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ORIGINAL RESEARCH

Morphological Changes of Peri-Coronary Adipose Tissue Together with Elevated NLR in Acute Myocardial Infarction Patients in-Hospital

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Background: Inflammation triggers atherosclerotic plaque rupture, leading to acute myocardial infarction (AMI). Following AMI, peri-coronary adipose tissue (PCAT) undergoes a transition from lipid-rich to hydrophilic characteristics due to vascular inflammation. This study investigates PCAT changes and neutrophil-to-lymphocyte ratio levels during AMI.

Patients and Methods: 60 AMI patients undergoing coronary computed tomography angiography and angiography (Jan 2020-Jun 2022) were studied 60 age, gender, BMI-matched stable angina, and 60 non-coronary artery disease patients were included. Siemens VB20.0 measured PCAT-volume and fat attenuation index (FAI). Neutrophil-to-lymphocyte ratio levels were calculated by peripheral blood tests.

Results: The PCAT volume and PCAT-FAI gradually increased across the control, stable angina, and AMI groups, with a corresponding gradual rise in NLR. NLR exhibited weak positive correlation with PCAT-FAI (r=0.35) and PCAT-volume (r=0.24). Multivariable logistic regression identified increased PCAT-volume, PCAT-FAI and neutrophil-to-lymphocyte ratio as possible independent AMI risk factors. No significant PCAT-volume difference was observed between infarct-related artery (IRA) and non-IRA for all three coronary arteries. Only PCAT-FAI around IRA-LAD was higher than non-IRA-LAD (−74.84±6.93 HU vs −79.04±8.68 HU). PCAT-FAI around culprit vessels in AMI was higher than corresponding lesion related vessel in SA. PCAT-volume around narrowed non-IRA in AMI was higher than that of corresponding LRV in SA. PCAT-FAI of narrowed non-IRA-LADs and non-IRA-LCXs in AMI were elevated compared to LADs (−78.46 ±8.56HU vs −83.13±8.34 HU) and LCXs (−73.83±10.63 HU vs −81.38±7.88 HU) of lesion related vessel in stable angina.

Conclusion: We found an association between AMI and inflammation in the coronary perivascular adipose tissue and systemic inflammatory response.

Keywords: peri-coronary adipose tissue, neutrophil-to-lymphocyte ratio, fat attenuation index, acute myocardial infarction

Background

Adipose tissue is the largest energy metabolism, endocrine and immune organ in the human body.[1–3] Recent clinical research has shown that various adipose tissues play crucial roles in the pathophysiological processes of cardiovascular diseases.[4–7] Peri-coronary adipose tissue (PCAT) refers to the epicardial adipose tissue that surrounds the coronary arteries and their branches.[8,9] It is an essential component of the coronary artery microenvironment and plays a vital role in bidirectional communication with the coronary vessel wall, influencing the regulation and function of the coronary arteries.[9–11] Previous research has shown that under the influence of pathogenic factors, PCAT recruits and activates inflammatory cells around the coronary vessels.[12,13] It secretes pro-inflammatory cytokines and reduces the secretion of anti-inflammatory adipokines, thereby promoting endothelial dysfunction and local lipid deposition, leading to the formation of atherosclerotic plaques and participating in the process of atherosclerosis. Simultaneously, the inflammatory cells released from inflamed blood vessels secrete inflammatory mediators into the

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local PCAT.[13,14] This induces lipolysis in the local PCAT and inhibits adipogenesis, resulting in an increase in the water content of PCAT. Due to recent progress in medical imaging technology, it is now possible to non-invasively identify alterations in PCAT resulting from vascular inflammation using Coronary Computed Tomography Angiography (CCTA). This technique relies on the fact that inflamed or metabolically active fat tissue tends to exhibit different attenuation patterns compared to healthy fat tissue. By quantifying the attenuation values in specific regions of interest, often expressed in Hounsfield Units (HU), medical professionals can identify and analyze severity of fat inflammation.[15–17]

Vascular inflammation-induced formation of high-risk plaques is a major contributing factor in the progression of atherosclerosis and the development of atherosclerotic thrombi.[17–19] This process can further exacerbate the occurrence and advancement of Acute Coronary Syndrome (ACS).[18] Therefore, it is possible to differentiate the severity of coronary artery disease by detecting the Coronary Artery Fat Attenuation Index (FAI), which measures the attenuation of adipose tissue surrounding the coronary arteries. Prior research indicates a connection between acute myocardial infarction and increased adipose tissue volume surrounding the coronary arteries.[20,21] However, there is no observed correlation with the average FAI of adipose tissue in the coronary arteries.[22] Subsequent investigations have revealed that the average FAI of this adipose tissue is linked to compromised coronary artery flow reserve following emergency interventions for acute myocardial infarction.[23] Recent studies have demonstrated that the FAI of adipose tissue around the proximal section of the right coronary artery (RCA) can differentiate between three distinct stages of coronary artery disease (CAD):[24] acute myocardial infarction, stable coronary heart disease, and absence of lesions. Moreover, it independently predicts long-term MACEs (Major Adverse Cardiac Events) in patients with acute myocardial infarction.[25,26] Nevertheless, previous research has not examined the relationship between adipose tissue volume and FAI around the left anterior descending artery (LAD) and the circumflex artery (LCX) in relation to acute myocardial infarction, nor has it analyzed the adipose tissue surrounding non-culprit lesion vessels during acute myocardial infarction. As a result, it remains unclear whether plaque rupture triggered by vascular inflammation during acute myocardial infarction solely induces inflammation in the corresponding culprit coronary artery adipose tissue, or if it also provokes inflammation in the entire epicardial vascular adipose tissue. Consequently, a more in-depth exploration is essential to shed light on these aspects.

