Jian Wang[1], Jianjun Chu[2], Chunju Jiang[3], Menghong Cao[4]

[1] Department of Imaging, General Hospital of the Yangtze River Shipping (Wuhan Brain Hospital), Wuhan, China

[2] Department of Medical Imaging, Henan Tianyou Integrative Medicine Cancer Hospital, Zhengzhou, China

[3] Department of Imaging, Western Theater Command Air Force Hospital, Chengdu, China

[4] Department of Medical Imaging, Shanghai Pudong Hospital (Fudan University Pudong Medical Center), Shanghai, China

Coronary CT Angiography in Acute Coronary Syndrome and Analysis of Factors That Influence This Assessment

Objective	To evaluate coronary CT angiography (CCTA) combined with Coronary Artery Disease Reporting and Data System (CAD-RADS) grading and with high-risk plaque characteristics for predicting 30-day major adverse cardiovascular events (MACE) in patients with acute coronary syndrome (ACS).
Material and methods	A prospective, multicenter cohort study was conducted by enrolling 300 ACS patients admitted to four tertiary hospitals from January 2023 to June 2024. All patients underwent CCTA examination within 24 h of admission. Coronary artery stenosis severity was assessed using CAD-RADS 2.0 criteria, and high-risk plaque characteristics, including low-density plaque, positive remodeling, spotty calcification, and napkin-ring sign, were analyzed. Baseline clinical data were collected, Global Registry of Acute Coronary Events (GRACE) scores were calculated, and the 30-day MACE incidence was evaluated. Logistic regression analysis was used to evaluate risk factors, and receiver operating characteristic (ROC) curves were used to assess diagnostic performance.
Results	The incidence of 30-day MACE was 22.7% (68/300 cases). Spearman's rank correlation analysis demonstrated that MACE incidence showed a significant positive correlation with the CAD-RADS grade (ρ=0.658, $p<0.05$), increasing from 0% in CAD-RADS grade 0 to 100% in CAD-RADS grade 5. Patients in the MACE group were older, had higher prevalence of diabetes and higher GRACE scores (all $p<0.05$). High-risk plaque characteristics, i.e., low-density plaque, positive remodeling, and napkin-ring sign, were detected more frequently in the MACE group (all $p<0.05$). Multivariate analysis showed that the GRACE score and positive remodeling were independent predictors of 30-day MACE (both $p<0.05$). The comprehensive prediction model combining GRACE score, CAD-RADS grading, and high-risk plaque characteristics achieved an area under the ROC curve (AUC) of 0.789, significantly superior to the GRACE score model alone (AUC=0.723, $p=0.018$), representing a 9.1% improvement in discriminative ability.
Conclusion	A non-invasive imaging examination, CCTA, combined with CAD-RADS grading and high-risk plaque assessment can improve the prediction of 30-day MACE risk in ACS patients beyond traditional risk scores, providing important reference for clinical risk stratification and precision treatment decision-making.

Keywords	Acute coronary syndrome; coronary CT angiography; CAD-RADS; high-risk plaque; major adverse cardiovascular events; prognostic assessment
For citations	Jian Wang, Jianjun Chu, Chunju Jiang, Menghong Cao. Coronary CT Angiography in Acute Coronary Syndrome and Analysis of Factors That Influence This Assessment. Kardiologiia. 2025;65(12):81–89. [Russian: Значение компьютерной томографической коронарной ангиографии при остром коронарном синдроме и анализ показателей, влияющих на прогноз. Кардиология. 2025;65(12):81–89].

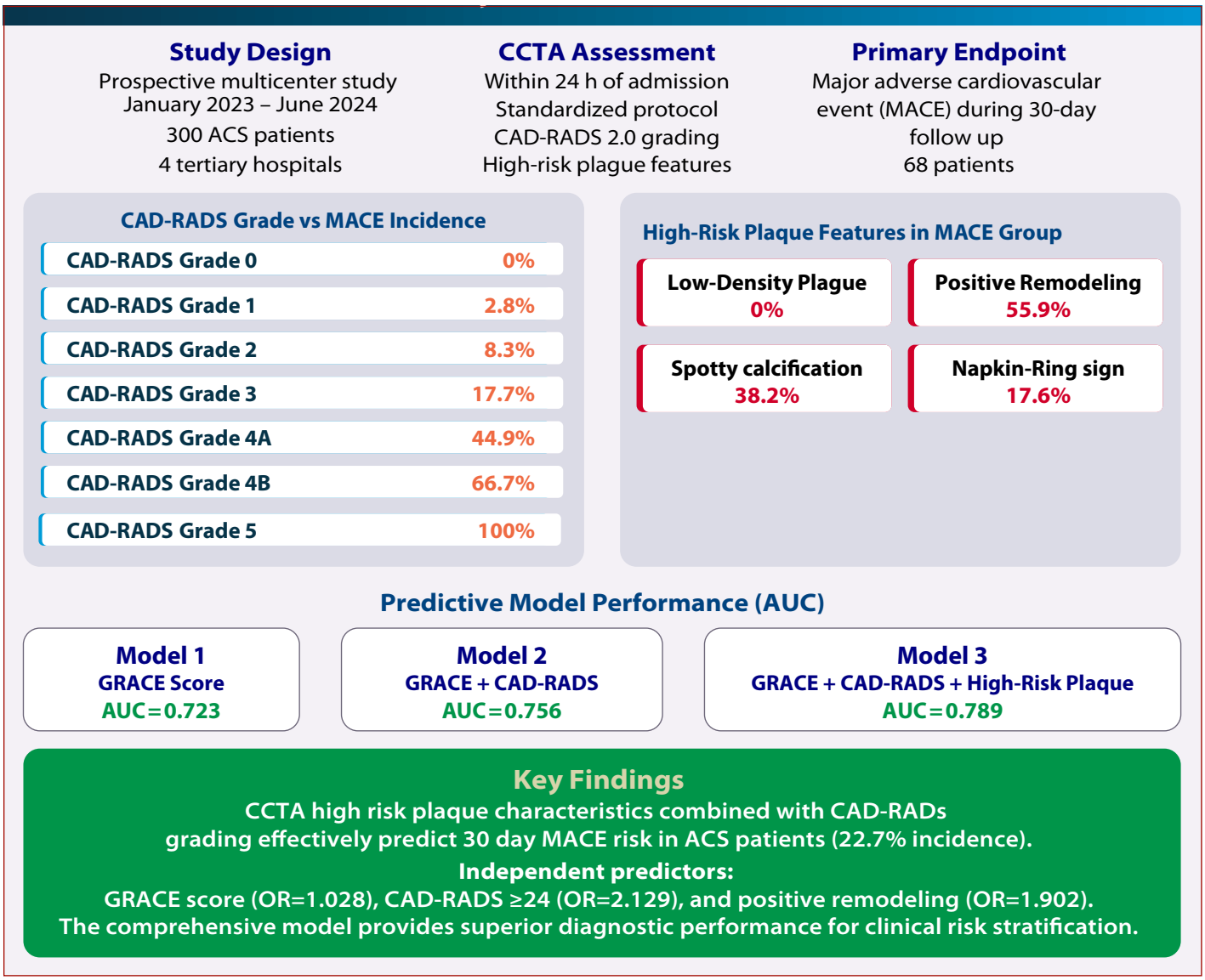
Corresponding author Menghong Cao. Email: menghongcao5676@sina.com

