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ORIGINAL RESEARCH

Impact of pericoronary adipose tissue attenuation on clinical outcomes after percutaneous coronary intervention

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ABSTRACT

BACKGROUND: Pericoronary adipose tissue (PCAT) attenuation, measured using coronary computed tomography angiography (cCTA), is a potential marker of coronary inflammation.

AIMS: We aimed to examine the association between coronary inflammation, as assessed by measuring PCAT attenuation before percutaneous coronary intervention (PCI), and clinical outcomes of PCI using current-generation drug-eluting stents (DES).

METHODS: We retrospectively studied consecutive patients who underwent cCTA before PCI with current-generation DES. Adverse plaque characteristics, calcified plaque (CP) burden, and PCAT attenuation of the proximal right coronary artery ($PCAT_{RCA}$) were assessed using cCTA. The primary outcome was a patient-oriented composite endpoint (PoCE), including cardiovascular death, non-fatal myocardial infarction, any revascularisation, and stroke.

RESULTS: During a median follow-up of 1,540 days, 77 of 490 patients experienced PoCE. Patients with PoCE had higher $PCAT_{RCA}$ (–76.3±6.4 Hounsfield units [HU] vs –82.5±8.1 HU; p<0.001). Multivariable analysis showed that the presence of adverse plaque, greater CP burden and higher $PCAT_{RCA}$ were independently associated with PoCE (hazard ratio [HR] 2.05, 95% confidence interval [CI]: 1.26-3.34; p=0.004; HR 1.04, 95% CI: 1.02-1.07; p=0.002; and HR 2.20, 95% CI: 1.63-2.97; p<0.001, respectively). PoCE incidence was 3.9 times higher in patients with high $PCAT_{RCA}$ (≥–79.9 HU) than those with low $PCAT_{RCA}$ (<–79.9 HU). Adding $PCAT_{RCA}$ to traditional cardiovascular risk factors and cCTA findings (adverse plaque and CP burdens) improved the predictive and reclassification abilities for PoCE.

CONCLUSIONS: High $PCAT_{RCA}$ was independently associated with PoCE after PCI using current-generation DES. Combining $PCAT_{RCA}$ with traditional cardiovascular risk factors and cCTA findings may enhance risk assessment for PoCE after PCI.

KEYWORDS: coronary computed tomography angiography; coronary inflammation; current-generation drug-eluting stents; pericoronary adipose tissue

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Current-generation drug-eluting stents (DES) have dramatically reduced target lesion revascularisation (TLR) and stent thrombosis in patients with coronary artery disease (CAD). Despite notable advancements in medical management and device technology, patients undergoing percutaneous coronary intervention (PCI) remain at subsequent cardiovascular risk[1,2]. Although aggressive management of conventional cardiovascular risk factors is effective, it only addresses part of the overall cardiovascular risk, and residual risk persists even with optimal medical therapy.

Recent studies have highlighted the role of coronary inflammation in atherosclerotic progression and vulnerable plaque rupture, leading to subsequent cardiovascular events in patients with CAD[3]. Clinical trials, such as the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) and the Low Dose Colchicine 2 trial, have further substantiated that reducing systemic inflammation through anti-inflammatory medications significantly decreases recurrent cardiovascular events[4-6]. This underscores the relevance of evaluating coronary artery inflammation as a residual risk factor, providing an opportunity to enhance cardiovascular risk stratification in patients with CAD.

Recent advances in coronary computed tomography angiography (cCTA) have enabled the non-invasive quantification of coronary inflammation by analysing changes in pericoronary adipose tissue (PCAT) attenuation[7]. PCAT attenuation is a novel marker of coronary inflammation on cCTA, capturing changes in adipocyte size and lipid accumulation caused by inflammatory mediators from the vascular wall. Previous reports have demonstrated an association between increased PCAT attenuation and future adverse events in patients with CAD[8,9]. However, the prognostic impact of coronary inflammation, assessed using PCAT attenuation, in patients undergoing PCI with current-generation DES remains unexplored. This study aimed to investigate the relationship between pre-PCI PCAT attenuation and clinical outcomes after PCI with current-generation DES.

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Impact on daily practice

Coronary inflammation is recognised as a significant residual risk factor for cardiovascular events, with pericoronary adipose tissue (PCAT) attenuation on coronary computed tomography angiography (cCTA) being a novel marker linked to higher risks of cardiac mortality and major adverse events. This study demonstrates that PCAT attenuation is independently associated with the patient-oriented composite endpoint after percutaneous coronary intervention with current-generation drug-eluting stents, and its inclusion alongside traditional cCTA findings and cardiovascular risk factors enhances patient risk discrimination. Measuring PCAT attenuation may be useful for identifying patients who would benefit the most from anti-inflammatory drugs.

Methods

STUDY DESIGN

In this retrospective, multicentre, observational cohort study, we enrolled consecutive patients at four institutions between January 2016 and December 2020; an external cohort of additional patients was enrolled between January 2021 and December 2021. The inclusion criteria were (1) patients who had undergone PCI using current-generation DES for *de novo* native coronary stenotic lesions, (2) patients who had undergone cCTA within the 120 days preceding PCI, and (3) patients who were aged ≥20 years. The exclusion criteria were (1) patients diagnosed as having ST-segment elevation myocardial infarction, (2) patients with coronary artery bypass grafted lesions, (3) patients with chronic total occlusion, (4) patients with left main coronary artery lesions, (5) patients undergoing intervention of more than one native coronary vessel during a single PCI procedure, and (6) patients with insufficient computed tomography (CT) data quality. The study protocol complied with the Declaration of Helsinki and was approved by the ethics committee of Kobe University Hospital. Informed consent was obtained as an opt-out form on the website of the Division of Cardiovascular Medicine at Kobe University Graduate School of Medicine. The study was registered in the University Hospital Medical Information Network Clinical Trial Registry (UMIN000051353).

CCTA IMAGE ACQUISITION AND ANALYSIS OF PLAQUE CHARACTERISTICS

cCTA images were obtained in accordance with the Society of Cardiovascular Computed Tomography guidelines[10]. Acquisition details are described in **Supplementary Appendix 1**. Reconstructed images were transferred to a processing workstation (SYNAPSE VINCENT [FUJIFILM Corporation]) and analysed by two independent investigators who were blinded to the patients' clinical characteristics, except for information regarding the PCI target lesion. The centreline and vessel contours were automatically detected and manually corrected, if necessary.

The lesions that underwent PCI were deemed target lesions. In cases with multiple lesions, the target lesion was defined as the most severe stenotic lesion. Non-target lesions were defined as the other (non-PCI) lesions with percentage diameter stenosis (%DS) >30% on cCTA. The reference and minimal lumen diameters, lesion length, minimal lumen area, and %DS were measured using axial and multiplanar reconstruction images.

Abbreviations

APC	adverse plaque characteristics	**HU**	Hounsfield unit	**PCI**	percutaneous coronary intervention
cCTA	coronary computed tomography angiography	**LAP**	low-attenuation plaque	**PoCE**	patient-oriented composite endpoint
		MI	myocardial infarction	**RCA**	right coronary artery
CP	calcified plaque	**NCP**	non-calcified plaque	**TLR**	target lesion revascularisation
DES	drug-eluting stent	**PCAT**	pericoronary adipose tissue	**TVR**	target vessel revascularisation

Plaque burdens were measured for the following subtypes in the entire coronary artery, target lesions, and non-target lesions: total plaque, low-attenuation plaque (LAP), non-calcified plaque (NCP), and calcified plaque (CP)[11]. When there were multiple non-target lesions, the average value was used for analysis.

Adverse plaque characteristics (APCs), such as positive remodelling, low-attenuation plaque, spotty calcification, and the napkin-ring sign, were assessed for PCI target and non-target lesions[12]. In cases with multiple lesions, the lesions with the highest number of APCs, including both target and non-target lesions, were used for patient-level analysis. The number of APCs per lesion was calculated, and adverse plaques were defined as those with two or more APCs. Details of cCTA image analysis are described in **Supplementary Appendix 1**.

PCAT ANALYSIS

PCAT attenuation was measured using dedicated cCTA analysis software (SYNAPSE VINCENT). Within the predefined volume of interest, voxels with tissue attenuation ranging from –190 Hounsfield units (HU) to –30 HU were considered adipose tissues, and PCAT attenuation was defined as the mean attenuation within such contamination-free volumes of interest. These measurements were performed for each patient around the proximal right coronary artery (RCA; $PCAT_{RCA}$), proximal target vessels ($PCAT_{Vessel}$), and the specific target lesions ($PCAT_{Lesion}$) **(Figure 1)**. PCAT attenuation measurements at the patient level are represented by $PCAT_{RCA}$[8,9]. PCAT analysis details are described in **Supplementary Appendix 1**.

OUTCOMES

The primary outcome of the study was a patient-oriented composite endpoint (PoCE), defined as a composite of cardiovascular death, non-fatal myocardial infarction (MI), any revascularisation, and stroke. Based on the Academic Research Consortium (ARC)-2 definition[13], we investigated other clinical outcomes such as major adverse cardiovascular events (MACE), target vessel failure (TVF), target lesion failure (TLF), all-cause death, cardiovascular death, any MI, non-fatal MI, any revascularisation, target vessel revascularisation (TVR), TLR, heart failure hospitalisation, and periprocedural myocardial infarction (PMI). Clinical outcomes were ascertained using hospital records and follow-up data from outpatient visits. Further details of the outcomes and statistical analyses are provided in **Supplementary Appendix 1**.

EXTERNAL COHORT

We determined the optimal cutoff value of $PCAT_{RCA}$ for predicting PoCE after PCI using receiver operating characteristic (ROC) curve analysis. To externally validate this cutoff value, an external cohort of patients from the same institution was identified. These patients met the same inclusion and exclusion criteria as the current study. External cohort details are described in **Supplementary Appendix 1**.

Results

STUDY POPULATION

In total, 702 patients underwent cCTA before PCI using current-generation DES for *de novo* native lesions during the study period. After applying various exclusion criteria, 490 patients were included in the analysis. During a median follow-up of 1,540 (interquartile range: 1,070-1,990) days, 77 (15.7%) experienced PoCE (PoCE group) **(Supplementary Figure 1)**. Ten patients experienced cardiovascular death, 8 experienced non-fatal MI, 52 underwent any type of revascularisation, and 16 experienced strokes.

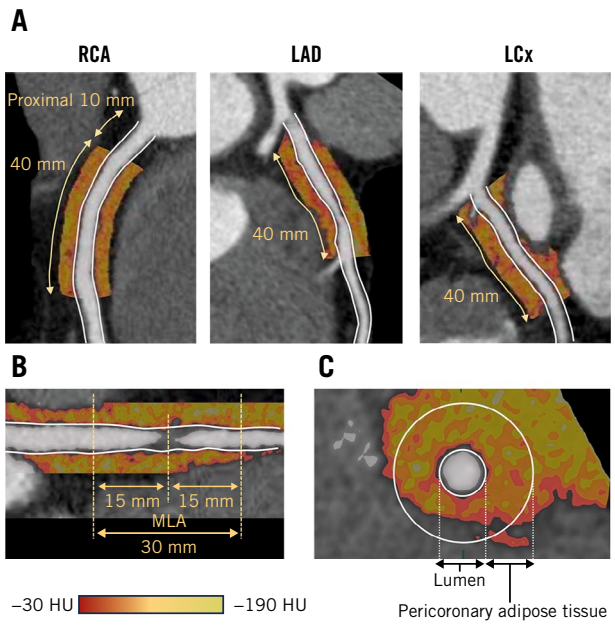


Figure 1. *PCAT analysis. Pericoronary adipose tissue (PCAT) attenuation measurements are performed at (A) the proximal target vessels ($PCAT_{Vessel}$) and (B) the target lesions ($PCAT_{Lesion}$). C) PCAT is defined as the adipose tissue within a radial distance equal to the vessel diameter.*
HU: Hounsfield unit; LAD: left anterior descending artery; LCx: left circumflex artery; MLA: minimal lumen area; RCA: right coronary artery

COMPARISON OF BASELINE CHARACTERISTICS BETWEEN THE POCE AND NON-POCE GROUPS

Table 1 shows baseline patient, lesion, and procedural characteristics. The PoCE group had significantly higher frequencies of haemodialysis and multivessel disease, lower left ventricular ejection fraction, higher brain natriuretic peptide values, and less frequent statin use at discharge than the non-PoCE group. High sensitivity C-reactive protein (hs-CRP) was comparable between the groups.

Table 2 and **Supplementary Table 1** summarise the pre-PCI cCTA findings. In the patient-level analysis, total plaque, LAP, NCP, and CP burdens were significantly higher and napkin-ring signs and adverse plaques were significantly more prevalent in the PoCE group than in the non-PoCE group. In the target lesion-level analysis, CP burden tended to be higher in the PoCE group. In the non-target lesion-level analysis, total plaque, LAP, NCP, and CP burdens were significantly higher and spotty calcification, napkin-ring signs and adverse plaques were significantly more prevalent in the PoCE group.

Table 1. Baseline patient, lesion, and procedural characteristics.

