Original Article

Is there an association between coronary artery inflammation and coronary atherosclerotic burden?

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Background: As for the coronary artery inflammation and coronary atherosclerotic burden, which are used to assess the risk of adverse cardiac events in patients, it is unclear whether there is any certain correlation between them. Therefore, the purpose of this study was to explore the potential relationship between coronary artery inflammation and coronary atherosclerotic burden.

Methods: A total of 346 eligible patients underwent assessment of computed tomography (CT) attenuation values of pericoronary adipose tissue (PCAT) in the right coronary artery and Agatston coronary artery calcium (CAC) based on coronary CT angiography. These measurements were utilized to evaluate coronary inflammation and atherosclerotic burden, respectively. Patients with a CAC score of 0 were categorized into groups based on the presence or absence of coronary artery disease (CAD). CAC scores of 10, 100, and 400 were chosen as cutoff values to compare differences in PCAT attenuation values across different CAC scores.

Results: When comparing all CAD patients to non-CAD patients, a significantly higher PCAT attenuation was observed in CAD patients (–87.54±9.39 *vs.* –93.45±7.42 HU, P=0.000). The PCAT attenuation in CAD patients with a CAC score of 0 was significantly higher than that in patients with a CAC score greater than 0 and in non-CAD patients with a CAC score of 0 (–82.63±8.70 *vs.* –90.38±8.59 *vs.* –93.45±7.42 HU, P=0.000). The PCAT attenuation values did not exhibit significant differences among different CAC scores (all P>0.05); however, it was highest in CAD patients with a CAC score of 0 (P<0.05). Body mass index, hyperlipidemia, hypertension, and PCAT attenuation were identified as independent risk factors in both CAD patients with a CAC score of 0 and patients with a CAC score greater than 0 (all P<0.05).

Conclusions: The results of this study suggest that a direct relationship between coronary inflammation and coronary atherosclerotic burden is not evident. Nonetheless, it is noteworthy that coronary inflammation was most pronounced in CAD patients with a CAC score of 0, while CAC score did not demonstrate an association with inflammation.

Keywords: Pericoronary adipose tissue (PCAT); coronary artery calcium (CAC); coronary computed tomography angiography (CCTA); coronary artery disease (CAD)

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Introduction

Cardiovascular diseases continue to be the leading cause of morbidity and mortality worldwide, accounting for a significant proportion of global deaths (1). Among these conditions, coronary artery disease (CAD) remains a significant concern, with acute myocardial infarctions often being overlooked in patients without a history of chest pain (2). Early identification of individuals at risk of myocardial infarction is critical for timely prevention, personalized treatment, and improved survival rates for CAD patients.

Previous studies have highlighted the importance of detection of coronary inflammation and coronary atherosclerotic burden in assessing the risk of adverse cardiac events (3-5). However, noninvasive detection of these factors remains challenging (6). Cardiac ultrasound and magnetic resonance imaging face limitations in accurately detecting coronary inflammation. While ^{18}F-sodium fluoride positron emission tomography-computed tomography (^{18}F-NaF PET-CT) has shown promising performance in detecting coronary artery inflammation, its higher cost and radiation dose impede widespread clinical application (7).

Coronary computed tomography angiography (CCTA) is a well-established noninvasive imaging technique widely used for qualitative and quantitative assessment of coronary plaque, atherosclerotic burden and inflammatory changes (8,9). By measuring coronary artery calcium (CAC) through CCTA, clinicians can evaluate the burden of coronary atherosclerosis. CAC score has been demonstrated as an independent predictor of mortality and a reliable method to assess the risk of future cardiovascular events, particularly in asymptomatic patients (10-12). Recent studies have also identified the attenuation of pericoronary adipose tissue (PCAT) in proximity to the right coronary artery (RCA) as a potential biomarker for coronary vascular inflammation (13-15). This PCAT attenuation, assessed through CCTA measurements, has shown promising performance in predicting future cardiac events in CAD patients (13-15).

Despite the significance of coronary inflammation and coronary atherosclerotic burden in assessing the risk of adverse cardiac events, it remains unclear whether a direct correlation exists among those factors. Therefore, the objective of this study is to investigate the potential association between coronary inflammation and coronary atherosclerotic burden by analyzing CCTA measurements of CAC scores and RCA proximal PCAT attenuation.

Methods

Patients

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethics Board of Lanzhou University Second Hospital, China (No. 2021A-165) and individual consent for this retrospective analysis was waived. The patients who underwent CCTA scans in our hospital from April 2021 to November 2021 were retrospectively collected and screened strictly according to the following inclusion and exclusion criteria. The inclusion criteria were as follows: (I) excellent image quality, (II) CAC and PCAT attenuation can be calculated, (III) patients older than 18 years old, and (IV) complete clinical and imaging data. The exclusion criteria were as follows: (I) previous coronary artery bypass surgery or stent placement; (II) clinical instability or atrial fibrillation; (III) with coronary artery malformation, prosthetic valve, and pacemaker; and (IV) concurrent or previous myocarditis or vasculitis within 6 months. Finally, a total of 346 patients were included, with 215 males and 131 females, with an average age of 56.60±10.82 years old. *Figure 1* shows the flow diagram of patient selection.

