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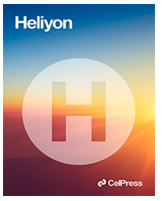

Research article

# The relationship between different exercise conditions and pericoronary inflammation as quantified by coronary CTA in coronary artery disease

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ABSTRACT

*Objectives:* The correlation between exercise type and intensity and coronary artery inflammation in patients with stable coronary artery disease (CAD) is unknown. Therefore, this study assessed the relationship between coronary inflammation quantified by coronary computed tomography angiography (CCTA) and exercise intensity and pattern in patients with CAD.

*Materials and methods:* Patients who underwent CCTA between 2019 and 2023 in the second hospital of Lanzhou University were retrospectively examined. We calculated the pericoronary fat attenuation index (FAI) on the right coronary artery (RCA) as a marker of coronary inflammation. We compared basic information, exercise status, and RCA-FAI values between the two groups, and described the relationship between different exercise durations and RCA-FAI using analysis of variance and restricted cubic splines.

*Results:* In total, 1222 patients were included: 774 had no CAD and 448 patients had CAD. Sex (P = 0.016; odds ratio [OR]: 0.673), high-density lipoprotein (P = 0.006; OR: 0.601), low-density lipoprotein (P = 0.001; OR. 0.762), hypertension (P = 0.000; OR: 0.762), smoking (P = 0.005; OR: 0.670), and postprandial glucose (P = 0.030; OR: 0.812), household income (P = 0.038; OR:1.117), and body mass index (P = 0.000; OR:1.084) were the risk factors for elevated RCA-FAI values in the patients with coronary artery disease group. And when the exercise modality was running and aerobics, the correlation between RCA-FAI values and exercise time showed a "U"-shaped relationship. Follow-up revealed that short periods of high-intensity exercise resulted in lower RCA-FAI values.

*Conclusion:* RCA-FAI was significantly associated with coronary artery inflammation. Although appropriate physical activity reduced the risk of pericoronary inflammation and coronary atherosclerosis, overly prolonged exercise could exacerbate the coronary inflammatory response and increase the likelihood of CAD.

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## 1. Introduction

Coronary artery disease (CAD) is an atherosclerotic disorder with high incidence which is expected to rise further in the next decade with the continuous socioeconomic development and changes in the population's diet; moreover, it tends to affect progressively younger individuals and remains the leading cause of death in upper-middle and high income economies [1,2]. Inflammation is the main driver of atherosclerosis and a key factor in the development of atherosclerotic plaques [3,4]; therefore, the detection of coronary inflammation is important for risk stratification and targeted therapy in patients with coronary atherosclerosis. In clinical practice, the treatment for this disease is based on conventional medication to reduce the coronary inflammatory response and plaque formation, increase the myocardial blood supply, and improve cardiac function. Additionally, for some patients with chronic or in the early stage of the disease, exercise intervention can have a positive effect on multiple organs and systems [5,6]. In particular, long-term exercise interventions can reduce the incidence of cardiovascular diseases. However, a 3-year study conducted by Isern et al. Isern CB [7] showed an increased risk of sudden cardiac arrest in patients while performing exercise or immediately afterwards compared to those not usually exercising. Therefore, how to exercise properly and the specific effects of exercise on the coronary inflammatory response in patients with stable CAD are still unclear.

The current clinical tools to assess vascular inflammation are insufficient. The typical blood tests, such as complete blood count and high-sensitivity C-reactive protein, are more indicative of systemic inflammation than local inflammatory response. Intravascular ultrasound and optical coherence tomography can assess the plaque type in patients with CAD, though not vascular inflammation [8,9]. Fluorine 18–sodium fluoride ($^{18}$FNaF) positron emission tomography/computed tomography (PET/CT) [10,11], the gold standard for evaluating local vascular inflammation in the coronary arteries, is difficult to use as a screening tool because of its high price and radiation dose.

In contrast, recent studies have shown that the pericoronary adipose tissue (PCAT) can be used as a marker of coronary artery inflammation [12,13]. and is closely associated with a variety of cardiovascular diseases [14]. Therefore, the purpose of this study was to quantify the fat attenuation index (FAI) values of PCAT using coronary computed tomography angiography (CCTA) images, and to evaluate the correlation between pericoronary inflammation and exercise patterns and levels and provide a guide for stable CAD patients on the benefits of proper physical exercise.

## 2. Materials and Methods

### 2.1. Study subjects

Patients who underwent CCTA within 3 days of hospital admission and diagnosed with stable CAD between 2019 and 2023 in the second hospital of Lanzhou University, were retrospectively collected. The inclusion criteria were as follows: complete imaging data; adequate CCTA image quality; full clinical examination, and complete clinical data. The exclusion criteria were the following: history of stent implantation, bypass, coronary artery malformation, prosthetic valve, or pacemaker; myocarditis, vasculitis, or acute coronary syndrome diagnosed within the previous six months; Severe liver and kidney diseases and respiratory diseases; myocardial bridges located at coronary plaques; absence of ambulatory electrocardiogram findings; and a history of medication with beta-blockers and non-dihydropyridine calcium channel blockers within one week before heart rate measurement. The diagnostic criteria for patients in the CAD group (CAD-group) adhered to the 2019 European Society of Cardiology Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes [15]. The non-CAD group was defined as patients without coronary artery stenosis or plaque. The study

