Radiology: Cardiothoracic Imaging

ORIGINAL RESEARCH

Diagnostic and Prognostic Performance of Pericoronary Adipose Tissue Attenuation in Suspected Acute Coronary Syndrome: Insights from the RAPID-CTCA Trial

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Author affiliations, funding, and conflicts of interest are listed at the end of this article.

Radiology: Cardiothoracic Imaging 2026; 8(1):e250074 • https://doi.org/10.1148/ryct.250074 • Content codes: CA CT

Purpose: To assess whether pericoronary adipose tissue (PCAT) attenuation on coronary CT angiography (CCTA) aids in the diagnosis of acute coronary syndrome (ACS) or provides additive prognostic value at 1 year in intermediate-risk individuals.

Materials and Methods: This study was a secondary post hoc analysis of the multicenter prospective randomized Rapid Assessment of Potential Ischemic Heart Disease with CT Coronary Angiography trial (ClinicalTrials.gov identifier, NCT02284191), which enrolled intermediate-risk patients with suspected ACS from 37 sites in the United Kingdom between March 2015 and June 2019. The current study evaluated the diagnostic and prognostic performance of PCAT attenuation, the Global Registry of Acute Coronary Events (GRACE) score, coronary artery diameter stenosis, and low-attenuation plaque (LAP) burden, using receiver operating characteristic curve analysis and Cox proportional hazards regression, respectively.

Results: The study included 353 participants (median age, 63 years [IQR, 54–73 years]; 231 [65%] male participants), of whom 169 (48%) had a discharge diagnosis of ACS. The strongest predictors were diameter stenosis (C statistic, 0.74) and LAP burden (C statistic, 0.73), followed by the GRACE score (C statistic, 0.62). PCAT attenuation (C statistic, 0.57) did not provide additive discrimination for diagnosis ($P > .05$ for all comparisons). Both LAP burden (adjusted hazard ratio, 1.16; 95% CI: 1.02, 1.32) and PCAT attenuation (adjusted hazard ratio, 1.12; 95% CI: 1.00, 1.26) were independent predictors of death or recurrent myocardial infarction at 1 year. However, adding PCAT attenuation (C statistic, 0.63; 95% CI: 0.50, 0.76) to LAP burden (C statistic, 0.69; 95% CI: 0.62, 0.77) did not improve event discrimination (ΔC statistic, 0; 95% CI: −0.11, 0.11; $P = .97$).

Conclusion: In intermediate-risk individuals with suspected ACS, PCAT attenuation showed weak diagnostic and prognostic performance, inferior or nonadditive compared with the GRACE score or other CCTA metrics.

Supplemental material is available for this article.

Clinical trial registration no. NCT02284191

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Coronary CT angiography (CCTA) is a sensitive noninvasive test that is increasingly used to evaluate and manage patients with chest pain (1,2). In addition to assessment of diameter stenosis, it enables quantitative evaluation of coronary atherosclerosis and characterization of high-risk plaque features, such as low-attenuation plaque (LAP), which independently predict adverse clinical events (3). Pericoronary adipose tissue (PCAT) attenuation has recently emerged as a novel CCTA-derived imaging biomarker that may reflect coronary inflammation (4).

Vascular inflammation is a key driver of atherosclerosis progression and atherothrombosis leading to acute coronary syndrome (ACS) (5). Initial reports demonstrated higher PCAT attenuation in 10 patients with acute myocardial infarction (6). PCAT attenuation around the proximal right coronary artery has since been associated with plaque instability and the presence of high-risk plaque on CCTA scans (7). Subsequent studies linked PCAT attenuation with death owing to coronary heart disease or myocardial infarction in patients with stable chest pain (8). Pericoronary fat stranding in ACS may also arise from other causes, including spontaneous coronary artery dissection (9), edema, hematoma, or epicardial fat necrosis. Although PCAT attenuation is an emerging noninvasive biomarker of coronary inflammation, its role in the diagnosis or risk stratification of patients with acute chest pain remains uncertain.

In the emergency department, the role of CCTA continues to be debated, particularly with the availability of high-sensitivity cardiac troponin testing assays. Nevertheless, CCTA offers rapid assessment of patients with acute chest pain, may reduce unnecessary invasive coronary angiography, and can assist in challenging diagnostic cases. The Rapid Assessment of Potential Ischemic Heart Disease with CT Coronary Angiography (RAPID-CTCA) trial previously demonstrated that in intermediate-risk patients with suspected ACS, CCTA reduced the rate of invasive coronary angiography but did not alter clinical outcomes at 1 year (10). However, quantitative plaque analysis of CCTA from this trial showed that LAP burden was an important predictor of death or recurrent myocardial infarction at 1 year (11).