Neutrophils and lymphocytes are two significant subgroups within white blood cells. The neutrophil-to-lymphocyte ratio (NLR), functioning as a composite inflammatory marker, effectively combines the inflammatory and immune status of these crucial cellular components.[27,28] It signifies the equilibrium between the activation and regulation of the inflammatory response, offering a more comprehensive portrayal of the body's inflammatory state and immune regulatory function.[27] Due to its ease of measurement and low testing costs, NLR has garnered substantial attention from clinical practitioners and has increasingly been employed to assess the disease progression and prognosis of cardiovascular system ailments in recent years.[29–31] In prior investigations, we observed a correlation between inflammation in the pericardial adipose tissue and coronary heart disease.[32] This was evident through heightened macrophage presence in the pericardial adipose tissue of coronary heart disease patients, along with an elevated proportion of pro-inflammatory M1 subtype cells. At present, research on utilizing NLR as a marker to indicate the inflammation status of PCAT is yet to be conducted.

In this retrospective study, we analyzed the peri-coronary fat inflammation in patients with acute myocardial infarction (AMI) using CCTA images obtained before percutaneous coronary intervention (PCI). We evaluated the inflammation level of peri-coronary adipose tissue by measuring the peri-coronary fat attenuation value. The results were compared with matched subjects having stable angina and controls with no CAD. Additionally, we performed peripheral blood tests to measure neutrophil and lymphocyte counts, from which we calculated the NLR. We investigated the correlation between NLR and peri-coronary fat inflammation, aiming to explore the potential association between peri-coronary fat inflammation and the progression to an unstable phase of CAD, as well as whether NLR could reflect peri-coronary fat inflammation. We also aimed to examine whether NLR could serve as a reference index for assessing the degree of peri-coronary fat inflammation in patients after AMI.

Materials and Methods

Study Population

This is a retrospective clinical study that included 60 patients who visited the Chest Pain Center at HuaDong hospital between January 2020 and June 2022. This study complies with the Declaration of Helsinki. These patients underwent emergency

CCTA within 1 hour and were subsequently diagnosed with acute myocardial infarction. They were admitted to the hospital and underwent percutaneous coronary angiography, including cases of ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction (The enrolled STEMI patients had no ST-segment elevation in the electrocardiogram at admission. After the completion of CCTA examination, the Re-examining electrocardiogram showed ST-segment elevation. Therefore, these patients had no problems in the diagnosis and treatment process). The presence of culprit lesions was confirmed during invasive coronary angiography by a cardiac specialist. The diagnosis of AMI conforms to the Fourth Universal Definition of Myocardial Infarction.[33] All AMI patients belonged to type 1 myocardial infarction (Emphasis on the causal relationship of plaque disruption with coronary athero-thrombosis). The most severe lesion site with complete occlusion, thrombotic lesion, or treated with percutaneous coronary intervention during coronary angiography is defined as the culprit vessel. The exclusion criteria include: left main coronary artery lesion, history of previous myocardial infarction or revascularization, acute infection period, severe autoimmune diseases or long-term use of corticosteroids, coexisting tumors, missing clinical data, unclear or missing image sequences.

The 60 patients in the Stable Angina (SA) group were enrolled during the same period and were well-matched with AMI patients in terms of age, gender, and body mass index (BMI). Additionally, all patients in the SA group underwent both CCTA and percutaneous coronary angiography. Stable angina is defined as exertional chest pain that has not shown any changes in frequency, intensity, or duration of symptoms during the preceding 4 weeks.[34]

Furthermore, 60 non-CAD patients serve as the control group. These patients received CCTA examination and CCTA showed that all coronary vessels were smooth without plaque.

The study design and patient selection are depicted in Figure 1. This research has obtained ethical approval from Huadong Hospital Affiliated to Fudan University.

Definition of Risk Factors

The past medical history and smoking history of the three patient cohorts were collected. Diabetes was defined as a fasting blood glucose level ≥7.0 mmol/L or the use of diabetes medications.[35] Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or receiving treatment for hypertension.[36] A history of atrial fibrillation was defined as the presence of atrial fibrillation rhythms on electrocardiogram or Holter

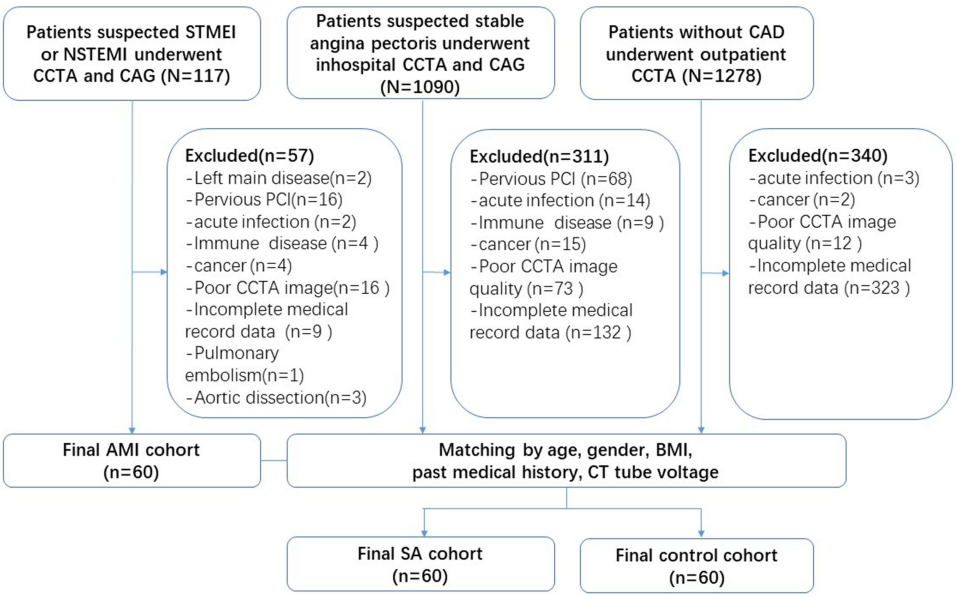

Figure 1 Flow diagram.

Abbreviations: STMEI, ST-segment elevation myocardial infarction; NSTEMI, Non-ST-segment elevation myocardial infarction; CCTA, coronary computed tomography angiography; CAG, coronary angiography; CAD, Coronary artery disease: AMI, acute myocardial infarction; SA, stable angina; BMI, body mass index. PCI, percutaneous coronary intervention; CT, computed tomography.

monitoring records. Cerebrovascular disease was defined as a history of ischemic or hemorrhagic stroke. Smoking history referred to current smoking or previous smoking habits.

