia in men without CAD (rs=0.339, P<0.001; Table S1).

Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by BMI

In patients without CAD having BMI ≥24.91 kg/m^2, we observed that patients with hypertension [–84.00 (–92.00, –78.00) HU] or dyslipidemia [–81.50 (–88.00, –76.00) HU] had a higher $PCAT_{MA}$ than those without hypertension [–87.00 (–95.00, –81.00) HU, P=0.004] and dyslipidemia [–89.00 (–96.50, –81.00) HU, P<0.001, *Table 3*]. However, in the group with BMI <24.91 kg/m^2, $PCAT_{MA}$ was

Table 2 Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by sex

Characteristics	Women (n=432)		Men (n=374)	
	$PCAT_{MA}$ (HU)	P value	$PCAT_{MA}$ (HU)	P value
Age (years)		0.790		0.900
≥55	−87.00 (−94.50, −80.00)		−87.00 (−95.25, −79.00)	
<55	−88.00 (−94.00, −80.00)		−86.00 (−93.00, −80.00)	
BMI (kg/m^2)		0.270		0.329
≥24.91	−87.00 (−94.00, −79.00)		−86.00 (−94.00, −79.00)	
<24.91	−88.00 (−94.00, −81.00)		−87.00 (−94.00, −80.00)	
Smoking		0.037		0.369
Yes	−84.00 (−94.00, −78.00)		−87.00 (−95.00, −80.00)	
No	−88.00 (−95.00, −81.00)		−87.00 (−93.50, −79.00)	
Hypertension		0.315		0.077
Yes	−87.00 (−93.50, −79.00)		−85.50 (−92.75, −79.00)	
No	−88.00 (−95.00, −81.00)		−87.00 (−95.00, −80.00)	
Hyperglycaemia		0.873		0.548
Yes	−85.00 (−96.00, −79.00)		−87.00 (−95.25, −80.00)	
No	−88.00 (−94.00, −80.50)		−86.50 (−93.00, −79.00)	
Dyslipidemia		<0.001		<0.001
Yes	−82.00 (−89.00, −77.00)		−82.00 (−88.00, −77.00)	
No	−89.00 (−97.00, −82.00)		−89.00 (−97.00, −81.75)	

Data are presented as median (interquartile range). $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; BMI, body mass index; HU, Hounsfield unit.

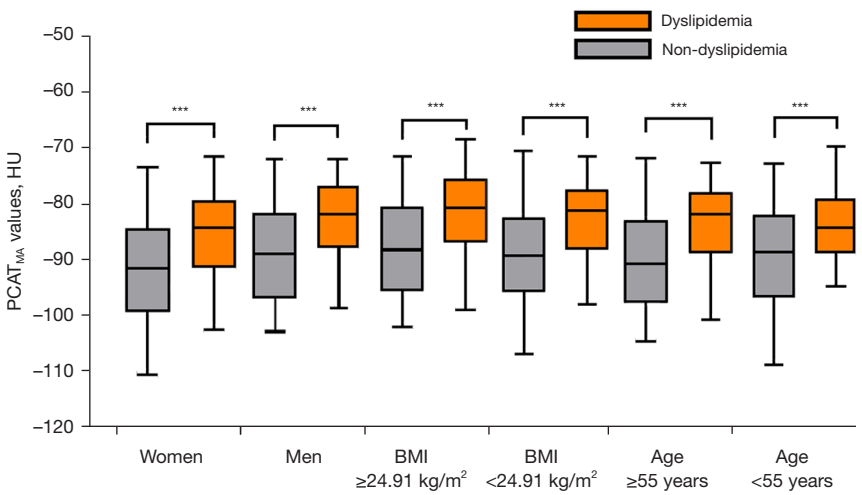

Figure 3 Box plot showing the difference in $PCAT_{MA}$ values between dyslipidemia and non-dyslipidemia in subgroups stratified by sex, BMI, and age. ***, P<0.001. $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; HU, Hounsfield unit; BMI, body mass index.