Introduction

Acute coronary syndrome (ACS) is one of the most critical clinical syndromes in cardiovascular disease. ACS includes ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, and unstable angina and is characterized by high morbidity and mortality [1]. Accurate assessment of coronary lesion severity and short-term prognostic risk in ACS patients is of significant clinical importance for developing individualized treatment strategies and, thus, for improving patient outcomes [2]. Traditional risk assessment primarily relies on clinical presentation, electrocardiographic changes, myocardial biomarkers (including cardiac troponin I and creatine kinase-MB), and Global Registry of Acute Coronary Events (GRACE) scores, but this assessment has limitations for predicting major adverse cardiovascular events (MACE) [3].

Coronary CT angiography (CCTA) is a non-invasive imaging examination that can directly visualize coronary anatomy, luminal stenosis severity, and plaque characteristics. It provides a new approach for risk stratification in ACS patients [4]. The CAD-RADS classi-

Central illustration. Predictive Value of CAD-RADS Grading and High-Risk Plaque Characteristics for 30-Day MACE in Patients with ACS



fication system provides a unified framework for standardized reporting of CCTA results, since coronary plaque morphological characteristics, such as low-density plaque, positive remodeling, spotty calcification, and napkin-ring sign, are closely associated with acute coronary events [5].

Large-scale prospective studies on the value of CCTA in prognostic assessment of ACS patients and its influencing factors are relatively limited [6]. Recent guidelines emphasize the importance of non-invasive imaging in coronary disease evaluation, with CCTA playing an increasingly significant role in patient management [7].

This study systematically evaluated the predictive value of CCTA combined with CAD-RADS grading and high-risk plaque characteristics for 30-day MACE in ACS patients. This multicenter, prospective, cohort study aimed to provide scientific evidence needed for making improved decisions regarding clinical precision treatment [8].

Material and methods

Study Design and Patient Selection

This was a prospective multicenter cohort study of patients admitted from January 2023 to June 2024 to four tertiary hospitals (Changjiang Navigation General Hospital, Henan Tianyou Integrated Traditional Chinese and Western Medicine Oncology Hospital, Western Theater Air Force Hospital, and Shanghai Pudong Hospital). The ethics committees of all participating hospitals approved the study protocol, and all patients signed informed consent forms. Inclusion criteria: age 18–80 yrs, meeting ACS diagnostic criteria, completion of CCTA examination within 24 h of admission, complete clinical data. Exclusion criteria: severe renal dysfunction (serum creatinine >1.5 mg/dl), history of iodine contrast allergy, severe arrhythmia affecting image quality, expected survival <6 mos, pregnancy or lactation, history of coronary artery bypass grafting (CABG).

ISSN 0022-9040. Кардиология. 2025;65(12). DOI: 10.18087/cardio.2025.12.n2900

CCTA Examination Protocol

All patients were examined with 64-slice or higher multidetector computed tomography (CT). Pre-examination preparation included oral metoprolol 25–50 mg if heart rate >70 beats/min and sublingual nitroglycerin 0.5 mg. Dual-phase, contrast-enhanced scanning protocol was used with iohexol or iopromide contrast agent, dose 80–100 ml, injection rate 4.5–5.0 ml/s. Scanning parameters: tube voltage 100–120 kVp, tube current 200–400 mAs, slice thickness 0.625 mm, reconstruction interval 0.3 mm. Image reconstruction used electrocardiogram (ECG) gating technique, selecting mid-diastole for reconstruction. All images were independently read by two double-blinded radiologists with more than five yrs of experience in cardiovascular imaging diagnostics. Consensus was reached through discussion when opinions differed.

Image Analysis and CAD-RADS Assessment

CAD-RADS 2.0 classification criteria were used to assess coronary stenosis severity: CAD-RADS grade 0 (normal, 0% stenosis), CAD-RADS grade 1 (minimal, 1–24% stenosis), CAD-RADS grade 2 (mild, 25–49% stenosis), CAD-RADS grade 3 (moderate, 50–69% stenosis), CAD-RADS grade 4A (severe, 70–99% stenosis, left main <50%), CAD-RADS grade 4B (severe, 70–99% stenosis, left main ≥50%), CAD-RADS grade 5 (total occlusion, 100% stenosis). All coronary segments were included in the atherosclerotic plaque analysis, with focus on symptom-related arteries. High-risk plaque characteristics were defined as: low-density plaque (CT value <30 Hounsfield units [HU]), positive remodeling (remodeling index >1.1), and spotty calcification, napkin-ring sign. Quantitative analysis parameters included plaque volume, calcium score, and lipid core volume ratio.

Treatment Protocol and Management

All patients received standardized treatment according to guideline recommendations. Medical treatment included: dual antiplatelet therapy (aspirin 100 mg/d combined with either clopidogrel 75 mg/d or ticagrelor 90 mg twice daily), statin therapy (atorvastatin 20-40mg/d or rosuvastatin 10–20 mg/d), beta-blockers (metoprolol 25–100 mg twice daily), angiotensin-converting enzyme inhibitors (ACEI), or angiotensin receptor blockers (ARB). Revascularization therapy (percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)) was determined based on clinical symptoms, ECG changes, myocardial biomarker concentrations, and coronary lesion severity. PCI indications were hemodynamically significant stenosis (luminal stenosis ≥70% or left main ≥50%), or moderate stenosis (50–69%) with evidence of myocardial ischemia. CABG indications included left main stenosis ≥50%, three-vessel disease, or complex multivessel disease with reduced left ventricular function. Detailed records were kept of all patient treatment regimens, drug dosages, and intervention timing and method.