CCTA Protocol

The participants were subjected to CCTA scans using a Siemens CT scanner (Siemens, Definition Flash, Erlangen, Germany) by skilled technicians following a standardized protocol. The CT scan covered the region from the level of the tracheal bifurcation to the apex of the heart. The scan parameters included detector collimation (256×0.625 mm), reconstruction slice thickness (0.625 mm), slice interval (0.625 mm), gantry rotation time (0.28 s), tube voltage (100 kV), and smart-mA adjusted based on the patient's condition. The field of view (FOV) was set at 25 cm.

All participants had an 18G intravenous catheter inserted into the upper limb vein. The injection of the contrast agent, iopromide (370 mg iodine/mL, Bracco, Italy), was administered at a rate of 4.5 to 5.5 mL/s, based on their BMI and venous condition, with a total volume of 50 to 60 mL. After the contrast agent injection, a flush of 30 to 40 mL of normal saline was administered at the same injection rate.

Analysis of PCAT Volume and Attenuation

The Siemens VB20.0 workstation and post-processing software were used to measure the PCAT volume and PCAT attenuation. The coronary arteries of interest were manually selected, and the heart was separated to remove the blood pool, retaining only the coronary artery tree. The segmentation tool was used to fine-tune the region of interest (ROI) around the coronary artery tree, and the fat threshold was set to −190 HU to −30 HU. After the evaluation, quantitative data of the attenuation index and volume of PCAT surrounding the coronary artery tree within the ROI were obtained (refer to Figure 2). The PCAT volume represented the total peri-coronary adipose tissue volume around the LAD, LCX and RCA, while PCAT-FAI represented the average attenuation index of adipose tissue around the LAD, LCX, and RCA.

Measurement of NLR

For inpatients, blood samples were collected within the first 24 hours after admission through the median cubital vein, and placed in ethylene diamine tetraacetic acid (EDTA) tubes for total blood cell count measured using an automated hematology analyzer. For outpatient cases, the total blood cell count was obtained within 24 hours before and after the completion of the CCTA procedure. The NLR is defined as the ratio between the absolute neutrophil count and the absolute lymphocyte count.[27]

Definition of IRA, Non-IRA and LRV

The IRA (infarct-related artery) was defined as the main coronary artery branch that caused the attack of myocardial infarction, which was determined by electrocardiogram and coronary angiography. Non-IRA was defined as unrelated other coronary artery branch that caused the onset of this myocardial infarction. It is the coronary artery branch excluding IRA. LRV (lesion related vessel) was defined as a coronary artery branch that causes chest pain in patients with stable angina and was determined by electrocardiogram and coronary angiography.

Statistical Analysis

All data were subjected to statistical analysis using SPSS 23.0. Normally distributed continuous variables were presented as mean ± standard deviation, while non-normally distributed continuous variables were described as median (interquartile range). Categorical data were presented as frequency and percentage [n (%)]. For comparisons among three or more groups of continuous variables, analysis of variance (ANOVA) was utilized, with independent sample *t*-tests used for inter-group comparisons. The correlation between continuous variables was analyzed using the Spearman correlation test. The comparison of categorical data among groups was conducted using the chi-square test or Fisher's exact chi-square test. Univariate and multivariate logistic regression analysis was used to identify possible risk factors. Variables with $P < 0.05$ in univariate analysis were further included in multivariate analysis. A significance level of $P < 0.05$ was considered statistically significant.