Table 3 Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by BMI

Characteristics	BMI ≥24.91 kg/m^2 (n=403)		BMI <24.91 kg/m^2 (n=403)	
	$PCAT_{MA}$ (HU)	P value	$PCAT_{MA}$ (HU)	P value
Age (years)		0.695		0.678
≥55	−86.00 (−94.00, −79.00)		−87.00 (−95.00, −79.00)	
<55	−86.00 (−94.00, −79.00)		−88.00 (−93.75, −81.00)	
Sex		0.706		0.675
Men	−86.00 (−94.00, −79.00)		−87.00 (−94.00, −80.00)	
Women	−87.00 (−94.00, −79.00)		−88.00 (−94.00, −81.00)	
Smoking		0.751		0.466
Yes	−86.00 (−93.75, −79.00)		−86.50 (−96.00, −79.00)	
No	−87.00 (−94.00, −79.00)		−88.00 (−94.00, −81.00)	
Hypertension		0.004		0.851
Yes	−84.00 (−92.00, −78.00)		−88.00 (−96.00, −80.00)	
No	−87.00 (−95.00, −81.00)		−87.50 (−94.00, −80.00)	
Hyperglycaemia		0.468		0.286
Yes	−85.00 (−94.00, −79.00)		−88.00 (−96.50, −80.00)	
No	−87.00 (−94.00, −79.00)		−87.50 (−93.00, −80.75)	
Dyslipidemia		<0.001		<0.001
Yes	−81.50 (−88.00, −76.00)		−82.00 (−89.00, −78.00)	
No	−89.00 (−96.50, −81.00)		−90.00 (−97.00, −83.00)	

Data are presented as median (interquartile range). $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; BMI, body mass index; HU, Hounsfield unit.

only found to be significantly higher in dyslipidemia [−82.00 (−89.00, −78.00) HU] than in those without dyslipidemia [−90.00 (−97.00, −83.00) HU, P<0.001; *Table 3*, *Figure 3*]. Furthermore, $PCAT_{MA}$ values in the BMI ≥24.91 kg/m^2 group were positively associated with hypertension (rs=0.144, P=0.004) and dyslipidemia (rs=0.342, P<0.001; Table S1), whereas $PCAT_{MA}$ values in the BMI <24.91 kg/m^2 group were only positively related to dyslipidemia (rs=0.326, P<0.001; Table S1).

Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by age

In patients without CAD aged ≥55 or <55 years, higher $PCAT_{MA}$ values were present in patients with dyslipidemia [−81.00 (−88.25, −77.00) HU, −83.50 (−88.00, −78.00) HU] than in those without dyslipidemia [−90.00 (−97.00, −82.00) HU, −88.00 (−96.00, −81.00) HU; all P<0.001, *Table 4*, *Figure 3*]. The results of the correlation analysis showed a positive relationship between $PCAT_{MA}$ values and dyslipidemia in either the age ≥55 years group or the <55 years group, with rs 0.367 (P<0.001) and 0.298 (P<0.001), respectively (Table S1).

Discussion

The significant strength of this study is the inclusion of a large number of patients without CAD and stratification by sex, BMI, and age to explore the relationship between different demographic factors and $PCAT_{MA}$. The major findings of this study are as follows: $PCAT_{MA}$ values were higher in patients with dyslipidemia than in those without dyslipidemia and showed a positive relationship with dyslipidemia, which was not influenced by sex, BMI, or age stratification. Furthermore, smoking women and hypertensive patients with BMI ≥24.91 kg/m^2 had higher