This secondary post hoc analysis of the RAPID-CTCA trial aimed to determine whether PCAT attenuation aids in the diagnosis of ACS or provides additive prognostic value at 1 year.

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Abbreviations

ACS = acute coronary syndrome, CCTA = coronary CT angiography, GRACE = Global Registry of Acute Coronary Events, LAP = low-attenuation plaque, PCAT = pericoronary adipose tissue, RAPID-CTCA = Rapid Assessment of Potential Ischemic Heart Disease with CT Coronary Angiography

Summary

Coronary CT angiography markers, including pericoronary adipose tissue attenuation and low-attenuation plaque burden, showed limited diagnostic and prognostic value in individuals with suspected acute coronary syndrome.

Key Points

- In intermediate-risk individuals with acute chest pain, pericoronary adipose tissue (PCAT) attenuation was a weak discriminator for the index diagnosis of acute coronary syndrome (C statistic, 0.57).
- PCAT attenuation and low-attenuation plaque burden predicted 1-year clinical outcomes of death or recurrent myocardial infarction (adjusted hazard ratio for PCAT, 1.12 [95% CI: 1.00, 1.26]; adjusted hazard ratio for low attenuation plaque, 1.16 [95% CI: 1.02, 1.32]), independent of baseline risk, but did not provide additive value to each other (P = .97).
- The findings did not support incorporating pericoronary adipose tissue attenuation for diagnosis or prognostication in intermediate-risk participants with suspected acute coronary syndrome.

Keywords

Pericoronary Adipose Tissue Attenuation, Acute Chest Pain, CT Coronary Angiography

Materials and Methods

Trial Overview

This study was a secondary post hoc analysis of the multicenter prospective randomized RAPID-CTCA trial (ClinicalTrials.gov identifier, NCT02284191), which investigated the effect of early CCTA on adverse events and health care costs in intermediate-risk patients with suspected ACS; the design and primary results have been reported previously (10,12). Participants were recruited from 37 sites in the United Kingdom between March 2015 and June 2019. Eligible patients presented with acute chest pain and at least one of the following: history of coronary artery disease, electrocardiographic abnormality, or elevated cardiac troponin concentration, consistent with European Society of Cardiology criteria for intermediate risk (13). The exclusion criteria included high-risk features (eg, ST-segment elevation, ST-segment depression > 3 mm), contraindications to CCTA, known obstructive coronary artery disease within 2 years, or angiographically normal coronary arteries (within 5 years). Participants were randomized 1:1, stratified by site and with variable block sizes (4–8), to undergo early CCTA in addition to standard of care or standard of care alone. The trial was approved by the South East Scotland Research Ethics Committee, and all participants provided written informed consent.

Study Sample

The trial recruited 1749 intermediate-risk patients, of whom 887 were randomized to CCTA and 767 completed the scan. Subsequently, 422 consecutive scans were available from a quality assurance cohort collected across all participating centers (n = 121) and from the five highest recruiting centers (Southampton, n = 79; Plymouth, n = 71; Edinburgh, n = 61; Milton Keynes, n = 49; Reading, n = 41). The remaining 345 scans were unavailable owing to logistical, contractual, and resource restrictions (11). The final study sample included 404 participants with adequate image quality for both quantitative plaque and PCAT analysis (Fig 1).

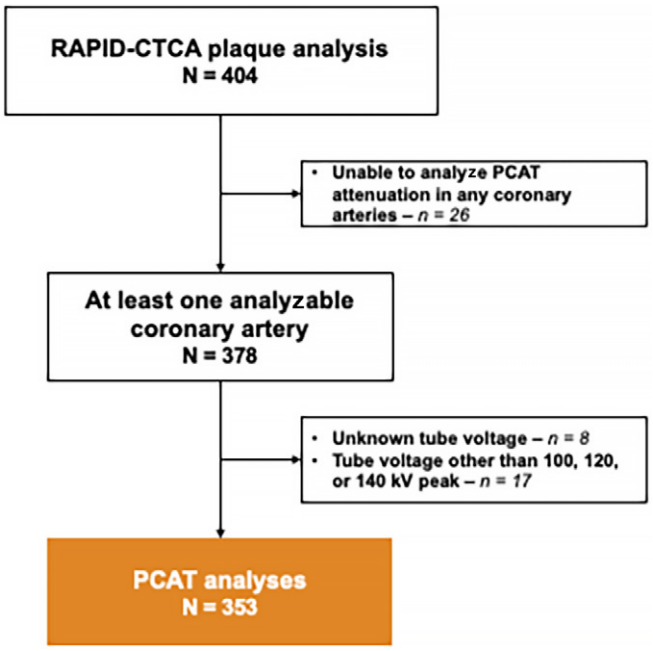

Figure 1: Substudy flowchart of Rapid Assessment of Potential Ischemic Heart Disease with CT Coronary Angiography (RAPID-CTCA) trial shows the participants included in this study. PCAT = pericoronary adipose tissue.