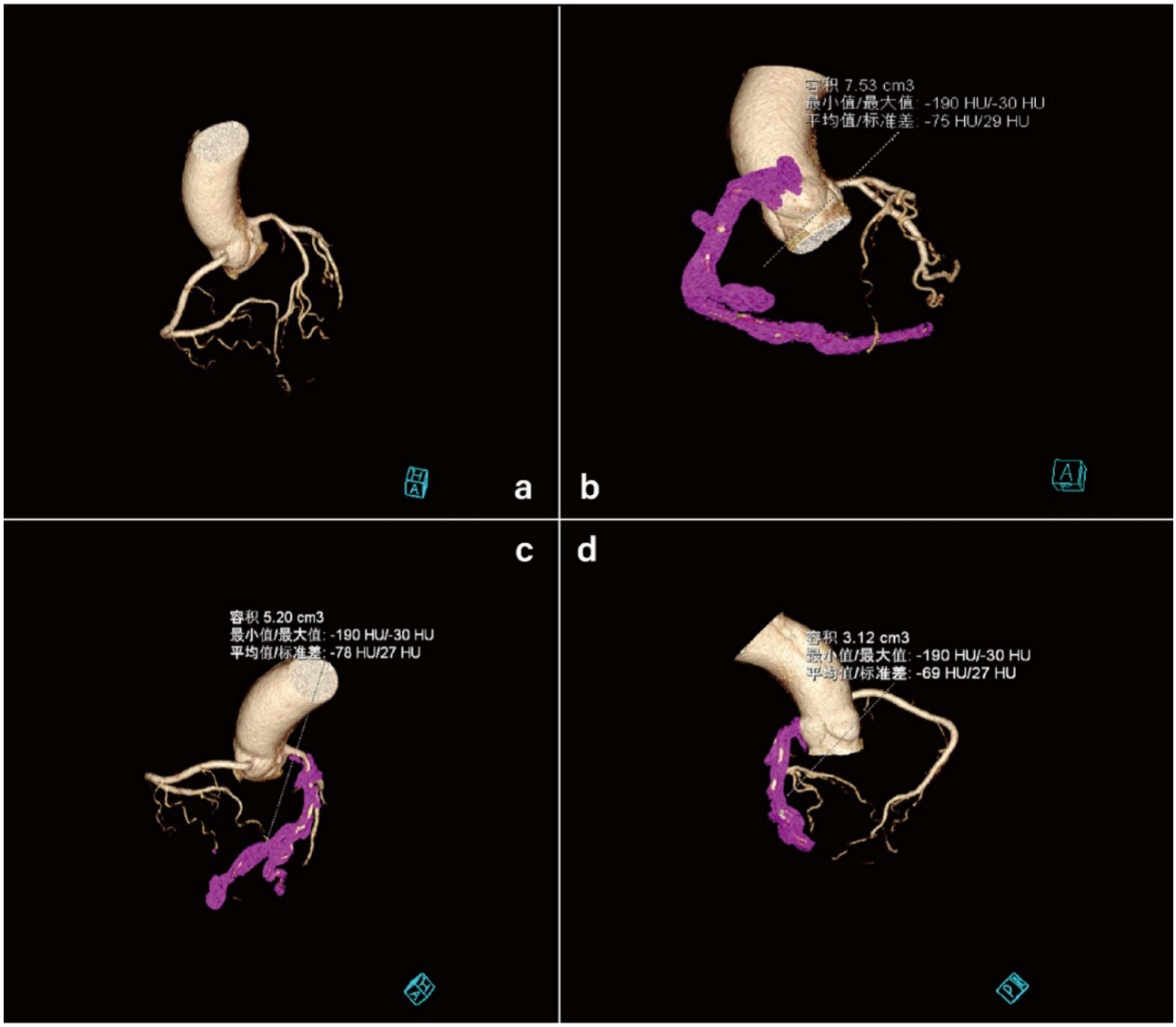

Figure 2 A 65-year-old female. (**a**) Three-dimensional reconstruction of the ascending aorta and coronary arteries; (**b**) PCAT-volume around the RCA is 7.53 cm^3 with an average FAI of −75 HU; (**c**) PCAT-volume around the LAD is 5.20 cm^3 with an average FAI of −78 HU; (**d**) PCAT-volume around the LCX is 3.12 cm^3 with an average FAI of −69 HU.
Abbreviations: PCAT, peri-coronary adipose tissue; FAI, fat attenuation index; RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery.

Results

Baseline Characteristics and Coronary Stenosis

Table 1 summarizes the general characteristics of the three study groups. There were no statistically significant differences among the groups in terms of age, gender, body mass index, medical history, cholesterol, triglycerides, low-density lipoprotein, and others. The smoking rate in the acute myocardial infarction group was higher than that in the control group, but there was no significant difference compared to the stable angina group (35%, 26.7%, and 15%, respectively). The levels of glycated hemoglobin in the acute myocardial infarction group and stable angina group were significantly higher than those in the control group (6.72 ± 2.62%, 6.84 ± 1.58%, and 5.85 ± 0.52%, respectively), but there was no statistically significant difference between the two groups ($p<0.05$). Regarding blood lipids, the HDL-C level in the acute myocardial infarction group (1.14 ± 0.26 mmol/L) was lower than that in the control group (1.32 ± 0.43 mmol/L), but there was no significant difference compared to the stable angina group (1.24 ± 0.28 mmol/L).

In terms of coronary artery involvement, compared to the stable angina group, patients with acute myocardial infarction had a higher incidence of triple vessel disease (46.7% vs 25%). The incidence of left anterior descending

Table 1 Baseline Characteristics of Study Participants

	AMI group (n=60)	SA group (n=60)	Control group (n=60)	t, x^2 or H	p value	p1–p2	p1–p3	p2–p3
Clinical characteristics								
Age(years)	67.65±13.85	69.55±10.40	66.97±6.18	0.95	0.387	–	–	–
Gender (M/F)	45/15	39/21	40/20	1.61	0.448	–	–	–
BMI(kg/m^2)	24.87±4.01	23.85±4.73	24.28±3.26	0.85	0.429	–	–	–
Hypertension, n(%)	45(75.0%)	47(78.3%)	44(73.3%)	0.42	0.810	–	–	–
Diabetes, n(%)	29(48.3%)	28(46.7%)	22(36.7%)	1.94	0.379	–	–	–
Atrial fibrillation, n(%)	4(6.7%)	4(6.7%)	6(10.0%)	0.17	0.920	–	–	–
Stroke, n(%)	3(5.0%)	8(13.3%)	5(8.33%)	2.61	0.272	–	–	–
Smoking, n(%)	21(35.0%)	16(26.7%)	9(15.0%)	6.37	0.041	0.323	0.011	0.116
Laboratory analysis								
Total cholesterol(mmol/L)	4.17[3.55–4.89]	4.14[3.34–4.74]	4.66[4.13–4.99]	5.71	0.058	–	–	–
Triglycerides(mmol/L)	1.50[1.20–2.08]	1.64[1.10–2.30]	1.43[1.02–2.30]	0.32	0.852	–	–	–
HDL–cholesterol(mmol/L)	1.16[0.98–1.27]	1.23[1.03–1.34]	1.34[1.04–1.51]	6.77	0.034	0.101	0.002	0.154
LDL–cholesterol(mmol/L)	2.47[1.87–3.05]	2.37[1.66–3.10]	2.63[2.22–3.12]	3.70	0.157	–	–	–
HbA1C(%)	6.40[5.60–7.70]	6.30[5.70–7.40]	5.80[5.40–6.20]	20.04	<0.001	0.711	0.015	0.005
CRP(mg/L)	6.90[3.73–18.12]	1.78[1.28–5.63]	2.26[1.28–5.72]	24.88	<0.001	<0.001	<0.001	1.000
CTnT(ng/mL)	0.40[0.14–1.84]	0.01[0.01–0.02]	0.01[0.01–0.02]	117.60	<0.001	<0.001	<0.001	0.151
Coronary artery characteristics								
Triple vessel lesion, n(%)	29(46.7%)	15(25.0%)	–	7.03	0.008		–	–
LAD lession, n(%)	55(91.7%)	47(78.3%)	–	4.18	0.041		–	–
LCX lession, n(%)	38(63.3%)	24(40.0%)	–	6.54	0.011		–	–
RCA lession, n(%)	42(70.0%)	28(46.6%)	–	6.72	0.010		–	–

Note: Data are expressed as n(%), mean ± SD.