Table 4 Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by age

Characteristics	Age ≥55 years (n=411)		Age <55 years (n=395)	
	$PCAT_{MA}$ (HU)	P value	$PCAT_{MA}$ (HU)	P value
Sex		0.862		0.528
Men	−87.00 (−95.25, −79.00)		−86.00 (−93.00, −80.00)	
Women	−87.00 (−94.50, −80.00)		−88.00 (−94.00, −80.00)	
BMI (kg/m^2)		0.524		0.144
≥24.91	−86.00 (−94.00, −79.00)		−86.00 (−94.00, −79.00)	
<24.91	−87.00 (−95.00, −79.00)		−88.00 (−93.75, −81.00)	
Smoking		0.762		0.357
Yes	−86.50 (−96.00, −79.00)		−85.50 (−93.00, −79.25)	
No	−87.00 (−94.00, −80.00)		−88.00 (−94.00, −81.00)	
Hypertension		0.192		0.130
Yes	−86.00 (−93.50, −79.00)		−86.00 (−93.00, −78.25)	
No	−87.00 (−95.25, −80.00)		−88.00 (−94.00, −81.00)	
Hyperglycaemia		0.831		0.900
Yes	−87.00 (−95.50, −79.50)		−86.00 (−96.00, −80.00)	
No	−87.00 (−94.00, −79.00)		−88.00 (−93.00, −80.00)	
Dyslipidemia		<0.001		<0.001
Yes	−81.00 (−88.25, −77.00)		−83.50 (−88.00, −78.00)	
No	−90.00 (−97.00, −82.00)		−88.00 (−96.00, −81.00)	

Data are presented as median (interquartile range). $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; BMI, body mass index; HU, Hounsfield unit.

$PCAT_{MA}$ values and a positive correlation with $PCAT_{MA}$.

Vascular inflammation inhibits local fat formation in PCAT, which can be detected using CCTA, as $PCAT_{MA}$ levels are elevated (6). It was determined that $PCAT_{MA}$ proximal to the RCA measured by conventional CCTA is the most standardized method for PCAT analysis (18). Goeller *et al.* (7) revealed that an increase in $PCAT_{MA}$ values proximal to the RCA, as measured using conventional CCTA, was an independent predictor of major adverse cardiac events. Relevance studies have also shown that $PCAT_{MA}$ values in the proximal segment of the RCA are associated with the progression of noncalcified plaques and total plaque burden (10). In addition, Bittner *et al.* (19) demonstrated that higher levels of eicosapentaenoic acid, which reduces cardiovascular mortality, were related to lower $PCAT_{MA}$ values proximal to the RCA, as acquired through CCTA. Therefore, the present study was performed to explore the information on $PCAT_{MA}$ in the coronary arteries of patients without CAD, which is lacking in current studies, by measuring $PCAT_{MA}$ values in the proximal segment of the RCA.

In the exploration of different demographic factors in $PCAT_{MA}$ values, different studies have reported different results (20-23). Yu *et al.* (20) found that in patients with stable CAD, $PCAT_{MA}$ values in the proximal segment of the RCA were higher in the type 2 diabetic group than in the non-diabetic group, whereas no differences were observed between the two groups in the left anterior descending and left circumflex. van Rosendael *et al.* (21) observed that $PCAT_{MA}$ values in individuals without CAD measured in the proximal segment of the left anterior descending artery, left circumflex artery, and RCA were higher in men than in women. A retrospective study showed that $PCAT_{MA}$ values in the proximal segment of the RCA were significantly correlated with sex in patients with CAD and that men were independently determined (22). Moreover, other studies

have reported that in patients without plaque on CCTA images, $PCAT_{MA}$ values were significantly related to age and sex but not to BMI (23). In contrast to the results of previous findings (20-22), in patients without CAD, no significant differences in $PCAT_{MA}$ values by age, sex, BMI, or history of diabetes were found in our study. This may be because the population, type of disease, scanning equipment, scanning parameters, and PCAT analysis differed among studies (18,24). In the future, the group type should be further expanded and PCAT scan parameters and analyses should be standardized to better explore the correlation between $PCAT_{MA}$ values and different demographic factors.

