

Pre-PCI C-reactive protein–triglyceride glucose index and angiographic no-reflow or slow flow in acute myocardial infarction: a single-centre retrospective study

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Abstract

Background

Angiographic no-reflow or slow flow after percutaneous coronary intervention (PCI) is linked to impaired myocardial reperfusion in acute myocardial infarction (AMI). The C-reactive protein–triglyceride glucose index (CTI) combines information on systemic inflammation and insulin resistance. This study examined the association of pre-PCI CTI with immediate post-PCI no-reflow or slow flow and assessed its additional predictive information beyond routine clinical variables.

Methods

This single-centre retrospective study included 429 patients with AMI who underwent PCI between January 2023 and January 2025. All variables used to calculate CTI were collected before PCI. Immediate post-PCI Thrombolysis in Myocardial Infarction (TIMI) flow was assessed by two experienced interventional cardiologists who were blinded during adjudication. TIMI grade 3 was classified as normal flow, and TIMI grades 0–2 as no-reflow or slow flow after excluding mechanical obstruction. Multivariable logistic regression, restricted cubic splines, receiver operating characteristic curves, bootstrap internal validation, and exploratory incremental-value and subgroup analyses were performed.

Results

Among 429 patients, 102 had no-reflow or slow flow. Pre-PCI CTI was higher in patients with the outcome than in those with normal flow (10.57 ± 0.96 versus 9.39 ± 0.86). After adjustment for age, sex, ST-elevation myocardial infarction, diabetes, hypertension, current smoking, estimated glomerular filtration rate, and left ventricular ejection fraction, each 1-unit increase in CTI was associated with higher odds of no-reflow or slow flow (odds ratio 3.34, 95% confidence interval 2.30–5.05; $P < 0.001$). The association was nonlinear (P for nonlinearity = 0.003). CTI alone had an area under the curve (AUC) of 0.830 (95% confidence interval 0.778–0.883). Adding CTI to the clinical model increased the AUC from 0.850 to 0.889 (difference 0.039, 95% confidence interval 0.010–0.067; $P = 0.008$). The optimism-corrected AUC was 0.875 (95% confidence interval 0.837–0.917). Diabetes did not show evidence of effect modification (P for interaction = 0.533).

Conclusions

Higher pre-PCI CTI was associated with immediate angiographic no-reflow or slow flow in this retrospective AMI cohort and added predictive information to a clinical model. The cut-off, reclassification measures, decision curves, and diabetes subgroup findings remain exploratory. Bootstrap internal validation cannot replace validation in an independent external cohort.

Background

Acute myocardial infarction (AMI) remains a major cause of cardiovascular morbidity and mortality worldwide [1]. Current guidelines support rapid diagnosis and reperfusion, usually with percutaneous coronary intervention (PCI), when clinically indicated [2–4]. Restoration of epicardial coronary patency does not always restore adequate downstream tissue perfusion. Angiographic no-reflow or slow flow can remain after the infarct-related artery has been opened, and proposed contributors include distal embolization, ischaemic injury, reperfusion injury, endothelial dysfunction, tissue oedema, and increased vulnerability of the coronary microcirculation [5, 6]. This complication has been associated with larger myocardial injury and worse short- and long-term outcomes [7, 8].

Inflammation and metabolic dysfunction may help explain why some patients are more susceptible to impaired flow after PCI. Inflammatory activation is central to acute coronary syndromes and evolves during myocardial injury and repair [9–11]. Insulin resistance is also linked to endothelial dysfunction, oxidative stress, altered vasomotor regulation, and adverse cardiovascular outcomes. The triglyceride-glucose (TyG) index, calculated from fasting triglyceride and glucose concentrations, is a practical surrogate measure of insulin resistance [12, 13]. Higher TyG values have been associated with adverse outcomes after PCI, although their performance varies across populations and clinical endpoints [14, 15].

The C-reactive protein–triglyceride glucose index (CTI) combines TyG with high-sensitivity C-reactive protein (hs-CRP), bringing metabolic and inflammatory information into one measure. Previous studies have reported joint associations of TyG and hs-CRP with cardiovascular outcomes [16–18]. More recent work found that CTI was associated with recurrent events after PCI, major adverse cardiovascular events after AMI, and cardiac magnetic resonance-defined microvascular obstruction [19–21]. Evidence for immediate angiographic no-reflow or slow flow after PCI remains limited. We therefore examined whether pre-PCI CTI was associated with immediate post-PCI no-reflow or slow flow in patients with AMI. We also assessed its discrimination and the additional information obtained when CTI was added to a clinical model. Cut-off analysis, reclassification measures, decision curve analysis, and diabetes subgroup analyses were treated as exploratory or supportive analyses.

Methods

Study design and setting

This single-centre retrospective study used the electronic inpatient record system of Zhengzhou Central Hospital Affiliated to Zhengzhou University. Consecutive patients admitted with AMI between January 2023 and January 2025 were screened. The report was prepared with reference to the STROBE and TRIPOD + AI reporting frameworks. AMI eligibility was evaluated retrospectively against contemporary diagnostic criteria [2–4].

Participants

Patients were eligible when they met the diagnostic criteria for AMI, underwent PCI during the index admission, had the first fasting blood sample required for CTI calculation collected before PCI, and had complete coronary angiographic records that permitted assessment of TIMI flow. Exclusion criteria were: PCI before the index hospitalization; major PCI-related complications, including coronary perforation, dissection, or pericardial effusion with haemodynamic instability; severe in-hospital complications, including ventricular septal or free-wall rupture, ventricular arrhythmia requiring cardiopulmonary resuscitation or electrical cardioversion, or severe congestive heart failure requiring invasive haemodynamic support such as intra-aortic balloon counterpulsation; acute infectious disease unrelated to AMI, autoimmune disease, or malignancy; severe hepatic or renal dysfunction, defined as alanine or aspartate aminotransferase greater than three times the upper limit of normal or estimated glomerular filtration rate (eGFR) below 30 mL/min/1.73 m²; and incomplete key clinical data. The analysis used complete cases. Because the source records did not permit reliable reconstruction of mutually exclusive reason-specific counts for all excluded patients, only the aggregate number excluded is reported.

Data collection

Demographic and clinical data were collected from the electronic medical record, including age, sex, systolic and diastolic blood pressure, current smoking, hypertension, dyslipidaemia, diabetes mellitus, and history of coronary artery disease. Laboratory variables included peripheral blood counts, haemoglobin, fasting plasma glucose (FPG), triglycerides (TG), high-density and low-density lipoprotein cholesterol, serum creatinine, eGFR, creatine kinase-MB (CK-MB), cardiac troponin I (cTnI), D-dimer, B-type natriuretic peptide (BNP), and hs-CRP. Clinical and imaging variables included Killip class, left ventricular ejection fraction (LVEF), pre-PCI TIMI flow, thrombus aspiration, infarct-related artery, and stent number, diameter, and length. In-hospital medication variables included aspirin, clopidogrel, ticagrelor, beta-blockers, statins, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and angiotensin receptor-neprilysin inhibitors.

