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Multimodal Cardiac CT–Derived High-Risk Coronary and Myocardial Features for Predicting Adverse Outcomes After PCI in Patients with Acute Myocardial Infarction: A Multicenter Prospective Cohort Study

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1. Study Background

Acute myocardial infarction (AMI) remains one of the leading causes of mortality in China. Even after successful percutaneous coronary intervention (PCI) and guideline-directed medical therapy, patients with coronary artery disease continue to face a substantial annual risk of adverse cardiovascular events, including heart failure, recurrent ischemic events, and malignant arrhythmias. Effective risk stratification is therefore essential for tailoring treatment strategies and optimizing patient outcomes. However, currently available tools for predicting adverse outcomes after PCI in patients with AMI are limited by suboptimal predictive accuracy or restricted accessibility.

Cardiac imaging plays a central role in post-AMI risk assessment, with echocardiography serving as the standard imaging modality. Current clinical guidelines recommend routine echocardiographic evaluation after PCI to assess left ventricular function, right ventricular function, and valvular abnormalities, as well as to exclude early post-infarction mechanical complications and left ventricular thrombus formation. However, its ability to predict subsequent left ventricular remodeling remains uncertain.

Cardiac magnetic resonance imaging (CMR) has emerged as the most powerful imaging modality for predicting adverse left

ventricular remodeling after AMI. Key prognostic indicators, including infarct size, microvascular obstruction, and intramyocardial hemorrhage, can be comprehensively evaluated using CMR and have been shown to be independent predictors of clinical outcomes in patients with AMI. Nevertheless, the routine implementation of CMR following AMI remains challenging due to limited availability, high cost, and logistical constraints. Moreover, although CMR provides comprehensive myocardial tissue characterization, it does not assess coronary artery anatomy, thereby limiting its ability to provide a comprehensive risk assessment that incorporates atherothrombotic components.

In recent years, cardiac computed tomography (CT) has evolved into a first-line imaging modality for the evaluation of patients with chest pain. In addition to assessing coronary artery stenosis and high-risk plaque characteristics, cardiac CT can also evaluate cardiac morphology, function, and myocardial tissue characteristics. A recent meta-analysis demonstrated that CT-based delayed iodine enhancement imaging shows excellent diagnostic accuracy compared with late gadolinium enhancement on CMR. Furthermore, CT-derived extracellular volume fraction (ECV) enables quantitative assessment of myocardial fibrosis. Therefore, multimodal cardiac

CT provides an unprecedented opportunity for comprehensive risk stratification in patients with AMI following PCI.

In this study, we plan to prospectively collect clinical and imaging data from 1,000 patients with AMI who have undergone PCI. The objectives are to evaluate the diagnostic performance of multimodal cardiac CT in assessing cardiac structure and function after PCI, identify key imaging biomarkers associated with adverse outcomes after AMI, and develop a machine learning–based predictive model for early risk stratification of adverse clinical outcomes in patients with AMI. The implementation of this study is expected to establish a novel risk assessment strategy for patients with AMI after PCI, thereby facilitating personalized management of coronary artery disease and reducing the incidence of future adverse cardiovascular events.

2. Study Objectives

Primary Objective: To investigate the association between high-risk coronary and myocardial features derived from multimodal cardiac CT and adverse clinical outcomes in patients with acute myocardial infarction (AMI) after PCI.

Secondary Objective: To evaluate the diagnostic performance of multimodal cardiac CT in assessing cardiac morphology and

function in patients with AMI after PCI.

3. Study Design, Methods, and Procedures

3.1 Study Design

This study is designed as a prospective, multicenter study.

3.2 Sample Size Calculation

Sample size was estimated according to the rule-of-thumb principle, which requires at least 10 events per predictor variable in predictive modeling. Based on previous studies, the estimated 2-year incidence of thrombotic events after PCI in patients with AMI is approximately 8%. The covariates included in the model consist of clinical variables such as age, sex, clinical presentation, hypertension, diabetes mellitus, and statin therapy. Considering a 5% dropout rate, at least 921 participants are required. The estimated 2-year incidence of heart failure and severe arrhythmic events after PCI in patients with AMI is approximately 20%, with the same set of clinical covariates included in the model. After accounting for a 5% dropout rate, at least 368 participants are required. To ensure adequate statistical power for both major endpoints, a total of 1,000 participants will be enrolled in the study.