It is well known that dyslipidemia is one of the most important risk factors for atherosclerosis and cardiovascular disease (25). Several studies have also shown a correlation between indicators associated with dyslipidemia and PCAT in patients with CAD (26-28). Ichikawa *et al.* (26) observed that highly oxidized high-density lipoprotein levels were related to higher $PCAT_{MA}$ values proximal to the RCA in CAD patients. A prospective study revealed that $PCAT_{MA}$ values were significantly higher around plaques with cholesterol crystals versus plaques without cholesterol crystals and that patients with cholesterol crystals had higher $PCAT_{MA}$ values proximal to the RCA (27). Furthermore, by exploring the relationship between PPAR-γ gene expression in peri-plaque PCAT of CAD patients and patient obesity, Marketou *et al.* (28) demonstrated that PCAT had a unique phenotype in obese individuals. Unlike previous studies (26-28), we found that in patients without CAD, those with dyslipidemia had higher $PCAT_{MA}$ values than those without dyslipidemia, indicating that dyslipidemic patients are more likely to present with coronary artery inflammation.

Additionally, we found that smoking in women was correlated with higher $PCAT_{MA}$ values. Smoking is also a leading cause of cardiovascular disease and death (29). Smoking not only causes direct physical damage to endothelial cells through multiple pathways but also induces tissue remodeling and thrombosis while activating systemic inflammatory signals (30,31). Furthermore, in female smokers, cardiovascular risk is complicated by hormonal factors, which may lead to higher relative risks (32). Consequently, smoking is associated with the risk of coronary inflammation in women without CAD, thereby detecting that $PCAT_{MA}$ values are elevated in CCTA.

Hypertension is a known cardiovascular risk factor that causes thickening of the fibromuscular lining of the intima and middle layers of blood vessels and narrowing of the lumen of small arteries and arterioles (33,34). Regarding the relationship between hypertension and PCAT, Chang *et al.* (35) found that PCAT thickness was significantly increased in hypertensive patients compared to the normotensive group and was an independent factor. Further, in the present study we found that hypertensive patients with BMI ≥24.91 kg/m^2 in patients without CAD were associated with $PCAT_{MA}$ values, whereas hypertensive patients with BMI <24.91 kg/m^2 were not correlated with $PCAT_{MA}$ values. This may be due to the fact that obesity not only elevates blood pressure but also increases left ventricular volume load and exacerbates inflammation (36). Moreover, there are overlapping and potentially synergistic mechanisms by which obesity and hypertension promote inflammation and M1 macrophage polarization, resulting in the release of proinflammatory cytokines that impair cardiac function (37). Thus, it is recommended that weight and blood pressure should be controlled clinically.

The present study had several limitations. First, further replication and validation in a multicenter study are needed despite the large sample size. Second, the optimal threshold for elevated $PCAT_{MA}$ is unknown, and the normal reference range for $PCAT_{MA}$ should be determined in more extensive studies. Finally, although the results of the current study are promising, these patients should be followed up in the future to improve the clinical significance of $PCAT_{MA}$ further.

Conclusions

In patients without CAD, $PCAT_{MA}$ values were higher in dyslipidemia patients than in non-dyslipidemia patients and were also higher in smoking women and in hypertensive patients with BMI ≥24.91 kg/m^2. This suggests that $PCAT_{MA}$ values may be useful in detecting patients at high risk for CAD with future events, even though they do not currently exhibit atherosclerosis.