All blood variables used to calculate CTI were collected before PCI. In the analysis dataset, CRP, cTnI, CK-MB, D-dimer, and BNP had been stored after $\ln(x + 1)$ transformation; descriptive summaries were reported on the original scale. TG and FPG were converted from mmol/L to mg/dL before TyG and CTI were calculated. The conversion factors used in the analysis code were 88.57 for TG and 18.0182 for FPG.

Calculation of TyG and CTI

The predefined formulas were retained without modification:

$$\text{TyG} = \ln[(\text{TG [mg/dL]} \times \text{FPG [mg/dL]}) / 2]$$

$$\text{CTI} = \text{TyG} + 0.412 \times \ln[\text{hs-CRP (mg/L)}]$$

The natural logarithm was used. CTI therefore combined the fasting lipid-glucose product with hs-CRP measured on the original mg/L scale.

Coronary angiography, PCI, and outcome adjudication

Coronary angiography used multiple projections, with each major coronary artery visualized in at least two views. Before PCI, patients received aspirin 300 mg with ticagrelor 180 mg, or aspirin 300 mg with clopidogrel 300–600 mg. Coronary angiography and PCI were performed by at least two experienced interventional cardiologists, and procedural decisions were based on angiographic findings and lesion characteristics.

The primary outcome was immediate post-PCI angiographic no-reflow or slow flow in the infarct-related artery. Two experienced interventional cardiologists assessed post-PCI TIMI flow while blinded to the study predictors. TIMI grade 3 was classified as normal flow, and TIMI grades 0–2 were classified as no-reflow or slow flow after coronary dissection, spasm, embolism, and other mechanical causes of reduced flow had been excluded. The 429 patients were divided into a normal-flow group (n = 327) and a no-reflow/slow-flow group (n = 102).

Statistical analysis

Analyses were performed with R version 4.4.2. Continuous variables that followed an approximately normal distribution were summarized as mean (standard deviation) and compared with the two-sided Welch t test. Other continuous variables were summarized as median [interquartile range] and compared with the Mann–Whitney U test. Categorical variables were reported as number (percentage) and compared with Fisher's exact test. The patient was the independent unit of analysis.

Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for immediate post-PCI no-reflow or slow flow. The clinical model contained age, sex, ST-elevation myocardial infarction (STEMI), diabetes, hypertension, current smoking, eGFR, and LVEF. The primary adjusted model added CTI as a single linear term to provide a parsimonious and readily interpretable average association. TG, FPG, and hs-CRP were not entered with CTI because they are components of the index. Sensitivity models additionally included Killip class or initial TIMI flow grade. Collinearity was assessed with variance inflation factors. The primary model contained 102 events and nine predictor parameters, corresponding to 11.3 events per parameter.

Restricted cubic splines were used as a secondary assessment of the functional form of the CTI association, with four knots at the 5th, 35th, 65th, and 95th percentiles and the median CTI as the reference. The linear-term OR was interpreted as an average association across the observed CTI range, and discrimination of the linear and spline-extended models was compared in a supportive analysis. Discrimination was summarized by the area under the receiver operating characteristic curve (AUC) with

DeLong 95% CIs. The primary comparison between the clinical and extended models used a paired DeLong test. Two component-marker comparisons, CTI versus TyG and CTI versus CRP, were adjusted with the Benjamini–Hochberg procedure.

The Youden cut-off, continuous net reclassification improvement (NRI), integrated discrimination improvement (IDI), decision curve analysis (DCA), and diabetes subgroup analyses were exploratory or supportive. Confidence intervals for the Youden cut-off and reclassification measures were obtained by 2,000 bootstrap resamples. Internal validation of the extended model used 2,000 patient-level bootstrap resamples with model refitting to estimate optimism-corrected AUC, calibration intercept and slope, Brier score, Nagelkerke R^2 , and maximum absolute calibration error. DCA was displayed over threshold probabilities from 0.05 to 0.50 and was also corrected by 2,000 bootstrap resamples. Diabetes effect modification was evaluated in a full-cohort model containing a CTI-by-diabetes interaction term; subgroup estimates were interpreted through the interaction test rather than through within-subgroup P values. All tests were two-sided, with $P < 0.05$ used as a descriptive threshold for statistical evidence.

Use of generative artificial intelligence in manuscript preparation

OpenAI Codex was used to assist with manuscript organization, English-language drafting, and language editing based on author-provided data and results. The tool was not used to collect or generate study data or to conduct the statistical analyses reported in this article. All manuscript content, numerical results, interpretations, and references were reviewed and verified by the authors, who take full responsibility for the final manuscript.

Results

Participant flow and baseline characteristics

A total of 1,567 patients with AMI were assessed. Of these, 303 did not undergo PCI and 1,264 underwent PCI. Among the PCI-treated patients, 835 were excluded because they did not meet the eligibility criteria and/or lacked key pre-PCI variables required for the complete-case analysis. Mutually exclusive counts for individual exclusion reasons were unavailable from the retrospective records. The final analysis included 429 patients, of whom 327 had normal flow and 102 had no-reflow or slow flow (Fig. 1).

Patients with no-reflow or slow flow more often had STEMI, diabetes, and current smoking, and they had lower eGFR and LVEF. Several inflammatory, metabolic, myocardial injury, angiographic, and procedural variables also differed between groups (Table 1). Pre-PCI CTI was higher in patients with no-reflow or slow flow than in patients with normal flow (10.57 ± 0.96 versus 9.39 ± 0.86 ; $P < 0.001$; Fig. 2).