3.3 Study Procedures

(1) Screening Phase

A total of 1,000 patients with AMI undergoing PCI will be screened. All participants will undergo multimodal cardiac CT within 7 days after PCI, either following the index procedure or staged PCI. In addition, 50 participants will undergo cardiac magnetic resonance imaging (CMR) within 2 days after cardiac CT for comparative imaging analysis.

(2) Clinical Data Collection

Clinical information will be collected, including: Demographic characteristics: age, sex, body weight, height, clinical symptoms, cardiovascular risk factors (hypertension, diabetes mellitus, smoking history, and chronic kidney disease), medication history, laboratory biomarkers (hematocrit, low-density lipoprotein cholesterol, lipoprotein a, blood glucose, high-sensitivity C-reactive protein, interleukin-6, and other biochemical markers), PCI-related procedural data

(3) Cardiac CT Follow-up

Participants who remain free of thrombotic events, heart failure, or severe arrhythmias within one year after the baseline cardiac CT

examination will be recommended to undergo repeat cardiac CT imaging. Blood biochemical parameters, including triglycerides, LDL cholesterol, blood glucose, hs-CRP, and IL-6, will also be analyzed during this follow-up period.

(4) Echocardiographic Follow-up

Participants will be recommended to undergo transthoracic echocardiography at the following time points:

6 months

12 months

2 years

3 years

4 years

5 years

(5) Clinical Follow-up

All participants will undergo clinical follow-up at 1 month, 3 months, 6 months, 12 months, 2 years, 3 years, and 4 years after PCI, and annually thereafter until the last enrolled participant completes 5 years of follow-up. Follow-up will be conducted through telephone interviews or outpatient clinic visits.

4. Coronary Angiography and PCI Procedures

Coronary angiography was performed according to standard clinical practice. All culprit lesions underwent successful PCI, which could be performed either during the index procedure or as a staged procedure within two months. These included lesions responsible for acute coronary syndrome (ACS) as well as other lesions with hemodynamically significant stenosis requiring revascularization. The decision to assess the hemodynamic significance of coronary lesions using fractional flow reserve (FFR), instantaneous wave-free ratio (iFR), or quantitative flow ratio (QFR) was made at the discretion of the interventional cardiologist. Eligible patients were required to undergo successful PCI of the culprit lesion without major procedural complications. Successful PCI was defined as residual diameter stenosis <50% at the target lesion with restoration of TIMI grade 3 coronary flow.

5. Multimodal Cardiac CT Acquisition and Analysis

5.1 Multimodal Cardiac CT Acquisition

All participants at the study center underwent multimodal cardiac CT

using a third-generation dual-source CT scanner (Siemens). Prior to scanning, 0.1 mg of sublingual nitroglycerin was administered 3–5 minutes before image acquisition. A breath-hold scout scan was performed from the thoracic inlet to the cardiac diaphragm. The acquisition range for coronary CT angiography (CCTA) extended from 2 cm below the tracheal carina to the cardiac diaphragm, with an additional 10–20 mm margin beyond the cardiac borders bilaterally. A dual-head power injector (Urich) was used to administer 60–80 mL of nonionic iodinated contrast agent (iopromide, 370 mg iodine/mL; Bayer, Germany) via a peripheral vein at an injection rate of 5.0 mL/s. Scan timing was determined using an artificial intelligence–assisted bolus tracking system, with the region of interest placed in the ascending aorta. Image acquisition was automatically triggered 7 seconds after the attenuation value reached 100 HU. Scanning parameters included: Tube voltag 80–120 kVp and automatic tube current modulation. For cardiac multiphase image reconstruction, images were reconstructed throughout the entire cardiac cycle (0%–95%) at 5% intervals of the R–R interval, with a slice thickness of 0.75 mm, generating 20 phases of cardiac cine images. After completion of CCTA acquisition, an additional 40 mL of contrast agent was injected, followed by a 5-minute delay before performing dual-energy CT delayed

enhancement imaging. Scanning parameters for delayed enhancement imaging were as follows:

Tube A: 90 kV, 165 mA

Tube B: 150 kV, 127mA

5.2 CCTA Image Analysis

All CCTA images were interpreted by experienced radiologists. The presence of a coronary plaque on CCTA was considered a positive finding. Coronary artery segments were analyzed according to the 18-segment model recommended by the American Heart Association (AHA). The number, location, and degree of stenosis of plaques were recorded, along with the total number of coronary segments involved by atherosclerotic lesions.