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Footnote

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References

1. Haberka M, Matla M, Siniarski A, Stępień K, Malinowski KP, Kubicius A, Gąsior Z. Cardiometabolic predictive value of anthropometric parameters, vascular ultrasound indexes, and fat depots in patients at high cardiovascular risk: an 8-year prospective cohort study. Pol Arch Intern Med 2022;132:16302.
2. Ishikawa H, Otsuka K, Kono Y, Hojo K, Yamaura H, Hirata K, Kasayuki N, Izumiya Y, Fukuda D. Extent of coronary atherosclerosis is associated with deterioration of left ventricular global longitudinal strain in patients with preserved ejection fraction undergoing coronary computed tomography angiography. Int J Cardiol Heart Vasc 2023;44:101176.
3. Berman DS, Kwiecinski J. Imaging Coronary Inflammatory Risk. JACC Cardiovasc Imaging 2022;15:472-5.
4. Raggi P, Stillman AE. Pericoronary adipose tissue attenuation is "all the rage" around the vessel wall. Atherosclerosis 2022;346:77-8.
5. van der Bijl P, Kuneman JH, Bax JJ. Pericoronary adipose tissue attenuation: diagnostic and prognostic implications. Eur Heart J Cardiovasc Imaging 2022;23:e537-8.
6. Antonopoulos AS, Sanna F, Sabharwal N, Thomas S, Oikonomou EK, Herdman L, et al. Detecting human coronary inflammation by imaging perivascular fat. Sci Transl Med 2017;9:eaal2658.
7. Goeller M, Achenbach S, Herrmann N, Bittner DO, Kilian T, Dey D, Raaz-Schrauder D, Marwan M. Pericoronary adipose tissue CT attenuation and its association with serum levels of atherosclerosis-relevant inflammatory mediators, coronary calcification and major adverse cardiac events. J Cardiovasc Comput Tomogr 2021;15:449-54.
8. Araki M, Sugiyama T, Nakajima A, Yonetsu T, Seegers LM, Dey D, Lee H, McNulty I, Yasui Y, Teng Y, Nagamine T, Kakuta T, Jang IK. Level of Vascular Inflammation Is Higher in Acute Coronary Syndromes Compared with Chronic Coronary Disease. Circ Cardiovasc Imaging 2022;15:e014191.
9. Ma R, van Assen M, Ties D, Pelgrim GJ, van Dijk R, Sidorenkov G, van Ooijen PMA, van der Harst P, Vliegenthart R. Focal pericoronary adipose tissue attenuation is related to plaque presence, plaque type, and stenosis severity in coronary CTA. Eur Radiol 2021;31:7251-61.
10. Goeller M, Tamarappoo BK, Kwan AC, Cadet S, Commandeur F, Razipour A, Slomka PJ, Gransar H, Chen X, Otaki Y, Friedman JD, Cao JJ, Albrecht MH, Bittner DO, Marwan M, Achenbach S, Berman DS, Dey D. Relationship between changes in pericoronary adipose tissue attenuation and coronary plaque burden quantified from coronary computed tomography angiography. Eur Heart J Cardiovasc Imaging 2019;20:636-43.
11. Duncker H, Achenbach S, Moshage M, Dey D, Bittner DO, Ammon F, Marwan M, Goeller M. Computed Tomography-derived Characterization of Pericoronary, Epicardial, and Paracardial Adipose Tissue and Its Association With Myocardial Ischemia as Assessed by Computed Fractional Flow Reserve. J Thorac Imaging 2023;38:46-53.
12. Nishihara T, Miyoshi T, Nakashima M, Ichikawa K, Takaya Y, Nakayama R, Miki T, Ito H. Association of perivascular fat attenuation on computed tomography and