Clinical Assessment and Follow-up

Baseline clinical data were collected at admission, including age, gender, medical history (hypertension, diabetes, dyslipidemia, smoking history), laboratory data (including myocardial biomarkers such as cardiac troponin I and creatine kinase-MB, lipids, and renal function), and results of ECG and echocardiographic analyses. The GRACE scoring system was used to assess 30-day MACE risk, with scoring elements including age, heart rate, systolic blood pressure, serum creatinine, cardiac arrest history, ST-segment changes, elevated myocardial biomarkers, and Killip classification. The primary study endpoint was defined as 30-day MACE, including cardiac death, non-fatal myocardial infarction, and urgent revascularization. Secondary endpoints included recurrent angina, heart failure hospitalization, and stroke. All patients underwent 30-day follow-up through outpatient visits, telephone follow-up, or medical record review to collect endpoint event information.

Statistical Analysis

Statistical analysis was performed using SPSS 26.0 software. Normally distributed continuous variables were expressed as mean ± standard deviation (SD), non-normally distributed variables as median (interquartile range), and categorical variables as number (percentage). Between-group comparisons were performed with t-tests or Mann-Whitney U tests as appropriate, and categorical variable comparisons were done with χ^2 tests or Fisher's exact tests. Spearman's rank correlation analysis was used to assess the relationship between ordinal variables (such as CAD-RADS grades) and MACE incidence. Logistic regression analysis was used to evaluate the predictive value of CT characteristics for adverse events by first performing univariate analysis and then including variables with $p<0.10$ in multivariate analysis models. Multivariate analysis used forward stepwise regression, with traditional cardiovascular risk factors (age, gender, diabetes, hypertension, smoking history), previous myocardial infarction, LDL–C levels, treatment regimen (emergency PCI), GRACE score, and CT parameters (CAD-RADS grade≥4, low-density plaque, positive remodeling, spotty calcification, napkin-ring sign) simultaneously entered as covariates for adjustment. ROC curves were used to evaluate diagnostic performance by calculating the area under the curve (AUC), sensitivity, specificity, positive predictive value, and negative predictive value. The DeLong test was used to compare diagnostic performance of different models. $p<0.05$ was considered statistically significant.

Table 1. Baseline patient characteristics

Variable	All patients (n=300)	MACE Group (n=68)	Non-MACE Group (n=232)	p Value
Age (yrs)	62.4±11.8	66.8±10.2	61.1±12.0	0.001
Males	195 (65.0)	45 (66.2)	150 (64.7)	0.823
Body mass index (kg/m²)	24.8±3.4	24.6±3.2	24.9±3.5	0.587
Hypertension	198 (66.0)	48 (70.6)	150 (64.7)	0.366
Diabetes	89 (29.7)	28 (41.2)	61 (26.3)	0.017
Dyslipidemia	167 (55.7)	42 (61.8)	125 (53.9)	0.252
Smoking history	142 (47.3)	40 (58.8)	102 (44.0)	0.032
Previous MI	56 (18.7)	18 (26.5)	38 (16.4)	0.048
Previous PCI history	45 (15.0)	12 (17.6)	33 (14.2)	0.485
Peak troponin I (μg/l)	2.8 (0.6–8.9)	6.2 (2.1–15.4)	2.1 (0.5–7.2)	<0.001
Peak CK-MB (μg/l)	18.5 (8.2–42.1)	35.6 (16.8–78.2)	15.2 (7.4–35.9)	<0.001
Total cholesterol (mmol/l)	4.6±1.2	4.8±1.3	4.5±1.2	0.089
LDL–C (mmol/l)	2.9±0.9	3.1±1.0	2.8±0.9	0.032
GRACE score	128.5±24.6	142.8±22.4	124.1±23.8	<0.001

Data are mean±SD, median (interquartile range), or number (percentage). MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; CK-MB, creatine kinase-MB (a myocardial biomarker); LDL–C, low-density lipoprotein cholesterol; GRACE, Global Registry of Acute Coronary Events.

Results

Patient Baseline Characteristics (Table 1)

This study enrolled 300 ACS patients. Based on the 30-day follow-up findings, 68 (22.7%) patients experienced MACE (MACE group), and 232 (77.3%) patients did not (non-MACE group). Between-group comparison showed that MACE group patients were older, had higher diabetes prevalence and smoking history, and had more frequent, previous myocardial infarctions (all p<0.05). MACE group patients had significantly elevated myocardial injury markers (cardiac troponin I and creatine kinase-MB), higher low-density lipoprotein cholesterol (LDL–C) levels, and higher GRACE scores (all p<0.05). No statistically significant differences were found between groups for gender, body mass index, hypertension, and dyslipidemia (all p>0.05).

CAD-RADS Grading Results (Table 2)

The CAD-RADS grade distribution showed that moderate to severe stenosis (CAD-RADS 3–5) accounted for 61.0% of the MACE incidence. Spearman's rank correlation analysis demonstrated a strong positive correlation between MACE incidence and CAD-RADS grade (ρ=0.658, p<0.001). Specifically, MACE incidence increased from 0% in CAD-RADS grade 0 to 100% in CAD-RADS grade 5. MACE incidence in patients with CAD-RADS grades 4A and 4B reached 44.9% and 66.7%, respectively, which was significantly higher than in the mild to moderate stenosis groups.

Table 2. MACE listed by CAD-RADS grade

CAD-RADS Grade	Patients	MACE Cases	MACE Incidence	p Value
0	6 (2.0)	0 (0)	0	<0.001
1	36 (12.0)	1 (1.5)	2.8	
2	72 (24.0)	6 (8.8)	8.3	
3	96 (32.0)	17 (25.0)	17.7	
4A	78 (26.0)	35 (51.5)	44.9	
4B	9 (3.0)	6 (8.8)	66.7	
5	3 (1.0)	3 (4.4)	100.0	

Data are number (percentage) or percentage.