Variables	All patients (n=490)	PoCE (n=77)	Non-PoCE (n=413)	*p*-value
Baseline patient characteristics				
Age, years	69.6±9.9	70.7±9.6	69.5±9.9	0.314
Male sex	368 (75.1)	63 (81.8)	305 (73.8)	0.153
Hypertension	363 (74.1)	53 (68.8)	310 (75.1)	0.259
Dyslipidaemia	360 (73.5)	51 (66.2)	309 (74.8)	0.123
Diabetes mellitus	221 (45.1)	40 (51.9)	181 (43.8)	0.213
Smoker	299 (61.0)	51 (66.2)	248 (60.0)	0.373
Chronic kidney disease	151 (30.8)	28 (36.4)	123 (29.8)	0.282
Haemodialysis	12 (2.4)	5 (6.5)	7 (1.7)	0.027
Prior PCI	83 (16.9)	14 (18.2)	69 (16.7)	0.742
Prior MI	41 (8.4)	6 (7.8)	35 (8.5)	0.999
Acute coronary syndrome	127 (25.9)	17 (22.1)	110 (26.6)	0.479
Laboratory data				
BNP, pg/mL	32.4 (14.2, 83.2)	65.0 (15.0, 128.9)	30.6 (14.2, 65.80)	0.005
Estimated GFR, mL/min/1.73 m^2	66.0 (57.0, 76.2)	66.0 (55.2, 76.0)	66.0 (57.3, 77.0)	0.480
Low-density lipoprotein cholesterol, mg/dL	113.0 (92.3, 137.7)	109.0 (86.4, 125.0)	115.0 (94.0, 138.0)	0.097
HbA1c, %	6.1 (5.8, 7.0)	6.2 (5.8, 7.2)	6.1 (5.8, 7.0)	0.411
WBC count, $\times10^3$/μL	6.1 (5.1, 7.4)	6.2 (5.1, 7.4)	6.1 (5.1, 7.4)	0.881
hs-CRP, mg/L	0.8 (0.4, 2.0)	1.3 (0.4, 3.6)	0.8 (0.4, 1.9)	0.204
LVEF, %	60.0 (55.0, 64.9)	58.5 (51.0, 63.0)	61.0 (55.0, 65.0)	0.007
Medications at cCTA				
Statins	259 (52.9)	39 (50.6)	220 (53.3)	0.710
Beta blockers	110 (22.4)	16 (20.8)	94 (22.8)	0.768
RAS inhibitors	220 (44.9)	39 (50.6)	181 (43.8)	0.318
Calcium channel blockers	204 (41.6)	31 (40.3)	173 (41.9)	0.803
Oral anticoagulants	33 (6.7)	9 (11.7)	24 (5.8)	0.079
Medications at discharge				
Statins	439 (89.6)	61 (79.2)	378 (91.5)	0.003
Beta blockers	193 (39.4)	32 (41.6)	161 (39.0)	0.704
RAS inhibitors	283 (57.8)	50 (64.9)	233 (56.4)	0.170
Calcium channel blockers	234 (47.8)	35 (45.5)	199 (48.2)	0.710
Oral anticoagulants	36 (7.3)	10 (13.0)	26 (6.3)	0.054
Lesion characteristics				
Target vessel: LAD/LCx/RCA, %	51.8/14.7/33.5	41.6/14.3/44.2	53.8/14.8/31.5	0.086
Lesion location: proximal/mid/distal, %	31.2/56.1/12.7	36.4/48.2/15.6	10.3/57.6/12.1	0.278
Multivessel disease	238 (48.6)	47 (61.0)	191 (46.2)	0.018
Patients undergoing FFR[§]	116 (32.0)	17 (28.3)	99 (32.7)	0.548
FFR value	0.70±0.08	0.68±0.09	0.70±0.08	0.497
Procedural characteristics				
Number of stents	1.17±0.39	1.23±0.43	1.16±0.38	0.125
Stent diameter, mm	3.12±0.50	3.19±0.50	3.11±0.50	0.195
Stent length, mm	28.4±13.6	28.5±15.9	28.4±13.1	0.967
Imaging device: IVUS/OCT	486 (99.2)	76 (98.7)	410 (99.3)	0.460
IVUS	319 (65.1)	47 (61.0)	272 (65.9)	0.436
OCT	167 (34.1)	29 (37.7)	138 (44.1)	0.430
Atherectomy*	50 (10.2)	40 (9.7)	10 (13.0)	0.411

Values are expressed as mean±standard deviation, median (2^{5th}, 75^{th} percentiles) or n (%), unless otherwise stated. [§]The proportion of patients who underwent FFR was calculated based on the CCS patient population (n=368). *Atherectomy includes rotational atherectomy and orbital atherectomy. BNP: brain natriuretic peptide; CCS: chronic coronary syndrome; cCTA: coronary computed tomography angiography; FFR: fractional flow reserve; GFR: glomerular filtration rate; hs-CRP: high-sensitivity C-reactive protein; IVUS: intravascular ultrasound; LAD: left anterior descending artery; LCx: left circumflex artery; LVEF: left ventricular ejection fraction; MI: myocardial infarction; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; PoCE: patient-oriented composite endpoint; RAS: renin-angiotensin system; RCA: right coronary artery; WBC: white blood cell

Table 2. cCTA findings at the patient level.

Variables	All patients (n=490)	PoCE (n=77)	non-PoCE (n=413)	*p*-value
Quantitative cCTA analysis				
Total plaque burden, %	40.3 (35.2, 44.9)	44.8 (40.1, 48.9)	39.4 (34.5, 43.8)	<0.001
LAP burden, %	6.66 (3.97, 8.61)	6.98 (5.81, 9.06)	6.47 (3.94, 8.44)	0.013
NCP burden, %	36.8 (30.8, 42.0)	40.8 (35.4, 45.4)	36.1 (30.5, 41.4)	<0.001
CP burden, %	1.61 (0.38, 4.23)	2.86 (0.96, 6.37)	1.40 (0.34, 3.99)	<0.001
Coronary artery calcium score, Agatston units (n=368)	398 (119, 1,120)	378 (112, 1,010)	635 (243, 1,620)	0.002
≥400, %	181 (49.2)	41 (62.1)	140 (46.4)	0.021
Qualitative cCTA findings*				
Positive remodelling	221 (45.1)	39 (50.6)	182 (44.1)	0.319
Low-attenuation plaque	201 (41.0)	36 (46.8)	165 (40.0)	0.313
Spotty calcification	142 (29.0)	29 (37.7)	113 (27.4)	0.076
Napkin-ring sign	74 (15.1)	19 (24.7)	55 (13.3)	0.015
Adverse plaque	241 (49.2)	51 (66.2)	190 (46.0)	0.001
PCAT attenuation analysis				
$PCAT_{RCA}$, HU	–81.5±8.1	–76.3±6.4	–82.5±8.1	<0.001
$PCAT_{Vessel}$, HU	–81.1±8.1	–76.7±7.5	–82.0±7.8	<0.001
$PCAT_{Lesion}$, HU	–81.0±8.9	–76.5±7.9	–81.8±8.9	<0.001

Values are expressed as mean±standard deviation, median (25^{th}, 75^{th} percentiles) or n (%). *Qualitative cCTA findings at the patient-level analysis are assessed in the lesions with the highest numbers of APCs among all lesions. APC: adverse plaque characteristic; cCTA: coronary computed tomography angiography; CP: calcified plaque; HU: Hounsfield unit; LAP: low-attenuation plaque; MLA: minimal lumen area; NCP: non-calcified plaque; PCAT: pericoronary adipose tissue; PCI: percutaneous coronary intervention; PoCE: patient-oriented composite endpoint; RCA: right coronary artery

Additionally, PCAT parameters, including $PCAT_{RCA}$, $PCAT_{Vessel}$, and $PCAT_{Lesion}$, were significantly higher in the PoCE group than those in the non-PoCE group (all p<0.001). Inter- and intraobserver intraclass correlation coefficient values for PCAT attenuation were excellent (0.982 and 0.972, respectively). In a sensitivity analysis of 363 stable patients with CAD, $PCAT_{RCA}$, $PCAT_{Vessel}$, and $PCAT_{Lesion}$ were also significantly higher in the PoCE group (all p<0.001) **(Supplementary Table 2)**.

FACTORS ASSOCIATED WITH POCE

The results of the univariable and multivariable Cox regression analyses examining cardiovascular risk factors and cCTA findings associated with PoCE are summarised in **Table 3** and **Supplementary Table 3**. At the patient level, the following were independently associated with PoCE occurrence: statin use at discharge; total plaque, LAP, NCP, and CP burdens; the presence of adverse plaque; and $PCAT_{RCA}$. At the target lesion level, the multivariable model showed that CP burden, the presence of adverse plaque, and $PCAT_{RCA}$ were independently associated with PoCE occurrence. At the non-target lesion level, $PCAT_{RCA}$ and total plaque, NCP, and CP burdens were independently associated with PoCE occurrence.

ROC analysis showed that the cutoff value of $PCAT_{RCA}$ for identifying patients with subsequent PoCE was –79.9 HU **(Supplementary Figure 2A)**. PoCE incidence was 3.9 times higher in patients with high $PCAT_{RCA}$ (≥–79.9 HU: n=208) than in those with low $PCAT_{RCA}$ (<–79.9 HU: n=282; 26.5% vs 7.8%, hazard ratio [HR] 3.85, 95% confidence interval [CI]: 2.33-6.35; p<0.001) **(Supplementary Figure 3)**. Additionally, the incidences of MACE, TVF, TLF, all-cause death, cardiovascular death, any MI, any revascularisation, TVR, TLR, and heart failure hospitalisation were significantly higher in patients with high $PCAT_{RCA}$ (≥–79.9 HU) than in those with low $PCAT_{RCA}$ (<–79.9 HU) **(Table 4)**. Of the 205 patients who had sufficient data for PMI evaluation, 39.0% (80/205) had PMI. Furthermore, consistent results were observed in the external cohort using the same cutoff value **(Supplementary Table 4, Supplementary Figure 4)**.

ROC analysis of the CP burden showed that the cutoff value of this parameter for identifying patients with subsequent PoCE was 2.1% **(Supplementary Figure 2B)**. Patients with adverse plaque had a 2.1 times higher incidence of PoCE compared to those with no adverse plaque, and those with high CP burden had a 2.4 times higher incidence of PoCE compared to patients with low CP burden **(Supplementary Figure 5A, Supplementary Figure 5B)**.

Patients with high $PCAT_{RCA}$ and adverse plaque had a significantly higher PoCE incidence than those with low $PCAT_{RCA}$ and no adverse plaque (HR 6.40, 95% CI: 3.10-13.22; p<0.001) **(Figure 2A)**, and those with high $PCAT_{RCA}$ and high CP burden had a significantly higher PoCE incidence than those with low $PCAT_{RCA}$ and low CP burden (HR 7.83, 95% CI: 3.90-15.73; p<0.001) **(Figure 2B)**.

DISCRIMINATORY DIAGNOSTIC ABILITY BY ADDING FACTORS FOR POCE

The **Central illustration** shows the Harrell's c-index, category-free net reclassification index (NRI), and integrated

Table 3. Cox regression analysis of factors associated with PoCE at the patient level.

Variables	Univariable analysis		Multivariable model	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Baseline patient characteristics				
Age	1.02 (0.99-1.04)	0.180		
Male sex	1.54 (0.86-2.75)	0.145	1.23 (0.68-2.23)	0.490
Hypertension	0.73 (0.45-1.19)	0.208		
Dyslipidaemia	0.65 (0.40-1.04)	0.069		
Diabetes mellitus	1.36 (0.87-2.13)	0.175		
Smoker	1.29 (0.80-2.07)	0.293		
hs-CRP (per 1 mg/L increase)	1.01 (0.98-1.02)	0.644		
LVEF	0.97 (0.95-1.00)	0.019	0.99 (0.97-1.01)	0.260
Statin use at discharge	0.38 (0.22-0.66)	0.001	0.45 (0.25-0.79)	0.005
cCTA findings				
Quantitative cCTA analysis				
Total plaque burden*	2.14 (1.66-2.77)	<0.001		
LAP burden*	1.15 (1.05-1.27)	0.004	1.10 (1.01-1.20)	0.035
NCP burden*	1.52 (1.23-1.87)	<0.001		
CP burden*	1.04 (1.01-1.06)	0.002	1.04 (1.02-1.07)	0.002
Qualitative cCTA findings				
Positive remodelling	1.27 (0.82-1.99)	0.287		
Low-attenuation plaque	1.29 (0.83-2.02)	0.261		
Spotty calcification	1.93 (1.15-3.23)	0.013		
Napkin-ring sign	1.52 (0.96-2.41)	0.074		
Adverse plaque	2.14 (1.33-3.43)	0.002	2.05 (1.26-3.34)	0.004
PCAT attenuation analysis				
$PCAT_{RCA}$ (per 10 HU increase)	2.31 (1.74-3.05)	<0.001	2.20 (1.63-2.97)	<0.001
$PCAT_{Lesion}$ (per 10 HU increase)	2.40 (1.79-3.23)	<0.001		
$PCAT_{Vessel}$ (per 10 HU increase)	2.40 (1.79-3.23)	<0.001		

*Per 1.2-fold increase. cCTA: coronary computed tomography angiography; CI: confidence interval; CP: calcified plaque; HR: hazard ratio; hs-CRP: high-sensitivity C-reactive protein; HU: Hounsfield unit; LAP: low-attenuation plaque; LVEF: left ventricular ejection fraction; NCP: non-calcified plaque; PCAT: pericoronary adipose tissue; PoCE: patient-oriented composite endpoint; RCA: right coronary artery

Table 4. Comparison of the clinical outcomes between the high and low $PCAT_{RCA}$ groups throughout the study.

Endpoint	High $PCAT_{RCA}$ (≥–79.9 HU) (n=208)	Low $PCAT_{RCA}$ (<–79.9 HU) (n=282)	HR (95% CI)	*p*-value
PoCE	26.5 (56)	7.8 (21)	3.85 (2.33-6.35)	<0.001
MACE	33.8 (72)	9.7 (28)	3.74 (2.42-5.79)	<0.001
Target vessel failure	12.1 (24)	2.3 (7)	4.90 (2.11-11.37)	<0.001
Target lesion failure	9.1 (18)	2.6 (4)	6.42 (2.17-18.97)	<0.001
All-cause death	10.5 (20)	2.3 (6)	4.65 (1.87-11.57)	<0.001
Cardiovascular death	4.8 (9)	NA (1)	12.62 (1.60-99.61)	0.016
Any MI	3.7 (7)	0.1 (2)	4.81 (1.00-23.16)	0.049
Non-fatal MI	3.2 (6)	0.1 (2)	4.13 (0.83-20.45)	0.083
Any revascularisation	17.4 (36)	6.0 (16)	3.25 (1.80-5.85)	<0.001
Target vessel revascularisation	7.4 (15)	1.9 (6)	3.54 (1.38-9.14)	0.009
Target lesion revascularisation	4.4 (9)	1.2 (3)	4.26 (1.15-15.76)	0.030
Heart failure hospitalisation	6.4 (13)	2.7 (7)	2.54 (1.01-6.38)	0.047
Stroke	5.1 (11)	1.8 (6)	2.45 (0.91-6.63)	0.078

Event rates are Kaplan-Meier estimates, presented as % (n of events). CI: confidence interval; HR: hazard ratio; HU: Hounsfield unit; MACE: major adverse cardiovascular events; MI: myocardial infarction; PCAT: pericoronary adipose tissue; PoCE: patient-oriented composite endpoint; RCA: right coronary artery