Table 1
Baseline characteristics according to immediate post-PCI flow status

Characteristic	Overall	Normal flow	No-reflow/slow-flow	P value	SMD
No. of patients	429	327	102		
Age, years	60.97 (11.89)	61.01 (12.12)	60.85 (11.16)	0.902	0.014
Male sex	327 (76.2)	240 (73.4)	87 (85.3)	0.016	0.297
ST-elevation myocardial infarction	162 (37.8)	83 (25.4)	79 (77.5)	< 0.001	1.220
Diabetes mellitus	144 (33.6)	89 (27.2)	55 (53.9)	< 0.001	0.565
Hypertension	205 (47.8)	148 (45.3)	57 (55.9)	0.069	0.214
Current smoking	152 (35.4)	94 (28.7)	58 (56.9)	< 0.001	0.593
History of coronary artery disease	78 (18.2)	63 (19.3)	15 (14.7)	0.378	0.122
Dyslipidemia	41 (9.6)	33 (10.1)	8 (7.8)	0.568	0.079
White blood cell count	10.29 [8.29, 12.71]	9.87 [7.98, 12.22]	12.21 [10.22, 15.15]	< 0.001	0.697
Neutrophil count	8.09 [6.36, 9.91]	7.77 [6.03, 9.57]	9.04 [7.31, 11.09]	< 0.001	0.538
Hemoglobin	134.10 (17.41)	133.70 (17.64)	135.37 (16.68)	0.384	0.098
Platelet count	218.00 [185.00, 259.00]	215.00 [184.00, 249.00]	231.00 [193.50, 262.00]	0.051	0.253
C-reactive protein, mg/L	3.35 [1.34, 9.64]	2.67 [1.09, 7.34]	8.96 [3.12, 18.31]	< 0.001	0.543
Cardiac troponin I	38.50 [3.95, 50.00]	37.73 [3.72, 50.00]	49.96 [4.50, 50.00]	0.467	0.071
Creatine kinase-MB	96.00 [31.00, 195.00]	70.00 [29.00, 175.00]	161.50 [84.00, 328.00]	< 0.001	0.697
D-dimer	0.55 [0.26, 1.15]	0.51 [0.24, 1.08]	0.69 [0.35, 1.35]	0.006	0.144
B-type natriuretic peptide	108.50 [34.00, 290.00]	100.00 [30.30, 244.25]	149.32 [55.65, 373.77]	0.001	0.263
Glycated hemoglobin	6.00 [5.60, 7.20]	5.90 [5.50, 6.75]	6.85 [5.70, 8.70]	< 0.001	0.595

Characteristic	Overall	Normal flow	No-reflow/slow-flow	P value	SMD
Fasting plasma glucose, mmol/L	7.00 [6.00, 9.30]	6.67 [5.80, 8.30]	8.80 [6.91, 11.90]	< 0.001	0.679
Total cholesterol	4.41 [3.68, 5.09]	4.41 [3.66, 5.07]	4.41 [3.94, 5.32]	0.162	0.223
Triglycerides, mmol/L	1.48 [1.00, 2.18]	1.35 [0.96, 1.96]	2.25 [1.42, 3.71]	< 0.001	0.792
HDL cholesterol	0.94 [0.81, 1.11]	0.96 [0.82, 1.12]	0.91 [0.75, 1.08]	0.023	0.264
LDL cholesterol	2.49 (0.91)	2.50 (0.90)	2.47 (0.92)	0.770	0.033
Serum creatinine	68.00 [58.20, 78.50]	67.50 [57.65, 77.05]	70.30 [60.35, 89.13]	0.014	0.322
Estimated glomerular filtration rate	93.13 (19.70)	94.80 (18.47)	87.79 (22.48)	0.005	0.341
Left ventricular ejection fraction, %	56.07 (6.61)	56.91 (6.31)	53.37 (6.85)	< 0.001	0.536
Killip class				0.008	0.340
I	283 (66.0)	227 (69.4)	56 (54.9)		
II	98 (22.8)	71 (21.7)	27 (26.5)		
III	48 (11.2)	29 (8.9)	19 (18.6)		

Table 1
Baseline characteristics according to immediate post-PCI flow status (continued)

Characteristic	Overall	Normal flow	No-reflow/slow-flow	P value	SMD
Initial TIMI flow grade				0.252	0.250
0	281 (65.5)	211 (64.5)	70 (68.6)		
1	31 (7.2)	28 (8.6)	3 (2.9)		
2	111 (25.9)	83 (25.4)	28 (27.5)		
3	6 (1.4)	5 (1.5)	1 (1.0)		
Thrombus aspiration	73 (17.0)	23 (7.0)	50 (49.0)	< 0.001	1.057
Aspirin	49 (11.4)	34 (10.4)	15 (14.7)	0.284	0.130
Clopidogrel	17 (4.0)	12 (3.7)	5 (4.9)	0.566	0.061
Ticagrelor	9 (2.1)	7 (2.1)	2 (2.0)	1.000	0.013
Statin	63 (14.7)	48 (14.7)	15 (14.7)	1.000	0.001
Beta-blocker	26 (6.1)	19 (5.8)	7 (6.9)	0.642	0.043
ACE inhibitor/ARB	44 (10.3)	35 (10.7)	9 (8.8)	0.710	0.063
Infarct-related artery				< 0.001	0.757
LAD	159 (37.1)	96 (29.4)	63 (61.8)		
RCA	178 (41.5)	159 (48.6)	19 (18.6)		
Other	92 (21.4)	72 (22.0)	20 (19.6)		
Stent implantation	245 (57.1)	206 (63.0)	39 (38.2)	< 0.001	0.511
C-reactive protein-triglyceride-glucose index	9.67 (1.01)	9.39 (0.86)	10.57 (0.96)	< 0.001	1.292

Data are mean (standard deviation), median [interquartile range], or n (%). P values were obtained from two-sided Welch t tests, Mann–Whitney U tests, or Fisher exact tests, as appropriate. SMD denotes standardized mean difference. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CTI, C-reactive protein–triglyceride glucose index; eGFR, estimated glomerular filtration rate; HDL, high-

density lipoprotein; LAD, left anterior descending coronary artery; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction.

Association between CTI and no-reflow or slow flow

In the primary multivariable model, each 1-unit increase in pre-PCI CTI was associated with higher odds of post-PCI no-reflow or slow flow (adjusted OR 3.34, 95% CI 2.30–5.05; $P < 0.001$; Table 2 and Supplementary Figure S1). The estimates were similar after Killip class was added (adjusted OR 3.31, 95% CI 2.28–5.01) and after initial TIMI flow grade was added (adjusted OR 3.31, 95% CI 2.29–5.00). Variance inflation factors were low, with a maximum value of 1.72.

Table 2
Primary multivariable logistic regression for immediate post-PCI no-reflow or slow flow

Predictor	Adjusted OR (95% CI)	P value
CTI, per 1-unit increase	3.337 (2.299–5.046)	< 0.001
Age, per year	1.022 (0.990–1.057)	0.183
Male sex (vs female)	2.607 (1.137–6.337)	0.028
STEMI (vs non-STEMI)	5.741 (3.082–10.985)	< 0.001
Diabetes mellitus	1.461 (0.789–2.687)	0.224
Hypertension	1.261 (0.682–2.340)	0.460
Current smoking	2.162 (1.160–4.049)	0.015
eGFR, per unit	0.991 (0.973–1.009)	0.331
LVEF, per percentage point	0.943 (0.898–0.987)	0.014

The outcome was immediate post-PCI TIMI grade 0–2 after exclusion of mechanical causes of reduced flow. CTI was modelled per 1-unit increase. The model included 429 patients, 102 events, and nine predictor parameters. CI, confidence interval; CTI, C-reactive protein–triglyceride glucose index; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; OR, odds ratio; STEMI, ST-elevation myocardial infarction.