CCTA acquisition

The examinations were performed with the dual source computed tomography (DSCT) scanner (SOMATOM Force, Siemens Healthcare, Forchheim, Germany), which scanned all layers from 1 cm below tracheal bifurcation to the bottom of the heart. For CT image scanning, all the CCTA data were acquired in retrospective electrocardiographic gating and craniocaudal direction with a slice of 0.75 mm, an acquisition of 192 mm × 0.6 mm, a pitch of 0.19, a rotation time of 0.25 s, and the tube voltage and tube current were automatically modulated using the CARE KV and CARE Dose 4D.

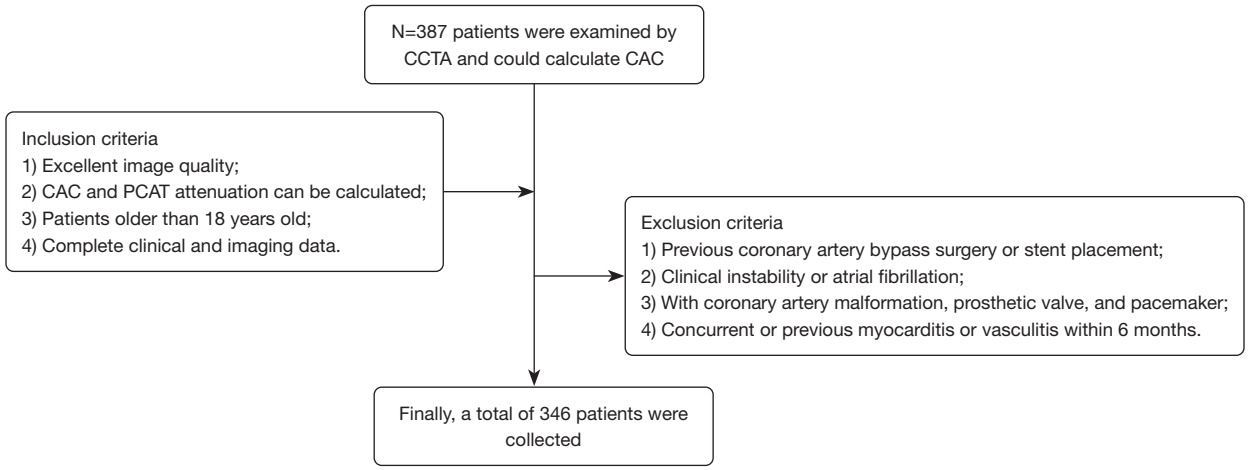

Figure 1 Flow diagram of patient selection. CCTA, coronary computed tomography angiography; CAC, coronary artery calcium; PCAT, pericoronary adipose tissue.

Subsequently, the soft reconstruction kernel (Bv40) and advanced modeled iterative reconstruction (ADMIRE) were used to perform the axial reconstruction of CCTA images with an increment of 0.5 mm and a field of view of 188 mm × 188 mm. For enhanced scanning, the contrast agent ioprolamine (370 mgI/mL) was injected through the elbow vein with an Ulrich high-pressure syringe (Ulrich Medical, Ulm, Germany) at a flow rate of 5.0 mL/s and followed by 40 mL of normal saline at the same rate for irrigation. The CAC parameters were as follows: tube voltage, 120 kV; tube current, 80 mAs; rotation time, 0.25 s; pitch, 0.24; and slice thickness, 3.0 mm.

Measurement of pericoronary CT fat attenuation index and CAC

After the scan was completed, the system can automatically push the CCTA scan image of each patient to 'CoronaryDoc' software (Shukun Technology, China), and the CCTA image reconstruction and coronary plaque analysis were automatically completed in about 3 min. The software has been approved by the National Medical Products Administration (NMPA) (Class III) for coronary artery reconstruction and stenosis diagnosis of CCTA. After that, the results of each patient's software analysis were ignored, and the CCTA images of each patient were diagnosed by 2 radiologists with more than 5 years of cardiovascular diagnosis experience respectively. By the visual analysis of the 2 radiologists, the criteria for CAD were defined according to whether the coronary artery was stenosed on the patient's CCTA image, and the plaques for CAD were classified as noncalcified plaque (NCP), calcified plaque (CP), and mixed plaque (MP) (16). If there was a discrepancy between the 2 radiologists or with the analysis of Shukun coronary analysis software, the final diagnosis was made by another cardiovascular radiologist with more experience.

Using the Shukun PCAT analysis software, the system can automatically calculate the RCA PCAT attenuation of a patient in about 30–40 s. According to the method proposed by Oikonomou (3), we extracted the PCAT along the center line of the RCA starting from 1 cm downstream of roots at the aorta with a length span of 4 cm. The transverse area was set to 3 times the diameter of the vessel lumen. In this area, tissues with a CT value of –190 to –30 HU were considered as the PCAT. Furthermore, we measured the total CAC score using the Shukun CAC score software to reflect the patient's overall coronary atherosclerotic burden. The CAC score was calculated by using the Agatston method, which is based on a weighted sum of lesions with a density greater than 130 HU (17). *Figures 2*,*3* show fully automated measurements of CAC and CT attenuation values of PCAT, respectively.