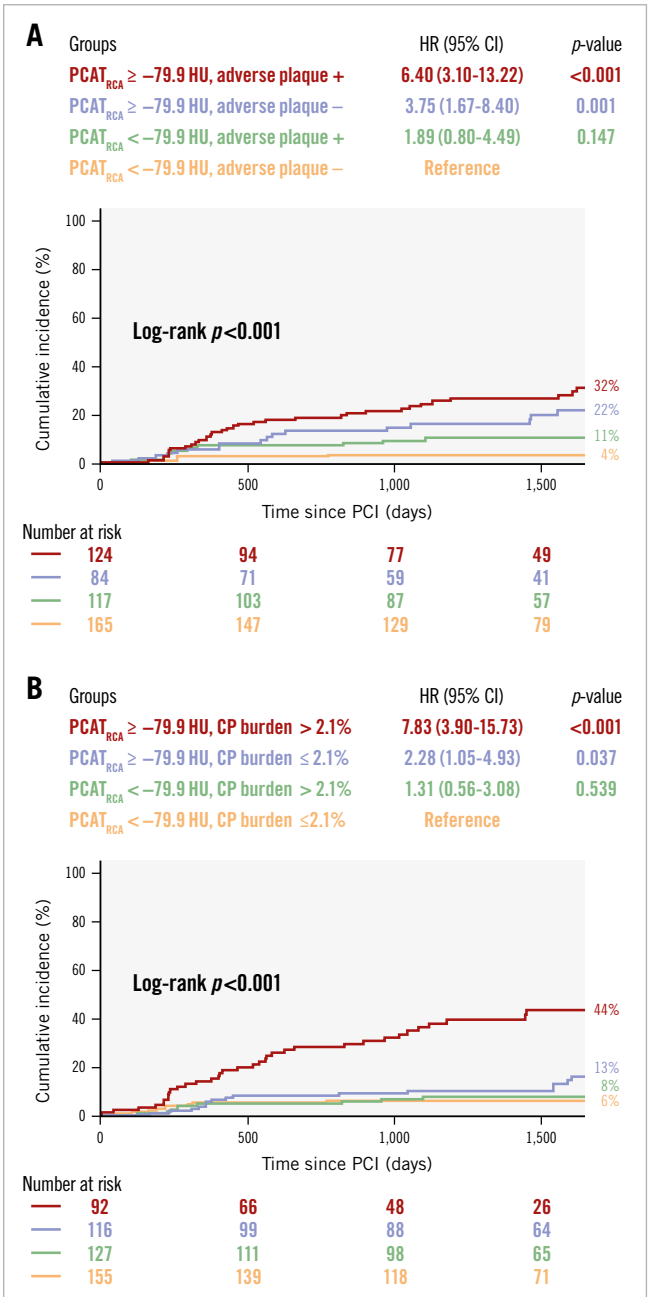


Figure 2. *Kaplan-Meier curves for PoCE in different patient subgroups. Kaplan-Meier curves show the cumulative incidence of PoCE in subgroups based on (A) $PCAT_{RCA}$ and adverse plaque and (B) $PCAT_{RCA}$ and CP burden. Patients with high $PCAT_{RCA}$ and adverse plaque or high CP burden have a significantly higher PoCE incidence compared to those with low $PCAT_{RCA}$ and no adverse plaque or low CP burden. CI: confidence interval; CP: calcified plaque; HR: hazard ratio; HU: Hounsfield unit; PCAT: pericoronary adipose tissue; PCI: percutaneous coronary intervention; PoCE: patient-oriented composite endpoint; RCA: right coronary artery*

discrimination improvement (IDI) values for the three models. Compared with model 1 (cardiovascular risk factors), model 2 (model 1 plus adverse plaque and CP burden) showed significantly higher discriminatory (c-index: 0.651 vs 0.725; p=0.010) and reclassification (NRI: 0.473; p<0.001; relative IDI: 0.044; p<0.001) abilities to identify patients with subsequent PoCE. Compared with model 2, model 3 (model 2 plus $PCAT_{RCA}$) showed significantly higher discriminatory (c-index: 0.725 vs 0.802; p=0.005) and reclassification (NRI: 0.632; p<0.001; relative IDI: 0.069; p<0.001) abilities.

FACTORS ASSOCIATED WITH POCE IN PATIENTS STRATIFIED BY HIGH AND LOW $PCAT_{RCA}$

Supplementary Table 5 summarises the results of univariable and multivariable Cox regression analyses examining patient characteristics and medications associated with PoCE in patients with high and low $PCAT_{RCA}$. In the high $PCAT_{RCA}$ group, the multivariable model showed that only non-statin use at discharge was independently associated with PoCE occurrence. Adjusted for patient characteristics (age, sex, smoking, and estimated glomerular filtration rate) and medications at discharge (beta blockers, renin-angiotensin system inhibitors, calcium channel blockers, and oral anticoagulants), the cumulative incidence of PoCE was 2.2 times lower in patients taking statins at discharge (22.7% vs 46.0%, HR 0.46, 95% CI: 0.24-0.88; p=0.018) **(Supplementary Figure 6A)**. Conversely, in the low $PCAT_{RCA}$ group, the multivariable model showed that neither statin nor other medication use was independently associated with PoCE after PCI. The cumulative incidence of PoCE did not significantly differ between patients taking or not taking statins at discharge (5.7% vs 6.9%, HR 0.94, 95% CI: 0.19-4.61; p=0.941) **(Supplementary Figure 6B)**.

RELATIONSHIP BETWEEN CCTA FINDINGS, TVR, AND TLR

The comparisons between the TVR and non-TVR groups are shown in **Supplementary Table 6**. $PCAT_{RCA}$, $PCAT_{Vessel}$, and CP burden were independently associated with TVR **(Supplementary Table 7)**. The area under the ROC curve (area under the curve [AUC]) values of $PCAT_{RCA}$, $PCAT_{Vessel}$, and CP burden for the identification of TVR were 0.711, 0.681, and 0.677, respectively, with no differences in diagnostic performance **(Supplementary Figure 7A)**.

Comparisons between the TLR and non-TLR groups are presented in **Supplementary Table 8**. $PCAT_{RCA}$, $PCAT_{Lesion}$, and CP burden were independently associated with TLR **(Supplementary Table 9)**. The AUC values of $PCAT_{RCA}$, $PCAT_{Lesion}$, and CP burden for identifying TLR were 0.720, 0.706, and 0.703, respectively, with no differences in diagnostic performance **(Supplementary Figure 7B)**.

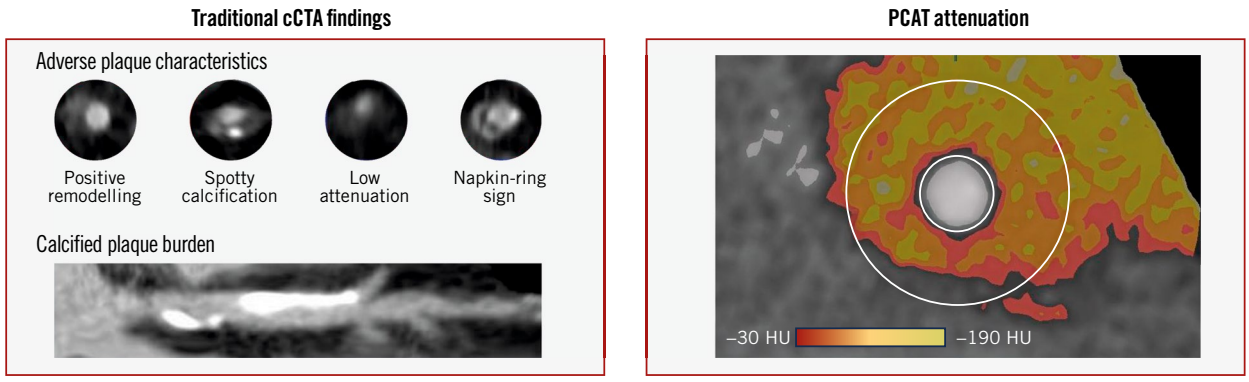
Discussion

To the best of our knowledge, this is the first study to investigate the relationship between PCAT attenuation measured on pre-PCI cCTA and subsequent adverse clinical outcomes in patients who underwent PCI using current-generation DES. The main findings can be summarised as follows: (1) patients who experienced post-PCI PoCE had a significantly higher level of vascular inflammation, as indicated by increased pre-PCI PCAT attenuation; (2) in addition to medications at discharge and cCTA findings such as higher LAP and CP burdens, increased pre-PCI PCAT attenuation was independently associated with PoCE occurrence, TVR, and TLR in patients undergoing PCI; (3)

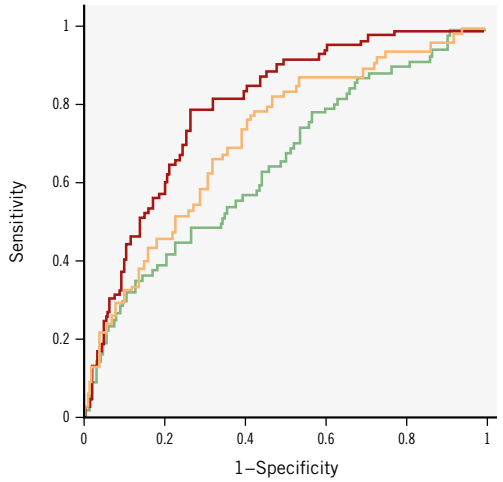
Discriminatory and reclassification abilities of predictive models for PoCE.

490 patients underwent cCTA before PCI with DES

A cCTA assessment before PCI



B Discriminatory and reclassification ability of predictive models for PoCE



Model 1: Cardiovascular risk factors
Model 2: model 1 + adverse plaque + CP burden
Model 3: model 2 + $PCAT_{RCA}$

Model	c-index	*p*-value	NRI	*p*-value	IDI	*p*-value
Model 1	0.651					
Model 2	0.725	vs model 1 0.010	0.473	vs model 1 <0.001	0.044	vs model 1 <0.001
Model 3	**0.802**	**vs model 2 0.005**	**0.632**	**vs model 2 <0.001**	**0.069**	**vs model 2 <0.001**

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A)The coronary computed tomography angiography (cCTA) assessment before percutaneous coronary intervention (PCI) included evaluation of traditional cCTA findings, adverse plaque characteristics and calcified plaque burden, and PCAT attenuation. B) Three analytical models were constructed: model 1, cardiovascular risk factors (green line); model 2, model 1+adverse plaque and CP burden (orange line); and model 3, model 2+$PCAT_{RCA}$ (red line). Adding PCAT attenuation to traditional cardiovascular risk factors and preprocedural cCTA findings, such as adverse plaque and CP burden, improves predictive abilities for identifying the patient-oriented composite endpoint (PoCE) after PCI. c-index: concordance statistics; CP: calcified plaque; DES: drug-eluting stent; HU: Hounsfield unit; IDI: relative integrated discrimination improvement; NRI: category-free net reclassification index; PCAT: pericoronary adipose tissue; RCA: right coronary artery

adding PCAT attenuation to traditional cardiovascular risk factors and cCTA findings improved the ability to identify post-PCI PoCE; (4) in the high $PCAT_{RCA}$ group, but not in the low $PCAT_{RCA}$ group, non-statin use at discharge was independently associated with PoCE occurrence; and (5) increased $PCAT_{Vessel}$ and $PCAT_{Lesion}$ were independently associated with TVR and TLR occurrence, respectively, but the predictive accuracy of these measurements was similar to that of $PCAT_{RCA}$. This study is the first real-world cohort with a long-term follow-up that clarifies the clinical relevance of PCAT attenuation measured on pre-PCI cCTA in identifying patients undergoing PCI using current-generation DES with subsequent PoCE.

RELATIONSHIP BETWEEN PRE-PCI PCAT ASSESSMENT AND POST-PCI CLINICAL OUTCOMES

Currently, PCI is the gold-standard treatment for patients with CAD. While current-generation DES have improved long-term

outcomes by reducing TLR and stent thrombosis, adverse events still occur. Coronary inflammation has emerged as a key residual risk factor for cardiovascular events[3] and a potential target for preventive therapy. In a previous randomised study comparing eicosapentaenoic acid (EPA) plus statin with statin-only therapy, we demonstrated that EPA stabilises thin-cap fibroatheromas better than statin-only therapy through greater suppression of vascular inflammation, assessed by hs-CRP and pentraxin-3[14]. Furthermore, the CANTOS placebo-controlled, randomised study demonstrated that canakinumab, a novel interleukin-1β inhibitor, significantly reduces the risk of recurrent cardiovascular events in patients with a history of MI and an elevated baseline hs-CRP[4]. These data highlight the potential utility of coronary inflammation assessments in the management of patients with CAD undergoing PCI.

Recently cCTA has emerged as a non-invasive method to evaluate PCAT attenuation, which potentially represents the inflammatory status of adjacent coronary arteries[9]. The ORFAN trial analysed 3,393 patients undergoing cCTA and showed that an increased fat attenuation index (FAI)-Score, which is a coronary inflammation marker like PCAT attenuation, in all three coronary arteries additively increased the risk of cardiac mortality or MACE[15]. In a recent *post hoc* analysis of the CRISP-CT study, Oikonomou et al demonstrated that the FAI was a strong predictor of all-cause and cardiac mortality over established cardiovascular risk factors and cCTA findings in 3,912 patients undergoing cCTA[8]. The FAI is calculated based on PCAT attenuation. Similarly to the FAI, crude PCAT attenuation has been validated in prior studies through histological and gene expression analyses[8,9]. We hypothesised that there might be a significant association between pre-PCI PCAT attenuation and post-PCI clinical outcomes and that clarifying this association would contribute to identifying patients who would benefit from therapies targeting plaque inflammation as secondary prevention of CAD.

In this study, using $PCAT_{RCA}$ as a patient-level coronary inflammation marker based on prior evidence[16,17], we found that increased $PCAT_{RCA}$ was independently associated with PoCE occurrence after PCI using current-generation DES. Specifically, the incidence of PoCE was 3.9 times higher in patients with high $PCAT_{RCA}$ than in those with low $PCAT_{RCA}$. Additionally, high $PCAT_{RCA}$ was significantly associated with adverse patient-level outcomes such as MACE, all-cause death, cardiovascular death, any MI, any revascularisation, and heart failure hospitalisation, as well as adverse vessel- and lesion-level outcomes such as TVF, TLF, TVR, and TLR. Regarding adverse clinical outcomes, 51.9% of patients with PoCE (40/77) required revascularisation due to significant non-target lesion progression. Although the mechanisms underlying high PCAT attenuation and subsequent adverse clinical outcomes remain uncertain, we speculate that the enhanced pan-coronary inflammatory status, as indicated by high $PCAT_{RCA}$, contributes to progressive plaque development and instability not only in target lesions but also in non-target lesions. Goeller et al analysed 111 stable patients who underwent sequential cCTA and demonstrated that baseline PCAT attenuation was independently associated with NCP progression, which was not suppressed by low-density lipid cholesterol reduction during follow-up[16].

In the present study, baseline hs-CRP levels were lower than in previous reports[18,19]. The median preprocedural hs-CRP level was 0.80 mg/L. According to a previous study, a large-scale prospective PCI registry in the USA in which 53% of patients had stable CAD, high inflammatory status is defined as baseline hs-CRP >2 mg/L, with 53% of that study's CAD patients meeting this criterion[20]. However, only 23.8% of our cohort met this high hs-CRP threshold. Thus, our lower baseline hs-CRP cohort may explain the lack of difference in hs-CRP levels between the PoCE and non-PoCE groups. However, even among the current cohort with relatively lower hs-CRP levels, PCAT attenuation demonstrated an improvement in the prediction of PoCE features, suggesting it may serve as a more specific and targeted biomarker for risk stratification and predicting clinical outcomes.

Our subgroup analysis showed that non-statin use was independently associated with PoCE in patients with high $PCAT_{RCA}$, but not in those with low $PCAT_{RCA}$. This suggests that statins may be more effective in patients with higher coronary inflammation, and measuring $PCAT_{RCA}$ could help identify those who would benefit most from anti-inflammatory treatment. This should be confirmed by further studies with larger sample sizes.

