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ORIGINAL RESEARCH

Evaluating Pericoronary Adipose Tissue Attenuation to Predict Cardiovascular Events

A Multicenter Study in East Asians

Takahiro Nishihara, MD, PhD,[a] Toru Miyoshi, MD, PhD,[a] Kentaro Ejiri, MD, PhD,[a] Kazuhiro Osawa, MD, PhD,[b] Soichiro Fuke, MD, PhD,[c] Kousuke Seiyama, MD,[d] Masayuki Doi, MD, PhD,[d] Mitsutaka Nakashima, MD, PhD,[a] Takashi Miki, MD, PhD,[a] Shinsuke Yuasa, MD, PhD[a]

ABSTRACT

BACKGROUND Pericoronary adipose tissue attenuation (PCATA) is a novel imaging biomarker of pericoronary inflammation associated with coronary artery disease. Several studies have reported the usefulness of PCATA among people of European ethnicity; however, data are lacking concerning those of Asian ethnicity.

OBJECTIVES This multicenter study aimed to evaluate the effect of PCATA on prognosis in East Asian patients.

METHODS Between August 2011 and December 2016, 2,172 patients underwent clinically indicated coronary computed tomography angiography (CTA) at 4 hospitals in Japan. Among them, 1,270 patients were analyzed. PCATA was evaluated using coronary CTA to measure pericoronary adipose tissue density surrounding the 3 major coronary arteries. The outcomes were composite cardiovascular events, including cardiovascular death and acute coronary syndrome; 33 cardiovascular events observed during a median follow-up of 6.0 years (Q1-Q3: 3.6-8.2 years).

RESULTS Right coronary artery (RCA)-PCATA was significantly higher in patients with cardiovascular events than in those without (-63.7 ± 8.9 HU vs -67.4 ± 9.1 HU, respectively; $P = 0.021$). High RCA-PCATA was significantly associated with cardiovascular events in a model that included the Hisayama risk score and adverse coronary CTA findings (HR: 1.55; 95% CI: 1.07-2.24; $P = 0.019$).

CONCLUSIONS High RCA-PCATA showed significant association with future cardiovascular events after adjusting conventional risk factors and adverse coronary CTA findings in East Asian patients who underwent clinically indicated coronary CTA. (JACC Asia. 2025;5:1-11) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Computed tomography angiography (CTA) is useful for evaluating the risk of future cardiovascular events through assessing stenosis and high-risk plaque (HRP) features that are prone to acute coronary syndrome.[1,2] Perivascular inflammation plays an important role in the formation of coronary atherosclerotic plaques, causing plaque rapture and subsequent acute myocardial infarction.[3]

From the [a]Department of Cardiovascular Medicine, Faculty of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, Okayama, Japan; [b]Department of General Internal Medicine 3, Kawasaki Medical School General Medicine Center, Okayama, Japan; [c]Department of Cardiovascular Medicine, Japanese Red Cross Okayama Hospital, Okayama, Japan; and the [d]Department of Cardiology, Kagawa Prefectural Central Hospital, Takamatsu, Japan.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CTA = computed tomography angiography

HRP = high-risk plaque

LAD = left anterior descending artery

LCX = left circumflex coronary artery

MACE = major adverse cardiac event(s)

PCATA = pericoronary adipose tissue attenuation

RCA = right coronary artery

Pericoronary adipose tissue attenuation (PCATA), quantified using coronary CTA, has been recognized as a novel imaging marker for pericoronary inflammation.[4] Furthermore, increased PCATA in the proximal right coronary artery (RCA) reflects pathophysiological changes in the entire coronary vasculature and improves the prediction of cardiac death when compared with plaque features.[5-8] The CRISP-CT (Cardiovascular RISk Prediction using Computed Tomography) study demonstrated that high RCA-PCATA was associated with cardiac mortality.[6] The multicenter SCOT-HEART (Scottish Computed Tomography of the Heart) trial also showed the additive values of RCA-PCATA and low-attenuation plaques for predicting the future risk of myocardial infarction.[7]

Coronary CTA features are closely associated with the development of coronary artery disease (CAD); however, ethnic differences are influential in terms of their effect on major adverse cardiac events (MACE) because of differences in the effect of cardiometabolic risks. In the PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial, the effect of HRP on MACE in Black populations was 1.5 times higher than that in White populations.[9] The CRISP-CT study showed that the effect of high PCATA on cardiac mortality tended to be greater in White than in Black populations; however, information was not provided concerning populations of Asian ethnicity.[6] Because PCATA is involved in plaque formation, the association between PCATA and MACE may depend on ethnicity. Therefore, this multicenter study aimed to investigate the usefulness of PCATA for predicting MACE in a population of East Asian ethnicity, namely, Japanese patients.

METHODS

STUDY DESIGN. This was a retrospective, observational, multicenter study (cardiovascular risk assessment using pericoronary adipose tissue attenuation [PCAT] on CT angiography: PCAT-CT). Data were retrospectively collected from patients examined across 4 hospitals in Japan (Okayama University Hospital, Kawasaki Medical School General Medicine Center, Japanese Red Cross Okayama Hospital, and Kagawa Prefectural Central Hospital) between August 2011 and December 2016. Clinical outcomes were examined as far as possible from the indexed coronary CTA scan to the end of December 2020. The study was conducted in accordance with the principles of the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Boards of Okayama University Graduate School of Medicine (2206-020) and each participating hospital. To ensure patient safety, all coronary CTA scans were performed in accordance with established guidelines.[10] The requirement for informed patient consent was waived because of the low-risk nature of the study and the inability to obtain consent directly from all study patients.