Patients grouping

According to the radiologists' diagnosis and CAC score, the patients were classified as follows to compare differences in their PCAT attenuation:

(I) A. CAC score >0 *vs.* B. CAC score =0 and no CAD

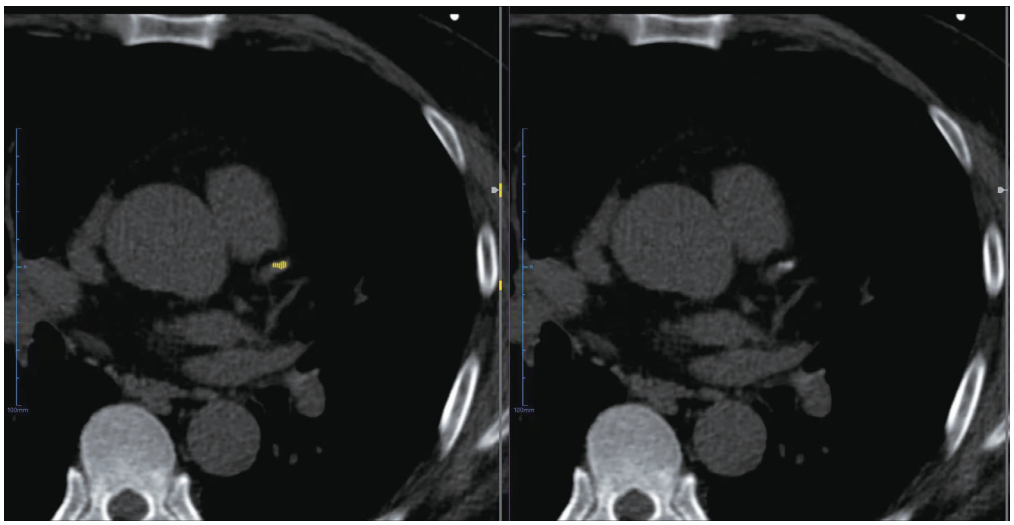

Figure 2 Schematic diagram of coronary artery calcium measurement.

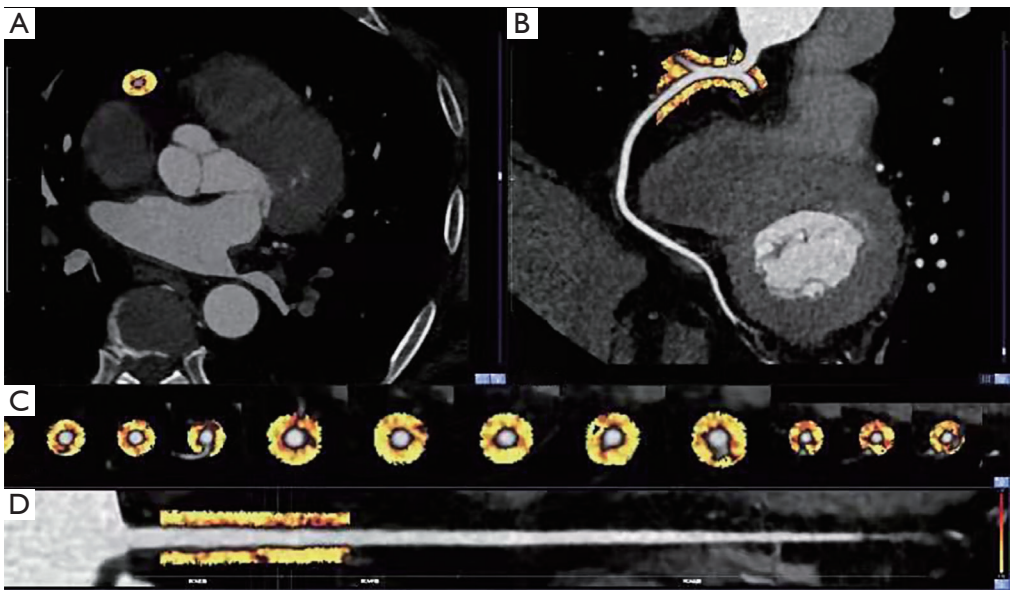

Figure 3 Schematic diagram of attenuation value measurement of pericoronary adipose tissue. (A) Axis position. (B) Curved planar reconstruction. (C) Cross-section multiplanar reconstruction. (D) Straightened curved planar reconstruction.

vs. C. CAC score =0 and with CAD;

(II) A_1. CAC score >10 *vs.* A_1'. 0< CAC score ≤10 *vs.* C. CAC score =0 and with CAD;

(III) A_2. CAC score >100 *vs.* A_2'. 0< CAC score ≤100 *vs.* C. CAC score =0 and with CAD; and

(IV) A_3. CAC score >400 *vs.* A_3'. 0< CAC score ≤400 *vs.* C. CAC score =0 and with CAD.

Statistical analysis

All the data were statistically analyzed by SPSS 23.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8.0.2 (GraphPad Software Inc., San Diego, CA, USA). The categorical variables were represented as frequency (percentage) and analyzed using the Chi-square test. The continuous variables were expressed as mean ± standard

Table 1 Patients' baseline characteristics

Characteristics	CAC >0 (n=117)	CAC =0 & No CAD (n=161)	CAC =0 & CAD (n=68)	χ^2/F	P value
Age (years, mean ± SD)	60.56±10.17#	53.99±11.09*	55.96±9.26*	13.564	0.000
Gender, n (%)					
Female	39 (33.33)	66 (40.99)	26 (38.24)	1.695	0.428
Male	78 (66.67)	95 (59.01)	42 (61.76)		
BMI (kg/m^2, mean ± SD)	25.68±3.60#	23.93±3.30*	26.29±3.33#	15.146	0.000
Hyperlipidemia, n (%)				37.546	0.000
Yes	86 (73.50)	65 (40.37)	49 (72.06)		
No	31 (26.50)	96 (59.63)	19 (27.94)		
Hypertension, n (%)				37.497	0.000
Yes	83 (70.94)	58 (36.02)	44 (64.71)		
No	34 (29.06)	103 (63.98)	24 (35.29)		
Hyperglycemia, n (%)				9.403	0.009
Yes	48 (41.03)	45 (27.95)	32 (47.06)		
No	69 (58.97)	116 (72.05)	36 (52.94)		
Smoking, n (%)				27.277	0.000
Yes	66 (56.41)	43 (26.71)	34 (50.00)		
No	51 (43.59)	118 (73.29)	34 (50.00)		
Tube voltage, KVP, n (%)				2.195	0.901
70	40 (34.19)	59 (36.65)	19 (27.94)		
80	62 (52.99)	80 (49.69)	37 (54.41)		
90	9 (7.69)	12 (7.45)	7 (10.29)		
100-120	6 (5.13)	10 (6.21)	5 (7.35)		