Image Analysis

Contrast-enhanced electrocardiographically gated CCTA was performed on 64-section or more multidetector row CT scanners, as per the study protocol (NCT02284191). CCTA datasets were anonymized and exported in Digital Imaging and Communications in Medicine format. Coronary arteries were segmented manually according to Society of Cardiovascular Computed Tomography guidelines. Scan acquisition characteristics are provided in Table S1. Coronary centerlines were extracted semiautomatically, and quantitative plaque analysis was performed using Autoplaque, version 2.5 (Cedars-Sinai Medical Center) (14). PCAT analysis was conducted with the same research software. Both analyses were performed independently in a core imaging laboratory (University of Edinburgh) by two experienced cardiology readers (M.N.M. and K.L.W.) with more than 3 years of experience who were blinded to clinical outcomes.

For plaque analysis, only segments (≥ 2 mm in diameter) containing atherosclerotic plaques were included. Plaque constituents were automatically defined using Hounsfield unit thresholds calibrated to attenuation in the ascending thoracic aorta, with manual adjustments when required (15). LAP was defined by a fixed threshold of less than 30 HU. Plaque burden was calculated as plaque volume divided by vessel volume. Diameter stenosis was computed automatically and reported with plaque metrics.

For PCAT analysis, the proximal 40 mm of the left anterior descending and left circumflex (from the ostium) and 10–50 mm

of the right coronary artery were evaluated. Per-participant PCAT attenuation was measured within a 3-mm radius of the outer vessel wall. Per-participant PCAT attenuation was calculated as the vessel volume–weighted average across the three coronary arteries. This method was adopted to ensure adequate power for our analysis. A sensitivity analysis confirmed no material differences between vessel-specific and weighted PCAT attenuation in relation to study outcomes. To harmonize attenuation across tube voltages, PCAT attenuation values from 100-kV and 140-kV scans were adjusted using validated conversion factors (divided by 1.11485 and 0.89095, respectively) to allow comparison with 120-kV scans (16).

Study Outcomes

The primary outcomes were index event diagnosis of ACS, defined by discharge diagnosis of myocardial infarction or unstable angina, and death or subsequent type 1 (spontaneous) or type 4b (stent thrombosis) myocardial infarction at 1 year. The outcomes were adjudicated by two independent cardiologists blinded to the trial intervention 1 year after randomization or death, whichever occurred first.

Statistical Analysis

Descriptive data are presented as medians (IQRs) for continuous variables and as frequencies (percentages) for categorical variables. Group differences were assessed with the Mann-Whitney *U* test or Fisher exact test, as appropriate. Logistic regression was used to assess determinants for the index diagnosis of ACS, with models adjusted for age, sex, diabetes mellitus, hypertension, dyslipidemia, and smoking habit. For death or recurrent myocardial infarction, Kaplan-Meier curves were used to illustrate event-free survival, and effect sizes were estimated with Cox proportional hazards regression, adjusted for fixed effects (age, sex, diabetes mellitus, hypertension, dyslipidemia, and smoking) and random effects (index ACS). A multivariable logistic regression that included all independent factors simultaneously was also performed. Receiver operating characteristic curve analysis was used to evaluate discrimination for both index diagnosis and 1-year outcomes; C statistics were compared using a nonparametric method (17). This study was exploratory, and no adjustment for multiplicity was applied. *P* less than .05 was considered statistically significant. All analyses were performed with a complete-case approach using R software (version 4.5.0; R Foundation).

Results

Study Sample Characteristics

Among 887 participants randomized to CCTA in the RAPID-CTCA trial, 353 (46%) participants with evaluable scans (median age, 63 years [IQR, 54–73 years]; 231 [65%] male, 122 [35%] female; Table 1) were available for both quantitative plaque and PCAT analysis and comprised the study sample (Fig 1). Participants diagnosed with ACS as the index event were more often men and had higher PCAT attenuation, higher Global Registry of Acute Coronary Events (GRACE) risk scores, greater coronary artery diameter stenosis, and greater LAP burden compared with participants without ACS (Table 1).

Diagnosis of ACS

At hospital discharge, 169 of 353 (48%) participants had a diagnosis of ACS (133 with myocardial infarction, 36 with unstable angina). In univariable regression analysis, GRACE score, LAP burden, diameter stenosis, and PCAT attenuation were associated with ACS diagnosis (Table 2). These associations persisted after adjustment for background clinical risk factors, although the association between PCAT attenuation and ACS diagnosis was attenuated (Table 2).