INCREMENTAL VALUE OF INFLAMMATION TO ADVERSE AND CALCIFIED PLAQUES

Previous studies have shown the prognostic value of adverse plaque features and coronary calcification via cCTA in patients who had undergone PCI[21,22]. Our study supports this, finding that adverse plaque and CP burden were independently associated with post-PCI PoCE. Combining cardiovascular risk factors with adverse plaque and CP burden improved prediction, but the discriminative power (c-index 0.725) remained insufficient for clinical use. We also found that $PCAT_{RCA}$ independently predicted PoCE and added incremental value over models with traditional risk factors and cCTA findings. This suggests that combining PCAT attenuation with cCTA findings may improve PoCE risk stratification. Oikonomou et al demonstrated that adverse plaque features with low inflammation, assessed using PCAT attenuation, were not associated with increased cardiovascular risk, whereas in the presence of inflammation, adverse plaque features identified a particularly high-risk group of patients[23]. These findings support our hypothesis.

Previous studies have shown that coronary inflammation leads to microcalcification, which accumulates into a large mass and becomes a spotty calcification that is more likely to be associated with plaque rupture, while reduced inflammation results in macrocalcification that stabilises plaques and limits inflammation[24]. Therefore, assessing coronary calcification alone is not sufficient to identify high-risk plaques, highlighting the importance of assessing intrinsic coronary artery inflammation. Considering these findings, the assessment of adverse or calcified plaques alone is insufficient for precise risk assessment of the target plaque, as most plaques identified at a single timepoint assessment heal naturally and do not always lead to clinical events. Indeed, in our study, patients with adverse plaque and high

CP burden had a higher PoCE incidence if they also had high $PCAT_{RCA}$ (32% and 44%, respectively) compared to those with low $PCAT_{RCA}$ (11% and 8%, respectively). Therefore, adverse or calcified plaques alone do not identify high-risk patients. By incorporating $PCAT_{RCA}$, higher-risk subgroups were identified more effectively, suggesting that measuring PCAT attenuation enhances risk stratification for post-PCI outcomes.

RELATIONSHIP BETWEEN VESSEL- OR LESION-LEVEL PCAT ATTENUATION AND TVR OR TLR

In this study, we examined the relationship between target vessel- or lesion-level coronary inflammation and clinical events such as TVR and TLR. Multivariable analyses showed that increased $PCAT_{Vessel}$ and $PCAT_{Lesion}$ were independently associated with TVR and TLR. Surprisingly, despite the hypothesis that $PCAT_{Vessel}$ and $PCAT_{Lesion}$ would reflect more specific local inflammation, their predictive abilities were similar to those of $PCAT_{RCA}$.

Currently, $PCAT_{RCA}$ is regarded as a global coronary inflammation biomarker, valuable for predicting cardiac mortality. Goeller et al found that longitudinal changes in $PCAT_{RCA}$ were associated with changes in NCP burden across the entire coronary tree[16]. Lin et al studied cCTA in patients with MI, stable CAD, and no CAD, and showed that $PCAT_{RCA}$ was progressively higher in patients with MI, then stable CAD, then no CAD, and could therefore help differentiate between CAD stages. Notably, these findings were unaffected by lesion distribution (RCA vs non-RCA), suggesting that $PCAT_{RCA}$ reflects overall coronary rather than just lesion-specific inflammation[17]. In general, the proximal RCA has the highest volume of surrounding adipose tissue and lacks confounding non-fatty structures (side branches, coronary veins, or myocardium). Additionally, the luminal diameter is stable. Thus, measuring $PCAT_{RCA}$ is the most standardised and reproducible patient-level approach to evaluate pan-coronary inflammation[8]. In light of these findings, the diagnostic performance of $PCAT_{RCA}$ for predicting TVR and TLR is comparable to that of $PCAT_{Vessel}$ and $PCAT_{Lesion}$, making it a comprehensive indicator of coronary artery inflammation and future adverse clinical events in patients undergoing PCI.

Limitations

First, the inclusion and exclusion criteria led to differences in baseline characteristics, including higher clinical risk profiles among excluded patients **(Supplementary Table 10)**, which may limit the generalisability of the findings. The levels of hs-CRP were relatively lower in the current study than in previous reports. Thus, the retrospective design introduces potential selection bias. Second, a relatively large number of patients (80/702) were excluded owing to insufficient CT image quality. Third, although the PoCE is a composite outcome whose associated factors might differ for each outcome, we might not have adequately assessed each clinical outcome due to the limited sample size. Fourth, we used crude PCAT attenuation, derived directly from CT values, instead of the artificial intelligence-adjusted FAI metric. While crude PCAT attenuation may be influenced by body composition and CT scanner differences, no significant scanner-related variability was observed in our cohort **(Supplementary Table 11)**. PCAT attenuation has been widely validated for assessing coronary inflammation in patients with high-risk lesions or major events, supporting its reliability as a measurement tool[16,17]. Finally, we did not directly measure coronary inflammation; however, recent studies have shown that PCAT attenuation is associated with biopsy-proven vascular inflammation[9]. This supports the potential of PCAT attenuation as a surrogate marker for coronary inflammation. Future studies are needed to explore whether the residual cardiovascular risk detected by PCAT attenuation can be reduced using targeted anti-inflammatory interventions.

Conclusions

This study demonstrates that PCAT attenuation is an independent factor associated with PoCE after PCI using current-generation DES. Adding PCAT attenuation to traditional cCTA findings and cardiovascular risk factors enables better discrimination of patients experiencing PoCE after PCI with current-generation DES.

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Conflict of interest statement

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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Supplementary data

Supplementary Appendix 1. Participating institutions and collaborators, definitions, supplementary methods, outcome, statistical analysis, and external cohort.

Supplementary Table 1. cCTA findings at the target lesion and non-target lesion level.

Supplementary Table 2. cCTA findings in stable CAD patients.

Supplementary Table 3. Cox regression analysis of factors associated with PoCE at the target lesion and non-target lesion level.

Supplementary Table 4. Patient characteristics and $PCAT_{RCA}$ in the internal and external cohorts.

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Supplementary Table 6. cCTA findings between TVR and non-TVR.

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Supplementary Table 10. Baseline patient characteristics in the inclusion and exclusion cohorts.

Supplementary Table 11. Comparison of PCAT attenuation across institutions.

Supplementary Figure 1. Study flowchart.

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Supplementary Figure 3. Kaplan-Meier curves for PoCE by $PCAT_{RCA}$.

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Supplementary Figure 5. Kaplan-Meier curves for PoCE by LAP and CP burden.

Supplementary Figure 6. Kaplan-Meier curves for PoCE, stratified by statin use and $PCAT_{RCA}$.

Supplementary Figure 7. Comparison of diagnostic performance of AUC for TVR and TLR.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00971

Supplementary data

Supplementary Appendix 1. Participating institutions and collaborators, definitions, supplementary methods, outcome, statistical analysis, and external cohort.

Participating institutions and investigators

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Definitions

Inclusion/exclusion criteria	**Definition**
ST-elevation myocardial infarction (STEMI)	New ST-segment elevation at the J point in two contiguous leads with the cut-points: ≥ 0.1 mV in all leads other than leads V1–V3 where the following cut-points apply: ≥ 0.2 mV
Clinical characteristics	**Definition**
Acute coronary syndrome	Acute ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina
Chronic kidney disease	Estimated glomerular filtration rate <30 ml/min/1.73 m^2 or serum creatinine level >1.5 mg/dl
Atherectomy	Rotational atherectomy and orbital atherectomy
cCTA (lesion analysis)	**Definition**
Target lesion	The lesions that underwent PCI were deemed target lesions
Percent diameter stenosis	(Reference vessel diameter – minimum lumen diameter) x 100 / reference vessel diameter
Lesion length	Length between proximal reference vessel diameter and distal reference vessel diameter
Minimal lumen area	Lumen area measured at the site of maximal stenosis using axial images
cCTA (adverse plaque characteristics [APC])	**Definition**
Adverse plaque	The number of APCs was calculated per lesion, and adverse plaques were defined as those with the presence with two or more APCs. In cases with multiple lesions, lesions with the highest numbers of APCs were included for the analysis
Positive remodelling	The external elastic membrane (EEM) cross-sectional area (CSA) of the target lesion divided by the average of the EEM CSAs of the proximal and distal references, with an index >1.1 representing positive remodelling[12,25]
Low attenuation plaque	A plaque containing any voxel <30 HU[12,25]

Spotty calcification	A calcified plaque comprising <90 degrees of the vessel circumference and <3 mm in length[12,25]
Napkin ring sign	A plaque core with low attenuation surrounded by a rim-like area of higher attenuation[12,25]
cCTA (plaque analysis)	**Definition**
Plaque volume	Plaque volumes (in mm^3) were measured for the following plaque subtypes; total plaque, low-attenuation plaque (defined by an attenuation of <30 HU), non-calcified plaque (defined by an attenuation of ≦350 HU) and calcified plaque (defined by an attenuation of >350 HU)[3]
Plaque burden	Plaque burden (as a percentage) was calculated for each of the total plaque, low-attenuation plaque, non-calcified plaque, and calcified plaque × 100%/vessel volume in the region of interest[3]
cCTA (calcium score)	**Definition**
Coronary artery calcium score	Quantified by the Agatston method on non-contrast cardiac CT scans
cCTA (PCAT analysis)	**Definition**
$PCAT_{RCA}$	Measurement around proximal 40 mm segments of right coronary artery (RCA). To avoid the effects of the aortic wall, we excluded the most proximal 10 mm of the RCA and analysed the proximal 10-50 mm of the vessel[8,9] . . . . . . Note: PCAT attenuation measurements at patient level was represented by $PCAT_{RCA}$
$PCAT_{Vessel}$	Measurement around proximal 40 mm segments of target major coronary arteries (right coronary artery [RCA], left anterior descending artery [LAD], and left circumflex artery [LCX]). To avoid the effects of the aortic wall, we excluded the most proximal 10 mm of the RCA and analysed the proximal 10-50 mm of the vessel. In the LAD and LCX, we analysed the proximal 40 mm of each vessel[8,9]
$PCAT_{Lesion}$	Measurement around target lesions, defined as proximal 15 mm segments and distal 15 mm segments of the most severely stenotic portion[26]
Clinical endpoints	**Definition**
Patient-oriented composite endpoint	Composite of cardiac death, non-fatal myocardial infarction, and any revascularization
Major adverse cardiac event	Composite of all-cause death, myocardial infarction, target lesion revascularization, any revascularization, stroke, and heart failure hospitalization
Target vessel failure	Composite of cardiac death, target-vessel related myocardial infarction, and ischemia-driven target vessel revascularization
Target lesion failure	Composite of cardiac death, target-lesion related myocardial infarction, and ischemia-driven target lesion revascularization
Cardiovascular death	Cardiac death according to ARC definition[13] Any death due to proximate cardiac cause (e.g. myocardial infarction, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, all procedure related deaths including those related to concomitant treatment

	. . . . . . Note: Unexpected death even in patients with coexisting and potentially fatal non-cardiac disease (e.g. cancer, infection) should be classified as cardiac unless the history related to the non-cardiac diagnosis suggests death was imminent
Myocardial infarction	Myocardial infarction includes acute myocardial infarction and prior myocardial infarction (1) Acute myocardial infarction Symptom of ischemia with serum creatinine kinase MB fraction ≥2 times upper limit of normal or serum troponin ≥ the 99th percentile (2) Prior myocardial infarction Any one of the following criteria meets the diagnosis for prior myocardial infarction (i) Abnormal Q wave in any two leads of a contiguous lead (grouping I, aVL; V1-V6; II, III, aVF) without symptom of ischemia within 1 month (ii) Imaging evidence of a region of loss of variable myocardium that thinned and fails to contract without symptom of ischemia within 1 month . . . . . . Electrocardiographic detection of myocardial infarction: Q wave (1) Q wave myocardial infarction Abnormal Q wave in any two leads of a contiguous lead (grouping I, aVL; V1-6; II, III, aVF) with or without serum creatinine kinase MB fraction ≥2 times upper limit of normal or serum troponin ≥ the 99th percentile (2) Non-Q wave myocardial infarction Myocardial infarction other than Q wave myocardial infarction . . . . . . Electrocardiographic detection of myocardial infarction: ST-segment (1) ST-segment elevation myocardial infarction New ST elevation at the J point in two contiguous leads with the cut-points: ≥0.1 mV in all leads other that leads V1–V3 where the following cut-points apply: ≥0.2 mV (2) Non-ST-segment elevation myocardial infarction Myocardial infarction other than ST-segment elevation myocardial infarction
Any revascularization	Repeat PCI or bypass graft placement after the index PCI . . . . . . Note: Any revascularization event was defined as an unplanned or late revascularization procedure performed due to the new onset of symptoms after the initial PCI. This does not include planned, staged PCI for a stenosis in another part of the vessel treated at the index PCI.

Ischemia-driven target vessel revascularization	Unplanned repeat PCI or bypass graft placement for a stenosis in another part of the vessel treated at the index PCI. . . . . . . Note: Target vessel revascularization is considered ischemia-driven if the lesion in the vessel treated at the index PCI was >70% diameter stenosis by quantitative coronary angiography analysis at the independent angiography core laboratory or for diameter stenosis between ≥50% and ≤70% if the event assessment committee determined there was objective evidence of recurrent angina pectoris or objective signs of ischemia in any diagnostic test. These events were driven by the new onset of symptoms indicating ischemia. Target vessel revascularization includes target lesion revascularization. Target vessel revascularization does not include planned, staged PCI for a stenosis in another part of the vessel treated at the index PCI
Ischemia-driven target lesion revascularization	Repeat PCI or bypass graft placement for restenosis or other complications at the lesion treated during index PCI, or occurring within 5 mm of the PCI site . . . . . . Note: Target lesion revascularization is considered ischemia-driven if the target lesion was >70% diameter stenosis by quantitative coronary angiography analysis at the independent angiography core laboratory or for diameter stenosis between ≥50% and ≤70% if the event assessment committee determined there was objective evidence of recurrent angina pectoris or objective signs of ischemia in any diagnostic test. These events were driven by the new onset of symptoms indicating ischemia
Heart failure hospitalization	Heart failure hospitalization according to HF-ARC definition[27] Admission for ≥24 hours with a primary diagnosis of heart failure, with ≥1 symptom and ≥2 physical examination, laboratory, or invasive findings of heart failure, and receives a heart failure-specific treatment
Stroke	Ischemic or hemorrhagic stroke requiring hospitalization with symptoms lasting >24 hours . . . . . . Note: Transient ischemic attack (TIA) (defined as a neurological event with the signs and symptoms of a stroke, but which go away within a short period of time [<24 hours]) is excluded

ARC = Australian Resuscitation Council; cCTA = coronary computed tomography angiography; HF-ARC = Heart Failure Academic Research Consortium; HU = Hounsfield unit; PCI = percutaneous coronary intervention.