Abbreviations: AMI, acute myocardial infarction; SA, stable angina; BMI, body mass index; HDL, high density lipoprotein; LDL, low density lipoprotein; CRP, c-reactive protein; CTnT, cardiac troponin-t; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

branch, right coronary branch, and circumflex branch lesions in the stable angina group was lower than that in the acute myocardial infarction group (p<0.05). The incidence of left anterior descending artery disease was higher than that of right coronary artery disease and circumflex artery disease in both the acute myocardial infarction group and stable angina group (p<0.05); There was no significant difference in the incidence of circumflex artery disease and right coronary artery disease (p>0.05) (Table 1).

PCAT Volume, PCAT-FAI and NLR Values

The volume of PCAT showed statistically significant differences among the AMI group, SA group, and control group. PCAT volume in AMI patients (11.61 ± 5.34 cm³) Significantly higher than the SA group (8.37 ± 4.06 cm³, $p < 0.001$) and control group (6.14 ± 3.20 cm ³, p< 0.001) (Figure 3A). The PCAT-FAI values in the control group, SA group, and AMI group gradually increased (p<0.05). The PCAT-FAI (−76.49 ± 6.67 HU) of AMI patients was significantly higher than that of the SA group (−81.52 ± 6.84 HU, p<0.001) and the control group (−84.73 ± 6.35 HU, p<0.001). The PCAT-FAI of the SA group was also significantly higher than that of the control group (p<0.01) (Figure 3B).

The NLR value is gradually increased in the control group, SA group, and AMI group. Compared to the SA group (2.60 ± 1.50, $p < 0.001$) and control group (2.04 ± 0.75) the NLR value was significantly increased in AMI group (5.45 ± 2.87). There was not significant between SA group and control group (p=0.097) (Figure 3C).

To further elucidate the correlation between perivascular fat and NLR, we conducted Spearman correlation analysis to evaluate the association between PCAT-FAI, PCAT volume and NLR. There is a weak positive correlation between NLR and PCAT-FAI (r=0.35, p<0.001) (Figure 3D), as well as between NLR and PCAT volume (r=0.24, p=0.001) (Figure 3E).

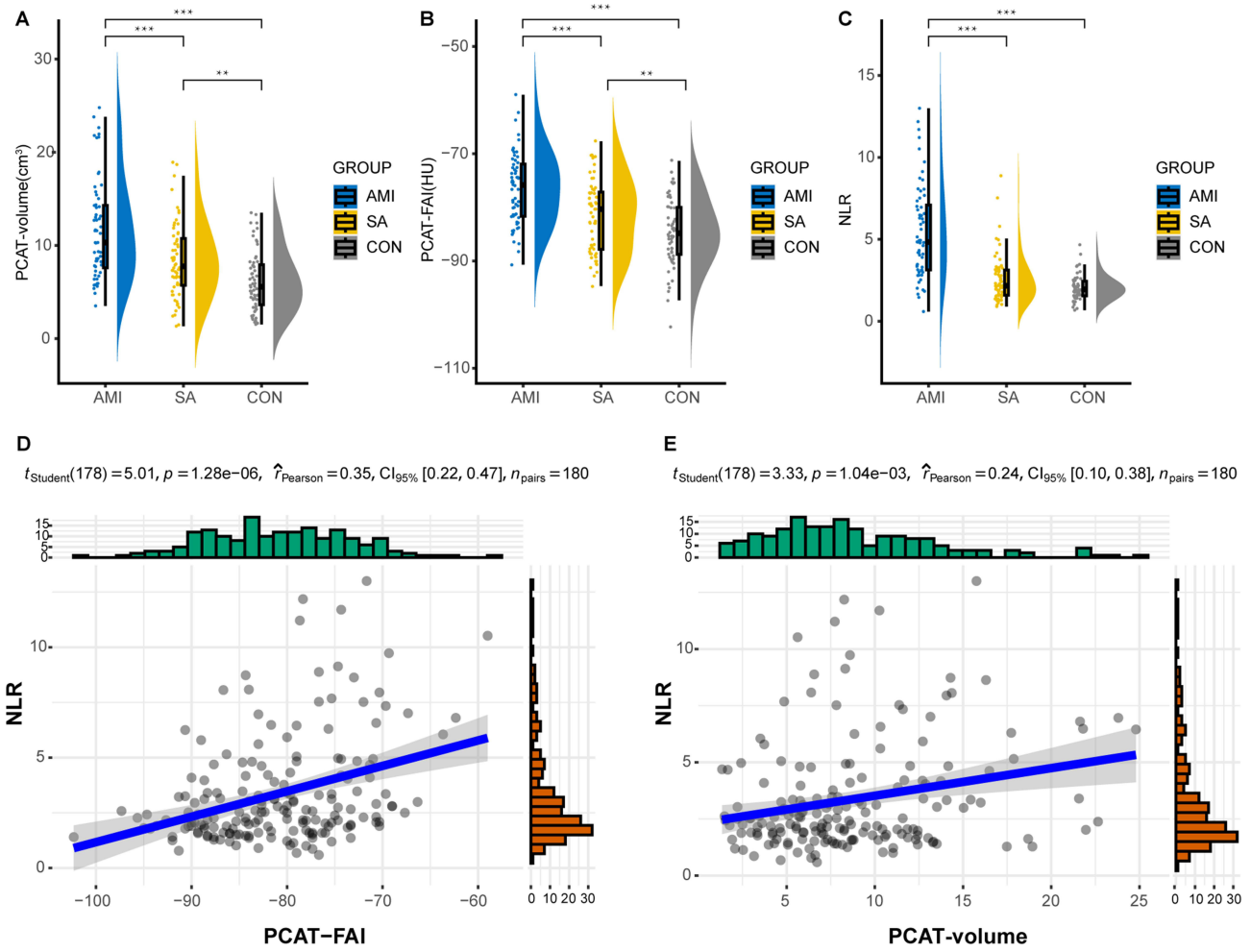

Figure 3 (**A**) PCAT volume in AMI patients significantly higher than the SA group and control group. (**B**) The PCAT-FAI values in the control group, SA group, and AMI group gradually increased. (**C**) The NLR value is gradually increased in the control group, SA group, and AMI group. Compared to the SA group (2.60 ± 1.50 cm ³) and control group (2.04 ± 0.75 cm³) the NLR value was significantly increased in AMI group (5.45 ± 2.87 cm³). (**D** and **E**) Spearman correlation analysis shows that there is a positive correlation between NLR and PCAT-FAI (r=0.35, p<0.001), as well as between NLR and PCAT volume (r=0.24, p=0.001). (**P<0.01; ***P<0.001).
Abbreviations: PCAT, peri-coronary adipose tissue; AMI, acute myocardial infarction; SA, stable angina; FAI, fat attenuation index; NLR, neutrophil-to-lymphocyte ratio.