Receiver operating characteristic curves demonstrated that diameter stenosis (C statistic, 0.74; 95% CI: 0.69, 0.80) and LAP burden (C statistic, 0.73; 95% CI: 0.68, 0.78) had the strongest discrimination for ACS diagnosis. The GRACE score (C statistic, 0.62; 95% CI: 0.56, 0.68) and PCAT attenuation (C statistic, 0.57; 95% CI: 0.51, 0.63) showed weaker discrimination (Fig 2). Receiver operating characteristic analysis demonstrated that PCAT attenuation added no incremental discrimination for ACS diagnosis beyond GRACE score, diameter stenosis, or LAP burden (DeLong test, $P > .05$ for all comparisons; Fig S1).

Death or Recurrent Myocardial Infarction

At 1-year follow-up, 20 of 353 (6%) participants had a clinical event (seven deaths, 14 type 1 or 4b myocardial infarctions). In univariable analyses, GRACE score (hazard ratio, 1.14; 95% CI: 1.01, 1.29), LAP burden (hazard ratio, 1.14; 95% CI: 1.01, 1.29), and PCAT attenuation (hazard ratio, 1.12; 95% CI: 1.00, 1.25) were associated with event risk, whereas diameter stenosis was not (hazard ratio, 1.05; 95% CI: 0.98, 1.12) (Fig 3, Table 3).

After multivariable adjusting for age, sex, diabetes mellitus, hypertension, dyslipidemia, and smoking, both LAP burden and PCAT attenuation remained independently associated with outcome (Table 3). Receiver operating characteristic analysis showed that LAP burden (C statistic, 0.69; 95% CI: 0.62, 0.77) and PCAT attenuation (C statistic, 0.63; 95% CI: 0.50, 0.76) independently predicted 1-year outcome, with no evidence of a difference between them (ΔC statistic, 0.06; 95% CI: −0.09, 0.21; $P = .44$). The addition of PCAT attenuation conferred no incremental value beyond LAP burden (ΔC statistic, 0; 95% CI: −0.11, 0.11; $P = .97$, Fig S2).

Discussion

In this post hoc analysis of a prospective randomized controlled trial of intermediate-risk participants with acute chest pain, we showed that PCAT attenuation on CCTA had weak discrimination for the index diagnosis of ACS (C statistic, 0.57; 95% CI: 0.51, 0.63). Both LAP burden and PCAT attenuation predicted death or recurrent myocardial infarction at 1 year, independent of other risk factors (adjusted hazard ratio for LAP, 1.16 [95% CI: 1.02, 1.32]; adjusted hazard ratio for PCAT, 1.12 [95% CI: 1.00, 1.26]). However, PCAT attenuation did not add incremental value to the clinical risk score or other quantitative CCTA metrics for the diagnosis of ACS or for the prediction of 1-year clinical outcome.

Acute local vascular inflammation is thought to play a crucial role in the initiation and pathogenesis of ACS, although it has been challenging to detect noninvasively. In this study, PCAT attenuation was associated with ACS diagnosis, although the discriminatory

Table 1: Baseline Participant Characteristics by Discharge Diagnosis

Variable	Overall (*n* = 353)	Acute Coronary Syndrome (*n* = 169)	Other Diagnoses (*n* = 184)
Age (y)	63 (54–73)	64 (54–74)	63 (52–70)
Sex			
Female	122 (35)	46 (27)	76 (41)
Male	231 (65)	123 (73)	108 (59)
Hypertension	157 (44)	79 (47)	78 (42)
Dyslipidemia	143 (41)	71 (42)	72 (39)
Smoking status			
Never	144 (41)	59 (35)	85 (46)
Former	141 (40)	72 (43)	69 (38)
Current	68 (19)	38 (22)	30 (16)
GRACE score	109 (88–137)	118 (96–142)	103 (83–132)
Diameter stenosis (%)	39 (23–61)	50 (37–78)	28 (17–43)
Low-attenuation plaque burden (%)	3 (1–5)	4 (2–6)	1 (0–3)
PCAT attenuation (HU)	−76 (−82 to −70)	−75 (−80 to −69)	−77 (−83 to −71)
Time from first symptom onset to CCTA (h)*	29 (14–46)	29 (15–45)	29 (13–48)
Preventative treatment at randomization			
Aspirin	209 (59)	127 (75)	82 (45)
$P2Y_{12}$ receptor antagonist	136 (39)	99 (59)	37 (20)
Statin	115 (33)	54 (32)	61 (33)
Renin-angiotensin system blocker	108 (31)	62 (37)	46 (25)
Beta-blocker	107 (30)	56 (33)	51 (28)
Preventative treatment at discharge			
Aspirin	221 (63)	150 (89)	71 (39)
$P2Y_{12}$ receptor antagonist	156 (44)	137 (81)	19 (10)
Statin	234 (66)	147 (87)	87 (47)
Renin-angiotensin system blocker	163 (46)	111 (66)	52 (28)
Beta-blocker	178 (50)	120 (71)	58 (32)
Coronary revascularization within 30 d of randomization	118 (33)	113 (67)	5 (3)

Note.—Data are medians with IQRs in parentheses or numbers with percentages in parentheses. CCTA = coronary CT angiography, GRACE = Global Registry of Acute Coronary Events, PCAT = pericoronary adipose tissue.
* Twelve participants (six from each group) had missing data on time from first symptom onset to CCTA.