Supplementary Methods

1. Study design

We retrospectively studied the consecutive patients who underwent percutaneous coronary intervention (PCI) using current-generation drug-eluting stents (DES) and cCTA within 120 days prior to the procedure. The cCTA in these patients was performed according to current guideline-directed clinical practices.[10] This current analysis included patients implanted with 5 different types of current-generation DES: cobalt-chromium durable polymer everolimus-eluting stents (CoCr-EES) (Xience Xpedition, Alpine, or Skypoint, Abbott Vascular), durable polymer Resolute-zotarolimus-eluting stents (Re-ZES) (Resolute Onyx, Medtronic Inc.), ultrathin strut biodegradable-polymer platinum-chromium EES (PtCr-EES) (Synergy, Boston Scientific), ultrathin strut biodegradable-polymer cobalt-chromium sirolimus-eluting stents (UT-SES) (Orsiro, Biotronik), and bioresorbable polymer sirolimus-eluting stents (BP-SES) (Ultimaster, Terumo Corporation).

2. cCTA protocol

cCTA scans were performed in a 320-slice scanner (Aquilion ONE Vision, Toshiba Medical Systems, Tokyo, Japan) (n=199, 40.6%), a 64-slice (LightSpeed VCT, GE Healthcare, Waukesha, WI, USA) (n=165, 33.7%), a 64-slice scanner (Ingenuity Core 64, Philips, Amsterdam, Netherlands) (n=79, 16.1%), and a 128-slice scanner (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany) (n=47, 9.6%). cCTA images were obtained in accordance with the Society of Cardiovascular Computed Tomography guidelines on cCTA.[10] Prior to scanning, 0.3 mg sublingual nitroglycerine spray was administered to all patients and, if necessary, oral beta-blockers was also administered aiming for a heart rate of <65 beats/min. cCTA was performed using retrospective ECG-gated spiral acquisition. The scan parameters included 120 kVp tube voltage, and 260–1,150 mA tube current (adjusting mA based on

patient's body size). All images were reconstructed using thin slices (0.5–0.75 mm) and medium smooth reconstruction filters in different phases.

3. cCTA post-processing and image analysis

The reconstructed images were transferred to a processing workstation (SYNAPSE VINCENT, Fujifilm, Tokyo, Japan). All scans were reviewed for their quality. Scans were excluded from the study if they exhibited severe artifacts, missing slices, coronary abnormalities, or were performed at a tube voltage other than 120 kVp, where PCAT has been validated.[9] The analysis of cCTA images was performed by two independent investigators who were blinded to the patients' clinical characteristics, except for information regarding PCI target lesion. The centreline and vessel contours were automatically detected and manually corrected if necessary. Coronary segments with a diameter 2.0 mm were included in the analysis. The lesions that underwent PCI were deemed target lesions. In cases with multiple lesions, the target lesion was defined as the most severe stenotic lesion. Non-target lesions were defined as the other (non-PCI) lesions with percent diameter stenosis (%DS) >30% on cCTA. The reference and minimal lumen diameters, lesion length, minimal lumen area, and %DS were measured using axial images and multiplanar reconstruction images.

4. Adverse plaque characteristics on cCTA

The presence of adverse plaque characteristics (APCs) on cCTA was defined as previous described. Remodelling index was defined as the external elastic membrane (EEM) cross-sectional area (CSA) of the target lesion divided by the average of the EEM CSAs of the proximal and distal references, with an index >1.1 representing positive remodelling. Low attenuation plaque was defined as a plaque containing any voxel <30 Hounsfield unit (HU). Spotty calcification was characterized by a calcified plaque comprising <90 degrees of the

vessel circumference and <3 mm in length. Napkin ring sign was defined by a plaque core with low attenuation surrounded by a rim-like area of higher attenuation.[12] In cases with multiple lesions, lesions with the highest number of APCs, including both target and non-target lesions, were included for patient-level analysis. The number of APCs per lesion was calculated, and adverse plaques were defined as those with two or more APCs. If there were multiple plaques with the same number of plaque characteristics, priority was determined in the following order: plaques with both positive remodelling and low-attenuated plaques, plaques with either positive remodelling or low-attenuated plaques, and plaques with none of the three. And if only one of positive remodelling or low-attenuated plaque was present in the plaque, the plaque with low-attenuated plaque was selected.

5. Plaque analysis on cCTA

For each patient, plaque volumes (in mm^3) were quantified for the following plaque subtypes in the entire coronary artery, target lesions, and non-target lesions: total plaque, low-attenuation plaque (LAP), non-calcified plaque (NCP), and calcified plaque (CP). Plaque composition was categorized based on HU ranges, with LAP defined as plaques <30 HU, NCP as plaques ≦350 HU, and CP as plaques >350 HU. Plaque burden (as a percentage) for each plaque subtype within the entire coronary artery, target lesions, and non-target lesions was calculated as 100% × (plaque volume/vessel volume) in the region of interest. For the analysis of the entire coronary artery, plaque volume and vessel volume were calculated as the volume of all coronary segments with a diameter of >2.0 mm. Vessel volume was measured regardless of whether they contain plaque or not.[3,28] When there were multiple non-target lesions, the average value was used for analysis.

6. Coronary artery calcium score (CACS) on cCTA

Coronary artery calcium score (CACS) was quantified by the Agatston method on non-contrast cardiac CT scans using available software (SYNAPSE VINCENT, Fujifilm, Tokyo, Japan), in those patients with an indication for CACS assessment.[29]

7. PCAT analysis on cCTA

To measure PCAT attenuation, 3-dimensional layers within radial distance from the outer coronary wall equal in thickness to the average diameter of the vessel were constructed automatically using a dedicated cCTA analysis software (SYNAPSE VINCENT, Fujifilm, Tokyo, Japan). Within the predefined volume of interest, voxels with tissue attenuation ranging from -190 up to -30 HU were considered as adipose tissue and PCAT attenuation was defined as the mean attenuation within such contamination-free volumes of interest. These measurements were performed in each patient around proximal right coronary artery ($PCAT_{RCA}$), proximal target vessels ($PCAT_{Vessel}$), and the specific target lesions ($PCAT_{Lesion}$). $PCAT_{Vessel}$ was measured proximal 40 mm segments of target major coronary arteries (right coronary artery [RCA], left anterior descending artery [LAD], and left circumflex artery [LCX]). To avoid the effects of the aortic wall, we excluded the most proximal 10 mm of the RCA and analysed the proximal 10-50 mm of the vessel. In the LAD and LCX, we analysed the proximal 40 mm of each vessel. $PCAT_{Lesion}$ was measured around target lesions, defined as proximal 15 mm segments and distal 15 mm segments of the most severely stenotic portion.[26] PCAT attenuation measurements at patient level was represented by $PCAT_{RCA}$.[8,9] We evaluated the inter- and intra-observer variability of PCAT attenuation across 300 vessels, including the proximal RCA, LAD, and LCX, in each of 100 patients randomly selected from the current cohort. Inter-observer variability was assessed between two independent observers, and intra-observer variability was determined by a repeat analysis conducted by one observer after an interval of at least one month.

Outcome

The primary outcome of the study was patient-oriented composite endpoint (PoCE), define as composite of cardiovascular death, non-fatal myocardial infarction (MI), any revascularization, and stroke. After the primary outcome analysis was performed, based on ARC-2 definition,[13] we further investigated the association between PCAT attenuation and other clinical outcomes such as major adverse cardiovascular events (MACE), target vessel failure (TVF), target lesion failure (TLF), all-cause death, cardiovascular death, any MI, non-fatal MI, any revascularization, target vessel revascularization (TVR), TLR, heart failure hospitalization, stroke, and peri-procedural myocardial infarction (PMI). We defined PMI as a 5-fold increase in high-sensitivity cardiac troponin I (cTnI) levels above the upper limit of the 99th percentile (URL) within 48 hours of PCI in patients with normal baseline cTnI levels. [30] Clinical outcomes were ascertained using hospital records and follow-up data from outpatient visits. There were 77 patients (15.4%) with PoCE, 100 patients (20.4%) with MACE, 31 patients (6.3%) with TVF, 22 patients (4.4%) with TLF. In details, 26 patients (5.3%) with all-cause death, 10 patients (2.0%) with cardiovascular death, 9 patients (1.8%) with any MI, 8 patients (1.6%) with non-fatal MI, 52 patients (10.6%) with any revascularization, 21 patients (4.3%) with TVR, 12 patients (2.4%) with TLR, 20 patients (4.1%) with heart failure hospitalization, 17 patients (3.5%) with stroke. Of the 205 patients who had sufficient data for PMI evaluation, 39.0% of the patients (80 of 205 patients) had PMI.

Statistical analysis

Continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. The mean ± standard deviation was presented when variables were normally distributed, and the median (interquartile range, IQR) when they were not. Categorical variables are presented

as numbers and percentages. Continuous variables were compared using the Student's t-test or Mann–Whitney U test, as appropriate. The Pearson's chi-squared test or Fisher's exact test was used to compare categorical variables. Plaque burdens were log transformed for analysis. The reliability of PCAT attenuation measurements was analyzed using the intraclass correlation coefficient.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the optimal cutoff values of PCAT attenuation and CP burdens for predicting PoCE after PCI. To validate the cutoff value of $PCAT_{RCA}$, we evaluated it in an external cohort consisting of patients treated at the same institution during January to December in 2021. Details regarding the external cohort were provided in the Supplementary material The Kaplan–Meier analysis was used to calculate the cumulative incidence of PoCE; the log-rank test was used to compare between-group differences. Cox regression analysis was performed to identify independent predictors of clinical outcomes. Three prediction models for PoCE were constructed to determine the incremental discriminatory and reclassification performance of PCAT attenuation. As a baseline, clinical model 1 was derived from traditional cardiovascular risk factors (age; sex; comorbidities, including hypertension, diabetes mellitus, dyslipidaemia, and multivessel disease; and smoking) and other baseline characteristics that are considered important factors associated with PoCE (left ventricular ejection fraction and estimated glomerular filtration rate). Clinical model 2 was constructed using model 1 and traditional cCTA findings (adverse plaque and CP burdens). Clinical model 3 was derived from model 2 and $PCAT_{RCA}$. The discriminatory ability was assessed using Harrell's concordance statistic (c-index), and the reclassification performance of each model was compared using the relative integrated discrimination improvement and category-free net reclassification index. Cox regression analysis was performed to examine the factors associated with PoCE in patients categorized into high and low $PCAT_{RCA}$ determined by the cutoff values identified through ROC analysis. All statistical

analyses were performed using the Microsoft R Open software version 4.3.1 (R Development Core Team, Vienna, Austria); $p<0.05$ was considered statistically significant.

External cohort

We determined the optimal cutoff value of $PCAT_{RCA}$ for predicting PoCE after PCI using ROC curve analysis. To externally validate this cutoff value, an external cohort of patients from the same institution was identified. These patients met the same inclusion and exclusion criteria as the current study. This external cohort consisted of 74 patients from the year 2021, with a median follow-up of 900 days (IQR: 730–1,090). During the follow-up period, 8 patients (10.8%) experienced PoCE, including 3 cardiovascular deaths, 1 non-fatal MI, 3 revascularizations, and 1 stroke.

When comparing patient characteristics and $PCAT_{RCA}$ between the internal cohort and the external cohort, no statistically significant differences were observed **(Supplementary Table 4)**. Furthermore, PoCE incidence was 4.2-times higher in patients with high $PCAT_{RCA}$ (≥-79.9 HU: n=22) than in those with low $PCAT_{RCA}$ (<-79.9 HU: n=52; 23.8% vs. 8.1%, hazard ratio [HR]: 4.22, 95% confidence interval: 1.01–17.72, p=0.032; **Supplementary Figure 4**).

Supplementary Table 1. cCTA findings at the target lesion and non-target lesion level.

Variables	All patients (n=490)	PoCE (n=77)	non-PoCE (n=413)	p value
PCI target lesion level analysis				
Quantitative cCTA analysis				
Diameter stenosis, %	51.6 (43.9, 59.9)	53.3 (44.2, 58.6)	52.5 (43.9, 60.3)	0.841
Lesion length, mm	24.0 (18.0, 34.0)	22.0 (12.0, 28.0)	26.0 (15.0, 38.0)	0.175
MLA, mm^2	2.13 (1.35, 2.71)	2.30 (1.33, 3.07)	1.98 (1.36, 2.67)	0.109
Total plaque burden, %	51.8 (44.0, 59.8)	52.4 (43.3, 61.0)	51.6 (44.1, 59.7)	0.914
LAP burden, %	9.66 (6.21, 14.65)	9.02 (6.05, 12.86)	9.75 (6.37, 15.05)	0.143
NCP burden, %	47.3 (36.5, 58.4)	46.5 (35.7, 55.6)	47.3 (36.9, 58.5)	0.540
CP burden, %	1.78 (0.06, 7.26)	3.14 (0.51, 9.11)	1.54 (0.04, 6.62)	0.055
Qualitative cCTA findings				
Positive remodelling, n (%)	182 (37.1%)	31 (40.3%)	151 (36.6%)	0.608
Low attenuation plaque, n (%)	146 (29.9%)	22 (28.6%)	124 (30.1%)	0.892
Spotty calcification, n (%)	68 (13.9%)	13 (16.9%)	55 (13.3%)	0.472
Napkin ring sign, n (%)	48 (9.8%)	9 (11.7%)	39 (9.4%)	0.533
Adverse plaque, n (%)	139 (28.4%)	28 (36.4%)	111 (26.9%)	0.099
Non-target lesion level analysis				
Quantitative cCTA analysis				
Total plaque burden, %	39.1 (33.2, 44.3)	44.1 (39.7, 48.9)	38.1 (32.3, 42.9)	<0.001
LAP burden, %	6.05 (3.55, 8.09)	6.58 (4.21, 8.80)	5.94 (3.52, 7.93)	0.026
NCP burden, %	35.8 (29.8, 40.9)	39.9 (34.6, 44.7)	34.7 (29.6, 40.5)	<0.001
CP burden, %	1.25 (0.29, 3.70)	2.53 (0.87, 5.49)	1.10 (0.23, 3.51)	<0.001
Qualitative cCTA findings				
Positive remodelling, n (%)	146 (29.8%)	25 (32.5%)	121 (29.3%)	0.589
Low attenuation plaque, n (%)	127 (25.9%)	24 (31.2%)	103 (24.9%)	0.259
Spotty calcification, n (%)	93 (19.0%)	23 (29.9%)	70 (16.9%)	0.011
Napkin ring sign, n (%)	54 (11.0%)	15 (19.5%)	39 (9.4%)	0.016
Adverse plaque, n (%)	161 (32.9%)	34 (44.2%)	127 (30.8%)	0.025

PCAT attenuation analysis				
$PCAT_{RCA}$, HU	-81.5 ± 8.1	-76.3 ± 6.4	-82.5 ± 8.1	<0.001
$PCAT_{Vessel}$, HU	-81.1 ± 8.1	-76.7 ± 7.5	-82.0 ± 7.8	<0.001
$PCAT_{Lesion}$, HU	-81.0 ± 8.9	-76.5 ± 7.9	-81.8 ± 8.9	<0.001

Values are expressed as mean ± standard deviation, median (25th, 75th percentiles) or n (%).
cCTA = coronary computed tomography angiography; CP = calcified plaque; HU = Hounsfield unit; LAP = low-attenuation plaque; MLA = minimum lumen area; NCP = non-calcified plaque; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint; RCA = right coronary artery

Supplementary Table 2. cCTA findings in stable CAD patients.