*, P<0.05, compared with CAC >0; #, P<0.05, compared with CAC =0 & No CAD. CAC, coronary artery calcium; CAD, coronary artery heart disease; SD, standard deviation; BMI, body mass index.

deviation or medians (interquartile range), and they were compared among the three groups using one-way ANOVA test or Kruskal-Wallis H test. The independent risk factors were screened using multiple logistic regressions.

Results

Patients' baseline characteristics

In this study, there were 117 patients with CAC score >0, 161 patients with no CAD with CAC score =0, and 68 patients with CAD with CAC score =0. There were significant differences in age, body mass index (BMI), hypertension, hyperlipidemia, hyperglycemia, and smoking among the three groups (P<0.05). On the other hand, there were no statistically significant differences in gender and tube voltage among the three groups (P>0.05, *Table 1*).

Comparison of PCAT attenuation values within each group

(I) In this study, patients with CAD had significantly higher PCAT attenuation than patients without CAD (−87.54±9.39 *vs.* −93.45±7.42 HU, P=0.000). Taking the CAC score =0 as the boundary, it was found that the PCAT attenuation of patients with CAD with CAC score =0 was significantly higher than that of patients with CAC score >0 and patients with no CAD

CAD (n=185)			No CAD (n=161)	P value
−87.54±9.39 HU			−93.45±7.42 HU	0.000
CAC >0 (n=117)		CAC =0 (n=68)	CAC =0 & No CAD (n=161)	0.000
−90.38±8.59 HU*#		−82.63±8.70 HU#	−93.45±7.42 HU*	
CAC >10 (n=94)	0<CAC≤10 (n=23)	CAC =0 (n=68)	–	0.000
−90.70±8.27 HU*	−89.09±9.87 HU*	−82.63±8.70 HU		
CAC >100 (n=51)	0<CAC≤100 (n=66)	CAC =0 (n=68)	–	0.000
−90.12±7.72 HU*	−90.59±9.26 HU*	82.63±8.70 HU		
CAC >400 (n=16)	0<CAC≤400 (n=101)	CAC =0 (n=68)	–	0.000
−89.69±6.04 HU*	−90.50±8.94 HU*	82.63±8.70 HU		

Figure 4 Comparison of PCAT attenuation values between groups. *, P<0.05, compared with CAC =0 & CAD; #, P<0.05, compared with CAC =0 & No CAD. PCAT, pericoronary adipose tissue; CAD, coronary artery heart disease; CAC, coronary artery calcium.

with CAC score =0 (−82.63±8.70 *vs.* −90.38±8.59 *vs.* −93.45±7.42 HU, P=0.000). In addition, patients with CAC score >0 also had significantly higher PCAT attenuation than patients with no CAD with CAC score =0 (*Figure 4*).

(II) The CAC scores of 10, 100, and 400 were taken as the cutoff values. It was found that the PCAT attenuation was significantly higher in patients with CAD with a CAC score =0 (−82.63±8.70 HU) than that of patients with CAC score >10 (−90.70±8.27 HU, P=0.000), 0< CAC score ≤10 (−89.09±9.87 HU, P=0.000); CAC score >100 (−90.12±7.72 HU, P=0.000), 0< CAC score ≤100 (−90.59±9.26 HU, P=0.000); and CAC score >400 (−89.69±6.04 HU, P=0.000), 0< CAC score ≤400 (−90.50±8.94 HU, P=0.000). In contrast, there was no significant difference in the PCAT attenuation between patients with CAC score >10, 0< CAC score ≤10; CAC score >100, 0< CAC score ≤100; and CAC score >400, 0< CAC score ≤400 (*Figure 4*).

The results of multiple logistic regressions

In the multiple logistic regression analysis, the study set patients with no CAD with CAC score =0 as the reference group, the independent risk factors of patients with CAC score >0 were age [odds ratio (OR): 1.076, 95% CI: 1.045–1.108, P=0.000], BMI (OR: 1.153, 95% CI: 1.056–1.259, P=0.001), hyperlipidemia (OR: 0.327, 95% CI: 0.180–0.597, P=0.000), hypertension (OR: 0.355, 95% CI: 0.195–0.645, P=0.001), smoking (OR: 0.248, 95% CI: 0.156–0.518, P=0.000) and PCAT attenuation (OR: 1.041, 95% CI: 1.002–1.081, P=0.040); the independent risk factors of patients with CAD with CAC score =0 were BMI (OR: 1.186, 95% CI: 1.067–1.319, P=0.002), hyperlipidemia (OR: 0.416, 95% CI: 0.198–0.874, P=0.021), hypertension (OR: 0.385, 95% CI: 0.185–0.798, P=0.010), and PCAT attenuation (OR: 1.175, 95% CI: 1.120–1.232, P=0.000; *Table 2*, *Figure 5*).