Table 3. Coronary plaque characteristics

Plaque Characteristic	All Patients (n=300)	MACE Group (n=68)	Non-MACE Group (n=232)	p Value
Mean number of plaques per patient	4.3±2.1	5.1±2.3	4.0±2.0	0.001
Calcium score	186 (45-413)	298 (87-586)	156 (39-369)	0.002
Plaque type				
Calcified plaque	212 (70.7)	45 (66.2)	167 (72.0)	0.365
Non-calcified plaque	189 (63.0)	52 (76.5)	137 (59.1)	0.009
Mixed plaque	156 (52.0)	42 (61.8)	114 (49.1)	0.068
High-risk plaque features				
Low-density plaque	132 (44.0)	42 (61.8)	90 (38.8)	0.001
Positive remodeling	126 (42.0)	38 (55.9)	88 (37.9)	0.009
Spotty calcification	87 (29.0)	26 (38.2)	61 (26.3)	0.059
Napkin-ring sign	27 (9.0)	12 (17.6)	15 (6.5)	0.005
High-risk plaque number	1.2±1.1	1.7±1.2	1.1±1.0	<0.001
Plaque volume (mm³)	126±79	168±89	112±73	<0.001
Lipid core ratio (%)	18.6±12.4	24.8±14.2	16.8±11.3	<0.001

Data are mean±SD, median (interquartile range), or number (percentage).

Analysis of Coronary Plaque Characteristics (Table 3)

A total of 1,286 plaques were detected across all 300 patients, with calcified plaques being the most common. On average, patients had 4.3±2.1 plaques per individual. Patients in the MACE group had significantly higher rates of high-risk plaque characteristics, with detection rates of low-density plaques, positive remodeling, and napkin-ring signs all significantly higher than in the non-MACE group (all p<0.05). Accordingly, the MACE group patients had heavier plaque burden, manifested as increased plaque number, elevated calcium score, enlarged plaque volume, and increased lipid core ratio (all p<0.01).

Treatment Strategy Analysis (Table 4)

All patients received standardized medical treatment as recommended by accepted guidelines. There was no significant difference in medical treatment regimens between the groups (all p>0.05). The overall revascularization rate was 78.0% (234/300 patients), with PCI being the prima-

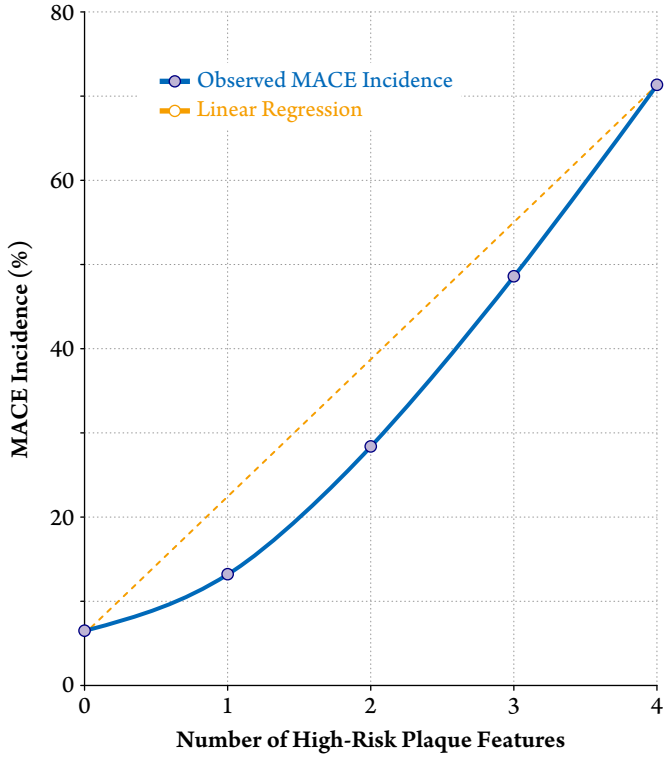
ISSN 0022-9040. Кардиология. 2025;65(12). DOI: 10.18087/cardio.2025.12.n2900

Table 4. Treatment strategies

Strategy	All Patients (n=300)	MACE Group (n=68)	Non-MACE Group (n=232)	p Value
Pharmacological treatment				
Dual antiplatelet	300 (100)	68 (100)	232 (100)	–
Aspirin and clopidogrel	186 (62.0)	38 (55.9)	148 (63.8)	0.242
Aspirin and ticagrelor	114 (38.0)	30 (44.1)	84 (36.2)	–
Statin therapy	298 (99.3)	68 (100)	230 (99.1)	0.999
Atorvastatin	189 (63.0)	43 (63.2)	146 (63.0)	0.967
Rosuvastatin	109 (36.3)	25 (36.8)	84 (36.2)	
Beta-blockers	286 (95.3)	65 (95.6)	221 (95.3)	0.999
ACEI/ARB	274 (91.3)	62 (91.2)	212 (91.4)	0.962
Revascularization treatment				
PCI	228 (76.0)	60 (88.2)	168 (72.4)	0.007
CABG	6 (2.0)	2 (2.9)	4 (1.7)	0.618
Conservative treatment	66 (22.0)	6 (8.8)	60 (25.9)	0.003
PCI timing				
Emergency PCI (<12 h)	108 (36.0)	32 (47.1)	76 (32.8)	0.036
Early PCI (12–72 h)	84 (28.0)	19 (27.9)	65 (28.0)	0.987
Elective PCI (>72 h)	36 (12.0)	9 (13.2)	27 (11.6)	0.726
Number of stents implanted	1.6±0.8	1.9±0.9	1.5±0.7	0.003

Data are number (percentage). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Figure 1. Correlation Between Number of High-Risk Plaque Features and MACE Incidence



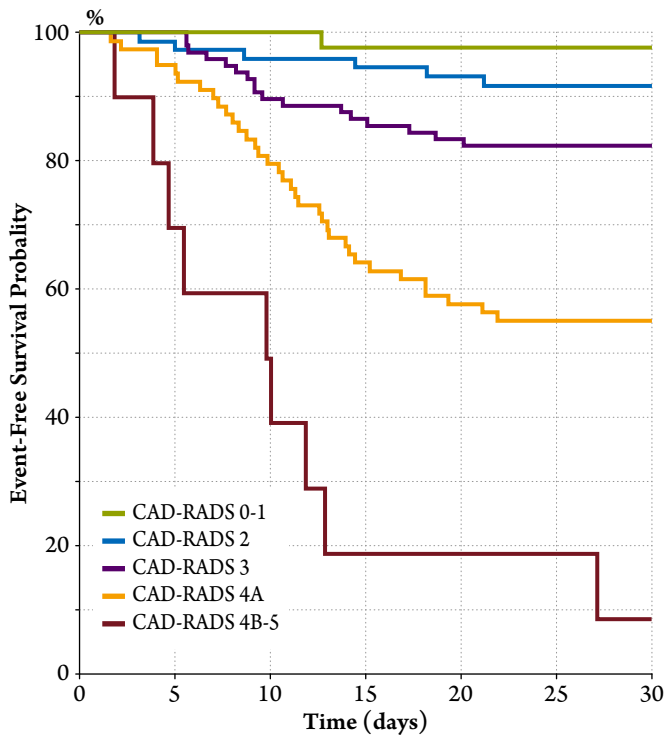
Linear regression analysis revealed a significant positive correlation between the number of high-risk plaque features and MACE incidence (R^2=0.952, p<0.001).