Supplementary Figure S1. Primary multivariable regression estimates. Points show adjusted odds ratios and horizontal lines show 95% confidence intervals from the primary logistic regression model.

The adjusted spline model showed evidence of an overall association ($P < 0.001$) and nonlinearity ($P = 0.003$). The odds of no-reflow or slow flow generally increased as CTI rose, with variation in the slope across the observed range (Fig. 3). Accordingly, the primary linear OR should be read as an average association rather than as a constant effect at every CTI value.

Discrimination and incremental predictive information

The AUC was 0.830 (95% CI 0.778–0.883) for CTI, 0.762 (95% CI 0.703–0.820) for TyG, and 0.704 (95% CI 0.646–0.762) for CRP (Fig. 4). The AUC difference was 0.069 for CTI versus TyG (Benjamini–Hochberg-adjusted $P < 0.001$) and 0.126 for CTI versus CRP (adjusted $P < 0.001$). The exploratory Youden cut-off for CTI was 10.344, with sensitivity 76.5% and specificity 88.1%.

Adding CTI to the clinical model increased the AUC from 0.850 (95% CI 0.807–0.894) to 0.889 (95% CI 0.849–0.929). The AUC difference was 0.039 (95% CI 0.010–0.067; $P = 0.008$; Fig. 5). A model using a spline form of CTI had an AUC of 0.897 (95% CI 0.860–0.934), but the difference from the linear CTI model was small and not statistically evident (AUC difference 0.008; $P = 0.224$).

In exploratory incremental analyses, the continuous NRI was 0.902 (95% CI 0.575–1.144), with an event NRI of 0.569 and a nonevent NRI of 0.333. The IDI was 0.119 (95% CI 0.060–0.189). These measures describe improvement in reclassification and average separation of predicted risks within this development sample and require external confirmation (Table 3).

Table 3
Incremental predictive performance after adding CTI to the clinical model

Measure	Estimate	95% CI	P value
AUC, clinical model	0.850	0.807–0.894	—
AUC, clinical model + CTI	0.889	0.849–0.929	—
AUC difference	0.039	0.010–0.067	0.008
Event NRI	0.569	0.353–0.686	0.001
Nonevent NRI	0.333	0.174–0.498	0.001
Continuous NRI	0.902	0.575–1.144	0.001
IDI	0.119	0.060–0.189	0.001

The clinical model included age, sex, STEMI, diabetes, hypertension, current smoking, eGFR, and LVEF. AUC comparison used a two-sided paired DeLong test. NRI and IDI estimates, confidence intervals, and bootstrap P values were based on 2,000 resamples and are exploratory. AUC, area under the curve; CI, confidence interval; CTI, C-reactive protein–triglyceride glucose index; IDI, integrated discrimination improvement; NRI, net reclassification improvement.

Internal validation and exploratory clinical utility

Bootstrap internal validation with 2,000 resamples gave an optimism-corrected AUC of 0.875 (95% CI 0.837–0.917), a calibration intercept of -0.058 , a calibration slope of 0.916, and a Brier score of 0.106.

The optimism-corrected Nagelkerke R^2 was 0.492 and the maximum absolute calibration error was 0.052 (Fig. 6). These estimates quantify internal performance and do not provide external validation.

The exploratory decision curve analysis showed a higher point estimate of net benefit for the extended model than for the clinical model, treat-all strategy, and treat-none strategy across threshold probabilities from 0.07 to 0.50. For the contrast between the extended and clinical models, pointwise empirical 95% intervals were above zero from 0.18 to 0.465 and from 0.475 to 0.50. These intervals were not adjusted for repeated assessment across thresholds (Fig. 7).

Exploratory analysis by diabetes status

Among 285 patients without diabetes, 47 experienced no-reflow or slow flow. Among 144 patients with diabetes, 55 experienced the outcome. The adjusted ORs per 1-SD increase in CTI were 3.09 (95% CI 1.90–5.02) in patients without diabetes and 3.98 (95% CI 2.05–7.69) in patients with diabetes. The CTI-by-diabetes interaction was not supported (P for interaction = 0.533). The nonlinear interaction sensitivity test was also not supported (P = 0.360). The subgroup findings are exploratory and do not indicate a difference in the CTI association according to diabetes status (Supplementary Figure S2).

Supplementary Figure S2. CTI association according to diabetes status. Estimates are adjusted odds ratios per 1-SD increase in CTI from a single full-cohort model containing the CTI-by-diabetes interaction and adjusted for age, sex, STEMI, hypertension, current smoking, eGFR, and LVEF. The primary interaction P value used a 1-degree-of-freedom likelihood-ratio test. The cohort included 285 patients without diabetes (47 events) and 144 with diabetes (55 events). Effect modification is assessed by the interaction test.

Discussion

In this single-centre retrospective study, higher pre-PCI CTI was associated with immediate angiographic no-reflow or slow flow after PCI for AMI. Several linked analyses supported the same central observation. CTI values differed between the two flow groups, the adjusted association remained strong after accounting for routine clinical variables, and sensitivity models that included Killip class or initial TIMI flow produced similar estimates. The spline analysis added evidence that the relation may not be constant across the full CTI range. Because every component used to calculate CTI was obtained before PCI, the index represents the inflammatory and metabolic state present before the angiographic outcome was assessed. The linear-term OR should therefore be interpreted as an average summary across the observed CTI range.

The prediction analyses also followed a consistent pattern. CTI had better discrimination than TyG or CRP alone, and its addition improved the AUC of the clinical model. Reclassification measures and DCA pointed in the same direction. Bootstrap correction reduced the AUC from its apparent value, while a substantial part of the discrimination remained. Together, the results show that CTI carries information beyond the selected clinical covariates in this sample. The estimated cut-off, NRI, IDI, and DCA results

are exploratory. They are useful for generating testable clinical hypotheses, but they are not ready to define treatment decisions or a universal threshold.

These findings can be placed within the current understanding of no-reflow. Opening the infarct-related artery does not ensure recovery of the coronary microcirculation. Distal microembolization, endothelial injury, tissue swelling, vasoconstriction, and reperfusion injury can act together during and after PCI [5, 6]. Earlier human studies linked no-reflow with greater myocardial damage and poorer prognosis [7, 8]. A marker available before PCI may therefore help identify patients whose downstream circulation is more vulnerable, although an observational association cannot establish a causal pathway.