STUDY POPULATION. A flow diagram of the study design is shown in **Figure 1**. First, 2,172 consecutive patients who underwent clinically indicated coronary CTA between August 2011 and December 2016 were enrolled in the study. Exclusion criteria comprised a history of percutaneous coronary intervention or coronary artery bypass grafting, congenital heart disease, poor coronary CTA image quality, and <1 year of follow-up. In total, 1,270 study patients were included.

CLINICAL DATA AND DEFINITION OF RISK FACTORS. Details of clinical characteristics, smoking status, medical history, comorbidities, and laboratory data were collected from a review of patients' medical records. Risk factor definitions have been previously presented.[11] A history of CAD was defined as having undergone percutaneous coronary intervention or coronary artery bypass grafting. The Hisayama risk score was calculated based on established risk factors (sex, systolic blood pressure, glucose intolerance, and serum lipid levels, and smoking status) for atherosclerotic cardiovascular disease within 10 years, with patients defined as being at low (<2%), intermediate (2%-10%), or high (≥10%) risk.[12]

ACQUISITION OF CORONARY CTA. Imaging was performed using a 128-slice CT scanner (SOMATOM Definition Flash, Siemens Healthineers) at Okayama University, a 64-slice CT scanner (Aquilion Prime, Canon Medical Systems Corporation) at the Kawasaki Medical School General Medicine Center, and a 320-slice CT scanner (Aquilion One, Canon Medical Systems Corporation) at the Japanese Red Cross Okayama Hospital and Kagawa Prefectural Central Hospital using standard protocols.[13] The tube voltage of all CT scanners was 120-kVp. All analyses were conducted using a dedicated workstation (AZE Virtual Place, Canon Medical Systems Corporation) at the core laboratory of Okayama University Hospital.

CORONARY PLAQUE ANALYSIS. We evaluated coronary artery segments with a diameter >2 mm and defined plaque characteristics in accordance with Society of Cardiovascular Computed Tomography guidelines.[14] Plaques were categorized as calcified (>130 HU) or noncalcified (<130 HU). Plaques

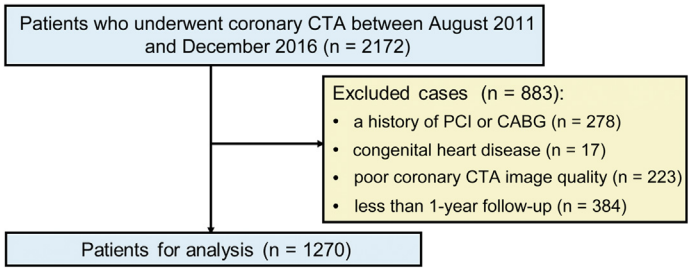
measuring <30 HU were defined as having a low attenuation. HRPs were defined as lesions with ≤2 of the following features: positive remodeling, spotty calcification, and low-attenuation plaques, as previously described.[15] Positive remodeling was defined when the outer vessel diameter at the plaque was ≥1.1 times that of the adjacent, uninvolved vessel. Spotty calcification was defined as a calcium burden length <1.5 times the vessel diameter and a width less than two-thirds of the vessel diameter. Significant stenosis was defined as a luminal narrowing of ≥50% in any main coronary artery. This visual evaluation was conducted in accordance with the Society of Cardiovascular Computed Tomography guidelines.[14]

PCAT QUANTIFICATION. PCAT was defined as adipose tissue located within a radial distance from the outer vessel wall equal to the diameter of the coronary vessel.[4] Adipose tissue was defined as all voxels with an attenuation between −190 and −30 HU. PCATA was defined as the average CT attenuation (in HU) of the adipose tissue within the defined volume of interest. PCATA was analyzed for the 3 main coronary vessels, and PCAT analysis was performed using a dedicated workstation (Aquarius iNtuition Edition, version 4.4.13. P3, TeraRecon Inc). The proximal 10 to 50 mm segment of the RCA and proximal 40 mm segments of the left anterior descending artery (LAD) and left circumflex coronary artery (LCX) were traced, as previously described.[6] Mean-PCATA was defined as the average PCATA in all 3 coronary arteries. The CT measurement of PCATA was fully automated with additional minor manual optimization. Representative examples of PCATA quantification in the study patients are shown in Supplemental Figure 1. The epicardial adipose tissue volume was quantified using a dedicated workstation (AZE Virtual Place).

INTRAOBSERVER AND INTEROBSERVER AGREEMENT IN RELATION TO PCATA. Bland-Altman plots were created to evaluate interobserver and intraobserver reproducibility of the PCATA measurement in 27 random patients. For intraobserver agreement, 2 cardiologists (T.N. and M.N.) with 7 and 12 years of experience, respectively, evaluated PCATA independently. For interobserver agreement, the cardiologist with 7 years of experience evaluated the PCATA at least 1 month afterwards to minimize recall bias.

OUTCOME DATA. Clinical follow-up was performed through reviewing medical records or telephone interviews. MACE was defined as a composite of cardiovascular and acute coronary syndromes. Each outcome was reviewed according to the relevant criteria by clinical event review members (M.N. and T.M.) who were blinded to the CT results. Details of the event definitions are provided in the Supplemental Appendix. Cardiac death was defined as death from any of the following causes: acute coronary syndrome, heart failure, arrhythmic death, or unclear causes of death wherein a cardiac origin could not be excluded. Acute coronary syndromes included myocardial infarction and unstable angina.

FIGURE 1 Flow Diagram of This Study



First, 2,172 consecutive patients who underwent clinically indicated coronary computed tomography angiography (CTA) between August 2011 and December 2016 were enrolled in the study. After exclusion of patients with history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), congenital heart disease, poor coronary CTA image quality, and <1 year of follow-up, 1,270 patients were analyzed in this study.