Table 5. 30-day follow-up occurrence of endpoint events

Endpoint Event	Cases	95% Confidence Interval
Primary endpoint (MACE)	68 (22.7)	18.1–27.9
Cardiac death	6 (2.0)	0.7–4.3
Non-fatal myocardial infarction	38 (12.7)	9.1–17.1
Urgent revascularization	24 (8.0)	5.2–11.7
Secondary endpoints		
Recurrent angina	89 (29.7)	24.6–35.2
Heart failure hospitalization	15 (5.0)	2.8–8.1
Stroke	3 (1.0)	0.2–2.9
All-cause mortality	8 (2.7)	1.2–5.2

Data are number (percentage). The 95% confidence intervals represent the estimated range for the incidence proportion of each endpoint event.

Figure 2. 30-Day Event-Free Survival Stratified by CAD-RADS Classification



Survival curves demonstrate significant differences in prognosis among patients with different CAD-RADS grades (log-rank test p<0.001).

ry treatment modality, accounting for 76.0% (228/300 patients) of all cases. The MACE group had a higher proportion receiving revascularization treatment (p<0.01), with significantly higher proportion of emergency PCI and average number of implanted stents (both p<0.05), reflecting the complexity and severity of the lesions.

30-Day Follow-up Results (Table 5; Figures 1 and 2)

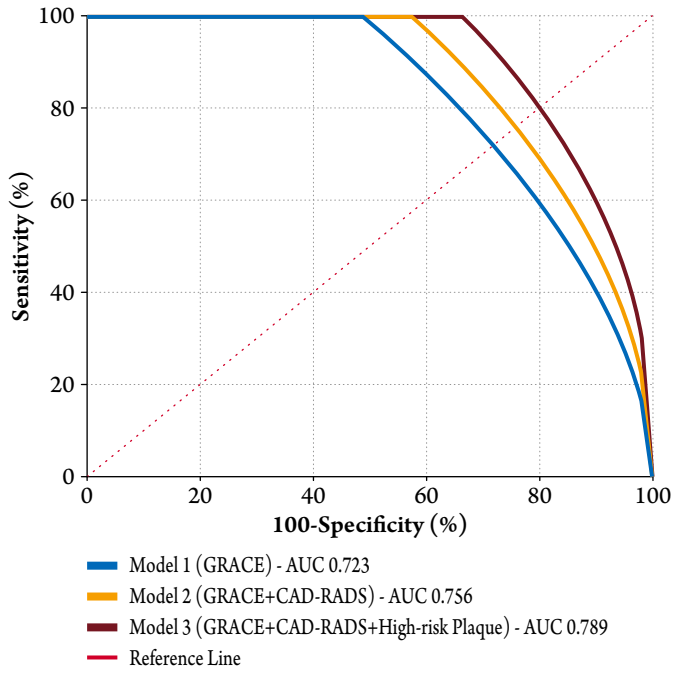
During the 30-day follow-up period, MACE incidence was 22.7%, with non-fatal myocardial infarction being

Table 6. Univariate logistic regression analysis of MACE risk factors

Variable	OR	95% Confidence Interval	p Value
Age (per 1-yr increase)	1.048	1.018–1.079	0.001
Male	1.070	0.607–1.886	0.823
Hypertension	1.299	0.723–2.333	0.378
Diabetes	1.954	1.124–3.398	0.018
Dyslipidemia	1.378	0.793–2.396	0.253
Smoking history	1.816	1.048–3.145	0.034
Previous myocardial infarction	1.822	0.987–3.365	0.055
Previous PCI history	1.290	0.635–2.620	0.485
LDL–C (per 1 mmol/l increase)	1.356	1.025–1.794	0.033
GRACE score (per 1-point increase)	1.034	1.022–1.047	<0.001
CAD-RADS grade ≥4	3.248	1.896–5.564	<0.001
Low-density plaque	2.541	1.486–4.346	0.001
Positive remodeling	2.089	1.234–3.538	0.006
Spotty calcification	1.728	1.005–2.969	0.048
Napkin-ring sign	3.047	1.398–6.641	0.005
High-risk plaque number (per 1 value increase)	1.524	1.235–1.881	<0.001
Emergency PCI	1.842	1.089–3.114	0.023
Statin therapy	0.686	0.298–1.578	0.378

OR, odds ratio; PCI, percutaneous coronary intervention; LDL–C, low-density lipoprotein cholesterol; GRACE, Global Registry of Acute Coronary Events.

Figure 3. ROC Curves for Predictive Models of 30-Day MACE



Model 1: GRACE score only; Model 2: GRACE + CAD-RADS; Model 3: GRACE + CAD-RADS + High-risk plaque features. AUC comparison: Model 3 vs Model 1 (p=0.018), Model 3 vs Model 2 (p=0.041)

the most common. Among secondary endpoints, recurrent angina had the highest rate at 29.7%. CAD-RADS grading and number of high-risk plaque characteristics showed significant positive correlations with MACE incidence. The relationship between the number of high-risk plaque features and MACE incidence is demonstrated. As the number of high-risk plaque features increases, MACE incidence shows an upward trend. Linear regression analysis revealed a significant positive correlation between the two variables (R^2=0.952, p<0.001). It should be noted that when the number of high-risk plaque features is low (0–1), MACE incidence is relatively low with minimal variation, whereas when the number of high-risk plaque features increases to 3 or more, MACE incidence rises substantially. This trend suggests that the cumulative effect of high-risk plaque features has an important impact on prognosis. The 30-day event-free survival curves stratified by CAD-RADS classification are illustrated. Kaplan-Meier survival analysis demonstrated significant differences in prognosis among patients with different CAD-RADS grades (log-rank test p<0.001). At the end of the 30-day follow-up period, the event-free survival rates were 97.6% for CAD-RADS grades 0–1, 91.7% for grade 2, 82.3% for grade 3, 55.1% for grade 4A, and only 8.6% for grades 4B-5. These findings confirm the important value of the CAD-RADS grading system in short-term prognostic assessment of ACS patients, with higher CAD-RADS grades being closely associated with increased risk of early adverse events.