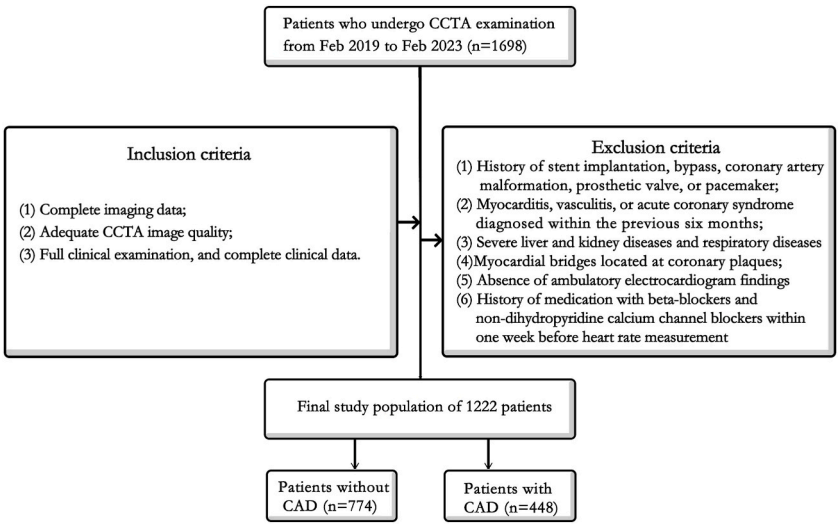


**Fig. 1.** Flowchart with inclusion and exclusion criteria.

was conducted in accordance with the tenets of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of our institution (grant No. 2021A-165); the need for written informed consent was waived because of the retrospective nature of the study. Fig. 1 illustrates the patient screening process.

### 2.2. Coronary computed tomography angiography

CCTA was performed using a Revolution CT (GE Healthcare, Milwaukee, WI, USA) and the patient was trained to breathe before the examination. Scanning was performed using prospective cardiac gating and covered all levels from 1 cm below the tracheal bifurcation to the base of the heart. The scanning protocol for CCTA images was as follows: field of view, 240 mm × 240 mm; matrix, 512 × 512; tube voltage, 100 kV; tube current, 400–700 mA; adaptive statistical iterative reconstruction Veo, 60 %; rotation time, 0.28 s; layer thickness, 0.625 mm. Enhancement scans were performed using a double-barrel high-pressure syringe (Bayer Health Care, Berlin, Germany) to inject 0.9 mL/kg of iopromide (370 mg/mL) through an elbow vein at an injection rate of 5.0–5.5 mL/s. Subsequently, 40 mL of normal saline was injected at the same rate for flushing.

### 2.3. Image analysis

Reviewers A and B used multi-plane reconstruction (MPR) and surface reconstruction (CPR) images to evaluate FAI measurements in enrolled patients. When the diagnoses of the two physicians did not agree, a third radiologist with more than 15 years of experience (Reviewer C) performed another independent assessment and a conclusion was reached after deliberation.

### 2.4. Fully automatic analysis of PCAT

The original CCTA images were pushed by Reviewer B to the Shukun Technology Analysis Software (Version 1150.1150.1142, China Shukun Technology Co., Ltd., Shanghai, China) through blinded analysis. After about 40 s, the software would automatically outline the PCAT range and calculate the FAI values of PCAT at the openings of the right coronary arteries. The width distance was the average diameter of the vessel [16], and the length distance from the right coronary artery (RCA) was set from the beginning of the vessel to 10–50 mm. The range of CT values for PCAT was set from −190 Hounsfield Unit (HU) to 30 HU, and the FAI was defined as the average computed tomography value of the adipose tissue in the above range [17]. A schematic diagram of the detection of the FAI value is shown in Fig. 2.

### 2.5. Patient data collection

The Hospital Information System (HIS) was used to collect the clinical testing indicators routinely performed on the patients,