Discussion

This study explored the potential association between coronary inflammation and coronary atherosclerotic burden based on the RCA proximal PCAT attenuation value and total CAC scores measured by the CCTA. The results showed that PCAT attenuation value was not necessarily associated with CT calcification but rather with the presence of CAD, especially in patients with NCP (patients with CAD with CAC score =0). In addition, BMI, hyperlipidemia, hypertension, and PCAT attenuation were independent risk factors for patients with CAD with CAC score =0 and patients with CAC score >0, when patients with no CAD with CAC score =0 were taken as the reference group.

The CAC score is a valid surrogate for the burden of coronary atherosclerosis, and its presence and magnitude are related to the increased risk of cardiovascular events; whereas, patients with a CAC score of 0 have always been considered to have a lower cardiovascular risk in the future (12,18). However, CAD patients with NCP were overlooked by the concept of a CAC score of 0 which could be caught by the CCTA but proven to be dangerous by

Table 2 The results of multiple logistic regression

Characteristics	Multivariable (CAC =0 & No CAD *vs.* CAC >0)			Multivariable (CAC =0 & No CAD *vs.* CAC =0 & CAD)		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.076	1.045–1.108	0.000	1.030	0.995–1.065	0.092
BMI	1.153	1.056–1.259	0.001	1.186	1.067–1.319	0.002
Hyperlipidemia	0.327	0.180–0.597	0.000	0.416	0.198–0.874	0.021
Hypertension	0.355	0.195–0.645	0.001	0.385	0.185–0.798	0.010
Hyperglycemia	0.859	0.463–1.592	0.629	0.584	0.278–1.228	0.156
Smoking	0.248	0.156–0.518	0.000	0.559	0.269–1.161	0.119
PCAT attenuation	1.041	1.002–1.081	0.040	1.175	1.120–1.232	0.000

CAC, coronary artery calcium; CAD, coronary artery heart disease; OR, odds ratio; CI, confidence interval; BMI, body mass index; PCAT, pericoronary adipose tissue.