heart failure with preserved ejection fraction. ESC Heart Fail 2023;10:2447-57.
13. Lin A, Dey D, Wong DTL, Nerlekar N. Perivascular Adipose Tissue and Coronary Atherosclerosis: from Biology to Imaging Phenotyping. Curr Atheroscler Rep 2019;21:47.
14. Baritussio A, Williams MC. Gaining evidence on coronary inflammation. J Cardiovasc Comput Tomogr 2021;15:455-6.
15. Pasqualetto MC, Tuttolomondo D, Cutruzzolà A, Niccoli G, Dey D, Greco A, Martini C, Irace C, Rigo F, Gaibazzi N. Human coronary inflammation by computed tomography: Relationship with coronary microvascular dysfunction. Int J Cardiol 2021;336:8-13.
16. Hoshino M, Yang S, Sugiyama T, Zhang J, Kanaji Y, Hamaya R, et al. Characteristic findings of microvascular dysfunction on coronary computed tomography angiography in patients with intermediate coronary stenosis. Eur Radiol 2021;31:9198-210.
17. Lin A, Nerlekar N, Yuvaraj J, Fernandes K, Jiang C, Nicholls SJ, Dey D, Wong DTL. Pericoronary adipose tissue computed tomography attenuation distinguishes different stages of coronary artery disease: a cross-sectional study. Eur Heart J Cardiovasc Imaging 2021;22:298-306.
18. Ma R, Fari R, van der Harst P, N De Cecco C, E Stillman A, Vliegenthart R, van Assen M. Evaluation of pericoronary adipose tissue attenuation on CT. Br J Radiol 2023;96:20220885.
19. Bittner DO, Goeller M, Dey D, Zopf Y, Achenbach S, Marwan M. High levels of eicosapentaenoic acid are associated with lower pericoronary adipose tissue attenuation as measured by coronary CTA. Atherosclerosis 2021;316:73-8.
20. Yu Y, Ding X, Yu L, Dai X, Wang Y, Zhang J. Increased coronary pericoronary adipose tissue attenuation in diabetic patients compared to non-diabetic controls: A propensity score matching analysis. J Cardiovasc Comput Tomogr 2022;16:327-35.
21. van Rosendael SE, Kuneman JH, van den Hoogen IJ, Kitslaar PH, van Rosendael AR, van der Bijl P, Reiber JHC, Ajmone Marsan N, Jukema JW, Knuuti J, Bax JJ. Vessel and sex differences in pericoronary adipose tissue attenuation obtained with coronary CT in individuals without coronary atherosclerosis. Int J Cardiovasc Imaging 2022;38:2781-9.
22. Sugiyama T, Kanaji Y, Hoshino M, Yamaguchi M, Hada M, Ohya H, Sumino Y, Hirano H, Kanno Y, Horie T, Misawa T, Nogami K, Ueno H, Hamaya R, Usui E, Murai T, Lee T, Yonetsu T, Sasano T, Kakuta T. Determinants of Pericoronary Adipose Tissue Attenuation on Computed Tomography Angiography in Coronary Artery Disease. J Am Heart Assoc 2020;9:e016202.
23. Ma R, Ties D, van Assen M, Pelgrim GJ, Sidorenkov G, van Ooijen PMA, van der Harst P, van Dijk R, Vliegenthart R. Towards reference values of pericoronary adipose tissue attenuation: impact of coronary artery and tube voltage in coronary computed tomography angiography. Eur Radiol 2020;30:6838-46.
24. Yuvaraj J, Cheng K, Lin A, Psaltis PJ, Nicholls SJ, Wong DTL. The Emerging Role of CT-Based Imaging in Adipose Tissue and Coronary Inflammation. Cells 2021;10:1196.
25. Gaggini M, Gorini F, Vassalle C. Lipids in Atherosclerosis: Pathophysiology and the Role of Calculated Lipid Indices in Assessing Cardiovascular Risk in Patients with Hyperlipidemia. Int J Mol Sci 2022;24:75.
26. Ichikawa K, Miyoshi T, Kotani K, Osawa K, Nakashima M, Nishihara T, Ito H. Association between high oxidized high-density lipoprotein levels and increased pericoronary inflammation determined by coronary computed tomography angiography. J Cardiol 2022;80:410-5.
27. Lin A, Nerlekar N, Munnur RK, Kataoka Y, Andrews J, Dey D, Nicholls SJ, Wong DT. Cholesterol crystal-induced coronary inflammation: Insights from optical coherence tomography and pericoronary adipose tissue computed tomography attenuation. J Cardiovasc Comput Tomogr 2020;14:277-8.
28. Marketou M, Lazopoulos G, Kontaraki J, Kalogerakos P, Plevritaki A, Chlouverakis G, Fragiadakis K, Maragkoudakis S, Zervakis S, Savva E, Kampanieris E, Kochiadakis G. PPAR-γ gene expression in pericoronary adipose tissue: A focus on obesity. Hellenic J Cardiol 2023;69:67-8.
29. Kondo T, Nakano Y, Adachi S, Murohara T. Effects of Tobacco Smoking on Cardiovascular Disease. Circ J 2019;83:1980-5.
30. Messner B, Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. Arterioscler Thromb Vasc Biol 2014;34:509-15.
31. Rana JS, Moffet HH, Liu JY, Nasir K, Blankstein R, Karter AJ, Sidney S. Smoking and Risk of Premature Atherosclerotic Cardiovascular Disease. Am J Prev Med 2022;62:466-8.
32. Villablanca AC, McDonald JM, Rutledge JC. Smoking and cardiovascular disease. Clin Chest Med 2000;21:159-72.