Assessment of Coronary Artery Stenosis

The degree of coronary artery stenosis was classified as follows: no stenosis; minimal stenosis (1–24%); mild stenosis (25–40%); moderate stenosis (50–69%); severe stenosis (70–99%); and total occlusion. Stenosis of ≥50% was defined as significant stenosis.

Qualitative Plaque Analysis

High-risk plaque (HRP) features included low-attenuation plaque,

napkin-ring sign, positive remodeling, and spotty calcification.

a) Low-attenuation plaque was defined as a non-calcified plaque with an attenuation value of <30 Hounsfield units (HU) measured within the plaque.

b) Napkin-ring sign was defined as a central low-attenuation plaque core adjacent to the coronary lumen surrounded by a higher-attenuation rim.

c) Spotty calcification was defined as calcified foci within plaques with a diameter <3 mm on any cross-sectional image and occupying less than one-quarter of the vessel circumference.

d) Positive remodeling was defined as a ratio of the maximum vessel diameter at the lesion site (including plaque and lumen) to the mean diameter of the proximal and distal reference segments $\geqslant$1.1.

The presence of two or more of these features was defined as a high-risk plaque.

Quantitative Plaque Analysis

Quantitative plaque analysis was performed using a semi-automated plaque analysis software (Medis). The following parameters were measured:

Degree of stenosis

Plaque length

Total plaque volume

Calcified plaque volume

Non-calcified plaque volume

Minimum lumen area (MLA)

Remodeling index (RI)

Plaque burden (PB)

Total plaque volume (TPV)

Percent atheroma volume (PAV)

Plaque volume was calculated as: Plaque volume = vessel volume − lumen volume. At the patient level, plaque volume was defined as the sum of all plaque volumes. The minimum lumen area (MLA) was defined as the lumen area at the site of maximal stenosis. The remodeling index (RI) was calculated as: RI = lumen area at the most stenotic site / mean lumen area of the proximal and distal reference segments. Positive remodeling was defined as RI > 1.1. Local plaque burden (PB) was defined as: PB = plaque area / vessel area at the site of the minimum lumen area. Percent atheroma volume (PAV) was calculated as: PAV = 100% × (plaque volume /

vessel volume). Plaque components were classified based on CT attenuation values:

Lipid plaque: <30 HU

Fibrofatty plaque: 30–130 HU

Fibrous plaque: 130–350 HU

Calcified plaque: >350 HU

Non-calcified plaque volume was defined as the sum of: fibrous plaque volume + fibrofatty plaque volume + lipid plaque volume.

CT-Derived Fractional Flow Reserve (CT-FFR) Analysis

CT-FFR analysis was performed using a fully automated CT-FFR analysis software (Shukun Technology). The software automatically measured CT-FFR values throughout the entire coronary tree without manual adjustment. The following parameters were recorded:

CT-FFR value 2 cm distal to the lesion

Terminal CT-FFR value of the vessel

Translesional ΔCT-FFR

Pericoronary Adipose Tissue Inflammation Analysis

Pericoronary adipose tissue inflammation analysis was conducted

using a fully automated analysis software (Shukun Technology), which automatically quantified pericoronary fat inflammation along the coronary artery tree. The following parameters were recorded:

Patient-level FAI measured in the proximal 1–5 cm segment of the right coronary artery (RCA)

Lesion-specific FAI surrounding the culprit lesion

Cardiac Function and Strain Analysis

Multiphasic cardiac CT images were transferred to the CVI42 post-processing workstation for analysis. The software automatically delineated the endocardial and epicardial borders, with manual adjustment performed when necessary. After segmentation, the software automatically calculated cardiac structural parameters.

Dual-Energy Delayed Enhancement Analysis and Extracellular Volume (ECV)

Dual-energy delayed enhancement images were transferred to the Siemens post-processing workstation (syngo.via VB60) for analysis. In the MM Reading module, delayed iodine enhancement of the left ventricular myocardium was evaluated by comparing with coronary CT angiography images. The delayed enhancement data were then imported into the Heart-PBV module, where the software

automatically generated iodine maps based on material decomposition algorithms, displaying iodine distribution throughout the myocardium. Delayed iodine density values were obtained from left ventricular myocardium and blood pool. Regions of interest (ROIs) were manually drawn within the left ventricular myocardium, avoiding artifacts such as beam hardening. On the same slice, a ROI with a minimum size of 200 mm² was placed in the left ventricular blood pool. Finally, the extracellular volume fraction (ECV) was calculated using the following formula:

$ECV = (HU_m / HU_b) \times (1 - HCT) \times 100\%$

HU_m = delayed iodine density of the myocardium

HU_b = delayed iodine density of the blood pool

HCT = hematocrit

6. Follow-up

The follow-up assessment included composite clinical outcomes at both the vessel level and the patient level, comprising:

Thrombotic events, including cardiac death, recurrent myocardial infarction, and urgent or clinically driven revascularization.