Univariate Analysis of MACE Risk Factors (Table 6)

Univariate analysis identified potential risk factors associated with 30-day MACE occurrence. Among the clinical factors, age (per 1-yr increase: OR=1.048, 95% CI: 1.018–1.079), diabetes (OR=1.954, 95% CI: 1.124–3.398), smoking history (OR=1.816, 95% CI: 1.048–3.145), and LDL–C levels (per 1 mmol/l increase: OR=1.356, 95% CI: 1.025–1.794) were associated with MACE occurrence (all p<0.05). GRACE score showed a strong predictive value (per 1-point increase: OR=1.034, 95% CI: 1.022–1.047, p<0.001). Among the imaging parameters, CAD-RADS grade ≥4 had the strongest predictive value (OR=3.248, 95% CI: 1.896–5.564, p<0.001). All the high-risk plaque characteristics were significantly associated with MACE occurrence (all p<0.05), including low-density plaque (OR=2.541, 95% CI: 1.486–4.346), positive remodeling (OR=2.089, 95% CI: 1.234–3.538), spotty calcification (OR=1.728, 95% CI: 1.005–2.969), and napkin-ring sign (OR=3.047, 95% CI: 1.398–6.641), with napkin-ring sign having the highest predictive value.

ISSN 0022-9040. Кардиология. 2025;65(12). DOI: 10.18087/cardio.2025.12.n2900

Table 7. Multivariate logistic regression analysis of MACE risk factors

Variable	β Coefficient	Standard Error	OR	95% Confidence Interval	p Value
Age (per 1-yr increase)	0.025	0.018	1.025	0.989–1.063	0.167
Diabetes	0.445	0.334	1.560	0.811–3.000	0.183
Smoking history	0.298	0.321	1.347	0.718–2.526	0.354
Previous myocardial infarction	0.412	0.368	1.510	0.734–3.105	0.263
LDL–C (per 1 mmol/l increase)	0.189	0.145	1.208	0.910–1.604	0.194
GRACE score (per 1-point increase)	0.028	0.007	1.028	1.015–1.042	<0.001
CAD-RADS grade≥4	0.756	0.346	2.129	1.080–4.194	0.029
Low-density plaque	0.612	0.325	1.844	0.977–3.478	0.060
Positive remodeling	0.643	0.318	1.902	1.021–3.544	0.043
Spotty calcification	0.347	0.322	1.415	0.754–2.656	0.281
Napkin-ring sign	0.789	0.421	2.201	0.963–5.028	0.061
Emergency PCI	0.486	0.334	1.626	0.845–3.129	0.146

Constant β=–3.892, Model χ^2=67.234, p<0.001, Nagelkerke R^2=0.298. OR, odds ratio; PCI, percutaneous coronary intervention; LDL–C, low-density lipoprotein cholesterol; GRACE, Global Registry of Acute Coronary Events.

Table 8. Comparison of diagnostic performance of different prediction models

Prediction Model	AUC	95% Confidence Interval	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	p Value*
Model 1 (GRACE score)	0.723	0.667–0.775	70.6	68.1	39.3	88.8	–
Model 2 (GRACE + CAD-RADS)	0.756	0.701–0.807	72.1	72.4	43.6	90.3	0.041
Model 3 (GRACE + CAD-RADS + high-risk plaque)	0.789	0.737–0.836	75.0	76.7	48.1	91.8	0.018

*p value compared to Model 1 using DeLong test; AUC, area under the curve; GRACE, Global Registry of Acute Coronary Events.

Multivariate Analysis of MACE Risk Factors (Table 7)

After adjusting for confounding factors in the multivariate analysis, GRACE score, CAD-RADS grade ≥4, and positive remodeling remained independent predictors of MACE (all p<0.05). Although low-density plaque did not reach statistical significance, it showed a predictive trend (p=0.060). Traditional risk factors such as age, diabetes, and smoking history lost statistical significance in the multivariate model (all p>0.05). The overall predictive ability of the model was good (Nagelkerke R^2=0.298).

Diagnostic Performance Evaluation of Prediction Models (Table 8, Figure 3)

Three progressive prediction models showed that the comprehensive model (Model 3) combining GRACE score, CAD-RADS grade, and high-risk plaque characteristics had the best diagnostic performance, with AUC significantly superior to the other two models (both p<0.05). This model demonstrated excellent performance in sensitivity, specificity, and predictive values

Subgroup Analysis (Table 9)

Subgroup analysis of different clinical characteristics confirmed the universal predictive value of high-risk plaque characteristics, with no significant interaction effects found between subgroups (all interactions p>0.05). In diabetic patients, low GRACE score patients, and patients receiving PCI treatment, the predictive value of high-risk plaque characteristics was more prominent (all p<0.05), while predictive efficacy was relatively weaker in elderly patients, female patients, and high GRACE score patients.

Discussion

In this study, the 30-day MACE incidence among ACS patients was 22.7%, consistent with international, large-scale ACS registry data [9]. MACE incidence increased significantly along with CAD-RADS grading, from 0% in CAD-RADS grade 0 to 100% in CAD-RADS grade 5, consistent with the recognized relationship between coronary stenosis severity and prognosis [10]. In fact, MACE incidence in CAD-RADS grade 4A and 4B patients reached 44.9% and 66.7% respectively, suggesting that patients with severe coronary stenosis require aggressive treatment [11].