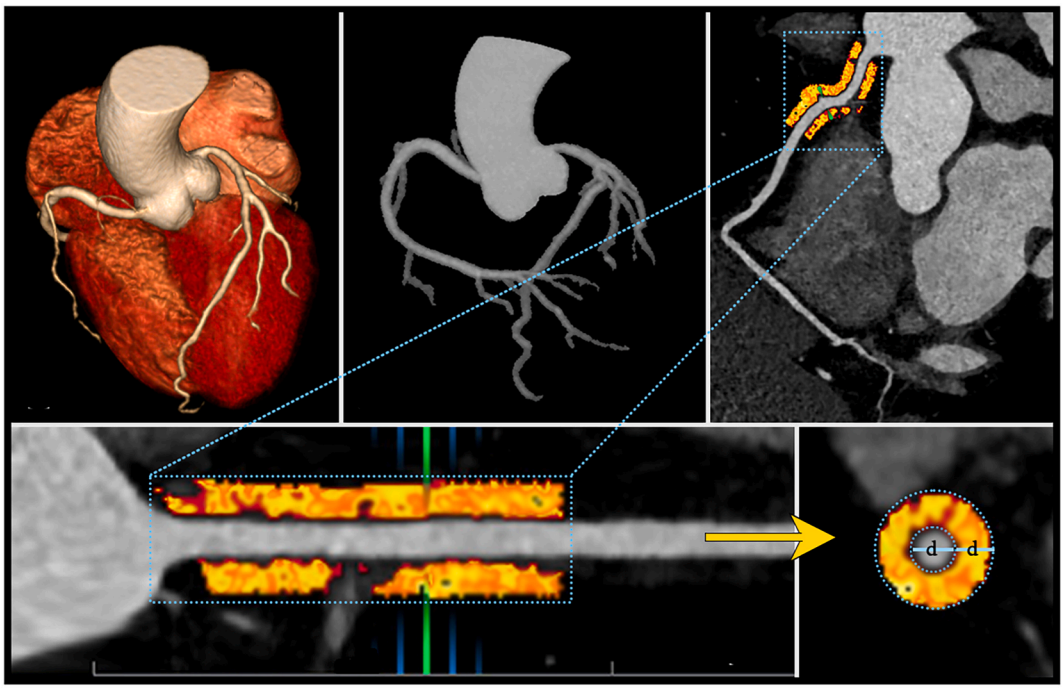


**Fig. 2.** Analysis of pericoronary fat attenuation.

including routine blood, fasting blood glucose, and lipid tests. The rest of the basic patient information was followed up by telephone, including annual family income, the weekly time the patients performed sports, and the intensity of sports and the mode of sports. The patients' exercise time included the time of maintaining the exercise habit and the weekly exercise time. The percentage maximum heart rate (HRmax%) was used to measure exercise intensity, and the formula for calculating the maximum heart rate of the subjects was HRmax = 206.9–0.67 × age. The heart rate was measured by 24-h ambulatory electrocardiography, and the average of three heart rate values was taken during the exercise period.

### 2.6. Statistical methods

Data statistics and analysis were performed using SPSS 26.0 (IBM, Armonk, NY). The qualitative information was expressed as frequency or percentage, and the chi-square test to compare categorical variables. If the quantitative data obeyed normal distribution, it was expressed as'x±SD, and non-normal distribution was expressed as M [Q25,Q75], and a K–S test was used to assess the normality, The independent sample's *t*-test and the Wilcoxon rank test were used to compare continuous variables. One-way ANOVA was used to analyze whether there were differences in FAI values at the coronary artery openings at different exercise durations. Independent predictors of elevated RCA-FAI values were screened using multivariate regression analyses. Pearson or Spearman correlation was used to analyze whether there was an association between these independent predictors and exercise duration in order to determine the correction factors. After correcting for factors that might affect both coronary plaques and exercise duration, the relationship between exercise duration and FAI values at coronary artery openings was analyzed using the restricted cubic spline (RCS).

**Table 1**
Differences in clinical characteristics and PCAT parameters analyzed between different groups of patients.

| | All (n = 1222) | Patients without CAD (n = 774) | Patients with CAD (n = 448) | P-value |
|---|---|---|---|---|
| **Age (Y)** | 45 ± 11.8 | 41 ± 10.5 | 48.0 ± 13.1 | 0.157 |
| **Female (%)** | 569 (46.6) | 279 (36.0) | 290 (64.7) | 0.462 |
| **BMI (kg/m$^2$)** | 24.3 (21.9–27.1) | 24.3 (21.9–27.1) | 25.1 (22.3–29.2) | 0.068 |
| **Smoking (%)** | 429 (35.1) | 164 (21.2) | 265 (59.2) | 0.019 |
| **Drinking(%)** | 511 (41.8) | 179 (23.1) | 332 (74.1) | 0.036 |
| **Hypertension (%)** | 672 (55.0) | 185 (13.3) | 88 (19.6) | 0.023 |
| **Hyperlipidemia (%)** | 336 (27.5) | 225 (29.1) | 111 (24.8) | 0.041 |
| **Hyperglycemia (%)** | 613 (50.2) | 395 (50.1) | 218 (18.7) | 0.329 |
| Household income (%) rowhead | | | | |
| **<** 30,000 CNY | 132 (10.8) | 101 (13.0) | 31 (6.9) | 0.000* |
| 30,000–59999 CNY | 434 (35.5) | 267 (34.4) | 167 (37.3) | |
| 60,000–99999 CNY | 368 (30.1) | 265 (34.2) | 103 (23.0) | |
| 100,000–150,000 CNY | 248 (20.3) | 134 (17.3) | 114 (25.4) | |
| **>** 150,000 CNY | 40 (3.3) | 7 (0.1) | 33 (7.4) | |
| Mode of Exercise (%) rowhead | | | | |
| Running | 293 (24.0) | 195 (25.2) | 98 (21.9) | 0.273 |
| Walking | 403 (33.0) | 265 (34.2) | 177 (39.5) | |
| Swimming | 273 (22.3) | 178 (23.0) | 95 (21.2) | |
| Aerobics | 253 (20.7) | 136 (17.6) | 78 (17.4) | |
| Other | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| Exercise time (Group) (h) rowhead | | | | |
| **<** 3 | 195 (24.0) | 91 (11.8) | 105 (23.4) | 0.000 |
| 3h-5.9 | 273 (22.3) | 175 (22.6) | 150 (33.5) | |
| 6h-10 | 410 (33.6) | 301 (38.9) | 109 (24.3) | |
| **>** 10 | 344 (28.1) | 207 (26.7) | 84 (18.8) | |
| **Exercise time(h)** | 7.03 ± 3.61 | 7.76 ± 2.29 | 5.12 ± 3.21 | 0.000 |
| **TG (mmol/L)** | 1.72 ± 1.69 | 1.612 ± 0.75 | 1.813 ± 0.77- | 0.012 |
| **HDL(mmol/L)** | 1.25 ± 0.50 | 1.157 ± 0.31 | 1.399 ± 0.42 | 0.029 |
| **LDL(mmol/L)** | 3.17 ± 4.66 | 3.14 ± 0.66 | 3.21 ± 0.58 | 0.047 |
| **TC(mmol/L)** | 5.21 ± 1.28 | 5.35 ± 0.87 | 4.97 ± 0.99 | 0.000 |
| **WBC(10^9/L)** | 5.8 [4.8,7.3] | 6.5 [4.3,11.5] | 6.1 [4.2,8.1] | 0.513 |
| **NE#(10^9/L)** | 5.2 [3.3,6.8] | 5.1 [3.9,6.8] | 5.8 [3.3,7.2] | 0.046 |
| **LYMPH#(10^9/L)** | 1.7 [1.2,2.2] | 1.7 [1.1,2.4] | 1.9 [1.2,2.7] | 0.743 |
| **MONO#(10^9/L)** | 0.41 [0.31,0.51] | 0.41 [0.31,0.51] | 0.33 [0.27,0.4] | 0.896 |
| **PLT(10^9/L)** | 268.67 ± 83.25 | 249.49 ± 45.61 | 287.33 ± 41.19 | 0.648 |
| **HGB(g/L)** | 139.55 ± 28.19 | 134.57 ± 22.67 | 145.31 ± 56.34 | 0.122 |
| **SII** | 163.18 [54.35,607.48] | 321 [157,471] | 356 [112,789] | 0.077 |
| **Fasting blood glucose(mmol/L)** | 4.59 ± 0.86 | 4.33 ± 0.47 | 4.86 ± 0.51 | 0.795 |
| **RCA-FAI**(HU) | −86.73 ± 9.91 | −89.73 ± 8.94 | −85.68 ± 7.71 | 0.003 |