STATISTICAL ANALYSIS. Normality testing for continuous variables was performed using a Shapiro-Wilk test. Continuous variables are expressed as mean ± SD or median (Q1-Q3) based on their distribution. Categorical variables are presented as numbers (n) and percentages (%). Statistical comparisons of continuous variables were performed using either a paired Student's *t*-test or a Mann-Whitney *U* test, as appropriate, while categorical variables were assessed using chi-square analysis or Fisher exact test. The Pearson correlation coefficient was used to measure the linear relationship between RCA-, LAD-, and LCX-PCATA. Cumulative survival estimates were calculated using the Kaplan-Meier method and compared using a log-rank test. We modeled Cox proportional hazards models to identify the association between PCATA and the occurrence of MACE. Multivariable models included adverse coronary CTA findings and the Hisayama risk score as confounders, which encompassed conventional risk factors to avoid overfitting. The results were reported as HRs with 95% CIs. The proportional hazard assumption was confirmed by the log-log plot. We determined the optimal cutoff of PCATA of RCA, LAD, LCX, and the mean value for all arteries using maximization of the

TABLE 1 Patient Characteristics

	MACE		
	Present (n = 33)	Absent (n = 1,237)	*P* Value
Age, y	69.4 ± 10.8	68.4 ± 9.2	0.538
Male	26 (79)	749 (61)	0.027
Body mass index, kg/m^2	23.1 (21.0-25.5)	23.0 (21.0-25.5)	0.776
Hypertension	23 (72)	797 (64)	0.46
Dyslipidemia	15 (47)	592 (48)	0.766
Diabetes mellitus	13 (42)	404 (33)	0.325
Chronic kidney disease	15 (46)	353 (29)	0.029
Current smoker	12 (36)	258 (21)	0.027
Beta-blocker	8 (24)	268 (22)	0.688
Calcium-channel blocker	14 (42)	447 (36)	0.419
ACEI or ARB	11 (33)	481 (39)	0.562
Statin	7 (21)	381 (31)	0.259
Oral antihyperglycemic drugs	8 (324)	232 (19)	0.401
eGFR, mL/min/1.73 m^2	63.8 (55.6-78.6)	68.1 (58.1-79.0)	0.546
Hemoglobin A1c, %	6.2 (5.7-6.5)	6.0 (5.7-6.6)	0.504
Triglyceride, mg/dL	118.0 (85.0-225.0)	113.0 (83.0-165.0)	0.485
Total cholesterol, mg/dL	177.5 (160.5-206.5)	187.0 (164.0-211.3)	0.456
HDL cholesterol, mg/dL	53.0 (49.0-60.0)	56.0 (46.0-67.0)	0.461
LDL cholesterol, mg/dL	99.0 (78.5-122.5)	109.0 (90.0-131.5)	0.129
C-reactive protein, mg/dL	0.12 (0.07-0.24)	0.10 (0.05-0.26)	0.455
BNP, pg/mL	67 (17-112)	38 (17-92)	0.126
Hisayama risk score, low/moderate/high group	1/15/17 (3/46/51)	119/765/353 (10/61/29)	0.013
Epicardial adipose tissue, cm^3	116 (85-140)	116 (88-146)	0.849

Values are mean ± SD, n (%), or median (Q1-Q3).

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; BNP = brain natriuretic peptide; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MACE = major adverse cardiovascular event(s).

log-rank statistic to discriminate patients with MACE. The incremental value of RCA-PCATA, compared with the Hisayama risk score and adverse coronary CTA findings for predicting MACE, was assessed by the improvement of c-statistic, decision curve analysis, and net reclassification improvement index (NRI). Because there are no clear cutoff values of risk category for the specific populations in the present study, we evaluated the continuous NRI. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using SPSS version 26 (IBM Corp) and R version 4.3.2 (R Foundation for Statistical Computing) software.

RESULTS

PATIENT CHARACTERISTICS. The baseline characteristics of patients with and without MACE are summarized in Table 1. The median patient age was 69 years, and 61% (775 of 1,270) of patients were men. Patients with MACE were older and significantly were more often men, had chronic kidney disease, and were current smokers than patients without MACE. The use of beta-blockers, calcium-channel blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and oral antihyperglycemic drugs did not differ between patients with and without MACE. Regarding laboratory data, the lipid profiles and C-reactive protein levels did not differ between the 2 groups. Patients with MACE had higher Hisayama risk scores than those without, whereas the epicardial adipose tissue volume did not differ between the 2 groups.

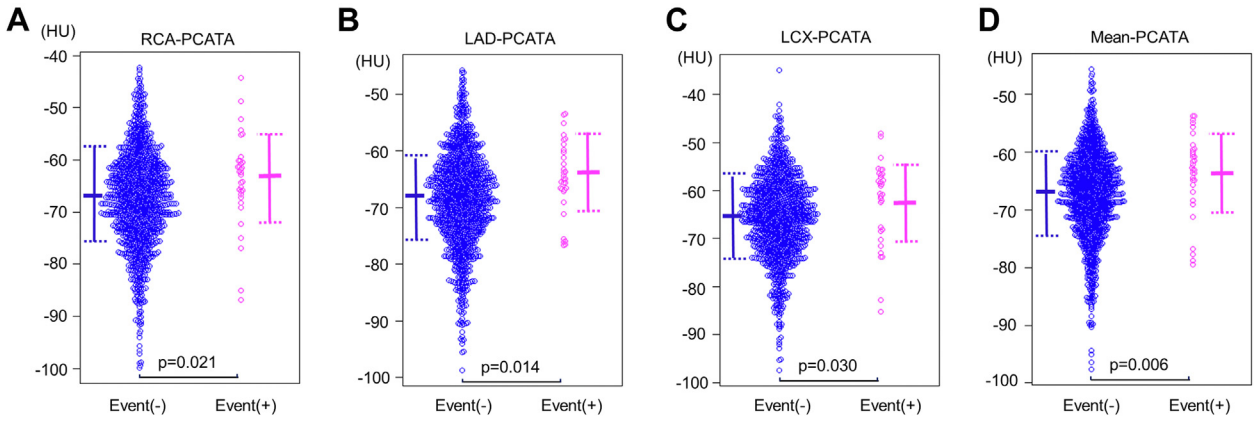
CORONARY CTA AND PCATA FINDINGS. Patients with MACE had a significantly higher prevalence of HRP and more significant stenosis than patients without MACE (49% [16 of 33] vs 30% [373 of 1,237]; $P = 0.02$; 49% [16 of 33] vs 32% [395 of 1,237]; $P = 0.04$, respectively). Additionally, patients with MACE had a greater prevalence of calcified plaques ($P = 0.03$), positive remodeling ($P = 0.03$), and low-density plaques ($P = 0.04$), but not noncalcified plaques ($P = 0.61$), than those without MACE.