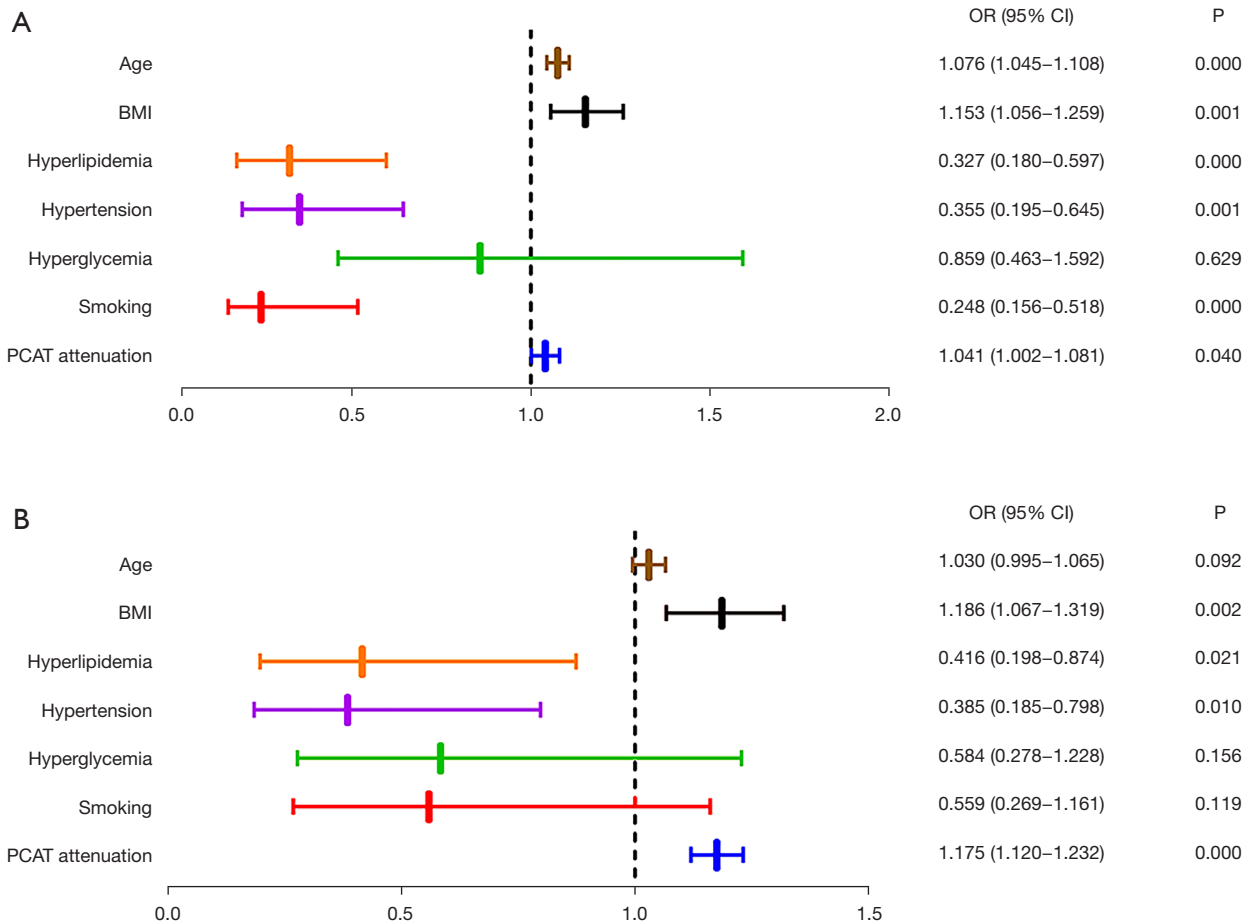

Figure 5 The forest plots show the results of the multiple logistic regression. (A) No CAD patients with CAC score =0 *vs.* patients with CAC score >0. (B) No CAD patients with CAC score =0 *vs.* CAD patients with CAC score =0. CAD, coronary artery heart disease; CAC, coronary artery calcium; BMI, body mass index; PCAT, pericoronary adipose tissue; OR, odds ratio; CI, confidence interval.

research (19-21). We, therefore, further subdivided patients with CAC score of 0 into patients with no CAD with CAC score =0 and CAD patients with CAC score =0 to better explore the potential association between PCTA attenuation and CAC score. Clinically, the age, BMI, hypertension, hyperlipidemia, hyperglycemia, and smoking are found to be significantly different among patients with CAD with CAC score =0, CAC score >0, and patients with no CAD with CAC score =0. Moreover, our results were similar to previous studies, which found BMI, hyperlipidemia, and hypertension were independent risk factors for patients with CAD with CAC score =0 and patients with CAC score >0 (22-24). Therefore, patients with hyperlipidemia, hypertension, and high BMI should be prompted for lipid, blood pressure and weight control, and regular CAC and CCTA examinations to prevent adverse cardiac events.

The attenuation value of PCAT is considered as a noninvasive biomarker of coronary inflammation (3,25). The mechanism is that inflammatory signals released from the inflamed vessels can diffuse directly to PCAT, inducing its breakdown and inhibiting its formation, while promoting pericoronary edema (26). When patients undergo a CCTA, the CT attenuation value of PCAT increases because of the lower lipid content and higher water content around the inflamed coronary artery (3). In patients, higher PCAT attenuation values suggest a higher danger of adverse cardiac events (27,28). In this study, compared to patients with no CAD, we found higher PCAT attenuation in patients with CAD, which is consistent with Antonopoulos *et al.* (26), who suggested that coronary artery inflammation plays an important part in the development and progression of atherosclerosis (29,30). In addition, we also found that the PCAT attenuation of patients with CAD with CAC score =0 was significantly higher than those with CAC score >0. This may be due to the fact that the calcium presence makes the plaque relatively stable, with only minimal inflammatory components and coronary inflammation may be more pronounced in the NCP (31,32).

Higher Agatston CAC scores indicate greater coronary atherosclerotic burden and higher cardiovascular risk, which however is inconsistent with the pathophysiological progression of coronary atherosclerotic plaques from unstable to stable stages (33). To further explore the relationship, our study, using the boundaries of the CAC scores of 10, 100, and 400, delved into finding the correlation between CAC scores and PCAT attenuation values. In this study, no significant differences in PCAT attenuation values between CAC scores were noted, which is in agreement with studies by Ma *et al.* (16) and Goeller *et al.* (34), which showed that the inflammatory information captured by PCAT attenuation is not associated with coronary artery calcification. Furthermore, this is to be anticipated because CPs are composed mainly of hydroxyapatite and do not comprise the main inflammatory element of atherosclerotic plaques (35). Moreover, patients with CAD with CAC score =0, also known as NCP, had higher PCAT attenuation values compared to all other groups with CAC scores. This is consistent with the hypothesis that NCP is an early stage of atherosclerosis, and plaque calcification is a late manifestation of atherosclerosis; whereas, inflammation can be comparatively reduced as plaques become more stable and calcified (36).

We observed that in addition to BMI, hyperlipidemia, and hypertension (23,37), which are often reported as risk factors, increased PCAT attenuation was also an independent risk factor for patients with CAD with CAC score =0 and patients with CAC score >0, which indicated that both PCAT attenuation and patient clinical information have important added value for the cardiovascular disease risk assessment. Furthermore, Sugiyama *et al.* (38) found that the RCA Agatston CAC score was a determinant of the PCAT attenuation value proximal to the RCA in male patients. Therefore, for patients with clinical risk factors, it is necessary to undergo a follow-up CCTA even if their CAC score is 0. It is not only to avoid missing NCPs, but also to obtain additional information about coronary inflammation, which is considered to be more important.

Limitations

There are several limitations of this study. Firstly, the present study was a retrospective single-center study; therefore, a larger multicenter study is needed to further validate our findings prospectively. Secondly, although the difference in tube voltage was not statistically significant among the three groups of patients, the CT values of fat varied with the tube voltage. Thirdly, patients with CAD were not followed up for subsequent major adverse cardiovascular events in this study, and we will follow up with patients in this study in the future to further reveal the relationship between coronary atherosclerotic burden and vascular inflammation. Finally, only the PCAT attenuation of the proximal RCA was analyzed, and the correlation between coronary inflammation around the plaque and

coronary atherosclerotic burden still needs to be further explored in the future.