BMI: body mass index; TC: Total cholesterol; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; HGB: Hemoglobin level; WBC: White blood cell count; NE#: Neutrophil count; LYMPH#: Lymphocyte count; MONO#: Monocyte count; PLT: Platelet count; SII: Systemic Immunoinflammatory Index.
RCA, right coronary artery; * : Fisher's Exact Test.

## 3. Results

### 3.1. Patients' characteristics

A total of 1222 patients were included in the analysis. Among them, 774 had no plaques (non-CAD group) and 448 had plaques in the coronary arteries (CAD group). The inclusion and exclusion criteria of the patients are shown in Fig. 1, the mean age of our patients was 44.28 ± 11.97 years, of which 569 were females, and there was a significant difference in the history of smoking, alcohol consumption, hypertension and hyperglycemia, family income, hours of exercise, total cholesterol (TC), triacylglycerol (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), neutrophilic granulocyte (NE), and RCA-FAI values between the two groups, as shown in Table 1.

### 3.2. Risk factors contributing to stable CAD

In the non-CAD group, univariate analysis showed that LDL, hypertension, BMI, and household income were strongly associated with higher RCA-FAI values. In multifactorial regression analysis, LDL (P = 0.019; OR:1.223; 95 % CI: 0.986 to 1.461), hypertension (P = 0.000; OR:0.503; 95 % CI: 0.333 to 0.673), BMI (P = 0.013; OR:1.094; 95 % CI: 1.049 to 1.140) and household income (P = 0.029; OR:1.600; 95 % CI: 0.647–2.553) were independently correlated with elevated RCA-FAI as shown in Table 2. In the CAD group, the univariate analysis showed that sex, triglycerides, LDL, HDL, hypertension, smoking, postprandial glucose, household income, and BMI were strongly associated with RCA-FAI elevation were strongly associated. In multifactorial regression analysis, after adjusting for other risk factors in patients with coronary artery stenosis, sex (P = 0.016; OR: 0.673; 95 % CI: 0.429 to 0.917), HDL (P = 0.006; OR: 0.601; 95 % CI: 0.361 to 0.842), LDL (P = 0.001; OR. 0.762; 95 % CI: 0.631 to 0.893), hypertension (P = 0.000; OR: 0.762; 95 % CI: 13.99 to 2.885), smoking (P = 0.005; OR: 0.670; 95 % CI: 0.464 to 0.876), and postprandial glucose (P = 0.030; OR: 0.812; 95 % CI: 0.645–0.978), household income (P = 0.038; OR:1.117; 95 % CI: 1.006–1.228), and BMI (P = 0.000; OR:1.084; 95 % CI:1.041–1.127) were independently correlated with elevated RCA-FAI in patients with coronary heart disease as shown in Table 3.

### 3.3. Differences in FAI values between different exercise groups of stable CAD

The people with different exercise time were divided into four groups, and the differences in RCA-FAI values in the coronary heart disease group and the non-CAD group in different four exercise modes were compared by ANOVA measurement analysis, and it was found that the coronary heart disease group's exercise duration was lower than that of the non-CAD group in any exercise modality, as shown in Fig. 3(a–d). There was a difference in RCA-FAI in the non-CAD group in the people with a running time of ‹3h versus› 9h, and in the people with an aerobics time of ‹3h versus 6–9h, as shown in Fig. 3(e–h). And at the same time, there was a difference in RCA-FAI