Analysis of Risk Factors for AMI

We conducted a multivariable logistic regression analysis to further examine the factors associated with the occurrence of acute myocardial infarction. In the initial single-variable analysis, smoking, decreased HDL-C, elevated HbA1C, increased PCAT volume, elevated PCAT-FAI, and higher NLR all exhibited statistically significant differences (p <0.05). These significant factors were subsequently included in the multivariable logistic regression analysis. The Results revealed that increased PCAT volume (OR=1.26, 95% CI: 1.15–1.38, P<0.001), elevated PCAT-FAI (OR=1.15, 95% CI: 1.08–1.22, P<0.001), and elevated NLR (OR=2.26, 95% CI: 1.67–3.07, P<0.001) were identified as possible independent risk factors for the occurrence of acute myocardial infarction (Figure 4).

The PCAT Volume and PCAT-FAI of Infarct Related Arteries (IRAs) in AMI

According to the locations of culprit lesions in the AMI group, 31 cases of IRAs were LAD (51.7%), 19 cases of IRA were LCX (31.7%), and 10 cases were RCA (16.7%). Based on whether each blood vessel in AMI patients is IRA, LAD, RCA, and LCX were further divided into IRA group and non-IRA group to analyze the differences in pericoronary fat between the two groups. The results indicated that there was no significant difference in PCAT volume between IRA -LAD and Non-IRA -LAD, IRA -LCX and Non-IRA -LCX, IRA -RCA and Non-IRA -RCA groups (p>0.05) (Figure 5A). Only the PCAT-FAI of IRA -LAD was higher than that around Non-IRA-LAD (−74.84±6.93 HU vs −79.04±8.68 HU, p=0.047), while the PCAT-FAI of IRA-LCX

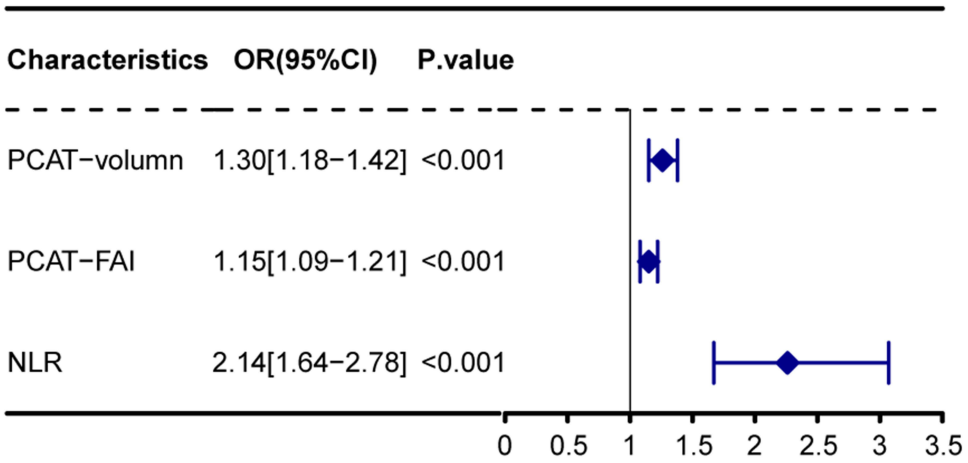

Figure 4 Multivariable logistic regression analysis of risk factors for AMI. AMI, acute myocardial infarction.