33. Oparil S, Acelajado MC, Bakris GL, Berlowitz DR, Cífková R, Dominiczak AF, Grassi G, Jordan J, Poulter NR, Rodgers A, Whelton PK. Hypertension. Nat Rev Dis Primers 2018;4:18014.
34. Hollander W. Role of hypertension in atherosclerosis and cardiovascular disease. Am J Cardiol 1976;38:786-800.
35. Chang S, Lee W, Kwag B, Chung YH, Kang IS. Maximal pericoronary adipose tissue thickness is associated with hypertension in nonobese patients with acute or chronic illness. Korean J Intern Med 2017;32:668-74.
36. Obokata M, Reddy YNV, Pislaru SV, Melenovsky V, Borlaug BA. Evidence Supporting the Existence of a Distinct Obese Phenotype of Heart Failure With Preserved Ejection Fraction. Circulation 2017;136:6-19.
37. Mouton AJ, Li X, Hall ME, Hall JE. Obesity, Hypertension, and Cardiac Dysfunction: Novel Roles of Immunometabolism in Macrophage Activation and Inflammation. Circ Res 2020;126:789-806.

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Supplementary

Table S1 Association of $PCAT_{MA}$ with different demographic factors in subgroups stratified by sex, BMI and age

Characteristics	$PCAT_{MA}$					
	Sex		BMI (kg/m^2)		Age (years)	
	Women	Men	≥24.91	<24.91	≥55	<55
Age (years)						
rs	0.013	−0.007	−0.020	0.021	–	–
P value	0.790	0.900	0.695	0.679	–	–
Gender						
rs	–	–	0.019	0.021	0.009	0.032
P value	–	–	0.707	0.676	0.863	0.529
BMI (kg/m^2)						
rs	0.053	0.051	–	–	0.031	0.074
P value	0.271	0.330	–	–	0.525	0.144
Smoking						
rs	0.101*	−0.046	0.016	0.036	0.015	0.046
P value	0.036	0.370	0.751	0.467	0.762	0.358
Hypertension						
rs	0.048	0.092	0.144**	−0.009	0.064	0.076
P value	0.315	0.077	0.004	0.851	0.193	0.130
Hyperglycaemia						
rs	0.008	−0.031	0.036	−0.053	−0.011	−0.006
P value	0.873	0.549	0.469	0.286	0.832	0.900
Dyslipidemia						
rs	0.328**	0.339**	0.342**	0.326**	0.367**	0.298**
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

**, significant association at the 0.01 level (two-tailed); *, significant association at the 0.05 level (two-tailed). $PCAT_{MA}$, mean pericoronary adipose tissue attenuation; BMI, body mass index.

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