Figure 2 shows a comparison of PCATA between patients with and without MACE. PCATA of RCA, LAD, LCX, and the mean value for all arteries in patients with MACE were significantly higher than those in patients without MACE (RCA, −63.7 ± 8.9 HU vs −67.4 ± 9.1 HU, respectively; $P = 0.021$; LAD, −64.8 ± 6.6 HU vs −68.5 ± 8.3 HU, respectively; $P = 0.014$; LCX, −62.4 ± 8.8 HU vs −65.7 ± 8.4 HU, respectively; $P = 0.030$; and mean, −63.6 ± 7.0 HU vs −67.2 ± 7.4 HU, respectively; $P = 0.006$). There was a significant correlation between RCA- and LAD-PCATA (r = 0.57 [95% CI: 0.53-0.61]; $P < 0.001$), RCA- and LCX-PCATA (r = 0.59 [95% CI: 0.55-0.62]; $P < 0.001$), and LAD- and LCX-PCATA (r = 0.68 [95% CI: 0.64-0.71]; $P < 0.001$) (Supplemental Figure 2). Table 2 shows the association between RCA-PCATA and baseline characteristics. RCA-PCATA was higher in patients with a lower body mass index ($P < 0.001$) and HRPs ($P = 0.010$) than in patients without, but lower in patients with dyslipidemia than in those without ($P = 0.025$). Other baseline characteristics did not differ between the 2 groups.

Bland-Altman analyses of PCATA showed excellent intraobserver and interobserver agreement with mean differences of 0.564 (95% CI: 0.086-1.042, limits of agreement: 0.939-0.980) for intraobserver agreement and 0.953 (95% CI: 0.351-1.556, limits of agreement: 0.921-0.983) for interobserver agreement (Figure 3).

ASSOCIATION BETWEEN RCA-PCATA AND MACE. During a median follow-up of 6.0 years (Q1-Q3: 3.6-8.2 years), we recorded 33 MACE (13 cases of cardiovascular death, 20 cases of acute coronary syndrome).

FIGURE 2 **PCATA of the Main Coronary Arteries**



Pericoronary adipose tissue attenuation (PCATA) of the right coronary artery (RCA) (A), left anterior descending artery (LAD) (B), left circumflex artery (LCX) (C), and mean value of all arteries (D) in patients with and without major adverse cardiac events (MACE).

The optimal cutoff value of RCA-PCATA for discriminating the presence of MACE using maximization of the log-rank statistic was −66.6 HU. We divided the patients into 2 groups based on this cutoff value (high RCA-PCATA >−66.6 HU, low RCA-PCATA ≤−66.6 HU). Kaplan-Meier curves revealed higher rates of MACE among patients with high RCA-PCATA than among those with low RCA-PCATA during follow-up (log-rank test; $P = 0.003$) (**Figure 4A**). When participants were categorized according to the combination of high/low RCA-PCATA and/or adverse coronary CTA findings, which included significant stenosis and/or HRPs, Kaplan-Meier curves showed that patients with both high RCA-PCATA and adverse coronary CTA findings had the highest event rates when compared with other groups (log-rank test; $P = 0.002$) (**Figure 4B**). In the subgroup analyses, a consistent trend was observed in the association between high vs low RCA-PCATA with MACE across all subgroups (**Figure 5**). However, when patients were divided into groups based on PCATA of -70.1 HU,[6] no significant difference in the rate of MACE was observed on Kaplan-Meier curves between patients with high and low RCA-PCATA (log-rank test; $P = 0.132$). As shown in **Table 3**, unadjusted Cox regression analysis revealed that the Hisayama risk score, adverse coronary CTA findings, and RCA-PCATA were associated with MACE. In the multivariable analysis that included the Hisayama risk score and adverse coronary CTA findings and PCATA, high RCA-PCATA was significantly associated with MACE (HR: 1.555 per SD; 95% CI: 1.074-2.249; $P = 0.019$). Furthermore, to evaluate the effect of factors related to image acquisition, such as scanner type and contrast density, institution was included in the multivariable analysis as a random intercept in addition to Hisayama score, adverse coronary CTA findings, and PCATA. High RCA PCATA remained significantly associated with MACE (HR: 1.512 per SD; 95% CI: 1.024-2.232; $P = 0.037$).

Furthermore, the association among MACE with LAD-, LCX-, and mean PCATA was assessed. Patients were divided into 2 groups based on the cutoff value for discriminating the presence of MACE determined using maximization of the log-rank statistic (high LAD-PCATA >−67.2 HU and low LAD-PCATA ≤−67.2 HU, high LCX-PCATA >-59.1 HU and low LCX-PCATA ≤−59.1 HU, and high mean PCATA >−64.9 HU and low mean PCATA ≤−64.9 HU). Kaplan-Meier curves showed that the rate of MACE in patients with high LAD-, LCX-, and mean PCATA was significantly greater than that in patients with low LAD-, LCX-, and mean PCATA during follow-up (all, log-rank test; $P < 0.001$) (Supplemental Figure 3). The multivariable analysis showed that high LAD-PCATA (HR: 1.612 per SD; 95% CI: 1.096-2.369; $P = 0.015$), LCX-PCATA (HR: 1.513 per SD; 95% CI: 1.033-2.217; $P = 0.033$), and mean-PCATA (HR: 1.733 per SD; 95% CI: 1.175-2.554; $P = 0.005$) were also significantly associated with MACE (Supplemental Table 1).