The analysis of the high-risk plaque characteristics showed their importance in MACE prediction. Low-density plaque, positive remodeling, spotty calcification, and napkin-ring sign had significantly higher presence in the MACE group, confirming that plaque morphological characteristics can better reflect plaque instability and rupture risk than does simply noting the presence of luminal stenosis [12]. The comprehensive prediction model achieved an AUC of 0.789, demonstrating statistically significant superiori-

Table 9. Predictive value of high-risk plaque features (≥2) for MACE in different subgroups

Subgroup	Patient Number	MACE Incidence (%)	OR Value	95% Confidence Interval	p Value	p Value for Interaction
Age						0.342
<65 yrs	167	18.6	2.156	1.089–4.269	0.028	
≥65 yrs	133	27.8	1.598	0.803–3.179	0.184	
Gender						0.567
Male	195	23.1	1.934	1.024–3.653	0.042	
Female	105	21.9	1.656	0.648–4.238	0.295	
Diabetes						0.089
Yes	89	31.5	2.845	1.134–7.136	0.026	
No	211	18.5	1.534	0.806–2.918	0.193	
GRACE score						0.078
≤140 points	178	15.7	2.589	1.156–5.793	0.021	
>140 points	122	32.8	1.356	0.594–3.093	0.468	
PCI						0.156
Yes	228	26.3	2.345	1.247–4.409	0.008	
No	72	12.5	1.134	0.267–4.814	0.864	

OR, odds ratio; MACE, major adverse cardiovascular events; GRACE, Global Registry of Acute Coronary Events, PCI: percutaneous coronary intervention.

ty over the GRACE score alone (AUC=0.723, p=0.018 by DeLong test), with a 9.1% improvement in discriminative ability. While this improvement is modest in absolute terms, it represents a clinically meaningful enhancement in risk stratification, as demonstrated by the improved sensitivity (75.0% vs. 70.6%) and specificity (76.7% vs. 68.1%) [13]. Multivariate analysis identified the GRACE score, CAD-RADS grade ≥4, and positive remodeling as independent predictors of 30-day MACE. As a marker of coronary artery plaque instability, positive remodeling has an independent predictive value that provides a new reference for clinical decision-making [14].

Subgroup analysis showed that high-risk plaque characteristics had more prominent predictive value in patients with diabetes, low GRACE scores, and in PCI-treated patients, thus providing further incentive for application of precision treatment [15]. High-risk plaque characteristics have clear pathophysiological basis for MACE occurrence. Low-density plaques contain large amounts of lipid core and inflammatory cells with thin fibrous caps, prone to rupture and cause acute thrombosis [16]. Positive remodeling reflects compensatory vascular wall expansion, often accompanied by intensified inflammatory reactions, leading to plaque instability [17]. A napkin-ring sign indicates large lipid cores covered by thin-walled fibrous caps, a typical manifestation of plaque vulnerability [18].

CAD-RADS grading identifies hemodynamically significant stenoses that reflect not only myocardial ischemia risk but often the accompanying complex plaque morphology [19]. In the current study, even patients with moderate stenosis had a MACE incidence of 17.7%, further supporting the importance of plaque characteristics in risk assessment [20].

This study has certain limitations. First, a single ethnic population was included in the study, so generalization of the results may be limited. Second, the 30-day follow-up period was relatively short; it did not permit evaluation of long-term prognosis. Third, some inter-reader inconsistency must be acknowledged. Fourth, the currently applied quantitative standards for evaluation of some high-risk plaque characteristic remain controversial [10].

Future studies should include multi-ethnic, large-sample prospective cohorts studied over extended follow-up periods. These studies should utilize artificial intelligence technology to develop tools for standardized, automated plaque analysis [21, 22]. Future studies should evaluate the success of individualized treatment strategies based on CCTA results [23].

Finally, it is important to recognize that recent advances in artificial intelligence and machine learning, as applied to coronary plaque analysis, show promising results for improving diagnostic accuracy and workflow efficiency [24]. The integration of AI-enabled automated plaque analysis with traditional risk assessment should further enhance prognostic stratification and clinical practice [25, 26].

Conclusions

This study confirms the importance of CCTA high-risk plaque characteristics combined with CAD-RADS grading in short-term prognostic assessment of ACS patients. The information provided by this approach should improve clinical risk stratification and provide a basis for precision treatment of ACS.

Acknowledgments

Jian Wang and Jianjun Chu are co-first authors; they contributed equally to this work.

No conflicts of interest are reported.

The article was received on 12/02/2025.

REFERENCES

1. Licordari R, Costa F, Garcia-Ruiz V, Mamas MA, Marquis-Gravel G, De La Torre Hernandez JM et al. The Evolving Field of Acute Coronary Syndrome Management: A Critical Appraisal of the 2023 European Society of Cardiology Guidelines for the Management of Acute Coronary Syndrome. Journal of Clinical Medicine. 2024;13(7):1885. DOI: 10.3390/jcm13071885