Inflammation provides one possible explanation for the CTI association. Plaque disruption and myocardial necrosis trigger leukocyte recruitment and cytokine release. Excessive or prolonged inflammation can increase oxidative stress, alter endothelial barrier function, and aggravate microvascular injury [9, 10]. Residual inflammatory activity also provides risk information beyond standard cardiovascular factors [11]. In our data, CRP alone showed moderate discrimination, while CTI performed better. This pattern is compatible with the view that inflammatory burden contributes to risk but does not capture the full clinical state.

The TyG component adds a metabolic dimension. TyG was developed as a practical surrogate for insulin resistance [12]. Insulin resistance is associated with reduced nitric oxide availability, oxidative stress, platelet activation, and impaired vasomotor responses, all of which may reduce the tolerance of the microcirculation to ischaemia and reperfusion [13, 29–31]. Studies in STEMI and pooled post-PCI cohorts have linked higher TyG values to adverse cardiovascular outcomes [14, 15]. TyG remains an indirect marker, and its interpretation differs from direct measurements such as the hyperinsulinaemic-euglycaemic clamp [28]. Acute stress during AMI may also influence fasting glucose and triglyceride concentrations.

Related human studies support combined assessment of inflammatory and metabolic status. Ma et al. found that hs-CRP modified TyG-associated cardiovascular risk in patients with acute coronary syndrome undergoing PCI [16]. National and multicentre cohorts also reported higher cardiovascular risk when TyG and hs-CRP were considered together [17, 18]. Gao et al. compared several inflammatory and insulin-resistance indices in PCI-treated patients and found that CTI was associated with recurrent cardiovascular events [19]. These studies used longer-term clinical outcomes, while our study focused on immediate angiographic flow. The agreement across different endpoints suggests that CTI may reflect a broader inflammatory-metabolic risk state.

Two recent AMI studies are especially relevant. Wang et al. reported that CTI was associated with long-term major adverse cardiovascular events and showed greater discrimination than TyG or hs-CRP alone [20]. Their laboratory measurements were obtained before discharge. Our measurements were obtained before PCI, and the outcome was assessed immediately after the procedure. Chen et al. subsequently found that CTI was associated with cardiac magnetic resonance-defined microvascular obstruction after AMI [21]. Their dose-response relation was close to linear, whereas ours was nonlinear. Cardiac

magnetic resonance assesses tissue-level obstruction, while TIMI flow describes angiographic forward flow. Differences in sampling time, case mix, and model specification may also contribute to the different curve shapes. These data support related, though not identical, clinical interpretations.

Evidence from other settings helps define the breadth and limits of CTI. The index was first developed in cancer populations, and later studies linked it to outcomes in critical illness and stroke [22–24]. Experimental work in mice showed that inflammation can promote insulin resistance through an IRF3-related reduction in FAHFA levels [29]. That result gives biological support to a connection between inflammation and altered metabolism. The pathway was not measured in our study, so it remains a contextual explanation rather than a demonstrated mechanism in this cohort.

Diabetes was considered because it commonly coexists with insulin resistance, chronic inflammation, and endothelial dysfunction [25, 26]. The adjusted CTI estimates appeared numerically different between the diabetes groups, but the formal interaction test gave $P = 0.533$. The analysis therefore provides no evidence that diabetes status changed the strength of the association. This interpretation is based on the interaction test. It does not depend on whether the separate subgroup estimates reached statistical significance. Previous work has reported that insulin-resistance surrogates may have different prognostic performance in AMI patients with and without diabetes [27], which supports further study in larger samples.

CTI is calculated from routine laboratory variables and could be available before PCI when the necessary samples are drawn promptly. It may complement clinical information on presentation, renal function, and ventricular function. At present, the model lacks external validation and a complete deployable equation, and several important procedural predictors were not fully available. CTI should therefore be viewed as a candidate risk marker for further evaluation. Prospective studies should test reproducibility across hospitals, assess incremental value over richer angiographic models, and determine whether CTI-guided management improves patient outcomes.

This study has several limitations. Its retrospective single-centre design allows selection bias, residual confounding, and incomplete measurement of symptom-to-PCI time, thrombus burden, collateral circulation, lesion complexity, and procedural treatment. Of 1,264 PCI-treated patients, 835 were excluded because eligibility criteria were not met and/or key pre-PCI variables were unavailable. Pre-PCI fasting glucose was unavailable for many excluded patients, but reason-specific counts and the characteristics of excluded patients could not be reconstructed reliably. Complete-case selection bias therefore cannot be excluded, and the final cohort may not represent all patients with AMI undergoing PCI. Some exclusion criteria concerned complications recorded during hospitalization, and their timing relative to the immediate angiographic outcome could not be verified uniformly. A single pre-PCI sample cannot represent changes in inflammation or metabolism, and acute stress may affect FPG, TG, and hs-CRP. TIMI flow provides an angiographic assessment and does not fully describe tissue-level perfusion. Two cardiologists adjudicated the endpoint, but interobserver agreement was not available. Finally,

bootstrap validation only estimates internal optimism in the development cohort and cannot replace independent external validation.

Conclusions

Higher pre-PCI CTI was associated with immediate angiographic no-reflow or slow flow after PCI in patients with AMI. CTI improved discrimination when added to the selected clinical model, and the association was supported by sensitivity and internal validation analyses. The cut-off, NRI, IDI, DCA, and diabetes subgroup findings should be considered exploratory. Prospective multicentre studies and independent external validation are required before clinical use.

Abbreviations

AMI

acute myocardial infarction

AUC

area under the curve

BNP

B-type natriuretic peptide

CI

confidence interval

CK-MB

creatinine kinase-MB

CRP

C-reactive protein

CTI

C-reactive protein–triglyceride glucose index

DCA

decision curve analysis

eGFR

estimated glomerular filtration rate

FPG

fasting plasma glucose

hs-CRP

high-sensitivity C-reactive protein

IDI

integrated discrimination improvement

LVEF

left ventricular ejection fraction

NRI

net reclassification improvement

OR
odds ratio
PCI
percutaneous coronary intervention
RCS
restricted cubic spline
STEMI
ST-elevation myocardial infarction
TG
triglycerides
TIMI
Thrombolysis in Myocardial Infarction
TyG
triglyceride-glucose index.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Zhengzhou Central Hospital Affiliated to Zhengzhou University (approval no. ZXY2026157). The requirement for informed consent was waived by the Ethics Committee because of the retrospective design of the study and the use of de-identified clinical data.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because of institutional privacy and ethical restrictions governing individual-level clinical data. De-identified participant-level data and the analysis code are available from the corresponding author on reasonable request, subject to institutional approval and the execution of an appropriate data-use agreement.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MG and HJ conceived and designed the study. MG and YM collected and curated the clinical data, performed the statistical analyses, prepared the tables and figures, interpreted the results, and drafted the manuscript. RX and HJ critically reviewed and revised the manuscript. HJ supervised the study and was responsible for project administration. All authors read and approved the final manuscript.