COMPARISON OF PREDICTIVE PERFORMANCES FOR MACE. We finally assessed whether the addition of RCA-PCATA to the Hisayama score and adverse coronary CTA findings could improve the prediction of

TABLE 2 RCA-PCATA According to Baseline Characteristics Variables

	RCA-PCATA (HU)	*P* Value
Age, y		0.299
<70	−67.6 ± 9.0	
≥70	−67.1 ± 9.2	
Sex		0.073
Male	−67.0 ± 8.7	
Female	−67.9 ± 9.7	
BMI, kg/m^2		<0.001
<25	−66.2 ± 9.1	
≥25	−69.6 ± 8.6	
Current Smoker		0.447
Yes	−67.0 ± 8.6	
No	−67.5 ± 9.2	
Hypertension		0.781
Yes	−67.5 ± 8.9	
No	−67.3 ± 9.6	
Diabetes mellitus		0.848
Yes	−67.6 ± 9.6	
No	−67.5 ± 8.9	
Dyslipidemia		0.025
Yes	−68.1 ± 9.0	
No	−66.9 ± 9.3	
Chronic kidney disease		0.062
Yes	−66.6 ± 8.8	
No	−67.7 ± 9.2	
Hisayama risk score		0.084
low	−66.8 ± 10.8	
intermediate	−67.8 ± 8.8	
high	−66.7 ± 9.0	
HRP		0.010
Yes	−66.4 ± 8.3	
No	−67.8 ± 9.4	
Significant stenosis		0.480
Yes	−67.6 ± 9.3	
No	−67.3 ± 9.0	
Adverse coronary CTA findings		0.430
Yes	−67.2 ± 8.9	
No	−67.6 ± 9.2	

Values are mean ± SD.

BMI = body mass index; CTA = coronary computed tomography angiography; HRP = high-risk plaque; PCATA = pericoronary adipose tissue attenuation; RCA = right coronary artery.

MACE. The c-statistic of the base model was 0.645 (95% CI: 0.544-0.745). Adding RCA-PCATA to the base model showed a higher c-statistic, but no significant improvement compared with the base model (0.687 [95% CI: 0.602-0.772]; Δc-statistic: 0.417 [95% CI −0.023 to 0.107]; $P = 0.208$). The decision curve analysis also showed a similar result as the c-statistic improvement (Supplemental Figure 4). We further evaluated the predictive performance of RCA-PCATA for future MACE using the continuous NRI. The positive NRI (ie, the number with an increase in predicted risk by adding PCAT in patients with MACE) was 0.282 (95% CI: −0.036 to 0.600), whereas the negative NRI (ie, the number with an increase in predicted risk by adding PCAT in patients without MACE) was 0.141 (95% CI: −0.004 to 0.289). Thus, the NRI was 0.423 (95% CI: 0.022-0.827).

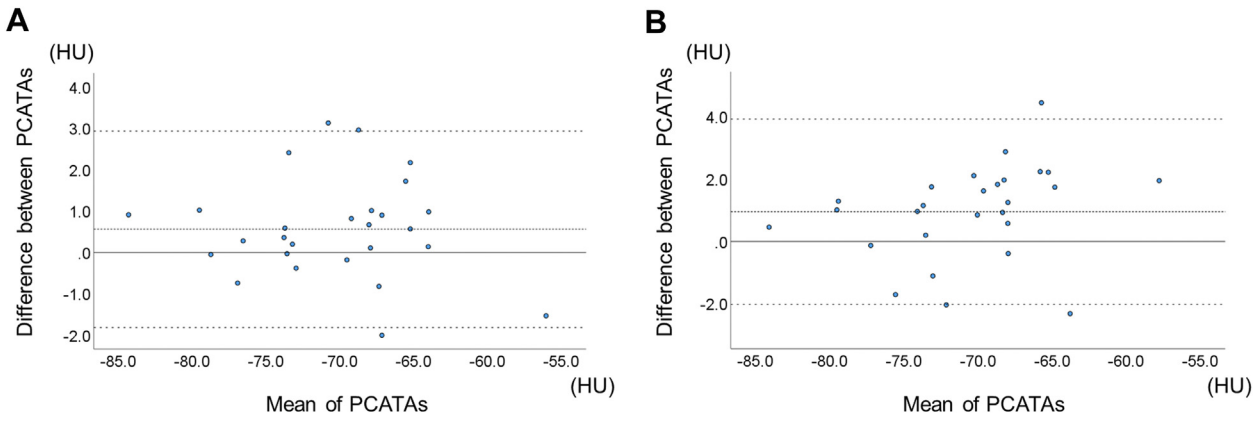
DISCUSSION

This study showed that high PCATA on coronary CTA was associated with the incidence of MACE among a cohort of Japanese patients, independent of adverse coronary CTA findings (**Central Illustration**). Adding RCA-PCATA to Hisayama score and adverse coronary CTA findings did not show significant improvement in predicting future MACE.