Table 2: Effect Estimates for Determinants of the Discharge Diagnosis of Acute Coronary Syndrome

Variable	Model 1	*P* Value	Model 2	*P* Value	Model 3	*P* Value
GRACE score, per 10 points	1.13 (1.06, 1.20)	<.001	1.14 (1.05, 1.24)	.003	1.11 (1.01, 1.22)	.03
Diameter stenosis, per 5 percentage points	1.16 (1.11, 1.21)	<.001	1.15 (1.10, 1.20)	<.001	1.08 (1.02, 1.14)	.005
Low-attenuation plaque burden, per 1 percentage point	1.34 (1.23, 1.47)	<.001	1.33 (1.21, 1.47)	<.001	1.23 (1.11, 1.38)	<.001
PCAT attenuation, per 2 HU	1.06 (1.01, 1.12)	.02	1.07 (1.01, 1.12)	.02	1.08 (1.02, 1.15)	.01

Note.—Effect sizes are odds ratios with 95% CIs in parentheses. Model 1 is a univariate model. Model 2 is a multivariable model that includes the variables from model 1, each separately adjusted for age, male sex, diabetes mellitus, hypertension, dyslipidemia, and smoking. Model 3 is a multivariable model that includes all independent variables from model 1, simultaneously adjusted for age, male sex, diabetes mellitus, hypertension, dyslipidemia, and smoking. GRACE = Global Registry of Acute Coronary Events, PCAT = pericoronary adipose tissue.

performance was weaker than that of coronary artery diameter stenosis or LAP burden. Higher PCAT attenuation has been reported in culprit plaques of patients with ACS (7,18), and this finding may underlie our observations. PCAT attenuation has been proposed as a marker of local coronary inflammation (4,6).

In a retrospective analysis of 198 patients with ACS, higher PCAT attenuation was observed at the site of culprit plaques and vessels compared with nonculprit lesions within the same patient or in control patients with stable coronary artery disease (19). In comparison to our study, PCAT attenuation values were higher, and there were more men and a greater prevalence of diabetes, hypertension, dyslipidemia, and active smoking in this study population (19). In another retrospective analysis, 106 patients with myocardial infarction with nonobstructive coronary arteries

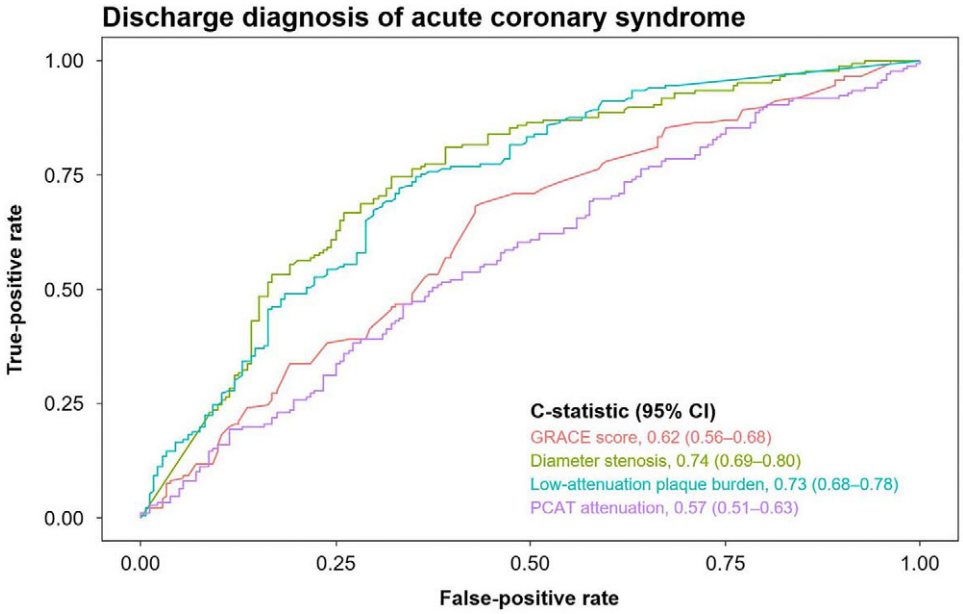

Figure 2: Line graph of receiver operating characteristic curves for discharge diagnosis of acute coronary syndromes. GRACE = Global Registry of Acute Coronary Events, PCAT = pericoronary adipose tissue.

or takotsubo syndrome were reported to have higher mean PCAT attenuation compared with controls with atypical chest pain and no obstructive disease (20). Unlike our study, neither of these retrospective studies reported the potential for PCAT attenuation to discriminate the diagnosis of ACS.