**Table 2**
Risk factors for elevated RCA-FAI values ( Non-CAD Group ) .

| | p | Exp(β) | Univariate | | p | Exp(β) | Multivariate | |
|---|---|---|---|---|---|---|---|---|
| | | | β coefficient (95 %CI) | | | | β coefficient (95 %CI) | |
| | | | lower-bound | upper-bound | | | lower-bound | upper-bound |
| **Age** | 0.653 | 1.004 | 0.987 | 1.021 | | | | |
| **Gender** | 0.401 | 0.910 | 0.543 | 1.276 | | | | |
| **TC(mmol/L)** | 0.549 | 0.963 | 0.798 | 1.128 | | | | |
| **TG(mmol/L)** | 0.061 | 1.155 | 0.994 | 1.317 | | | | |
| **HDL(mmol/L)** | 0.080 | 0.736 | 0.423 | 1.049 | | | | |
| **LDL(mmol/L)** | 0.030 | 1.053 | 1.005 | 1.101 | 0.019 | 1.223 | 0.986 | 1.461 |
| **Hypertension(%)** | 0.001 | 2.183 | 1.331 | 3.036 | 0.000 | 0.503 | 0.333 | 0.673 |
| **Hyperglycemia(%)** | 0.909 | 1.108 | 0.684 | 1.533 | | | | |
| **Hyperlipidemia (%)** | 0.066 | 1.525 | 0.978 | 2.072 | | | | |
| **Smoking** | 0.271 | 0.872 | 0.579 | 1.166 | | | | |
| **Drinking** | 0.514 | 1.109 | 0.916 | 1.303 | | | | |
| **WBC($10^{\wedge}9$/L)** | 0.555 | 1.099 | 0.852 | 1.346 | | | | |
| **HGB(g/L)** | 0.916 | 1.365 | 0.484 | 2.246 | | | | |
| **NE#(10^9/L)** | 0.624 | 0.982 | 0.893 | 1.070 | | | | |
| **LYMPH#($10^{\wedge}9$/L)** | 0.494 | 0.941 | 0.653 | 1.228 | | | | |
| **MONO#($10^{\wedge}9$/L)** | 0.338 | 1.299 | 1.053 | 1.545 | | | | |
| **Fasting blood glucose(mmol/L)** | 0.633 | 0.971 | 0.755 | 1.186 | | | | |
| **PLT(10^9/L)** | 0.604 | 0.999 | 0.996 | 1.003 | | | | |
| **BMI** | 0.013 | 1.511 | 0.961 | 2.060 | 0.000 | 1.094 | 1.049 | 1.140 |
| **SII** | 0.115 | 1.000 | 1.000 | 1.001 | | | | |
| **Exercise time(h)** | 0.603 | 1.066 | 0.876 | 1.256 | | | | |
| **Mode of Exercise (%)** | 0.509 | 0.955 | 0.778 | 1.133 | | | | |
| **Household income(%)** | 0.039 | 1.997 | 0.790 | 3.203 | 0.029 | 1.600 | 0.647 | 2.553 |

TC: Total cholesterol; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; HGB: Hemoglobin level; WBC: White blood cell count; NE#: Neutrophil count; LYMPH#: Lymphocyte count; PLT: Platelet count; SII: Systemic Immunoinflammatory Index.

**Table 3**
Risk factors for elevated RCA-FAI values (CAD Group).

| | p | Exp(β) | Univariate | | p | Exp(β) | Multivariate | |
|---|---|---|---|---|---|---|---|---|
| | | | lower-bound | upper-bound | | | lower-bound | upper-bound |
| **Age** | 0.672 | 1.004 | 0.988 | 1.019 | | | | |
| **Gender** | 0.006 | 0.615 | 0.381 | 0.848 | 0.016 | 0.673 | 0.429 | 0.917 |
| **TC(mmol/L)** | 0.625 | 1.087 | 0.842 | 1.332 | | | | |
| **TG(mmol/L)** | 0.048 | 1.137 | 1.001 | 1.272 | | | | |
| **HDL(mmol/L)** | 0.013 | 0.602 | 0.328 | 0.876 | 0.006 | 0.601 | 0.361 | 0.842 |
| **LDL(mmol/L)** | 0.010 | 0.737 | 0.552 | 0.923 | 0.001 | 0.762 | 0.631 | 0.893 |
| **Hypertension(%)** | 0.001 | 1.997 | 1.271 | 2.722 | 0.000 | 2.142 | 1.399 | 2.885 |
| **Hyperglycemia(%)** | 0.476 | 1.234 | 0.784 | 1.685 | | | | |
| **Hyperlipidemia (%)** | 0.231 | 0.872 | 0.752 | 0.993 | | | | |
| **Smoking** | 0.003 | 0.618 | 0.405 | 0.832 | 0.005 | 0.670 | 0.464 | 0.876 |
| **Drinking** | 0.824 | 1.051 | 0.822 | 1.279 | | | | |
| **WBC($10^9$/L)** | 0.560 | 0.977 | 0.887 | 1.067 | | | | |
| **HGB(g/L)** | 0.306 | 1.807 | 0.716 | 2.897 | | | | |
| **NE#(10^9/L)** | 0.662 | 0.986 | 0.912 | 1.060 | | | | |
| **LYMPH#($10^9$/L)** | 0.262 | 0.868 | 0.571 | 1.165 | | | | |
| **MONO#($10^9$/L)** | 0.457 | 1.346 | 1.013 | 1.679 | | | | |
| **Fasting blood glucose(mmol/L)** | 0.033 | 0.811 | 0.640 | 0.982 | 0.030 | 0.812 | 0.645 | 0.978 |
| **PLT(10^9/L)** | 0.101 | 1.003 | 0.999 | 1.006 | | | | |
| **BMI** | 0.000 | 1.080 | 1.035 | 1.125 | 0.000 | 1.084 | 1.041 | 1.127 |
| **SII** | 0.080 | 1.000 | 1.000 | 1.001 | | | | |
| **Exercise time(h)** | 0.474 | 1.450 | 0.692 | 2.207 | | | | |
| **Mode of Exercise (%)** | 0.334 | 0.941 | 0.806 | 1.076 | | | | |
| **Household income(%)** | 0.025 | 1.495 | 0.830 | 2.160 | 0.038 | 1.117 | 1.006 | 1.228 |

TC: Total cholesterol; TG: Triglycerides; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; HGB: Hemoglobin level; WBC: White blood cell count; NE#: Neutrophil count; LYMPH#: Lymphocyte count; PLT: Platelet count; SII: Systemic Immunoinflammatory Index.