Several large cohort studies have been conducted involving patients of European ethnicity.[6,7] Oikonomo et al[6] reported that RCA-PCATA ≥−70.1 HU predicted all-cause and cardiac mortality in 3,912 consecutive patients who underwent clinically indicated coronary CTA. Tzolos et al[7] reported similar findings in a post hoc analysis of the SCOT-HEART trial, which included 1,967 participants. However, data in relation to patients of Asian ethnicity were not available for these studies. Regarding patients of East Asian ethnicity, only 2 small, single-center studies on specific high-risk subgroups have reported an association between PCATA and cardiovascular events. Hoshino et al[16] reported that increased LAD-PCATA was a predictor of cardiovascular events in 220 patients with intermediate LAD stenosis. Ichikawa et al[17] reported that in 333 patients with type 2 diabetes mellitus, increased LAD-PCATA could significantly predict cardiovascular events. The current study is the largest multicenter cohort study in East Asia to demonstrate the incremental value of PCATA in the risk stratification of MACE and accords with previous studies involving patients of European ethnicity.[6,7]

The CRISP-CT study showed that the effect of high PCATA on cardiac mortality tended to be greater in White than in Black populations.[6] Similarly, the effect of PCATA on MACE may differ between patients of East Asian ethnicity and other ethnic groups. There are 2 possible explanations for this: one is that ethnicity affects PCATA and plaque differently or the relationship between the 2 as an underlying pathology, and the other is that the statistical effect of the relationship between PCATA and MACE may be modified by conventional cardiovascular risks, which vary according to ethnicity. The first possibility has been supported by several studies on coronary CTA. Epicardial fat volume measured on CT in populations of Southeast or East Asian ethnicity was found to be

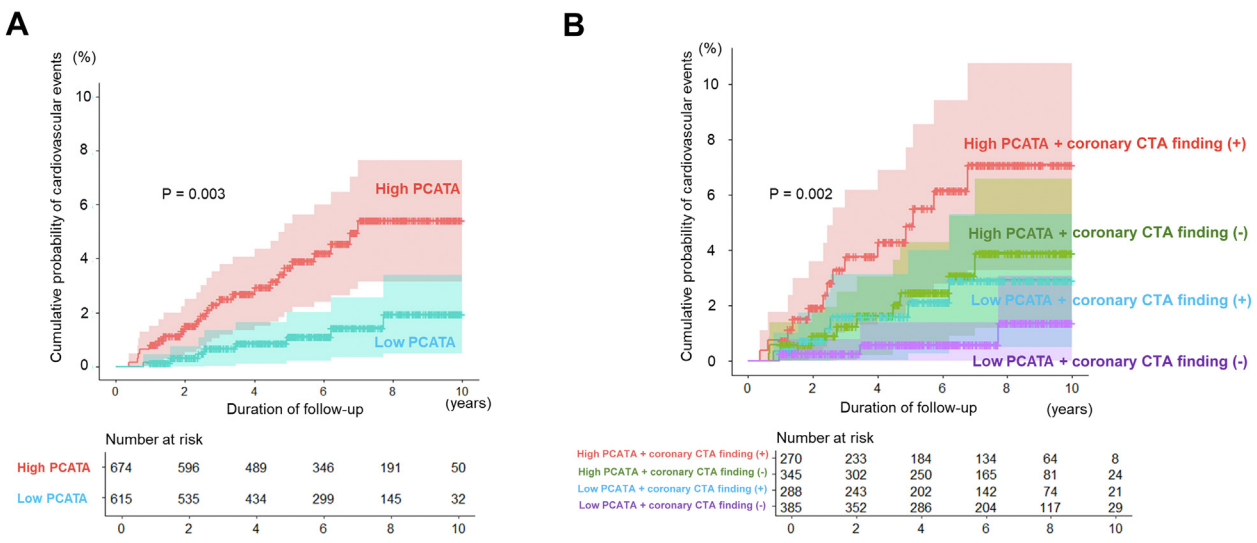
FIGURE 3 **Bland-Altman Plot of PCATA**



Interobserver (A) and intraobserver (B) agreement of pericoronary adipose tissue attenuation (PCATA). The center dotted lines represent the mean difference (bias), and the upper and lower dotted lines represent the limits of agreement.

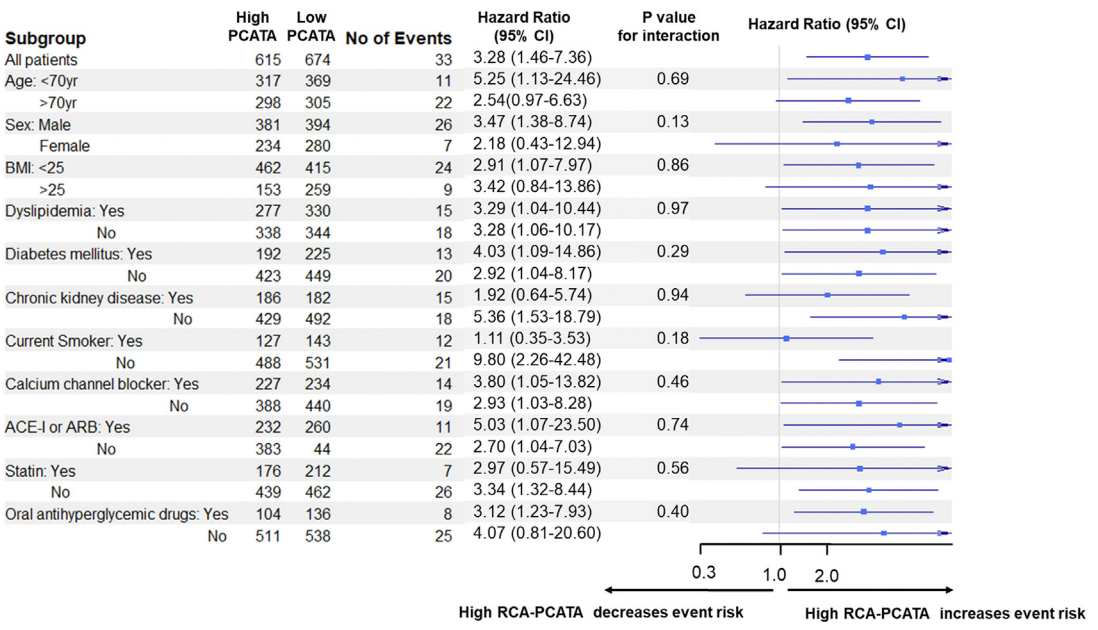
greater than that in populations of European ethnicity,[18] and significantly associated with severe coronary stenosis and HRP features.[19] These data suggest that difference in PCATA in terms of ethnicity may affect plaque morphology and progression. Moreover, PCATA is also influenced by inflammatory signals from the coronary arteries, because PCAT is in closer proximity to the coronary arteries.[20] A previous study showed that plaque formation in populations of East Asian ethnicity comprised less HRP such as fibrofatty and necrotic core plaque than in populations of European ethnicity,[21] which may explain the difference in PCATA between these ethnicities. Taken together, although the interaction between PCATA and plaque characteristics are bidirectional, this interaction may be affected by ethnicity. In terms