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Figures

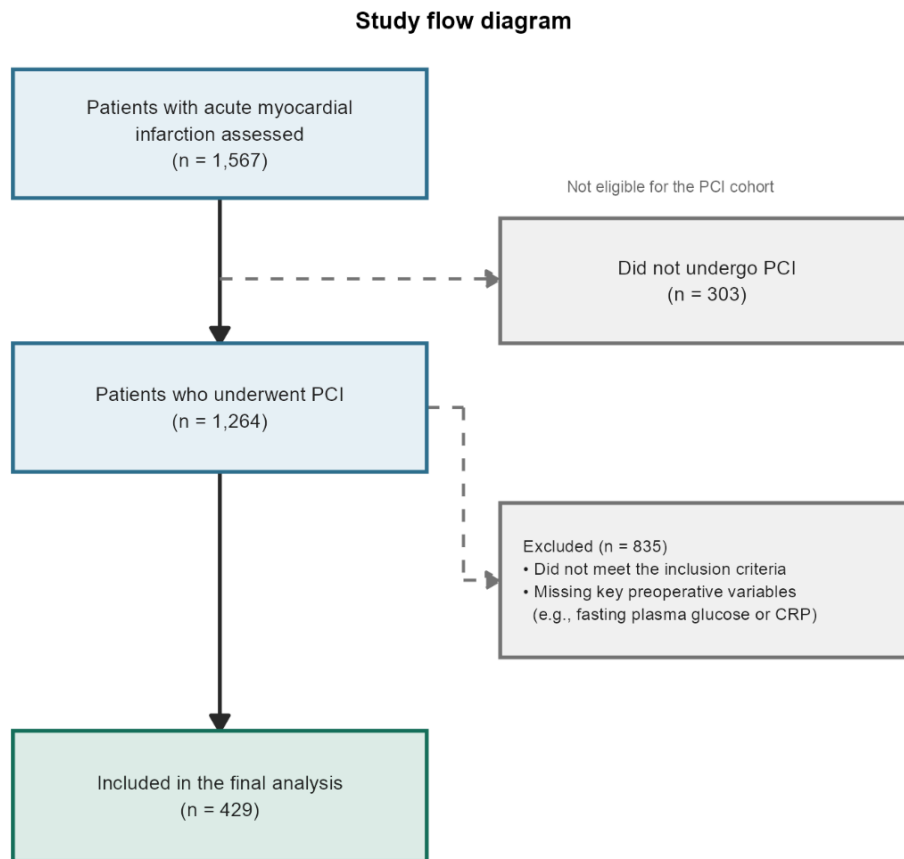


Figure 1

Study flow diagram. A total of 1,567 patients with acute myocardial infarction were assessed, of whom 1,264 underwent PCI. After 835 patients were excluded because eligibility criteria were not met or key pre-PCI variables were missing, 429 patients were included. The 303 patients who did not undergo PCI were not eligible for the PCI cohort. Individual counts for the exclusion reasons were unavailable.

Preoperative CTI distribution by post-PCI flow status

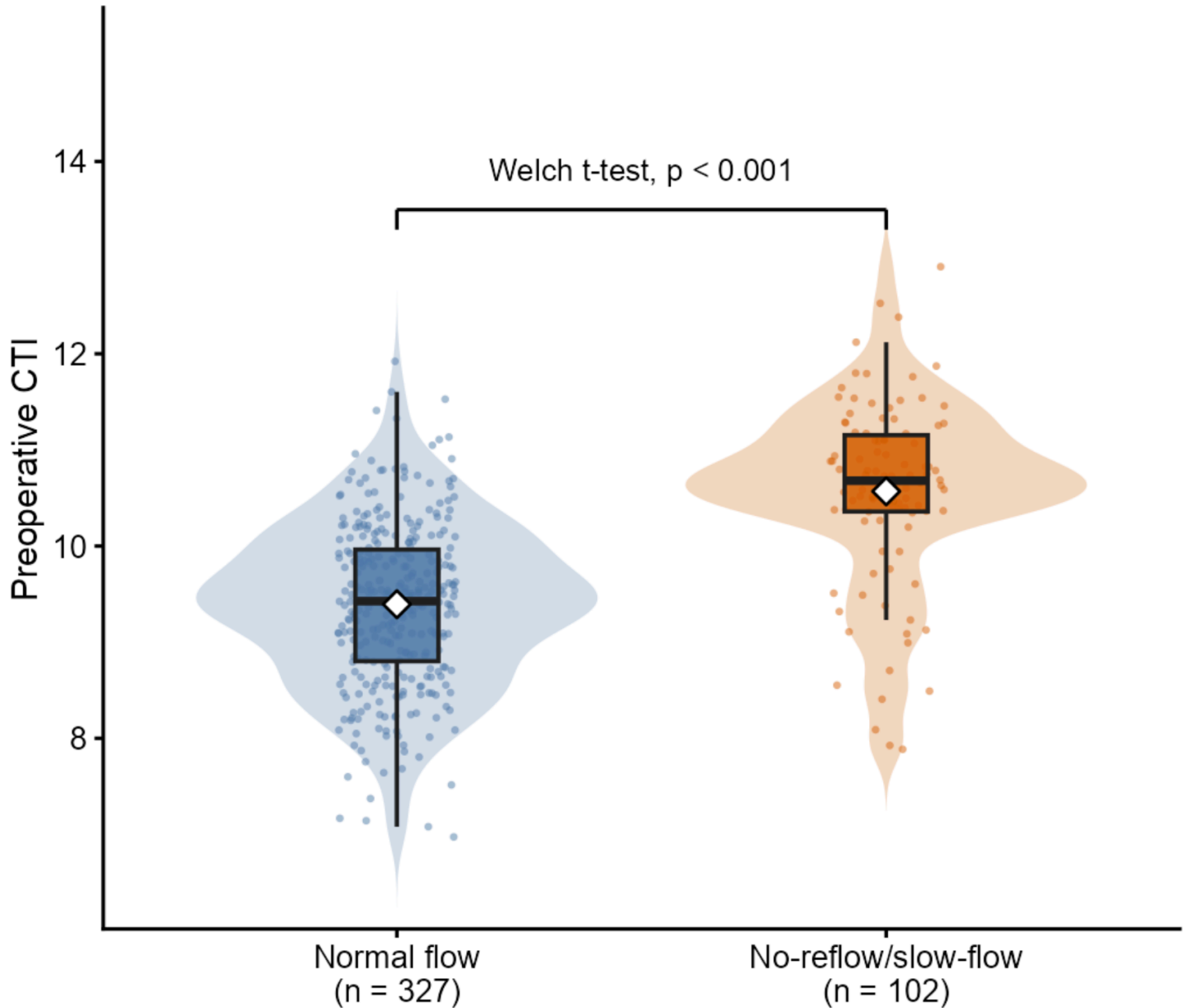


Figure 2

Distribution of pre-PCI CTI by post-PCI flow status. Each point represents one patient (normal flow, n = 327; no-reflow/slow-flow, n = 102). Violin width represents kernel density. Boxes show the median and interquartile range; whiskers extend to 1.5 times the interquartile range. White diamonds indicate means. The displayed P value was calculated with a two-sided Welch t test.