Variables	All patients (n=363)	PoCE (n=60)	non-PoCE (n=303)	p value
PCI target lesion level analysis				
Quantitative cCTA analysis				
Diameter stenosis, %	53.0 (42.5, 60.3)	53.6 (45.5, 58.8)	52.8 (41.9, 60.4)	0.717
Lesion length, mm	26.0 (18.0, 38.0)	28.0 (15.0, 38.0)	23.5 (12.0, 28.0)	0.080
MLA, mm^2	1.95 (1.33, 2.70)	2.07 (1.27, 2.76)	1.95 (1.35, 2.70)	0.518
Total plaque burden, %	49.9 (42.7, 58.9)	51.0 (42.2, 57.0)	49.8 (43.2, 58.9)	0.691
LAP burden, %	9.26 (6.11, 14.19)	8.79 (5.50, 12.71)	9.33 (6.15, 14.41)	0.200
NCP burden, %	45.3 (34.1, 57.3)	44.9 (32.3, 53.7)	45.4 (34.8, 57.7)	0.414
CP burden, %	2.81 (0.13, 8.49)	3.93 (0.67, 10.50)	2.49 (0.11, 8.29)	0.144
Qualitative cCTA findings				
Positive remodelling, n (%)	116 (32.0%)	20 (33.3%)	96 (31.7%)	0.880
Low attenuation plaque, n (%)	74 (20.4%)	12 (20.0%)	62 (20.5%)	0.999
Spotty calcification, n (%)	41 (11.3%)	5 (8.3%)	36 (11.9%)	0.510
Napkin ring sign, n (%)	29 (8.0%)	6 (10.0%)	23 (7.6%)	0.601
Adverse plaque, n (%)	72 (19.8%)	15 (25.0%)	57 (18.8%)	0.289
Non-target lesion level analysis				
Quantitative cCTA analysis				
Total plaque burden, %	39.4 (34.0, 44.3)	44.2 (39.7, 49.7)	38.4 (33.0, 42.8)	<0.001
LAP burden, %	6.02 (3.55, 8.23)	6.60 (4.12, 9.31)	5.85 (3.47, 7.94)	0.019
NCP burden, %	35.8 (29.9, 40.8)	39.7 (34.5, 44.7)	34.8 (29.7, 40.0)	<0.001
CP burden, %	1.72 (0.37, 4.25)	2.59 (1.37, 5.55)	1.32 (0.30, 3.78)	<0.001
Qualitative cCTA findings				
Positive remodelling, n (%)	93 (25.6%)	17 (28.3%)	76 (25.1%)	0.628
Low attenuation plaque, n (%)	72 (19.8%)	15 (25.0%)	57 (18.8%)	0.289
Spotty calcification, n (%)	61 (16.8%)	15 (25.0%)	46 (15.2%)	0.087
Napkin ring sign, n (%)	35 (9.6%)	10 (16.7%)	25 (8.3%)	0.055
Adverse plaque, n (%)	98 (27.0%)	22 (36.7%)	76 (25.1%)	0.079

Patient level analysis				
Quantitative cCTA analysis				
Total plaque burden, %	40.4 (35.9, 44.8)	44.2 (39.9, 49.5)	39.6 (35.2, 43.7)	<0.001
LAP burden, %	6.63 (3.95, 8.72)	7.02 (5.73, 9.26)	6.34 (3.90, 8.63)	0.012
NCP burden, %	36.6 (30.7, 41.7)	39.2 (35.3, 45.2)	36.0 (30.4, 41.2)	0.001
CP burden, %	2.13 (0.57, 4.77)	2.97 (1.22, 6.54)	1.82 (0.45, 4.37)	0.003
Coronary artery calcium score (Agatston units) (n=233)	506 (151, 1290)	834 (352, 1880)	399 (135, 1090)	0.001
≥ 400, n (%)	148 (53.4%)	37 (71.2%)	111 (49.3%)	0.005
Qualitative cCTA findings*				
Positive remodelling, n (%)	141 (38.8%)	26 (43.3%)	115 (38.0%)	0.470
Low attenuation plaque, n (%)	113 (31.1%)	24 (40.0%)	89 (29.4%)	0.127
Spotty calcification, n (%)	96 (26.4%)	20 (33.3%)	76 (25.1%)	0.201
Napkin ring sign, n (%)	45 (12.4%)	14 (23.3%)	31 (10.2%)	0.009
Adverse plaque, n (%)	143 (39.4%)	35 (58.3%)	108 (35.6%)	0.001
PCAT attenuation analysis				
$PCAT_{RCA}$, HU	-81.8 ± 8.1	-76.1 ± 6.1	-82.9± 8.0	<0.001
$PCAT_{Vessel}$, HU	-81.3 ± 8.8	-76.4 ± 7.5	-82.3 ± 7.9	<0.001
$PCAT_{Lesion}$, HU	-81.3 ± 8.1	-76.7 ± 7.9	-82.2 ± 8.7	<0.001

Values are expressed as mean ± standard deviation, median (25th, 75th percentiles) or n (%).
*Qualitative cCTA findings at the patient-level analysis are assessed at the lesions with the highest numbers of APCs among all lesions.
APCs = adverse plaque characteristics; CAD = coronary artery disease; cCTA = coronary computed tomography angiography; CP = calcified plaque; HU = Hounsfield unit; LAP = low-attenuation plaque; MLA = minimum lumen area; NCP = non-calcified plaque; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint; RCA = right coronary artery.

Supplementary Table 3. Cox regression analysis of factors associated with PoCE at the target lesion and non-target lesion level.

Variables	Univariate analysis		Multivariable model 1		Multivariable model 2	
	HR (95%CI)	p value	HR (95%CI)	p value	HR (95%CI)	p value
Baseline patient characteristics						
Sex, male	1.54 (0.86-2.75)	0.145	1.08 (0.59-1.98)	0.814	1.15 (0.63-2.09)	0.648
LVEF	0.97 (0.95-1.00)	0.019	0.98 (0.96-1.00)	0.050	0.99 (0.97-1.01)	0.250
Statin use at discharge	0.38 (0.22-0.66)	0.001	0.47 (0.26-0.83)	0.009	0.46 (0.26-0.81)	0.007
cCTA findings						
PCI target lesion-level analysis						
Quantitative cCTA analysis						
Diameter stenosis (per 10% increase)	1.00 (0.85-1.17)	0.953	1.00 (0.97-1.02)	0.892		
Lesion length (per 10mm increase)	1.33 (0.92-1.92)	0.134	0.97 (0.94-1.00)	0.083		
MLA	1.13 (0.93-1.38)	0.227	0.99 (0.75-1.31)	0.954		
Total plaque burden*	0.98 (0.85-1.12)	0.777				
LAP burden*	0.94 (0.89-1.00)	0.034	0.97 (0.92-1.03)	0.302		
NCP burden*	0.96 (0.87-1.06)	0.421				
CP burden*	1.01 (1.00-1.02)	0.058	1.01 (1.00-1.02)	0.016		
Qualitative cCTA findings						
Positive remodelling	1.15 (0.73-1.81)	0.554				
Low attenuation plaque	0.96 (0.58-1.57)	0.856				
Spotty calcification	1.20 (0.60-2.41)	0.603				
Napkin ring sign	1.35 (0.74-2.45)	0.326				
Adverse plaque	1.51 (0.95-2.41)	0.080	1.87 (1.13-3.07)	0.014		
Non-target lesion-level analysis						
Quantitative cCTA analysis						
Total plaque burden*	2.02 (1.61-2.54)	<0.001				
LAP burden*	1.10 (1.02-1.19)	0.020			1.05 (0.97-1.13)	0.216
NCP burden*	1.56 (1.27-1.90)	<0.001				
CP burden*	1.04 (1.02-1.06)	<0.001			1.04 (1.01-1.06)	0.001

Qualitative cCTA findings						
Positive remodelling	1.12 (0.70-1.81)	0.639				
Low attenuation plaque	1.29 (0.80-2.09)	0.302				
Spotty calcification	2.01 (1.14-3.54)	0.015				
Napkin ring sign	1.91 (1.17-3.11)	0.010				
Adverse plaque	1.66 (1.06-2.60)	0.028			1.50 (0.94-2.38)	0.090
PCAT attenuation analysis						
$PCAT_{RCA}$ (per 10 HU increase)	2.31 (1.74-3.05)	<0.001	2.35 (1.71-3.22)	<0.001	2.15 (1.61-2.88)	<0.001
$PCAT_{Lesion}$ (per 10 HU increase)	1.65 (1.30-2.08)	<0.001				
$PCAT_{Vessel}$ (per 10 HU increase)	2.41 (1.79-3.24)	<0.001				

* Per 1.2-fold increase.

cCTA = coronary computed tomography angiography; CI = confidence interval; CP = calcified plaque; HR = hazard ratio; HU = Hounsfield unit; LAP = low-attenuation plaque; LVEF = left ventricular ejection fraction; MLA = minimum lumen area; NCP = non-calcified plaque; PCAT = pericoronary adipose tissue; PoCE = patient-oriented composite endpoint; RCA = right coronary artery.

Supplementary Table 4. Patient characteristics and $PCAT_{RCA}$ in the internal and external cohorts.

Variables	All patients (n=564)	Internal cohort (n=490)	External cohort (n=74)	p value
Age, years	69.8 ± 9.9	69.7 ± 9.9	70.9 ± 10.2	0.339
Sex male, n (%)	424 (75.2%)	368 (75.1%)	56 (75.7%)	0.999
Hypertension, n (%)	422 (74.8%)	363 (74.1%)	59 (79.7%)	0.319
Dyslipidaemia, n (%)	411 (72.9%)	360 (73.5%)	51 (68.9%)	0.403
Diabetes mellitus, n (%)	252 (44.7%)	221 (45.1%)	31 (41.9%)	0.619
Smoking, n (%)	340 (60.3%)	299 (61.0%)	41 (55.4%)	0.374
Chronic kidney disease, n (%)	167 (29.6%)	151 (30.8%)	16 (21.6%)	0.132
Haemodialysis, n (%)	14 (2.5%)	12 (2.4%)	2 (2.7%)	0.704
Prior PCI, n (%)	96 (17.0%)	83 (16.9%)	13 (17.6%)	0.869
Prior MI, n (%)	50 (8.9%)	41 (8.4%)	9 (12.2%)	0.275
Acute coronary syndrome, n (%)	148 (26.2%)	127 (25.9%)	21 (28.4%)	0.671
$PCAT_{RCA}$, HU	-81.7 ± 8.1	-81.5 ± 8.1	-82.7 ± 8.1	0.226

Values are expressed as mean ± standard deviation or n (%).

HU = Hounsfield unit; MI = myocardial infarction; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; RCA = right coronary artery.

Supplementary Table 5. Cox regression analyses adjusted models for factors associated with PoCE between high (≥−79.9 HU) and low $PCAT_{RCA}$ (<−79.9 HU).

	HR (95% CI)	p value
High $PCAT_{RCA}$ (≥-79.9 HU)	0.94 (0.52-1.69)	0.834
Medications at cCTA	0.78 (0.39-1.56)	0.478
Statins	1.18 (0.66-2.12)	0.525
Beta-blockers	1.11 (0.62-2.00)	0.727
RAS-inhibitors	1.30 (0.56-3.03)	0.542
Calcium channel blockers	0.94 (0.52-1.69)	0.834
Oral anticoagulants		
Medications at discharge	0.46 (0.24-0.88)	0.018
Statins	1.05 (0.60-1.84)	0.865
Beta-blockers	1.01 (0.57-1.81)	0.959
RAS-inhibitors	1.09 (0.62-1.93)	0.762
Calcium channel blockers	1.15 (0.49-2.69)	0.756
Oral anticoagulants	0.46 (0.24-0.88)	0.018
Low $PCAT_{RCA}$ (<-79.9 HU)		
Medications at cCTA		
Statins	1.00 (0.40-2.49)	0.999
Beta-blockers	0.64 (0.18-2.29)	0.496
RAS-inhibitors	1.16 (0.44-3.04)	0.770
Calcium channel blockers	0.54 (0.19-1.51)	0.238
Oral anticoagulants	2.31 (0.46-11.67)	0.311
Medications at discharge		
Statins	0.94 (0.19-4.61)	0.941
Beta-blockers	0.64 (0.24-1.70)	0.370
RAS-inhibitors	1.82 (0.68-4.86)	0.229
Calcium channel blockers	0.58 (0.23-1.45)	0.241
Oral anticoagulants	3.14 (0.82-12.05)	0.096

Medication use was compared in multivariable cox regression analyses adjusted models by age, sex, smoking, and estimated GFR.
cCTA = coronary computed tomography angiography; CI = confidence interval; GFR = glomerular filtration rate; HR = hazard ratio; HU = Hounsfield unit; PCAT = pericoronary adipose tissue; PoCE = patient-oriented composite endpoint; RAS = renin-angiotensin system; RCA = right coronary artery.

Supplementary Table 6. cCTA findings between TVR and non-TVR.