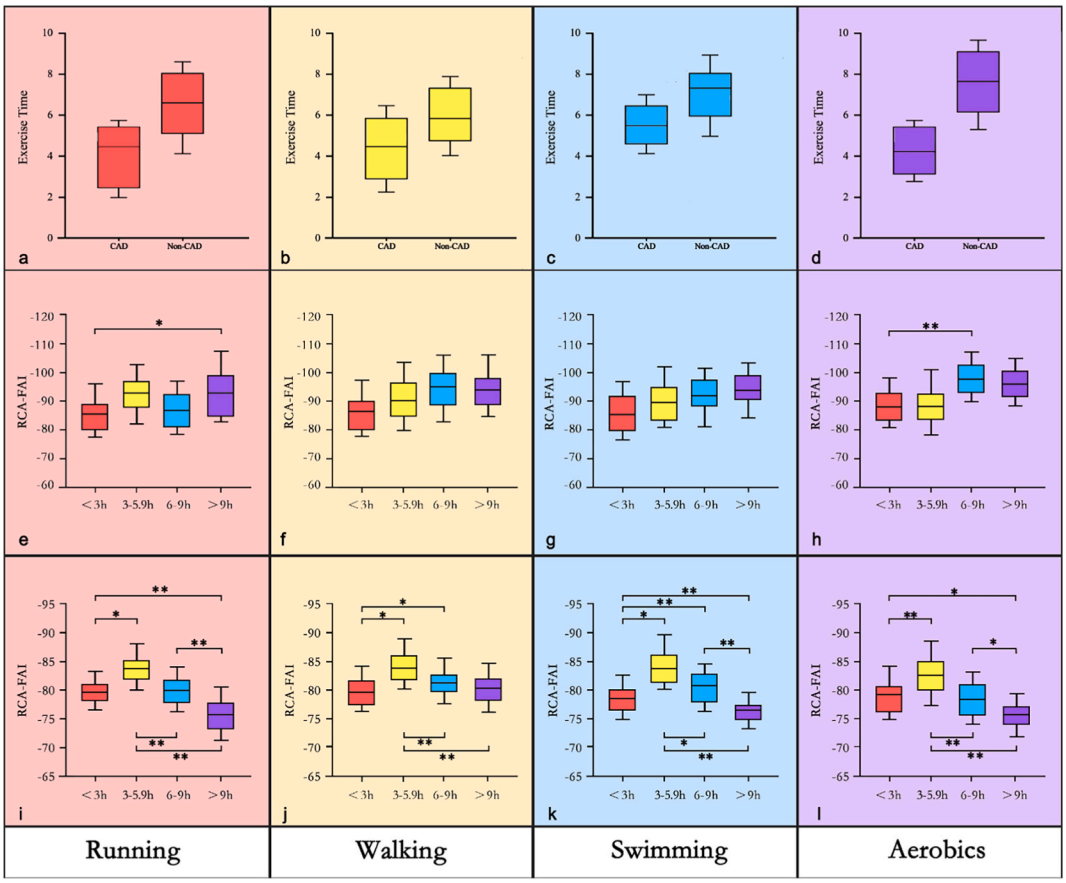


**Fig. 3.** ANOVA results in patients with different exercise durations.

in the CAD group patients with different exercise styles under different exercise time, as shown in Fig. 3(i–l).

### 3.4. Relationship between exercise status and FAI values

After identifying the significant independent predictors of elevated RCA-FAI, Pearson correlation analysis was used to analyze whether the above predictors were correlated with the length of exercise in the four different modalities, and only in the coronary artery disease group were found to be correlated with the length of exercise in the four different modalities of exercise: household income, BMI, and LDL (Table 4). After accounting for the above three factors, we additionally corrected for three potential confounders: age, sex, and smoking status. The relationship between exercise status and RCA-FAI values of patients in the coronary artery disease group was analyzed using restricted cubic spline, and after comprehensively considering the sample size and fitting accuracy, we set the number of nodes of the RCS to be 3, P10, P50, and P90, and using the median as a reference, we found that when the exercise modality was running and aerobics, the correlation between RCA-FAI values and exercise time showed a "U"-shaped relationship, and the rest did not show significant statistical significance, as shown in Fig. 4 (4a: Running; 4b: Aerobic gymnastics exercise). A second telephone follow-up was conducted to investigate the heart rate during exercise for patients with these two types of exercise modes, and the transverse time corresponding to the inflection point of the U-shaped distribution was used to group the above patients to compare the intensity of exercise, and it was found that people with a running time of less than 6.25 h per week and people with aerobics time of less than 7 h per week had higher exercise average heart rates, see Fig. 5 were higher, as shown in Fig. 5.

## 4. Discussion

CAD is an immune-mediated phenomenon influenced by various factors, including genetics, coronary atherosclerosis, and altered lipid metabolism. Accurate assessment and risk prediction in patients with CAD are crucial to prevent and treat this disease effectively and reduce the risk of acute cardiovascular events. Pathological investigations have shown that arterial wall inflammation triggers atherosclerosis, leading to the accumulation of monocytes, macrophages, and other cells at the inflammation sites [18]. Chronic inflammatory changes can cause rupture of vulnerable plaques, underscoring the significance of coronary inflammation in the prognosis of patients with CAD.