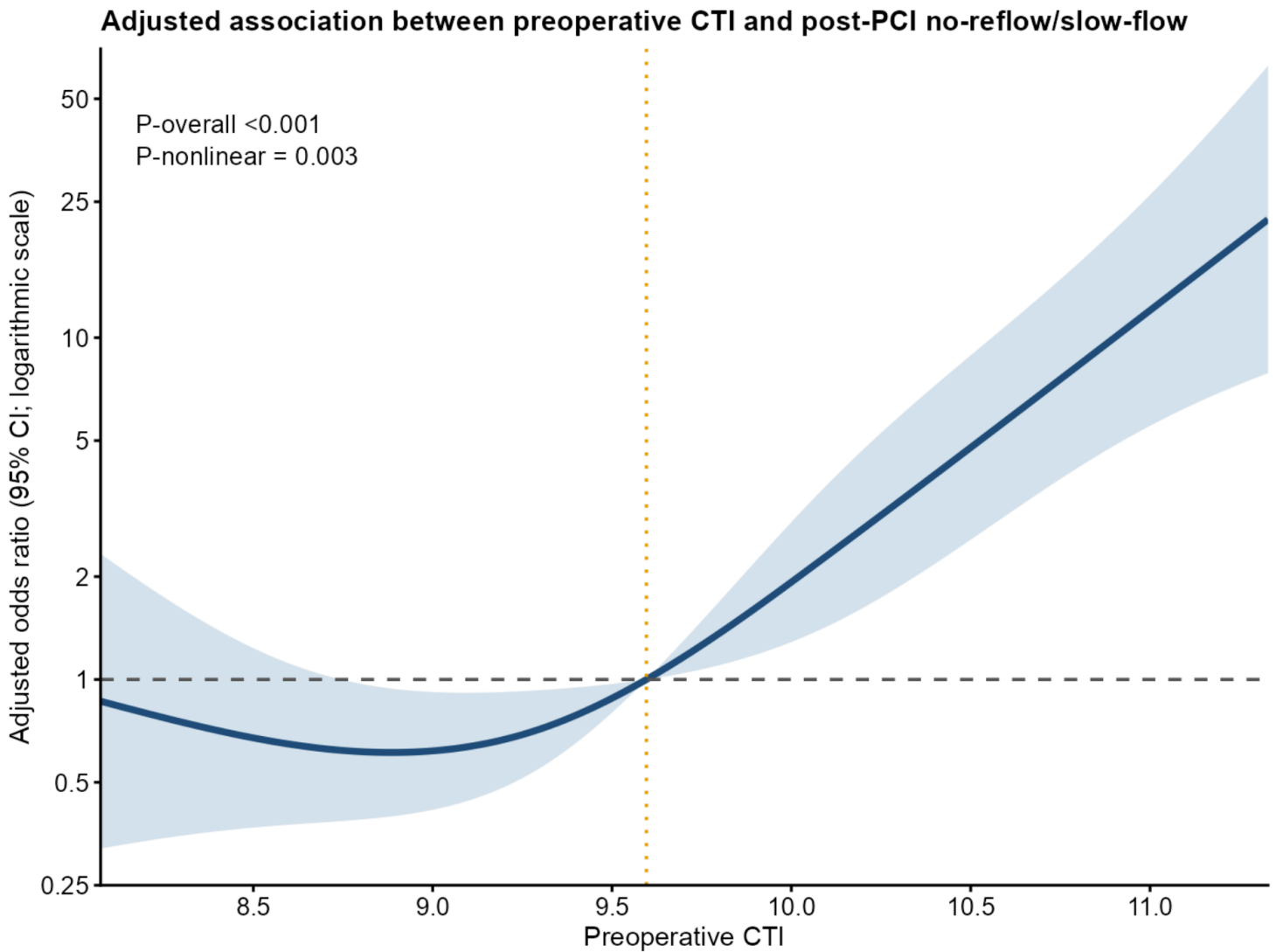


Figure 3

Adjusted spline association of CTI with no-reflow or slow flow. The solid line shows adjusted odds ratios and the shaded area shows 95% confidence intervals. The reference was the median CTI of 9.60. Four knots were placed at the 5th, 35th, 65th, and 95th percentiles. The model adjusted for age, sex, STEMI, diabetes, hypertension, current smoking, eGFR, and LVEF (n = 429; 102 events). The curve is shown from the 5th to 95th percentiles. P values are from two-sided Wald tests.