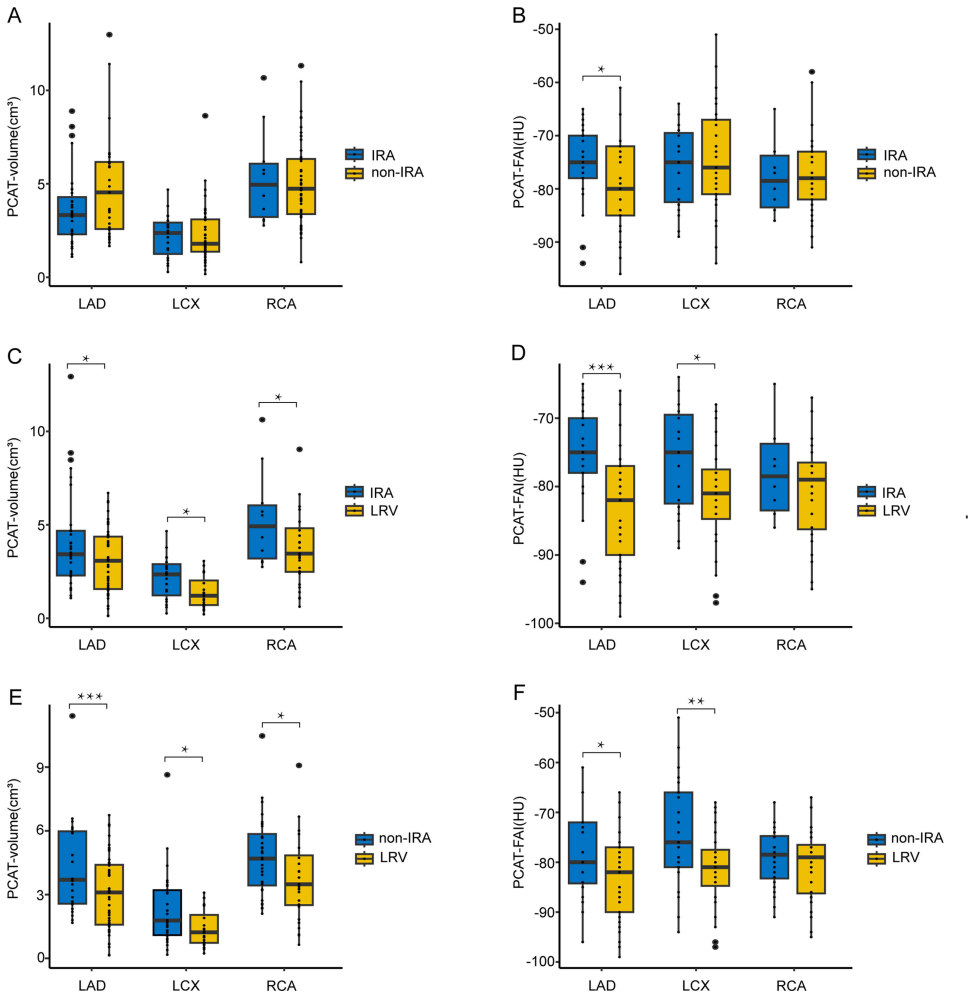

Figure 5 (**A**) There was no significant difference in PCAT volume between IRA -LAD and Non-IRA -LAD, IRA -LCX and Non-IRA -LCX, IRA -RCA and Non-IRA -RCA groups (p>0.05). (**B**) Only the FAI of adipose tissue around IRA -LAD was higher than that around Non-IRA-LAD, while the FAI of adipose around IRA-LCX and IRA-RCA showed no statistical difference compared to that around Non-IRA-LCX and Non-IRA-RCA. (**C**) PCAT volume of IRA-LADs, IRA-LCXs, and IRA-RCAs were significantly higher than that in the LRV-LADs, LRV-LCXs, and LRV-RCAs. (**D**) The FAI around the culprit vessels in AMI patients with LAD, LCX, and RCA were higher than those in the SA group. (**E**) The PCAT volumes of Non -IRA-LADs, Non -IRA-LCXs, and Non -IRA-RCAs were notably greater than that of the LRV-LADs, LRV-LCXs, and LRV-RCAs. (**F**) The FAIs of Non -IRA-LADs and Non -IRA-LCXs were higher than that of LRV-LADs and LRV-LCXs. There was no statistically difference of FAI between Non -IRA-RCAs and LRV-RCAs. (*P<0.05; **P<0.01; ***P<0.001).

Abbreviations: PCAT, peri-coronary adipose tissue; FAI, fat attenuation index; RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; IRA, infarct-related artery; LRV, lesion related vessel.

and IRA-RCA showed no statistical difference compared to that around Non-IRA-LCX (−76.00 ± 7.59 HU vs −74.37 ± 9.56 HU, p>0.05) and Non-IRA-RCA (−78.00 ± 6.50 HU vs −77.68 ± 6.87 HU, p>0.05) (Figure 5B).

Comparison of PCAT Volume and PCAT-FAI Between IRAs in AMI and Lesion Related Vessels (LRVs) in SA

Subsequently, we compared the PCAT volume and PCAT-FAI between IRA in AMI patients and LRVs in SA patients. Among them, there were 78 LAD lesions (31 IRA -LADs vs 47 LRV-LADs), 43 LCX lesions (19 IRA -LCXs vs 24 LRV-LCXs), and 38 RCA lesions (10 IRA -RCAs vs 28 LRV-RCAs). The results revealed that PCAT volume of IRA-LADs, IRA-LCXs, and IRA-RCAs were significantly higher than that in the LRV-LADs (4.14±2.70 cm^3 vs 3.05 ±1.76 cm^3, p=0.033), LRV-LCXs (2.2±1.19 cm^3 vs 1.41±0.87 cm^3, p=0.017), and LRV-RCAs (5.36±2.60 cm^3 vs 3.76 ±1.96 cm^3, p=0.03) (Figure 5C). In addition, the PCAT-FAI around the culprit vessels in AMI patients with LAD, LCX, and RCA were higher than those in the SA group, which were (−74.84 ± 6.93 HU vs −83.13 ± 8.34 HU, p<0.001), (−76.00 ± 7.59 HU vs −81.38 ± 7.88 HU, p=0.029), and (−78.00 ± 6.50 HU vs −80.86 ± 7.05 HU, p=0.027) (Figure 5D).

The PCAT Volume and PCAT-FAI of Narrowed Non-IRAs in AMI and LRVs in SA

Based on the results of CAG and CCTA, a total of 71 narrowed Non- IRAs in AMI group were selected to analysis, including 24 narrowed Non -IRA-LADs, 29 narrowed Non -IRA-LCXs, and 32 narrowed Non -IRA-RCAs. The differences of PCAT volume and PCAT-FAI were compared between narrowed Non-IRAs in AMI group and LRVs in SA group. The PCAT volumes of narrowed Non -IRA-LADs, narrowed Non -IRA-LCXs, and narrowed Non -IRA-RCAs were notably greater than that of the LRV-LADs (4.32±2.27 cm^3 vs 3.05±1.76 cm^3, p=0.001), LRV-LCXs (2.30±1.75 cm^3 vs 1.41±0.87 cm^3, p=0.028), and LRV-RCAs (4.76±1.86 cm^3 vs 3.76±1.96 cm^3, p=0.047), respectively (Figure 5E).

The PCAT-FAIs of Non -IRA-LADs and narrowed Non -IRA-LCXs were higher than that of LRV-LADs (−78.46±8.56 HU vs −83.13±8.34 HU, p < 0.001) and LRV-LCXs (−73.83±10.63 HU vs −81.38±7.88 HU, p=0.029). There was no statistically difference of PCAT-FAI between narrowed Non -IRA-RCAs and LRV-RCAs (−78.66 ± 6.23 HU vs −80.86 ± 7.05 HU, p=0.204) (Figure 5F).