Heart failure and arrhythmic events, including new-onset congestive heart failure, sustained ventricular arrhythmia, implantable

cardioverter-defibrillator (ICD) implantation, sudden cardiac death or resuscitated cardiac arrest.

Identification of culprit lesions was determined based on electrocardiographic findings, repeat coronary CT angiography (CCTA), or invasive coronary angiography. Clinical follow-up was conducted through outpatient visits, telephone interviews, and review of electronic medical records. All primary endpoint events were independently reviewed and adjudicated by a blinded clinical event adjudication committee.

7. Study Population

The study population consisted of patients with acute myocardial infarction (AMI) who underwent percutaneous coronary intervention (PCI). Patients were enrolled if they met the following criteria: age $\geqslant$18 years; AMI occurring within 4 weeks prior to enrollment, including ST-segment elevation myocardial infarction (STEMI) or non–ST-segment elevation myocardial infarction (NSTEMI); PCI performed for the culprit lesion of acute coronary syndrome (ACS) according to current clinical guidelines; hemodynamically stable condition; willingness to undergo multimodality cardiac CT examination within 7 days after PCI; and agreement to participate in telephone follow-up.

Patients were excluded if they met any of the following criteria: inability to undergo cardiac CT examination (such as estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m² or iodinated contrast allergy); prior coronary artery bypass grafting (CABG); previous diagnosis of congestive heart failure or prior myocardial infarction; severe arrhythmia or structural heart disease; poor-quality multimodality cardiac CT images or missing imaging data; or an expected life expectancy of less than 6 months.

8. Statistical Analysis

All analyses were conducted using SPSS software (IBM SPSS, version 26.0; SPSS Inc., Chicago, IL, USA), MedCalc (version 18.2.1, Ostend, Belgium), and R software (version 4.0.3, R Foundation for Statistical Computing). Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or as median with interquartile range (25th–75th percentiles) for non-normally distributed data. For comparisons between groups, categorical variables were analyzed using the Pearson χ^2 test, with continuity-corrected χ^2 test or Fisher's exact test applied when appropriate. Normally distributed continuous variables were compared using the independent

samples t-test, whereas non-normally distributed variables were compared using the Mann–Whitney U test. High-risk plaque morphological characteristics were defined as follows: high local plaque burden was defined as minimum lumen area (MLA) <4 mm^2 and plaque burden (PB) ⩾70%; high global plaque burden was defined as total plaque volume (TPV) or percent atheroma volume (PAV) ⩾ the median value; high low-attenuation plaque burden was defined as >4%; and high-risk plaque was defined as the presence of two or more high-risk plaque features. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive value of CT-derived fractional flow reserve (CT-FFR) for major adverse cardiovascular events (MACE), and the optimal cutoff value was determined using the Youden index to define high-risk hemodynamic characteristics. High-risk myocardial characteristics included the number of myocardial segments with delayed enhancement, extracellular volume fraction (ECV), myocardial ejection fraction, and myocardial strain parameters. Kaplan–Meier survival analysis with the log-rank test was used to estimate and compare cumulative event rates between groups with different high-risk coronary plaque and myocardial characteristics. Furthermore, Cox proportional hazards regression models were applied to evaluate the association between coronary plaque high-

risk features, myocardial high-risk characteristics, and clinical outcomes, with results reported as hazard ratios (HRs) and corresponding 95% confidence intervals (CIs).

9. Ethical Principles and Requirements for Clinical Research

This clinical study will be conducted in accordance with the ethical principles outlined in the Declaration of Helsinki issued by the World Medical Association.

10. Study Timeline

From January 2026 to April 2026, ethical approval will be obtained from the Ethics Committee and the study protocol will be finalized.

From April 2026 to December 2029, data collection, data analysis, and clinical follow-up will be conducted.

From December 2029 to December 2030, manuscript preparation, submission for publication, and dissemination of study results will be completed.

11. References

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