Moreover, studies examining the relationship between PCAT attenuation and the lesions possibly causing it have provided further insights for an accurate clinical prognosis. The FAI, an imaging index of PCAT, was recently introduced by Lin A et al. [19]. Meanwhile, Oikonomou et al. [16] and Lin A [20] et al. found that FAI in RCA segments may be a reliable indicator of coronary inflammatory response. RCA-FAI as a quantitative measure of global coronary inflammation independently distinguishes patients with MI vs. stable CAD vs. no CAD. Higher RCA-FAI values could be a predictor of all-cause and cardiac mortality events. Furthermore, RCA-FAI values could predict disease stability in patients with acute coronary syndrome, thus guiding early targeted clinical interventions [21–23]. However, current research on FAI values as a biomarker of coronary inflammation is lacking in terms of clinical outcomes between patient populations and health populations. Consequently, there is a dearth of studies conducted on healthy cohorts, and few have explored the associations between demographic characteristics and coronary inflammation.

This study identified significant differences between CAD group and non-CAD group. These discrepancies extend beyond the indicators of coronary inflammation, glucose levels, lipid profiles, and blood cell counts; they also include other elements, such as household income and exercise duration, highlighting the multifaceted nature of CAD, though the specific mechanisms connecting exercise and the inflammatory processes precipitating acute cardiovascular events remain elusive [24]. However, it is worth noting that appropriate physical activity can partially mitigate the risk of incurring such events. For instance, Balducci et al. [25] observed that a significant decrease in physical fitness and sedentary behavior were predictive of a high cardiometabolic risk among patients with type 2 diabetes. However, Rajan et al. [26] noted a 5–33-fold increase in sudden cardiac death associated with exercise in women compared to men. This significant difference appears to be strongly influenced by hormonal factors, blood pressure levels, and coronary inflammation, indicating that the effect of exercise on the coronary arteries defies a simple linear relationship. Consequently, it is imperative to first identify the risk factors that may affect the development of stenosis and plaques within the coronary arteries to determine the specific effects of exercise on coronary inflammation. Furthermore, investigating the potential association between these factors and the extent of physical activity is crucial. Previous studies [27–29] have revealed notable variations in several parameters, such as levels of HDL, triglycerides, postprandial glucose, and platelet and lymphocyte counts, between patients with and without stenosis. Elevated lipid levels and chronic hyperglycemia have been shown to induce vascular inflammation, thereby increasing the presence of inflammatory cells and blood viscosity, and both factors contribute to the formation and exacerbation of atherosclerosis. These findings are consistent with the disparities observed in the FAI values within the RCA segments between the two patient groups in this study.

**Table 4**
Correlation between coronary atherosclerosis risk factors and exercise duration.

| | Running Time | Walking Time | Swimming Time | Aerobics Time |
|---|---|---|---|---|
| Household income | 0.159* | 0.205* | 0.199** | 0.103* |
| BMI | 0.401* | 0.323** | 0.216* | 0.454** |
| LDL | 0.398** | 0.245* | 0.312* | 0.411* |

*p < 0.05 **p < 0.01.