FIGURE 4 **Kaplan-Meier Curves of the Cumulative Incidence of MACE**



Incidence of cardiovascular events during follow-up according to low or high RCA-PCATA (A) and the combination of RCA-PCATA and adverse coronary CTA findings (B). The shading indicates the 95% CIs. MACE includes cardiovascular death and acute coronary syndrome. Abbreviations as in Figures 1 and 2.

FIGURE 5 Subgroup Analysis of the Association Between RCA-PCATA and Cardiovascular Events



In the subgroup analyses, a consistent trend was observed in the association between high vs low RCA-PCATA with MACE across all subgroups. ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; BMI = body mass index; other abbreviations as in Figure 2.

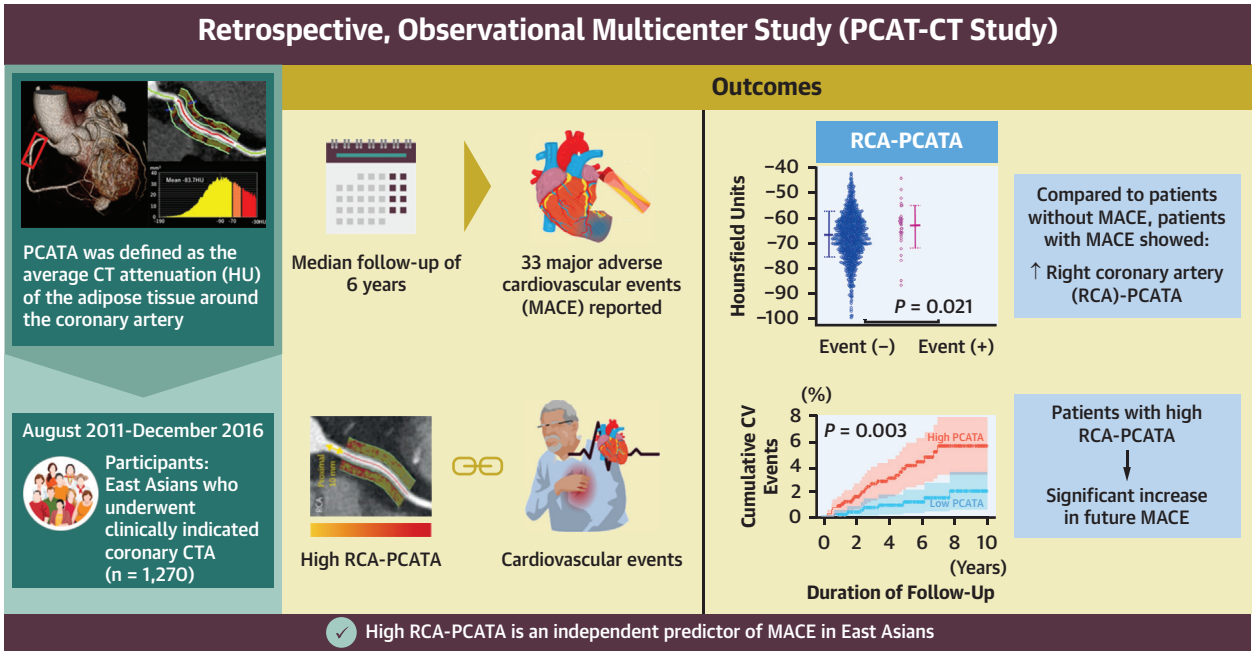
TABLE 3 Factors Associated With MACE

	Univariable		Multivariable	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age, y	1.019 (0.979-1.060)	0.366		
Male	2.627 (1.140-6.053)	0.023		
Body mass index, kg/m^2	0.987 (0.899-1.084)	0.792		
Hypertension	1.350 (0.624-2.918)	0.446		
Dyslipidemia	0.905 (0.456-1.795)	0.775		
Diabetes mellitus	1.300 (0.646-2.613)	0.462		
Chronic kidney disease	0.458 (0.231-0.909)	0.026		
Current smoker	2.188 (1.076-4.449)	0.031		
Statin	0.612 (0.265-1.409)	0.248		
Hisayama risk score				
Low-risk group	Reference		Reference	
Moderate-risk group	2.542 (0.335-19.25)	0.366	2.383 (0.310-18.32)	0.404
High-risk group	6.354 (0.845-47.80)	0.073	5.126 (0.663-39.65)	0.117
Adverse coronary CTA findings	2.147 (1.068-4.319)	0.032	1.736 (0.850-3.544)	0.130
RCA-PCATA, per SD	1.565 (1.089-2.249)	0.016	1.555 (1.074-2.249)	0.019

MACE included cardiovascular (CV) death and acute coronary syndrome.
RCA = right coronary artery; other abbreviations as in Tables 1 and 2.