Conclusions

Although PCAT attenuation values were not different among CAC scores, it was highest in patients with CAD with CAC score =0 and was also an independent risk factor for patients with CAD with CAC score =0 and CAC score >0. These suggest that direct relationship between coronary inflammation and coronary atherosclerotic burden is not evident, however, patients with CAD with CAC score =0 should not be ignored.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-147/coif). JZ reports that this work was supported by the National Natural Science Foundation of China (No. 82071872), and Medical Innovation and Development Project of Lanzhou University (No. lzuyxcx-2022-139). XZ was an employee of Siemens Healthineers Company, and ZX is an employee of Shukun Technology Company. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Lanzhou University Second Hospital (No. 2021A-165) and individual consent for this retrospective analysis was waived.

References

1. Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: results from global burden of disease study 2017. BMC Public Health 2021;21:401.
2. Meah MN, Maurovich-Horvat P, Williams MC, Newby DE. Debates in cardiac CT: Coronary CT angiography is the best test in asymptomatic patients. J Cardiovasc Comput Tomogr 2022;16:290-3.
3. Oikonomou EK, Marwan M, Desai MY, Mancio J, Alashi A, Hutt Centeno E, et al. Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. Lancet 2018;392:929-39.
4. Mortensen MB, Caínzos-Achirica M, Steffensen FH, Bøtker HE, Jensen JM, Sand NPR, Maeng M, Bruun JM, Blaha MJ, Sørensen HT, Pareek M, Nasir K, Nørgaard BL. Association of Coronary Plaque With Low-Density Lipoprotein Cholesterol Levels and Rates of Cardiovascular Disease Events Among Symptomatic Adults. JAMA Netw Open 2022;5:e2148139.
5. Nerlekar N, Ha FJ, Cheshire C, Rashid H, Cameron JD, Wong DT, Seneviratne S, Brown AJ. Computed Tomographic Coronary Angiography-Derived Plaque Characteristics Predict Major Adverse Cardiovascular Events: A Systematic Review and Meta-Analysis. Circ Cardiovasc Imaging 2018;11:e006973.
6. Goeller M, Achenbach S, Cadet S, Kwan AC, Commandeur F, Slomka PJ, Gransar H, Albrecht MH, Tamarappoo BK, Berman DS, Marwan M, Dey D. Pericoronary Adipose Tissue Computed Tomography Attenuation and High-Risk Plaque Characteristics in Acute Coronary Syndrome Compared With Stable Coronary Artery Disease. JAMA Cardiol 2018;3:858-63.
7. Zhou W, Dey A, Manyak G, Teklu M, Patel N, Teague H, Mehta NN. The application of molecular imaging to advance translational research in chronic inflammation. J

Nucl Cardiol 2021;28:2033-45.
8. Shaw LJ, Blankstein R, Bax JJ, Ferencik M, Bittencourt MS, Min JK, et al. Society of Cardiovascular Computed Tomography / North American Society of Cardiovascular Imaging - Expert Consensus Document on Coronary CT Imaging of Atherosclerotic Plaque. J Cardiovasc Comput Tomogr 2021;15:93-109.
9. Budoff MJ, Lakshmanan S, Toth PP, Hecht HS, Shaw LJ, Maron DJ, Michos ED, Williams KA, Nasir K, Choi AD, Chinnaiyan K, Min J, Blaha M. Cardiac CT angiography in current practice: An American society for preventive cardiology clinical practice statement (☆). Am J Prev Cardiol 2022;9:100318.
10. Agarwal S, Morgan T, Herrington DM, Xu J, Cox AJ, Freedman BI, Carr JJ, Bowden DW. Coronary calcium score and prediction of all-cause mortality in diabetes: the diabetes heart study. Diabetes Care 2011;34:1219-24.
11. Blaha M, Budoff MJ, Shaw LJ, Khosa F, Rumberger JA, Berman D, Callister T, Raggi P, Blumenthal RS, Nasir K. Absence of coronary artery calcification and all-cause mortality. JACC Cardiovasc Imaging 2009;2:692-700.
12. Shreya D, Zamora DI, Patel GS, Grossmann I, Rodriguez K, Soni M, Joshi PK, Patel SC, Sange I. Coronary Artery Calcium Score - A Reliable Indicator of Coronary Artery Disease? Cureus 2021;13:e20149.
13. Klüner LV, Oikonomou EK, Antoniades C. Assessing Cardiovascular Risk by Using the Fat Attenuation Index in Coronary CT Angiography. Radiol Cardiothorac Imaging 2021;3:e200563.
14. Gaibazzi N, Martini C, Botti A, Pinazzi A, Bottazzi B, Palumbo AA. Coronary Inflammation by Computed Tomography Pericoronary Fat Attenuation in MINOCA and Tako-Tsubo Syndrome. J Am Heart Assoc 2019;8:e013235.
15. Pergola V, Previtero M, Cecere A, Storer V, Castiello T, Baritussio A, Cabrelle G, Mele D, Motta R, Caforio AP, Iliceto S, Perazzolo Marra M. Clinical Value and Time Course of Pericoronary Fat Inflammation in Patients with Angiographically Nonobstructive Coronaries: A Preliminary Report. J Clin Med 2021;10:1786.
16. 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.
17. McCollough CH, Ulzheimer S, Halliburton SS, Shanneik K, White RD, Kalender WA. Coronary artery calcium: a multi-institutional, multimanufacturer international standard for quantification at cardiac CT. Radiology 2007;243:527-38.
18. Ferencik M, Pencina KM, Liu T, Ghemigian K, Baltrusaitis K, Massaro JM, D'Agostino RB Sr, O'Donnell CJ, Hoffmann U. Coronary Artery Calcium Distribution Is an Independent Predictor of Incident Major Coronary Heart Disease Events: Results From the Framingham Heart Study. Circ Cardiovasc Imaging 2017;10:e006592.
19. Motoyama S, Sarai M, Harigaya H, Anno H, Inoue K, Hara T, Naruse H, Ishii J, Hishida H, Wong ND, Virmani R, Kondo T, Ozaki Y, Narula J. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. J Am Coll Cardiol 2009;54:49-57.
20. van Werkhoven JM, Schuijf JD, Gaemperli O, Jukema JW, Kroft LJ, Boersma E, Pazhenkottil A, Valenta I, Pundziute G, de Roos A, van der Wall EE, Kaufmann PA, Bax JJ. Incremental prognostic value of multi-slice computed tomography coronary angiography over coronary artery calcium scoring in patients with suspected coronary artery disease. Eur Heart J 2009;30:2622-9.
21. Michaud K, Magnin V, Faouzi M, Fracasso T, Aguiar D, Dedouit F, Grabherr S. Postmortem coronary artery calcium score in cases of myocardial infarction. Int J Legal Med 2021;135:1829-36.
22. Avdan Aslan A, Erbaş G, Erdal ZS, Şendur HN, Cerit MN, Öncü F, Cindil E, Şahinarslan A, Kiliç K, Araç M. Prevalence and associated risk factors of coronary artery disease in patients with a zero coronary calcium score. Clin Imaging 2021;77:207-12.
23. Cho I, Suh JW, Chang HJ, Kim KI, Jeon EJ, Choi SI, Cho YS, Youn TJ, Chae IH, Kim CH, Choi DJ. Prevalence and prognostic implication of non-calcified plaque in asymptomatic population with coronary artery calcium score of zero. Korean Circ J 2013;43:154-60.
24. Senoner T, Plank F, Beyer C, Langer C, Birkl K, Steinkohl F, Widmann G, Barbieri F, Adukauskaite A, Friedrich G, Bauer A, Dichtl W, Feuchtner GM. Gender Differences in the Atherosclerosis Profile by Coronary CTA in Coronary Artery Calcium Score Zero Patients. J Clin Med 2021;10:1220.
25. Dong X, Zhu C, Li N, Shi K, Si N, Wang Y, Pan H, Shi Z, Wang S, Zhao M, Zhang T. Identification of patients with acute coronary syndrome and representation of their degree of inflammation: application of pericoronary adipose tissue within different radial distances of the proximal coronary arteries. Quant Imaging Med Surg