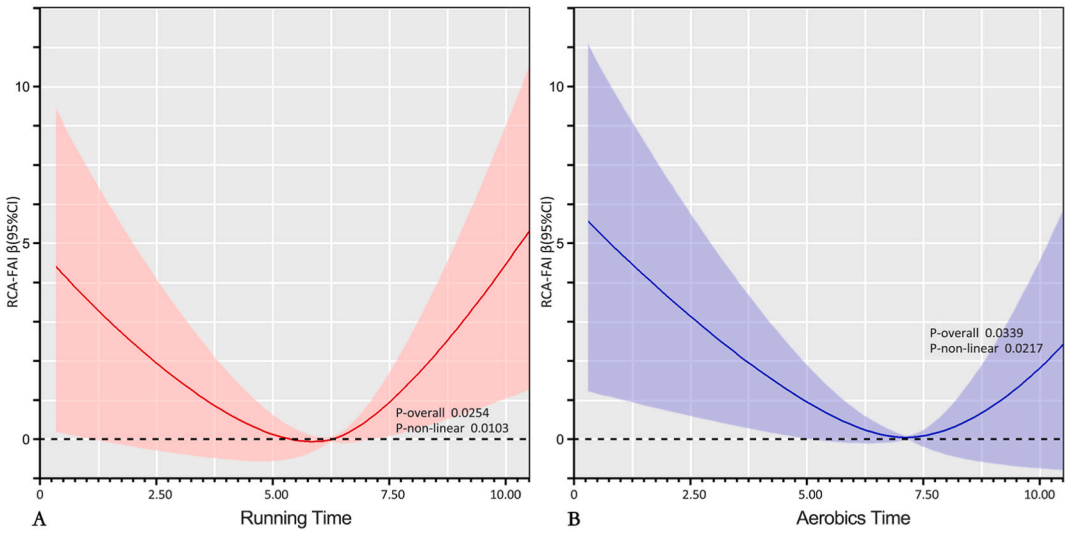


**Fig. 4.** Restricted cubic spline analysis of movement duration for the estimation of the RCA-FAI values.

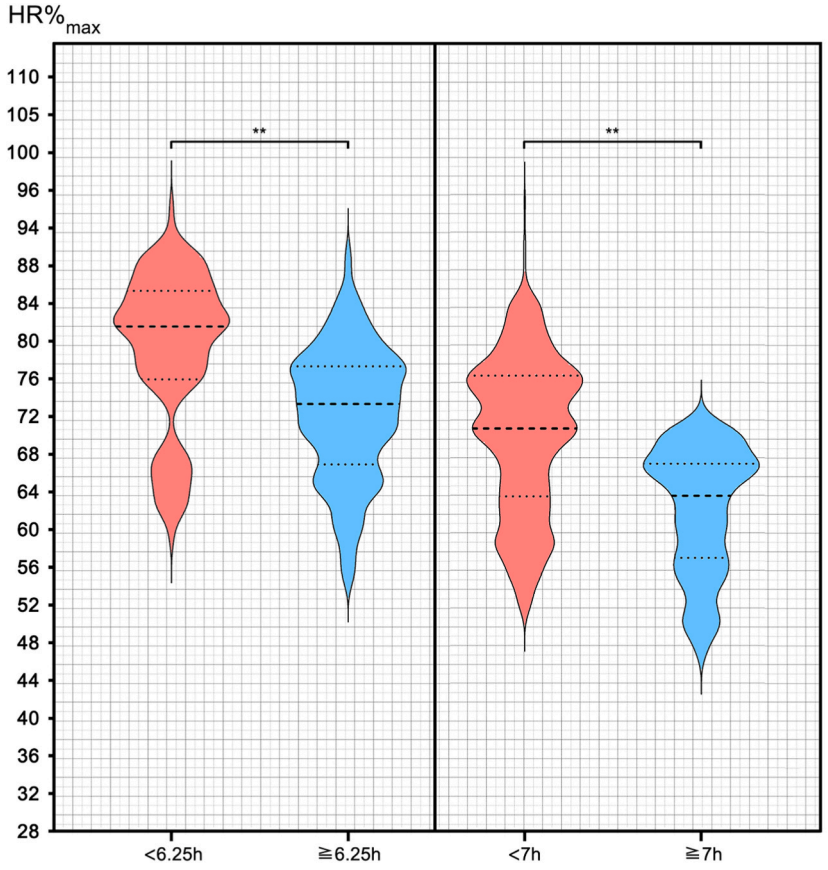


**Fig. 5.** Comparison of heart rate differences between groups with different exercise durations.

We also found that family income, LDL content, history of hypertension, and BMI were independent predictors of elevated RCA-FAI in the no-coronary-heart-disease group, and the coronary-heart-disease group added four new factors to the above: total cholesterol, HDL content, history of smoking, and fasting glucose. Furthermore, household income, BMI, and LDL level were significantly correlated with exercise duration. The restricted cubic spline model adjusted for the above three factors of household income, BMI, and LDL,

and we also adjusted for age, smoking, and sex. There was a curvilinear relationship between RCA-FAI and exercise intensity in patients with CAD, while no such relationship was evident in patients without CAD. This may be attributed to the myocardium of CAD patients being more susceptible to ischemia and hypoxia during exercise, leading to inflammatory changes around the coronary arteries. Specifically, in the CAD group, the inflammatory response in the RCA segment diminished with an increase in exercise duration (up to 6 h per week). However, beyond 6h, the inflammatory response gradually increased with the duration of exercise. Follow-up telephone inquiries revealed that exercise intensity tended to be higher among individuals with exercise durations lower than 6 h per week, whereas those engaging in prolonged exercise favored moderate-intensity aerobic exercise. Quindry et al. [30], in a retrospective comparison between high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) in patients with CAD, observed that HIIT is strongly associated with favorable body weight reduction, metabolic improvement, and aerobic capacity enhancement, particularly in obese patients. Additionally, HIIT is more effective than MICT in individuals with early CAD, in line with the findings of the present study. Similarly, Dun et al. [31] reported that HIIT provides superior improvements in lipid profiles compared with MICT in patients with myocardial infarction. Thus, increased exercise duration can enhance patients' aerobic capacity; however, excessive exercise may not reduce coronary inflammation and even increase the likelihood of acute cardiovascular events due to a higher exercise intensity. Therefore, it may be more beneficial for patients with CAD to increase exercise intensity while decreasing its duration.

Artificial intelligence techniques for assessing PCAT parameters offer a rapid, non-invasive, and easily implementable tool for large-scale clinical applications. However, their current use predominantly involves the evaluation of disease progression and risk in patients with CAD. In our study, we used PCAT attenuation to gauge the coronary inflammatory response to exercise, revealing the potential of appropriate exercise in reducing the risk of coronary inflammation.

This study was limited by its single-center design, necessitating further investigation in multi-center studies to validate our results. While our findings are promising, we did not stratify patients in greater detail according to CAD severity, nor did we consider the potential presence of peripheral vascular disease. Additionally, long-term follow-up of these patients is crucial to more thoroughly understand the relationship between FAI values and exercise.

In patients with CAD, an appropriate amount, type, and intensity of exercise can reduce the risk of coronary inflammation, whereas too long or too intense physical activity can have negative effects. Nonetheless, physical exercise is crucial for the clinical prevention and control of CAD progression.

## Statement

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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## CRediT authorship contribution statement

**Huaze Xi:** Writing – review & editing, Writing – original draft, Validation, Software, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Mengyuan Jing:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Data curation, Conceptualization. **Qiu Sun:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Investigation, Funding acquisition, Formal analysis. **Yuanyuan Wang:** Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Hao Zhu:** Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Junlin Zhou:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

## Declaration of competing interest

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

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