of the possibility of statistical modification of the association between PCATA and MACE by confounding factors, no clear data have been reported. However, the PROMISE trial showed that, although populations of European ethnicity had a higher prevalence of significant stenosis and high-risk plaque than Black populations, the MACE rate between the 2 ethnicities was similar.[9] One reason for this finding is likely to be the lower rate of conventional risks in the White population than that in the Black population.[22] Another reason is likely to be the influence of genetic factors. Lipoprotein(a) has been identified as a strong heritable risk factor for coronary artery disease.[23] Ethnic differences in Lp(a) levels have been reported, with the highest levels observed in populations of African ethnicity, followed by those of South Asian ethnicity, European ethnicity, and with the lowest in those of East Asian ethnicity.[24] Given those data, it is possible that the statistical effect of PCATA on MACE differs between populations of East Asian ethnicity compared with those of

CENTRAL ILLUSTRATION **Pericoronary Adipose Tissue Attenuation Predicts Cardiovascular Events in East Asians**



Nishihara T, et al. JACC Asia. 2025;5(1):1–11.

High right coronary artery (RCA) pericoronary adipose tissue attenuation (PCATA) on coronary computed tomography angiography (CTA) was significantly associated with major adverse cardiovascular events (MACE), a composite of cardiovascular (CV) and acute coronary syndromes in an East Asian patient cohort. CT = computed tomography.

European ethnicity. In the current study, RCA-PCATA >−70.1 HU, which has been reported to widely apply to populations of European ethnicity,[6,7] was not associated with the incidence of MACE. Further studies are needed to clarify whether the effects of PCATA on MACE differ between populations of East Asian ethnicity and other ethnicities.

Several previous studies have reported that RCA-PCATA was a representative marker for MACE among 3 major coronary arteries,[6,7] because of the absence of confounding nonfatty structures such as major side branches, accompanying coronary veins, and myocardium compared with LAD and LCX.[25,26] However, other studies have shown that LAD-PCATA predicts cardiovascular events, while LCX-PCATA does not.[6,27] Given the accuracy of RCA-PCATA measurements and the association with prognosis in observational studies, it would be reasonable to use the RCA as a prognostic indicator. Moreover, this study showed that the relationship between PCATA and MACE was consistent across all of the coronary arteries. Recently, Chan et al. reported that increased PCATA in all 3 coronary arteries had an additive effect on the risk for cardiac mortality,[28] which is in line with our study. These findings suggest that PCATA is a marker of overall coronary inflammation rather than focal inflammation.

Previous studies have shown that PCATA is involved in CAD severity.[29,30] Sugiyama et al[29] found that in 540 patients, significant stenosis on invasive coronary angiography significantly increased PCATA compared with patients without significant stenosis. Yuvaraj et al[30] showed that RCA-PCATA was higher in patients with HRP on coronary CTA than in those without. However, in our study, HRP was not always present in coronary arteries with increased PCATA (data not shown). In line with our findings, another study showed that RCA-PCATA was higher in patients with obstructive CAD or plaques with high-risk features anywhere in the coronary tree compared with those without.[7] Chan et al[28] reported that LAD-PCATA predicts MACE in patients without obstructive CAD. These studies suggest that patients with high PCATA are at high risk for future cardiovascular events regardless of plaque characteristics. Because our study showed that both high RCA-PCATA and adverse

coronary CTA findings predicted MACE, PCATA could be used in combination with coronary plaque characteristics for risk stratification in patients with CAD. Additionally, previous studies have reported that biological therapy for psoriasis and statin therapy are associated with reduced PCATA.[31,32] In contrast, the coronary artery calcium score, which is another marker of risk stratification, represents the coronary atherosclerotic burden. However, coronary artery calcification does not regress with medical treatment. Therefore, PCATA may serve as a measure of risk stratification, as well as an evaluation index for the treatment of CAD.

Image acquisition parameters on CT may affect PCATA. One important factor is tube voltage. Ma et al[33] reported that PCATA showed a positive linear association with tube voltage. To avoid its influence, all images used in this study were taken at 120 kVp as proof-of-concept studies concerning PCATA and other previous studies were performed on 120-kVp coronary CTA scans.[4-8] No data were available in relation to the effect of scanner type on PCATA because we did not perform a phantom study. However, a multivariable Cox regression analysis that included all of the institutions showed that PCATA remained a significant predicter for MACE, suggesting that the differences in scanner type and contrast density in the current study did not affect the results.

STUDY LIMITATIONS. Our results cannot be applied to the general population because all patients enrolled in the present study underwent coronary CTA for clinical reasons. They therefore had a higher risk than the general population, which was the case for patients in previous studies. This study was conducted retrospectively with a limited number of events. We did not investigate the underlying mechanisms that might explain the association between PCATA and cardiovascular events, and further studies are required to elucidate these underlying mechanisms. We did not compare the effect of PCATA on MACE between the current population and a non-East Asian cohort of patients. Therefore, further studies are needed to determine ethnic differences in terms of the association between PCATA and MACE.

CONCLUSIONS

This multicenter study showed that a high RCA-PCATA was an independent predictor of MACE above the clinical risk score and adverse coronary CTA findings in East Asians. The measurement of PCATA on coronary CTA is likely to facilitate identification of individuals at risk of future atherosclerotic cardiovascular disease among patients of East Asian ethnicity. However, further studies are needed to confirm the effects of ethnic differences in PCATA on adverse cardiac events.

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ADDRESS FOR CORRESPONDENCE: Dr Toru Miyoshi, Department of Cardiovascular Medicine, Faculty of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan. E-mail: miyoshit@cc.okayama-u.ac.jp.

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KEY WORDS acute coronary syndrome(s), coronary computed tomography angiography, high-risk plaque, obstructive stenosis, pericoronary adipose tissue attenuation

APPENDIX For a supplemental table and figures, please see the online version of this paper.

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