Variables	All patients (n=490)	TVR (n=21)	non-TVR (n=469)	p value
Baseline patient characteristics				
Age, years	69.6 ± 9.9	70.0 ± 11.1	69.7 ± 9.9	0.863
Sex male, n (%)	368 (75.1%)	19 (90.5%)	349 (74.4%)	0.123
Hypertension, n (%)	363 (74.1%)	18 (85.7%)	345 (73.6%)	0.309
Dyslipidaemia, n (%)	360 (73.5%)	12 (57.1%)	348 (74.2%)	0.125
Diabetes mellitus, n (%)	221 (45.1%)	11 (52.4%)	210 (44.8%)	0.510
Smoking, n (%)	299 (61.0%)	15 (71.4%)	284 (60.6%)	0.368
Chronic kidney disease, n (%)	151 (30.8%)	5 (23.8%)	146 (31.1%)	0.631
Haemodialysis, n (%)	12 (2.4%)	1 (4.8%)	11 (2.3%)	0.412
Prior PCI, n (%)	83 (16.9%)	7 (33.3%)	76 (16.2%)	0.066
Prior MI, n (%)	41 (8.4%)	3 (14.3%)	38 (8.1%)	0.406
Acute coronary syndrome, n (%)	127 (25.9%)	6 (28.6%)	121 (25.8%)	0.800
Laboratory data				
BNP, pg/mL	32.4 (14.2, 83.2)	30.2 (10.2, 86.4)	32.9 (14.3, 82.1)	0.597
estimated GFR, mL/min/1.73 m^2	66.0 (57.0, 76.2)	67.2 (60.2, 78.0)	66.0 (57.0, 76.1)	0.436
Low density lipoprotein cholesterol, mg/dL	113.0 (92.3, 137.7)	106.0 (86.0, 115.0)	114. 0 (93.0, 138.0)	0.077
HbA1c, %	6.1 (5.8, 7.0)	6.4 (5.9, 7.1)	6.1 (5.8, 7.2)	0.381
WBC count, $\times 10^3/\mu L$	6.1 (5.1, 7.4)	5.6 (5.1, 6.8)	6.2 (5.1, 7.5)	0.197
hs-CRP, mg/L	0.8 (0.4, 2.0)	1.4 (0.2, 3.8)	0.8 (0.4, 2.0)	0.512
LVEF, %	60.0 (55.0, 64.9)	58.0 (51.0, 63.8)	60.1 (55.0, 65.2)	0.173
Medications at cCTA				
Statins, n (%)	259 (52.9%)	10 (47.6%)	249 (53.1%)	0.660
Beta-blockers, n (%)	110 (22.4%)	4 (19.0%)	106 (22.6%)	1.000
RAS-inhibitors, n (%)	220 (44.9%)	13 (61.9%)	207 (44.1%)	0.121
Calcium channel blockers, n (%)	204 (41.6%)	13 (61.9%)	191 (40.7%)	0.070
Oral anticoagulants, n (%)	33 (6.7%)	2 (9.5%)	31 (6.6%)	0.645
Medications at discharge				

Statins, n (%)	439 (89.6%)	15 (71.4%)	424 (90.4%)	0.015
Beta-blockers, n (%)	193 (39.4%)	6 (28.6%)	187 (39.9%)	0.366
RAS-inhibitors, n (%)	283 (57.8%)	16 (76.2%)	267 (56.9%)	0.113
Calcium channel blockers, n (%)	234 (47.8%)	14 (66.7%)	220 (46.9%)	0.116
Oral anticoagulants, n (%)	36 (7.3%)	3 (14.3%)	33 (7.0%)	0.194
Lesion characteristics				
Target vessel: LAD/ LCX/ RCA, %	51.8/14.7/33.5	52.7/14.9/32.4	33.3/9.5/57.1	0.084
Lesion location: proximal/ mid/ distal, %	31.2/56.1/12.7	28.6/52.4/19.0	31.3/56.3/12.4	0.627
Multivessel disease, n (%)	238 (48.6%)	10 (47.6%)	228 (48.6%)	1.000
Procedural characteristics				
Number of stents, n	1.17 ± 0.39	1.29 ± 0.46	1.17 ± 0.39	0.168
Stent diameter, mm	3.12 ± 0.50	3.21 ± 0.58	3.11 ± 0.50	0.414
Stent length, mm	28.4 ± 13.6	28.5 ± 15.1	28.4 ± 13.5	0.972
Imaging device: IVUS/ OCT, %	65.1/34.1	52.4/47.6	65.7/33.5	0.362
Atherectomy*, n (%)	50 (10.2%)	6 (28.6%)	44 (9.4%)	0.014
cCTA findings				
PCI target lesion-level analysis				
Quantitative cCTA analysis				
Diameter stenosis, %	51.6 (43.9, 59.9)	52.2 (42.2, 58.0)	52.6 (43.9, 60.2)	0.712
Lesion length, mm	24.0 (18.0, 34.0)	26.0 (18.0, 33.0)	24.0 (18.0, 34.0)	0.965
Lesion MLA, mm^2	2.13 (1.35, 2.71)	2.48 (1.62, 3.16)	1.98 (1.35, 2.69)	0.115
Total plaque burden, %	51.8 (43.9, 59.8)	53.3 (42.7, 55.7)	51.6 (44.0, 60.2)	0.867
LAP burden, %	9.66 (6.21, 14.65)	9.02 (6.47, 14.08)	9.72 (6.20, 14.66)	0.822
NCP burden, %	47.25 (36.4, 58.4)	46.5 (35.7, 54.7)	47.3 (36.7, 58.5)	0.581
CP burden, %	1.78 (0.06, 7.26)	6.43 (1.77, 13.72)	1.68 (0.04, 6.76)	0.005
Qualitative cCTA findings				
Positive remodelling, n (%)	182 (37.1%)	9 (42.9%)	173 (36.9%)	0.646
Low attenuation plaque, n (%)	146 (29.9%)	7 (33.3%)	139 (29.7%)	0.808
Spotty calcification, n (%)	68 (13.9%)	1 (4.8%)	67 (14.3%)	0.336
Napkin ring sign, n (%)	48 (9.8%)	1 (4.8%)	47 (10.0%)	0.710

Adverse plaque, n (%)	139 (28.4%)	8 (38.1%)	131 (27.9%)	0.327
PCAT attenuation analysis				
$PCAT_{RCA}$, HU	-81.5 ± 8.1	-77.2 ± 5.6	-81.7 ± 8.2	0.013
$PCAT_{Vessel}$, HU	-81.1 ± 8.1	-77.6 ± 5.2	-81.3 ± 8.1	0.042

Values are expressed as mean ± standard deviation, median (25th, 75th percentiles) or n (%)
*Atherectomy includes rotational atherectomy and orbital atherectomy. BNP = brain natriuretic hormone; cCTA = coronary computed tomography angiography; CP = calcified plaque; GFR = glomerular filtration rate; hs-CRP = high sensitive C-reactive protein; HU = Hounsfield unit; IVUS = intravascular ultrasound; LAD = left anterior descending artery; LAP = low-attenuation plaque; LCX = left circumflex artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MLA = minimum lumen area; NCP = non-calcified plaque; OCT = optical coherence tomography; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; RAS = renin-angiotensin system; RCA = right coronary artery; TVR = target vessel revascularization; WBC = white blood cell.

Supplementary Table 7. Cox regression analysis of cCTA findings associated with TVR.

Variables	Univariable analysis		Multivariable model 1		Multivariable model 2	
	HR (95%CI)	p value	HR (95%CI)	p value	HR (95%CI)	p value
Clinical characteristics						
Age	1.01 (0.96-1.05)	0.754	1.00 (0.95-1.04)	0.897	1.00 (0.96-1.04)	0.954
Sex, male	3.19 (0.74-13.7)	0.118	2.51 (0.55-11.46)	0.235	2.42 (0.53-11.00)	0.254
Hypertension	2.06 (0.61-7.01)	0.245				
Dyslipidaemia	0.45 (0.19-1.08)	0.074	0.65 (0.26-1.57)	0.335	0.68 (0.28-1.65)	0.391
Diabetes mellitus	1.34 (0.57-3.16)	0.500				
Smoking	1.60 (0.62-4.13)	0.330				
Haemodialysis	2.51 (0.34-18.8)	0.369				
hs-CRP (per 1 mg/L increase)	1.01 (0.97-1.04)	0.631				
LVEF	0.98 (0.94-1.02)	0.264	0.99 (0.95-1.04)	0.809	0.99 (0.95-1.04)	0.746
cCTA findings						
PCI target lesion-level analysis						
Quantitative cCTA analysis						
Diameter stenosis (per 10% increase)	0.95 (0.73-1.24)	0.712				
Lesion length (per 10mm increase)	1.02 (0.75-1.38)	0.907				
Lesion MLA	1.26 (0.88-1.80)	0.200	1.26 (0.89-1.80)	0.189	1.23 (0.87-1.75)	0.248
Total plaque burden*	0.90 (0.72-1.13)	0.377				
LAP burden*	0.96 (0.86-1.07)	0.432				
NCP burden*	0.93 (0.77-1.12)	0.440				
CP burden*	1.04 (1.01-1.08)	0.020	1.05 (1.01-1.09)	0.013	1.05 (1.01-1.09)	0.013
Qualitative cCTA findings						
Positive remodelling	1.26 (0.53-3.00)	0.597				
Low attenuation plaque	1.19 (0.48-2.96)	0.702				
Spotty calcification	0.32 (0.04-2.38)	0.660				
Napkin ring sign,	0.46 (0.06-3.39)	0.442				
Adverse plaque	1.58 (0.65-3.80)	0.311				

PCAT attenuation analysis						
$PCAT_{RCA}$ (per 10 HU increase)	1.99 (1.16-3.40)	0.012			2.12 (1.17-3.82)	0.013
$PCAT_{Vessel}$ (per 10 HU increase)	1.67 (1.01-2.78)	0.048	1.94 (1.13-3.32)	0.016		

*Per 1.2-fold increase
cCTA = coronary computed tomography angiography; CI = confidence interval; CP = calcified plaque; HR = hazard ratio; HU = Hounsfield unit; LAP = low-attenuation plaque; LVEF = left ventricular ejection fraction; hs-CRP = high sensitive C-reactive protein; MLA = minimum lumen area; NCP = non-calcified plaque; PCAT = pericoronary adipose tissue; RCA = right coronary artery; TVR = target vessel revascularization.

Supplementary Table 8. cCTA findings between TLR and non-TLR.

Variables	All patients (n=490)	TLR (n=12)	non-TLR (n=478)	p value
Baseline patient characteristics				
Age, years	69.7 ± 9.9	65.5 ± 8.3	69.8 ± 9.6	0.140
Sex male, n (%)	368 (75.1%)	11 (91.7%)	357 (74.7%)	0.310
Hypertension, n (%)	363 (74.1%)	12 (100.0%)	351 (73.4%)	0.042
Dyslipidaemia, n (%)	360 (73.5%)	7 (58.3)	353 (73.8)	0.317
Diabetes mellitus, n (%)	216 (44.1%)	8 (66.7%)	213 (44.6%)	0.150
Smoking, n (%)	299 (61%)	8 (66.7%)	291 (60.9%)	0.773
Chronic kidney disease, n (%)	151 (30.8%)	3 (25.0%)	148 (31.0%)	0.763
Haemodialysis, n (%)	12 (2.5%)	0 (0.0%)	12 (2.5%)	1.000
Prior PCI, n (%)	83 (16.9%)	3 (25.0%)	80 (16.7%)	0.437
Prior MI, n (%)	41 (8.4%)	2 (16.7%)	39 (8.2%)	0.265
Acute coronary syndrome, n (%)	127 (25.9%)	2 (16.7%)	125 (26.2%)	0.739
Laboratory data				
BNP, pg/mL	34.4 (14.5, 85.1)	21.6 (14.1, 53.4)	32.7 (14.2, 83.2)	0.537
estimated GFR, mL/min/1.73 m^2	66.0 (57.0, 76.2)	70.5 (59.9, 80.3)	66.0 (57.0, 76.1)	0.402
Low density lipoprotein cholesterol, mg/dL	113.0 (92.3, 137.8)	100.0 (59.7, 80.3)	114.0 (93.0, 76.1)	0.028
HbA1c, %	6.1 (5.8, 7.0)	6.9 (6.2, 7.6)	6.1 (5.8, 7.2)	0.045
WBC count, $\times 10^3/\mu L$	6.1 (5.1, 7.4)	5.7 (4.6, 7.0)	6.2 (5.1, 7.4)	0.396
hs-CRP, mg/L	0.8 (0.4, 2.0)	1.6 (0.9, 5.4)	0.8 (0.4, 2.0)	0.168
LVEF, %	60.0 (55.0, 64.9)	56.2 (47.7, 60.2)	60.1 (55.0, 65.2)	0.046
Medications at cCTA				
Statins, n (%)	259 (52.9%)	5 (41.7%)	254 (53.1%)	0.561
Beta-blockers, n (%)	109 (22.2%)	2 (16.7%)	108 (22.6%)	1.000
RAS-inhibitors, n (%)	220 (44.9%)	8 (66.7%)	212 (44.4%)	0.148
Calcium channel blockers, n (%)	204 (41.6%)	9 (75.0%)	195 (40.8%)	0.033
Oral anticoagulants, n (%)	33 (6.7%)	0 (0.0%)	33 (6.9%)	1.000
Medications at discharge				

Statins, n (%)	259 (83.5%)	7 (58.3%)	432 (90.4%)	0.005
Beta-blockers, n (%)	192 (39.2%)	3 (25.0%)	190 (39.7%)	0.380
RAS-inhibitors, n (%)	283 (57.8%)	10 (83.3%)	273 (57.1%)	0.081
Calcium channel blockers, n (%)	204 (44.3%)	10 (83.3%)	224 (46.9%)	0.017
Oral anticoagulants, n (%)	36 (7.3%)	1 (8.3%)	35 (7.3%)	0.604
Lesion characteristics				
Target vessel: LAD/ LCX/ RCA, %	51.8/14.7/33.5	52.3/14.6/33.1	33.3/16.7/50.0	0.372
Lesion location: proximal/ mid/ distal, %	31.2/56.1/12.7	33.3/58.3/8.3	31.2/56.1/12.8	1.000
Multivessel disease, n (%)	238 (48.6%)	6 (50.0%)	232 (48.5%)	1.000
Procedural characteristics				
Number of stents, n	1.17 ± 0.39	1.17 ± 0.39	1.17 ± 0.39	0.966
Stent diameter, mm	3.12 ± 0.50	3.31 ± 0.64	3.11 ± 0.50	0.173
Stent length, mm	28.4 ± 13.6	29.8 ± 18.2	28.4 ± 13.5	0.716
Atherectomy*, n (%)	50 (10.2%)	4 (33.3%)	46 (9.6%)	0.026
cCTA findings				
PCI target lesion-level analysis				
Quantitative cCTA analysis				
Diameter stenosis, %	51.6 (43.9, 59.9)	54.0 (41.8, 58.3)	52.6 (43.9, 60.1)	0.965
Lesion length, mm	24.0 (18.0, 34.0)	25.0 (17.5, 30.5)	24.0 (18.0, 34.0)	0.983
Lesion MLA, mm^2	2.13 (1.35, 2.71)	2.84 (1.63, 3.17)	2.00 (1.35, 2.70)	0.108
Total plaque burden, %	51.83 (43.9, 59.8)	6.18 (1.84, 15.55)	51.71 (43.9, 60.1)	0.880
LAP burden, %	9.66 (6.21, 14.65)	10.08 (7.44, 16.71)	9.60 (6.19, 14.62)	0.375
NCP burden, %	47.25 (36.4, 58.4)	46.49 (35.6, 53.7)	47.30 (36.5, 58.4)	0.727
CP burden, %	1.78 (0.06, 7.26)	6.18 (1.84, 15.5)	1.71 (0.05, 7.01)	0.025
Qualitative cCTA findings				
Positive remodelling, n (%)	182 (37.1%)	5 (41.7%)	177 (37.0%)	0.768
Low attenuation plaque, n (%)	146 (29.9%)	4 (33.3%)	142 (29.8%)	0.757
Spotty calcification, n (%)	68 (13.9%)	1 (8.3%)	67 (14.0%)	1.000
Napkin ring sign, n (%)	48 (9.8%)	0 (0.0%)	48 (10.0%)	0.618
Adverse plaque, n (%)	139 (28.4%)	4 (33.3%)	135 (28.2%)	0.748

PCAT attenuation analysis				
$PCAT_{RCA}$, HU	-81.5 ± 8.1	-76.6 ± 5.1	-81.7 ± 8.2	0.031
$PCAT_{Lesion}$, HU	-81.0 ± 8.9	-75.9 ± 6.1	-81.1 ± 8.9	0.045

Values are expressed as mean ± standard deviation, median (25th, 75th percentiles) or n (%)
*Atherectomy includes rotational atherectomy and orbital atherectomy. BNP = brain natriuretic hormone; cCTA = coronary computed tomography angiography; CP = calcified plaque; GFR = glomerular filtration rate; hs-CRP = high sensitive C-reactive protein; HU = Hounsfield unit; LAD = left anterior descending artery; LAP = low-attenuation plaque; LCX = left circumflex artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MLA = minimum lumen area; NCP = non-calcified plaque; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; RAS = renin-angiotensin system; RCA = right coronary artery; TLR = target lesion revascularization; WBC = white blood cell.