Our study was not designed to capture lesion-specific PCAT attenuation, and the inflammatory milieu during an atherothrombotic event is dynamic. This may have contributed to the limited diagnostic potential for PCAT attenuation (21), although a strength of this study was that all CCTA examinations were performed before percutaneous coronary intervention, ensuring that culprit plaques had not been mechanically modified.

Natural history studies and pathologic data have shown that ACS is most commonly caused by rupture or erosion of a nonobstructive atherosclerotic plaque with a large necrotic core leading to luminal thrombosis (22). Atherosclerotic lesions with lipid-rich necrotic core correlate with LAP identified at CCTA (23,24). Consistent with this underlying pathobiology, our study demonstrated that luminal stenosis and a higher burden of LAP are stronger predictors of index diagnosis of ACS in patients who presented with intermediate- to high-risk acute chest pain. These findings are consistent with those of prior studies (25,26) and suggest that LAP burden portends high-risk plaque features, with increased susceptibility to plaque rupture.

The long-term prognostic value of PCAT attenuation and quantitative plaque characterization at CCTA has been established in patients with stable coronary artery disease, although the prognostic benefit of PCAT attenuation in patients with acute chest pain is unknown (27–29). The Cardiovascular Risk Prediction Using CT study showed that, in patients who underwent routine CCTA, higher PCAT attenuation was associated with increased all-cause and cardiac mortality, after accounting for clinical risk factors, severity of coronary artery disease, and high-risk plaque features (28).

The recent Oxford Risk Factors and Noninvasive Imaging study showed that the perivascular fat attenuation index score, an artificial intelligence–based proprietary risk algorithm that incorporated a variety of imaging factors, improved risk stratification beyond the cardiovascular risk scores and the Coronary Artery Disease Reporting and Data System 2.0 classification in patients with stable coronary artery disease referred for CCTA (30). However, a separate study of more than 400 patients reported that, although PCAT attenuation was an independent predictor of major adverse cardiovascular events, this was no longer demonstrable after adjustment for the coronary calcium score—a well-established prognostic surrogate for burden of atherosclerosis (31).

Our results showed that PCAT attenuation was modestly associated with adverse clinical outcomes of death or recurrent myocardial infarction at 1 year, although its prognostic value beyond LAP burden was not additive. These observations are consistent with those of a recent report of 1313 patients who presented with acute chest pain, in which both PCAT attenuation and severity of coronary artery disease identified by the Coronary Artery Disease Reporting and Data System were independent predictors of major adverse cardiac outcomes, although, similar to our results, there was no additional incremental benefit of PCAT attenuation compared with the severity of coronary artery disease (29). Prior analysis of the RAPID-CTCA trial demonstrated significant prognostic implications of plaque burden in patients with acute chest pain; patients who experienced the primary end point had nearly double the LAP burden compared with those who did not (11). Similar findings have been reported in the Rule Out Myocardial Infarction by Computer Assisted Tomography and the Rule Out Myocardial Infarction by Cardiac CT trials, in which LAP was associated with higher risk lesions (32,33). Together, these findings underscore the prognostic value of LAP burden as a robust predictor of adverse cardiovascular events in patients with acute chest pain.

This study had limitations. First, this was a post hoc analysis of a randomized controlled trial, and the results may be limited by sample size and selective entry criteria. Indeed, in the Oxford Risk Factors and Noninvasive Imaging study of more than 3000