ISSN 0022-9040. Кардиология. 2025;65(12). DOI: 10.18087/cardio.2025.12.n2900

2. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A et al. 2023 ESC Guidelines for the management of acute coronary syndromes. European Heart Journal. 2023;44(38):3720–826. DOI: 10.1093/eurheartj/ehad191
3. Kabiri A, Gharin P, Forouzannia SA, Ahmadzadeh K, Miri R, Yousefifard M. HEART versus GRACE Score in Predicting the Outcomes of Patients with Acute Coronary Syndrome; a Systematic Review and Meta-Analysis. Archives of Academic Emergency Medicine. 2023;11(1):e50. DOI: 10.22037/aaem.v11i1.2001
4. Sandoval Y, Leipsic JA, Collet C, Ali ZA, Azzalini L, Barbato E et al. Coronary Computed Tomography Angiography to Guide Percutaneous Coronary Intervention: Expert Opinion from a SCAI/SCCT Roundtable. Journal of the Society for Cardiovascular Angiography & Interventions. 2025;4(6):103664. DOI: 10.1016/j.jscai.2025.103664
5. Oikonomou EK, Antoniades C. The role of adipose tissue in cardiovascular health and disease. Nature Reviews Cardiology. 2019;16(2):83–99. DOI: 10.1038/s41569-018-0097-6
6. Van Rosendael AR, Crabtree T, Bax JJ, Nakanishi R, Mushtaq S, Pontone G et al. Rationale and design of the CONFIRM2 (Quantitative COroNary CT Angiography Evaluation For Evaluation of Clinical Outcomes: An InteRnational, Multicenter Registry) study. Journal of Cardiovascular Computed Tomography. 2024;18(1):11–7. DOI: 10.1016/j.jcct.2023.10.004
7. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. European Heart Journal. 2020;41(3):407–77. DOI: 10.1093/eurheartj/ehz425
8. Ichikawa K, Miyoshi T, Osawa K, Nakashima M, Miki T, Nishihara T et al. High pericoronary adipose tissue attenuation on computed tomography angiography predicts cardiovascular events in patients with type 2 diabetes mellitus: post-hoc analysis from a prospective cohort study. Cardiovascular Diabetology. 2022;21(1):44. DOI: 10.1186/s12933-022-01478-9
9. Blaha MJ, Mortensen MB, Kianoush S, Tota-Maharaj R, Cainzos-Achirica M. Coronary Artery Calcium Scoring: is it time for a change in methodology? JACC: Cardiovascular Imaging. 2017;10(8):923–37. DOI: 10.1016/j.jcmg.2017.05.007
10. Oeing CU, Matheson MB, Ostovaneh MR, Rochitte CE, Chen MY, Pieske B et al. Coronary artery disease grading by cardiac CT for predicting outcome in patients with stable angina. Journal of Cardiovascular Computed Tomography. 2023;17(5):310–7. DOI: 10.1016/j.jcct.2023.07.004
11. Maurovich-Horvat P, Ferencik M, Voros S, Merkely B, Hoffmann U. Comprehensive plaque assessment by coronary CT angiography. Nature Reviews Cardiology. 2014;11(7):390–402. DOI: 10.1038/nrcardio.2014.60
12. Suzuki K, Kinoshita D, Yuki H, Niida T, Sugiyama T, Yonetsu T et al. Higher Noncalcified Plaque Volume Is Associated With Increased Plaque Vulnerability and Vascular Inflammation. Circulation: Cardiovascular Imaging. 2024;17(1):e015769. DOI: 10.1161/CIRCIMAGING.123.015769
13. Hadamitzky M, Freißmuth B, Meyer T, Hein F, Kastrati A, Martinoff S et al. Prognostic Value of Coronary Computed Tomographic Angiography for Prediction of Cardiac Events in Patients With Suspected Coronary Artery Disease. JACC: Cardiovascular Imaging. 2009;2(4):404–11. DOI: 10.1016/j.jcmg.2008.11.015
14. Nannini G, Saitta S, Baggiano A, Maragna R, Mushtaq S, Pontone G et al. A fully automated deep learning approach for coronary artery segmentation and comprehensive characterization. APL Bioengineering. 2024;8(1):016103. DOI: 10.1063/5.0181281
15. Bauer MJ, Nano N, Adolf R, Will A, Hendrich E, Martinoff SA et al. Prognostic Value of Machine Learning–based Time-to-Event Analysis Using Coronary CT Angiography in Patients with Suspected Coronary Artery Disease. Radiology: Cardiothoracic Imaging. 2023;5(2):e220107. DOI: 10.1148/ryct.220107
16. Maurovich-Horvat P, Schlett CL, Alkadhi H, Nakano M, Otsuka F, Stolzmann P et al. The Napkin-Ring Sign Indicates Advanced Atherosclerotic Lesions in Coronary CT Angiography. JACC: Cardiovascular Imaging. 2012;5(12):1243–52. DOI: 10.1016/j.jcmg.2012.03.019
17. Feuchtner G, Kerber J, Burghard P, Dichtl W, Friedrich G, Bonaros N et al. The high-risk criteria low-attenuation plaque <60 HU and the napkin-ring sign are the most powerful predictors of MACE: a long-term follow-up study. European Heart Journal - Cardiovascular Imaging. 2017;18(7):772–9. DOI: 10.1093/ehjci/jew167
18. Otsuka K, Fukuda S, Tanaka A, Nakanishi K, Taguchi H, Yoshikawa J et al. Napkin-Ring Sign on Coronary CT Angiography for the Prediction of Acute Coronary Syndrome. JACC: Cardiovascular Imaging. 2013;6(4):448–57. DOI: 10.1016/j.jcmg.2012.09.016
19. Taron J, Foldyna B, Mayrhofer T, Osborne MT, Meyersohn N, Bittner DO et al. Risk Stratification With the Use of Coronary Computed Tomographic Angiography in Patients With Nonobstructive Coronary Artery Disease. JACC: Cardiovascular Imaging. 2021;14(11):2186–95. DOI: 10.1016/j.jcmg.2021.03.019
20. Tzolos E, Williams MC, McElhinney P, Lin A, Grodecki K, Flores Tomasino G et al. Pericoronary Adipose Tissue Attenuation, Low-Attenuation Plaque Burden, and 5-Year Risk of Myocardial Infarction. JACC: Cardiovascular Imaging. 2022;15(6):1078–88. DOI: 10.1016/j.jcmg.2022.02.004
21. Föllmer B, Williams MC, Dey D, Arbab-Zadeh A, Maurovich-Horvat P, Volleberg RHJA et al. Roadmap on the use of artificial intelligence for imaging of vulnerable atherosclerotic plaque in coronary arteries. Nature Reviews Cardiology. 2024;21(1):51–64. DOI: 10.1038/s41569-023-00900-3
22. Narula J, Stuckey TD, Nakazawa G, Ahmadi A, Matsumura M, Petersen K et al. Prospective deep learning–based quantitative assessment of coronary plaque by computed tomography angiography compared with intravascular ultrasound: the REVEALPLAQUE study. European Heart Journal - Cardiovascular Imaging. 2024;25(9):1287–95. DOI: 10.1093/ehjci/jeae115
23. Baeßler B, Götz M, Antoniades C, Heidenreich JF, Leiner T, Beer M. Artificial intelligence in coronary computed tomography angiography: Demands and solutions from a clinical perspective. Frontiers in Cardiovascular Medicine. 2023;10:1120361. DOI: 10.3389/fcvm.2023.1120361
24. Giesen A, Mouselimis D, Weichsel L, Giannopoulos AA, Schmermund A, Nunninger M et al. Pericoronary adipose tissue attenuation is associated with non-calcified plaque burden in patients with chronic coronary syndromes. Journal of Cardiovascular Computed Tomography. 2023;17(6):384–92. DOI: 10.1016/j.jcct.2023.08.008
25. Ihdayhid AR, Sehly A, He A, Joyner J, Flack J, Konstantopoulos J et al. Coronary Artery Stenosis and High-Risk Plaque Assessed With an Unsupervised Fully Automated Deep Learning Technique. JACC: Advances. 2024;3(9):100861. DOI: 10.1016/j.jacadv.2024.100861
26. Lee S, Giesen A, Mouselimis D, Weichsel L, Giannopoulos AA, Nunninger M et al. Composite cardiac computed tomography angiography score for improved risk assessment in chronic coronary syndromes. Scientific Reports. 2025;15(1):3089. DOI: 10.1038/s41598-025-87118-0