2023;13:3644-59.
26. 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.
27. Goeller M, Achenbach S, Duncker H, Dey D, Marwan M. Imaging of the Pericoronary Adipose Tissue (PCAT) Using Cardiac Computed Tomography: Modern Clinical Implications. J Thorac Imaging 2021;36:149-61.
28. Yuvaraj J, Lin A, Nerlekar N, Munnur RK, Cameron JD, Dey D, Nicholls SJ, Wong DTL. Pericoronary Adipose Tissue Attenuation Is Associated with High-Risk Plaque and Subsequent Acute Coronary Syndrome in Patients with Stable Coronary Artery Disease. Cells 2021;10:1143.
29. Harrington RA. Targeting Inflammation in Coronary Artery Disease. N Engl J Med 2017;377:1197-8.
30. Libby P, Tabas I, Fredman G, Fisher EA. Inflammation and its resolution as determinants of acute coronary syndromes. Circ Res 2014;114:1867-79.
31. Antonopoulos AS, Margaritis M, Coutinho P, Shirodaria C, Psarros C, Herdman L, Sanna F, De Silva R, Petrou M, Sayeed R, Krasopoulos G, Lee R, Digby J, Reilly S, Bakogiannis C, Tousoulis D, Kessler B, Casadei B, Channon KM, Antoniades C. Adiponectin as a link between type 2 diabetes and vascular NADPH oxidase activity in the human arterial wall: the regulatory role of perivascular adipose tissue. Diabetes 2015;64:2207-19.
32. Margaritis M, Antonopoulos AS, Digby J, Lee R, Reilly S, Coutinho P, Shirodaria C, Sayeed R, Petrou M, De Silva R, Jalilzadeh S, Demosthenous M, Bakogiannis C, Tousoulis D, Stefanadis C, Choudhury RP, Casadei B, Channon KM, Antoniades C. Interactions between vascular wall and perivascular adipose tissue reveal novel roles for adiponectin in the regulation of endothelial nitric oxide synthase function in human vessels. Circulation 2013;127:2209-21.
33. Rijlaarsdam-Hermsen D, Lo-Kioeng-Shioe MS, Kuijpers D, van Domburg RT, Deckers JW, van Dijkman PRM. Prognostic value of the coronary artery calcium score in suspected coronary artery disease: a study of 644 symptomatic patients. Neth Heart J 2020;28:44-50.
34. 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.
35. Fitzpatrick LA, Severson A, Edwards WD, Ingram RT. Diffuse calcification in human coronary arteries. Association of osteopontin with atherosclerosis. J Clin Invest 1994;94:1597-604.
36. Shioi A, Ikari Y. Plaque Calcification During Atherosclerosis Progression and Regression. J Atheroscler Thromb 2018;25:294-303.
37. Al-Muhaidb SM, Aljebreen AMM, AlZamel ZA, Fathala A. Prevalence of noncalcified plaques and coronary artery stenosis in patients with coronary calcium scores of zero. Coron Artery Dis 2021;32:179-83.
38. 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.

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