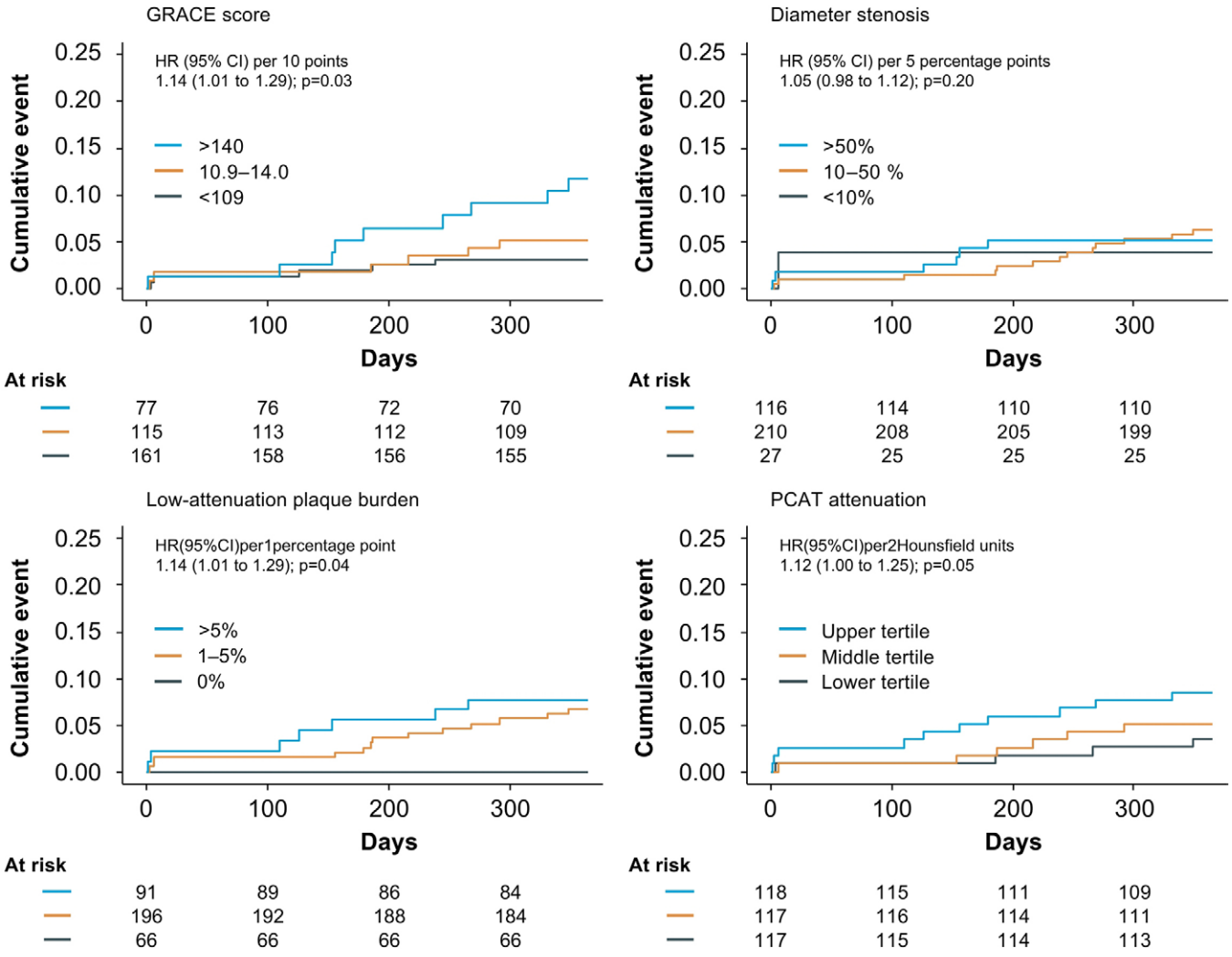

Figure 3: Line graphs of Kaplan-Meier curves for the associations of Global Registry of Acute Coronary Events (GRACE) score, diameter stenosis, low-attenuation plaque burden, and pericoronary adipose tissue (PCAT) with risk of subsequent death or myocardial infarction. HR = hazard ratio.

Table 3: Multivariable Regression for Death and Recurrent Myocardial Infarction

Variable	Model 1	*P* Value	Model 2	*P* Value	Model 3	*P* Value
GRACE score, per 10 points	1.14 (1.01, 1.29)	.03	1.06 (0.90, 1.26)	.48	1.05 (0.88, 1.24)	.60
Diameter stenosis, per 5 percentage points	1.05 (0.98, 1.12)	.20	1.04 (0.97, 1.13)	.27	…	…
Low-attenuation plaque burden, per 1 percentage point	1.14 (1.01, 1.29)	.04	1.16 (1.02, 1.32)	.03	1.23 (1.06, 1.42)	.006
PCAT attenuation, per 2 HU	1.12 (1.00, 1.25)	.047	1.12 (1.00, 1.26)	.049	1.17 (1.04, 1.33)	.01

Note.—Effect sizes are hazard ratios with 95% CIs in parentheses. Model 1 is a univariate model. Model 2 is a multivariable model that includes the variables from model 1, each separately adjusted for age, male sex, diabetes mellitus, hypertension, dyslipidemia, and smoking (as fixed-effects factors) and for index acute coronary syndrome (as a random-effects factor). Model 3 is a multivariable model that includes all independent variables from model 1, simultaneously adjusted for age, male sex, diabetes mellitus, hypertension, dyslipidemia, and smoking (as fixed-effects factors) and for index acute coronary syndrome (as a random-effects factor). GRACE = Global Registry of Acute Coronary Events, PCAT = pericoronary adipose tissue.