Discussion

This study focused on evaluating the PCAT volume and PCAT-FAI during the acute-phase in patients diagnosed with AMI. These assessments were then compared to those of patients with stable angina (SA) as well as individuals without coronary artery disease (non-CAD). The results revealed that both PCAT volume and PCAT-FAI in the acute-phase AMI patients were significantly higher compared to those in the SA and non-CAD control groups. Remarkably, both culprit and non-culprit vessels in AMI patients displayed heightened PCAT-FAI. It's worth noting that the PCAT-FAI around non-culprit vessels remained significantly elevated in acute-phase AMI patients when compared to those with stable angina. Furthermore, a noteworthy finding in our study was a substantial elevation in the NLR among AMI patients, and this ratio demonstrated a weak positive correlation with the PCAT-FAI. Our study demonstrates that in individuals experiencing acute myocardial infarction, the overall PCAT is in an inflamed condition, concomitant with plaque rupture and thrombus formation within related arteries. This inflammatory state is further accompanied by the activation of systemic inflammatory pathways.

Recent research indicates a bidirectional communication between the coronary artery vessel wall and PCAT.[9–11] PCAT can directly modulate signaling pathways in the vessel wall through paracrine and vasocrine actions.[12,13] Conversely, it can be influenced by inflammatory stimuli from diseased vessels.[13,14] Inflammatory stimuli from the underlying vessel can inhibit adipocyte differentiation and aggregation, inducing the perivascular adipose tissue to shift from a lipid to a more aqueous phase, resulting in increased attenuation of PCAT on CCTA.[15] Therefore, measuring PCAT attenuation values can be used to estimate the level of inflammation in the coronary arteries. Furthermore, other studies have indicated that elevated attenuation of PCAT is associated with increased cardiovascular mortality, and the culprit plaques in patients with acute coronary syndrome (ACS)[9,37,38] exhibit higher PCAT attenuation compared to those in SA patients.[17] These findings support the existence of a correlation between coronary artery inflammation measured through attenuation of PCAT and coronary artery disease. However, unlike previous studies where PCAT attenuation around ruptured plaque vessels was significantly higher than that around non-ruptured plaque vessels, our research found that only the perivascular adipose tissue attenuation around culprit vessels in the LAD was higher than

that around non-culprit vessels in AMI patients. Interestingly, we observed that not only did culprit plaque lesions in AMI patients have higher perivascular adipose tissue attenuation compared to those in SA patients, but non-culprit lesion vessels in AMI patients also exhibited higher perivascular adipose tissue attenuation compared to lesion vessels in SA patients. This indicates that during acute myocardial infarction, not only does the PCAT around the culprit plaque experience inflammation due to the diseased vessel, but the PCAT around non-culprit coronary artery lesions, as part of the epicardial adipose tissue, is also influenced by vascular inflammation. As a result, in the context of acute myocardial infarction, the inflammatory reaction of perivascular adipose tissue surrounding coronary arteries is not confined to specific areas.

In our previous investigations,[32] we confirmed that the epicardial adipose tissue exhibits a brown fat phenotype, and as a part of the epicardial adipose tissue, the PCAT also belongs to brown adipose tissue (BAT). Prior studies have found that inflammation of adipose tissue can lead to the whitening of BAT, manifested as decreased BAT activity, enlarged adipocyte volume, increased endoplasmic reticulum, increased cholesterol crystals, mitochondrial degradation, and increased surrounding collagen fibers. In this study, we observed that the total volume of PCAT in AMI patients was significantly higher than in SA patients and the controls. However, there were no significant differences in the PCAT volume around culprit and non-culprit vessels of the LAD, LCX, and RCA in AMI patients. Further analysis showed that regardless of whether the culprit vessel was involved, the PCAT volume around the LAD, LCX, and RCA in the AMI group was higher than the corresponding PCAT volume around the corresponding coronary arteries in the SA group, a finding not previously reported in existing research. We speculate that during acute myocardial infarction, the inflammation of perivascular adipose tissue around the coronary arteries leads to the whitening of brown fat, promoting an increase in adipocyte volume, which results in a significant increase in the volume of perivascular adipose tissue around the coronary arteries. Whether it is possible to improve cardiac remodeling and prognosis in patients with AMI by reducing the inflammation and volume of PCAT, as well as developing drugs or other therapeutic methods to reduce the inflammation and volume of PCAT, are worthy of future research.

Numerous scientific studies have demonstrated the vital role of inflammatory pathways in the initiation and progression of atherosclerosis.[17–19] During the advanced stages of atherosclerosis, neutrophils release various enzymes that render the affected arteries prone to vulnerable plaque formation, leading to plaque rupture and thrombus formation.[39–41] This process facilitates the transition from stable to unstable plaques. Additionally, lymphocytes play a pivotal role in inflammation regulation,[42] acting as key immune modulators that may decrease in number under stress conditions.[43] The NLR is a comprehensive marker that combines the strengths of neutrophils and lymphocytes in reflecting the severity of atherosclerotic lesions, thus compensating for their individual limitations.[27,28] It offers a more accurate assessment of the body's inflammatory and stress levels. In our study, we observed that NLR was notably elevated in patients with AMI. Furthermore, logistic regression analysis revealed that NLR independently predicted the risk of AMI. These findings align with the research conducted by Zalula et al[44] which also demonstrated a link between NLR and vulnerable plaques, supporting NLR as a robust independent predictor for acute coronary syndromes. Interestingly, we also discovered a positive correlation between NLR and PCAT-FAI in our study, suggesting a certain connection between NLR, AMI, and inflammation in perivascular adipose tissue surrounding the coronary arteries.

Conclusion, We found an association between AMI and inflammation in the coronary perivascular adipose tissue and systemic inflammatory response. This is reflected in elevated NLR levels, increased PCAT-FAI values on CCTA imaging, and an expansion in PCAT volume.

Limitations of the Study

There are some limitations in this study. 1. This study is a single-center study with a small sample size. In the future, we will increase the sample size in other clinical research centers to verify the research results; 2. Due to the limitation of research conditions, the analysis method of this study was logistic regression, which did not take into account the influence of time on the research results; 3. The baseline data of different groups of patients in the study did not reach the best matching degree; 4. This study did not include other representative immune-inflammatory indicators for statistical analysis to increase the credibility of the research results.

Ethics Statement

This study involving participants approved by the ethics committee of Huadong Hospital Affiliated to Fudan University, Shanghai, China (2019K072). All patients signed written informed consent.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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