Supplementary Table 9. Cox regression analysis of cCTA findings associated with TLR.

Variables	Univariable analysis		Multivariable model 1		Multivariable model 2	
	HR (95%CI)	p value	HR (95%CI)	p value	HR (95%CI)	p value
Clinical characteristics						
Age	0.96 (0.91-1.02)	0.164	0.94 (0.88-0.99)	0.031	0.94 (0.89-1.00)	0.051
Sex, male	3.67 (0.47-28.4)	0.213	2.71 (0.32-22.8)	0.359	2.04 (0.24-17.1)	0.512
Hypertension	-	-				
Dyslipidaemia	0.49 (0.16-1.56)	0.230				
Diabetes mellitus	2.44 (0.73-8.10)	0.146	2.03 (0.59-6.99)	0.260	2.14 (0.62-7.37)	0.230
Smoking	1.27 (0.38-4.23)	0.693				
Haemodialysis	-	-				
hs-CRP (per 1 mg/L increase)	1.02 (0.98-1.05)	0.309				
LVEF	0.96 (0.91-1.00)	0.078	0.98 (0.93-1.04)	0.559	0.98 (0.93-1.04)	0.592
cCTA findings						
PCI target lesion-level analysis						
Quantitative cCTA analysis						
Diameter stenosis (per 10% increase)	0.95 (0.66-1.37)	0.798				
Lesion length (per 10mm increase)	1.01 (0.97-1.05)	0.668				
Lesion MLA	1.39 (0.90-2.14)	0.133	1.45 (0.93-2.25)	0.097	1.39 (0.87-2.19)	0.166
Total plaque burden*	0.97 (0.70-1.36)	0.878				
LAP burden*	1.10 (0.92-1.31)	0.287				
NCP burden*	0.97 (0.75-1.25)	0.786				
CP burden*	1.07 (1.00-1.15)	0.048	1.11 (1.01-1.22)	0.023	1.10 (1.01-1.19)	0.026
Qualitative cCTA findings						
Positive remodelling	1.19 (0.38-3.75)	0.765				
Low attenuation plaque	1.19 (0.36-3.95)	0.779				
Spotty calcification	0.60 (0.08-4.62)	0.620				
Napkin ring sign,	-	-				
Adverse plaque	1.26 (0.38-4.62)	0.708				

PCAT attenuation analysis						
$PCAT_{RCA}$ (per 10 HU increase)	2.21 (1.08-4.50)	0.030			2.94 (1.23-6.99)	0.015
$PCAT_{Lesion}$ (per 10 HU increase)	1.91 (1.00-3.42)	0.049	2.47 (1.29-4.73)	0.006		

*Per 1.2-fold increase
cCTA = coronary computed tomography angiography; CI = confidence interval; CP = calcified plaque; HR = hazard ratio; HU = Hounsfield unit; LAP = low-attenuation plaque; LVEF = left ventricular ejection fraction; MLA = minimum lumen area; NCP = non-calcified plaque; PCAT = pericoronary adipose tissue; RCA = right coronary artery; TLR = target lesion revascularization.

Supplementary Table 10. Baseline patient characteristics in the inclusion and exclusion cohorts.

Variables	All patients (n=702)	Inclusion cohort (n=490)	Exclusion cohort (n=212)	p value
Age, years	70.1 ± 10.2	69.7 ± 9.9	71.2 ± 10.8	0.068
Sex male, n (%)	532 (75.8%)	368 (75.1%)	164 (77.4%)	0.565
Hypertension, n (%)	520 (74.1%)	363 (74.1%)	157 (74.1%)	0.999
Dyslipidaemia, n (%)	510 (72.6%)	360 (73.5%)	150 (70.8%)	0.462
Diabetes mellitus, n (%)	330 (47.0%)	221 (45.1%)	109 (51.4%)	0.138
Smoking, n (%)	422 (60.1%)	299 (61.0%)	123 (58.0%)	0.502
Chronic kidney disease, n (%)	225 (32.1%)	151 (30.8%)	74 (34.9%)	0.292
Haemodialysis, n (%)	25 (3.6%)	12 (2.4%)	13 (6.1%)	0.024
Prior PCI, n (%)	137 (19.5%)	83 (16.9%)	54 (25.5%)	0.013
Prior MI, n (%)	64 (9.1%)	41 (8.4%)	23 (10.8%)	0.318
Acute coronary syndrome, n (%)	166 (23.6%)	127 (25.9%)	39 (18.4%)	0.033
Multivessel disease, n (%)	408 (58.1%)	238 (48.6%)	170 (80.2%)	<0.001
Statins use at discharge, n (%)	625 (89.0%)	439 (89.6%)	186 (87.7%)	0.511
BNP, pg/mL	38.2 (15.0, 91.7)	32.4 (14.2, 83.2)	56.7 (21.8, 131.1)	<0.001
estimated GFR, mL/min/1.73 m^2	65.6 (56.7, 76.8)	66.0 (57.0, 76.2)	64.8 (54.9, 77.0)	0.127
LVEF, %	60.0 (52.7, 64.0)	60.0 (55.0, 64.9)	56.0 (48.8, 62.2)	<0.001

Values are expressed as mean ± standard deviation, median (25th, 75th percentiles) or n (%).
BNP = brain natriuretic hormone; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Supplementary Table 11. Comparison of PCAT attenuation across institutions.

Variables	Institution A (n=79)	Institution B (n=199)	Institution C (n=165)	Institution D (n=47)	p value
$PCAT_{RCA}$, HU	-80.9 ± 7.4	-81.9 ± 9.3	-81.6 ± 6.8	-80.7 ± 8.3	0.731
$PCAT_{Vessel}$, HU	-79.8 ± 6.9	-81.7 ± 9.2	-81.5 ± 6.5	-80.3 ± 9.1	0.257
$PCAT_{Lesion}$, HU	-80.4 ± 7.0	-80.5 ± 9.8	-81.7 ± 8.4	-81.5 ± 9.8	0.505

Values are expressed as mean ± standard deviation.
HU = Hounsfield unit; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; RCA = right coronary artery

Supplementary Figure 1. Study flowchart.

A total of 702 patients who underwent cCTA before PCI with current-generation DES for de novo native lesions during the study period were enrolled. After screening of enrollment criteria and image quality, 490 patients were finally analysed. 77 patients (15.7%) experienced PoCE (PoCE group), while 429 patients (84.3%) did not experienced PoCE (non-PoCE group). CABG = coronary artery bypass grafting; cCTA = coronary computed tomography angiography; DES = drug-eluting stents; LMCA = left main coronary artery; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint; STEMI =ST-segment elevation myocardial infarction.

Supplementary Figure 2. ROC analysis for identifying patients with subsequent PoCE.

ROC analysis showed that the cut-off value of the $PCAT_{RCA}$, and CP burden for identifying patients with subsequent PoCE was (A) -79.9 HU, (B) 2.1%, respectively. AUC = area under the curve; CI = confidence interval; CP = calcified plaque; HU = Hounsfield Unit; PCAT = pericoronary adipose tissue; PoCE = patient-oriented composite endpoint; RCA = right coronary artery; ROC = receiver operating characteristic curve.

Supplementary Figure 3. Kaplan-Meier curves for PoCE by $PCAT_{RCA}$.

Kaplan–Meier curves showing the cumulative incidence of PoCE according to $PCAT_{RCA}$ is shown. The incidence of PoCE is higher in patients with high $PCAT_{RCA}$ (≥-79.9 HU) than in those with low $PCAT_{RCA}$ (<-79.9 HU). HR = hazard ratio; HU = Hounsfield Unit; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint; RCA = right coronary artery

Supplementary Figure 4. Kaplan-Meier curves for PoCE by $PCAT_{RCA}$ in the external cohort.

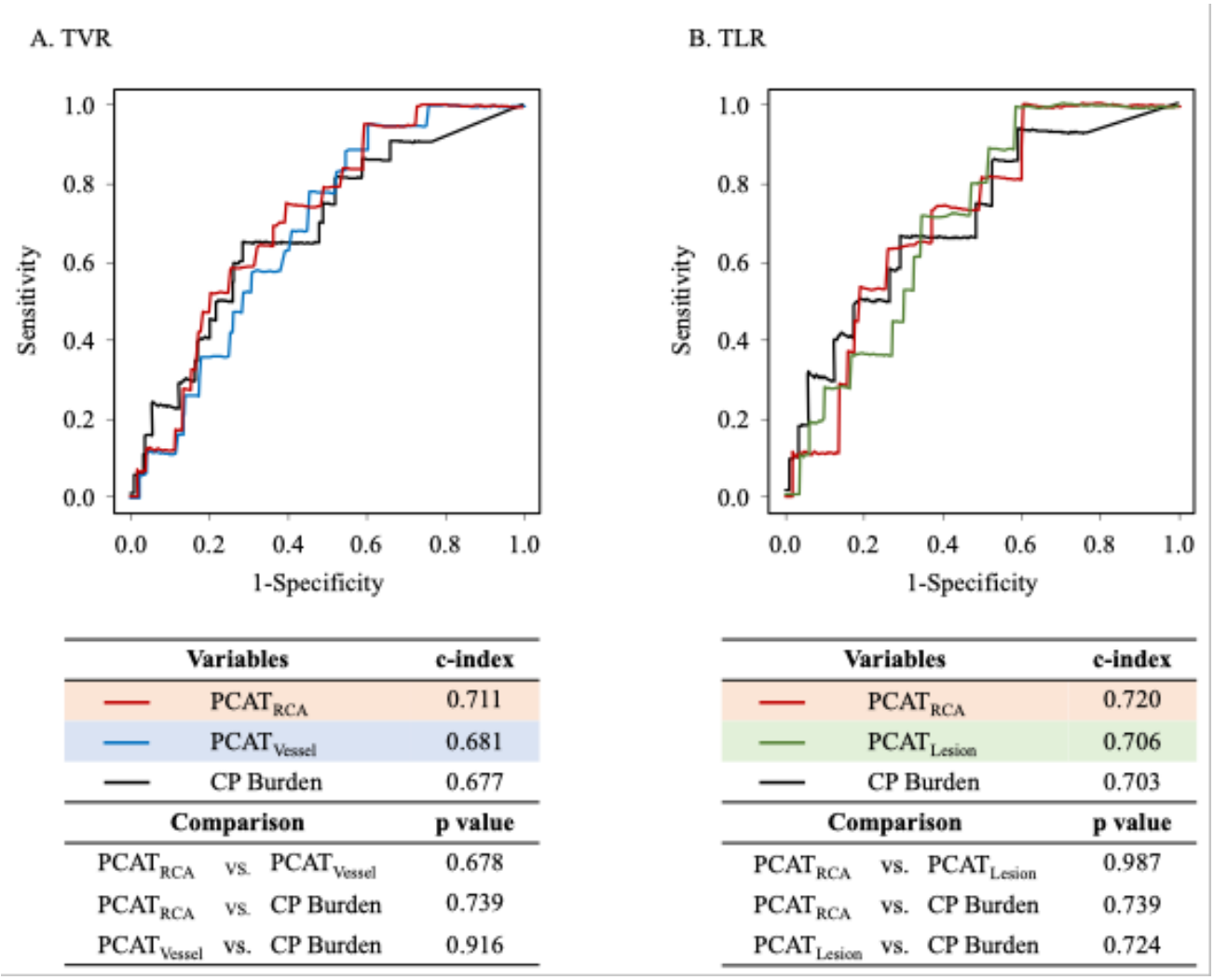
Kaplan–Meier curves showing the cumulative incidence of PoCE according to $PCAT_{RCA}$ in external cohort is shown. The incidence of PoCE is higher in patients with high $PCAT_{RCA}$ (≥-79.9 HU) than in those with low $PCAT_{RCA}$ (<-79.9 HU). HR = hazard ratio; HU = Hounsfield Unit; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint; RCA = right coronary artery

Supplementary Figure 5. Kaplan-Meier curves for PoCE by LAP and CP burden.

Kaplan–Meier curves showing the cumulative incidence of PoCE according to (A) Adverse plaque and (B) CP burden are shown. The incidence of PoCE is higher in patients with adverse plaque and CP burden (>2.1%) than in those with no adverse plaque and CP burden (≤2.1%), respectively. CP = calcified plaque; HR = hazard ratio; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint.

Supplementary Figure 6. Kaplan-Meier curves for PoCE, stratified by statin use and $PCAT_{RCA}$.

Kaplan–Meier curves show PoCE incidence in (A) high $PCAT_{RCA}$ (≥-79.9 HU) and (B) low $PCAT_{RCA}$ (<-79.9 HU). After adjustment for patient characteristics (age, sex, smoking, and eGFR) and discharge medications (beta-blockers, renin-angiotensin system inhibitors, calcium channel blockers, and oral anticoagulants), PoCE incidence was lower in statin users than in non-users in the high $PCAT_{RCA}$ group. In the low $PCAT_{RCA}$ group, PoCE incidence did not significantly differ based on statin use. eGFR = estimated glomerular filtration rate; HR = hazard ratio; HU = Hounsfield unit; PCAT = pericoronary adipose tissue; PCI = percutaneous coronary intervention; PoCE = patient-oriented composite endpoint; RCA = right coronary artery.



Variables	c-index
$PCAT_{RCA}$	0.711
$PCAT_{Vessel}$	0.681
CP Burden	0.677

Comparison	p value
$PCAT_{RCA}$ vs. $PCAT_{Vessel}$	0.678
$PCAT_{RCA}$ vs. CP Burden	0.739
$PCAT_{Vessel}$ vs. CP Burden	0.916

Variables	c-index
$PCAT_{RCA}$	0.720
$PCAT_{Lesion}$	0.706
CP Burden	0.703

Comparison	p value
$PCAT_{RCA}$ vs. $PCAT_{Lesion}$	0.987
$PCAT_{RCA}$ vs. CP Burden	0.739
$PCAT_{Lesion}$ vs. CP Burden	0.724

Supplementary Figure 7. Comparison of diagnostic performance of AUC for TVR and TLR.

(A) The AUC values of $PCAT_{RCA}$, $PCAT_{Vessel}$, and CP burden in identifying TVR are 0.711, 0.681, and 0.677, respectively. (B) The AUC values of $PCAT_{RCA}$, $PCAT_{Lesion}$, and CP burden in identifying TLR are 0.720, 0.706, and 0.703. AUC = area under the curve; c-index = concordance statistics; CP = calcified plaque; PCAT = pericoronary adipose tissue; RCA = right coronary artery; TLR = target lesion revascularization; TVR = target vessel revascularization.