patients, the prognostic algorithm that incorporated the perivascular fat attenuation index score changed the C statistic by 0.016 when added to cardiovascular risk scores and Coronary Artery Disease Reporting and Data System 2.0 (30). Given the modest sample size and number of clinical events, the diagnostic and prognostic potential of PCAT attenuation should be explored in larger prospective studies with greater power. Second, additional scan acquisition and reconstruction parameters may influence attenuation values, and only tube voltage was harmonized in this analysis. Third, PCAT attenuation was calculated as a vessel volume-weighted average, and lesion-specific PCAT attenuation could not be assessed because culprit lesions were not recorded

in the trial database. However, for patients presenting with acute chest pain, the site of the culprit plaque or vessel may not be initially apparent, and a global assessment of PCAT attenuation may be clinically relevant. Fourth, the GRACE score was used as the clinical risk score, a well-validated tool for prognostication in ACS (34,35). However, the GRACE score has received extensive validation in the emergency care setting for its diagnostic utility in undifferentiated acute chest pain, and it was modestly discriminative for ACS diagnosis in intermediate-risk patients (36–38). Prior analyses of RAPID-CTCA showed that most of the primary end points in this cohort occurred in participants with a GRACE score below the high-risk threshold of 140, and higher GRACE scores were associated with larger plaque burdens, including total plaque and LAP (11). Fifth, the diagnosis of ACS was site reported and not adjudicated independently, introducing misclassification bias.

In conclusion, PCAT attenuation showed limited diagnostic value for ACS in intermediate-risk participants with acute chest pain. PCAT attenuation was modestly associated with death or recurrent myocardial infarction at 1 year but did not provide additive or incremental prognostic value beyond established quantitative plaque burden measures. These findings do not support the addition of PCAT attenuation for diagnostic or prognostic assessment in this patient population. Larger prospective studies should evaluate the diagnostic and prognostic role of PCAT in intermediate-risk patients with acute chest pain.

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Received March 23, 2025; revision requested April 30; revision received October 25; accepted November 11.

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Supplemental material: Supplemental material is available at *Radiology: Cardiothoracic Imaging* online.

Funding: The RAPID-CTCA trial was investigator led, and oversight was delivered by a trial management group supported by independent trial steering and data monitoring committees. The RAPID-CTCA trial was coordinated by the Edinburgh Clinical Trials Unit, and governance and monitoring were provided by the Academic and Central Clinical Office for Research and Development on behalf of the trial sponsors (University of Edinburgh and NHS Lothian). D.E.N. and N.L.M. are supported by the British Heart Foundation (CH/09/002, CH/F/21/90010, RG/23/F/22/110093, RG/20/10/34966, RE/24/130012). K.L.W. is supported by the Yin Shu-Tien Foundation (111-V-A-010). D.E.N. is funded by the British Heart Foundation (CH/09/002, RG/F/22/110093, RE/24/130012 and SI/F/24/21170016) and the UK Research and Innovation Medical Research Council (MR/Y008944/1, G0701127 and MR/Z504658/1).

Author contributions: Suvasini Lakshmanan: Conceptualization, Investigation, Methodology, Writing - original draft, Writing - review & editing; Kang-Ling Wang: Conceptualization, Formal analysis, Investigation, Methodology, Validation, Writing - original draft, Writing - review & editing; Mohammed Meah: Data curation, Investigation, Methodology, Supervision; Evangelos Tzolos: Conceptualization, Formal analysis, Supervision; Anda Bularga: Conceptualization, Resources, Writing - review & editing; Marc Dweck: Conceptualization, Data curation, Investigation, Methodology, Resources, Supervision, Writing - review & editing; Nick Curzen: Conceptualization, Funding acquisition, Investigation, Methodology, Supervision, Writing - review & editing; Attila Kardos: Conceptualization, Supervision, Writing - review & editing; Liza Keating: Conceptualization, Resources, Supervision, Writing - review & editing; Robert Storey: Conceptualization, Investigation, Methodology, Supervision, Writing - review & editing; Nicholas L Mills: Conceptualization, Supervision, Writing - review & editing; Piotr Slomka: Conceptualization, Software, Writing - review & editing; Damini Dey: Investigation, Methodology, Software, Supervision, Writing - review & editing; Alasdair Gray: Conceptualization, Investigation, Methodology, Resources, Supervision, Writing - review & editing; Michelle C. Williams: Conceptualization, Formal analysis, Investigation, Methodology, Resources, Supervision, Writing - review & editing; and Carl A Roobottom: Conceptualization, Investigation, Methodology, Supervision, Writing - review & editing; David E. Newby: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing - review & editing.

Data sharing: Data generated or analyzed during the study are available from the corresponding author by request.

Disclosures of conflicts of interest: D.D. is a member of the *Radiology: Cardiothoracic Imaging* editorial board. M.C.W. is a deputy editor of *Radiology: Cardiothoracic Imaging*. Please see ICMJE form(s) for author conflicts of interest. These have been provided as supplemental materials.

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