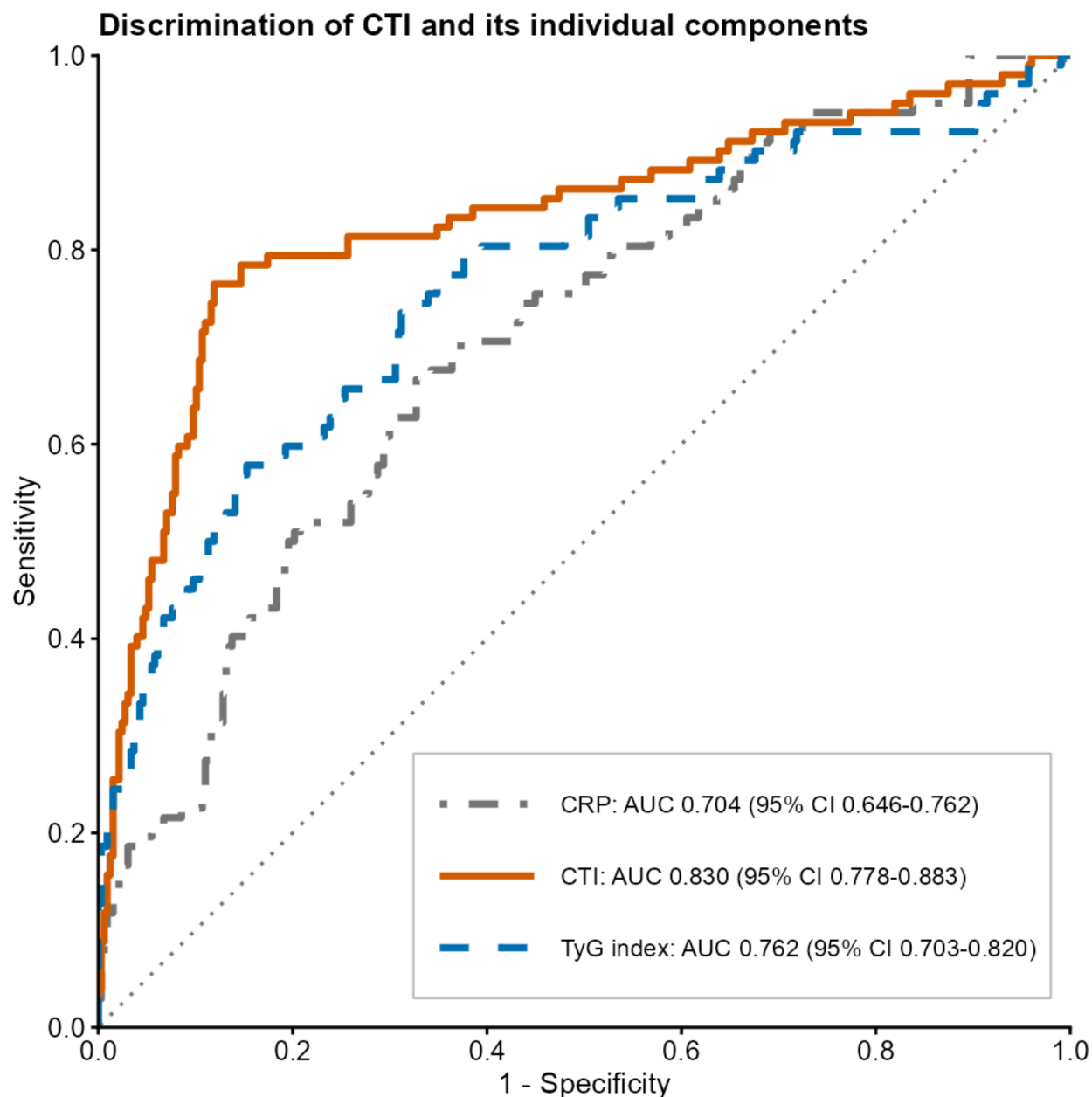


Figure 4

ROC comparison of CTI, TyG, and CRP. AUC confidence intervals were calculated with DeLong's method, and markers were compared with two-sided paired DeLong tests ($n = 429$; 102 events). Benjamini–Hochberg-adjusted P values were used for the two component comparisons. CRP was analysed in mg/L; its ROC curve is invariant to the monotonic $\ln(\text{CRP})$ transformation in the CTI formula.

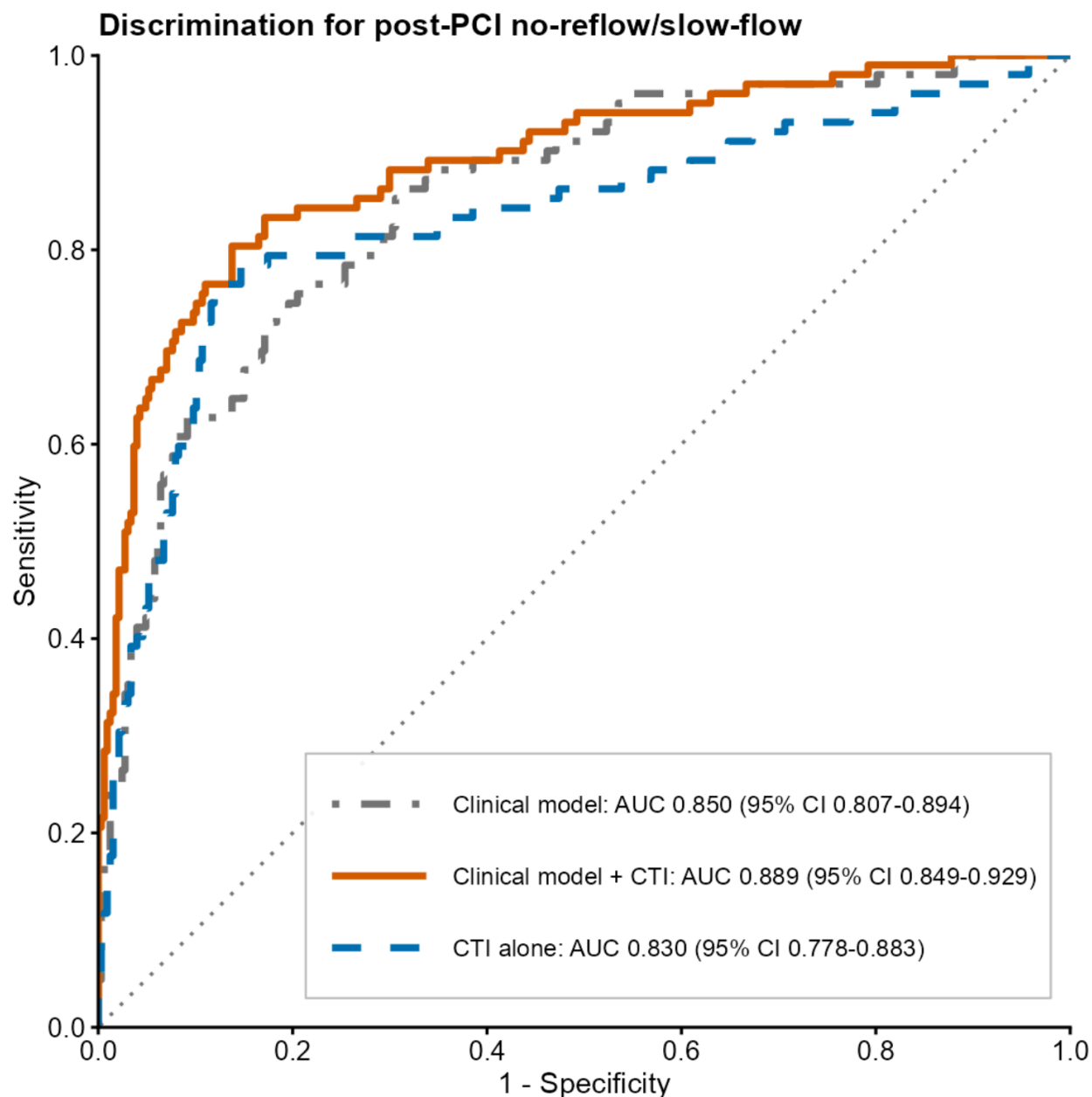


Figure 5

ROC curves for CTI and the clinical models. Curves show CTI alone, the pre-PCI clinical model, and the clinical model after adding linear CTI. The clinical model included age, sex, STEMI, diabetes, hypertension, current smoking, eGFR, and LVEF. AUC confidence intervals used DeLong's method, and the AUC increment after adding CTI used a two-sided paired DeLong test ($n = 429$; 102 events). These are apparent estimates from the development cohort.

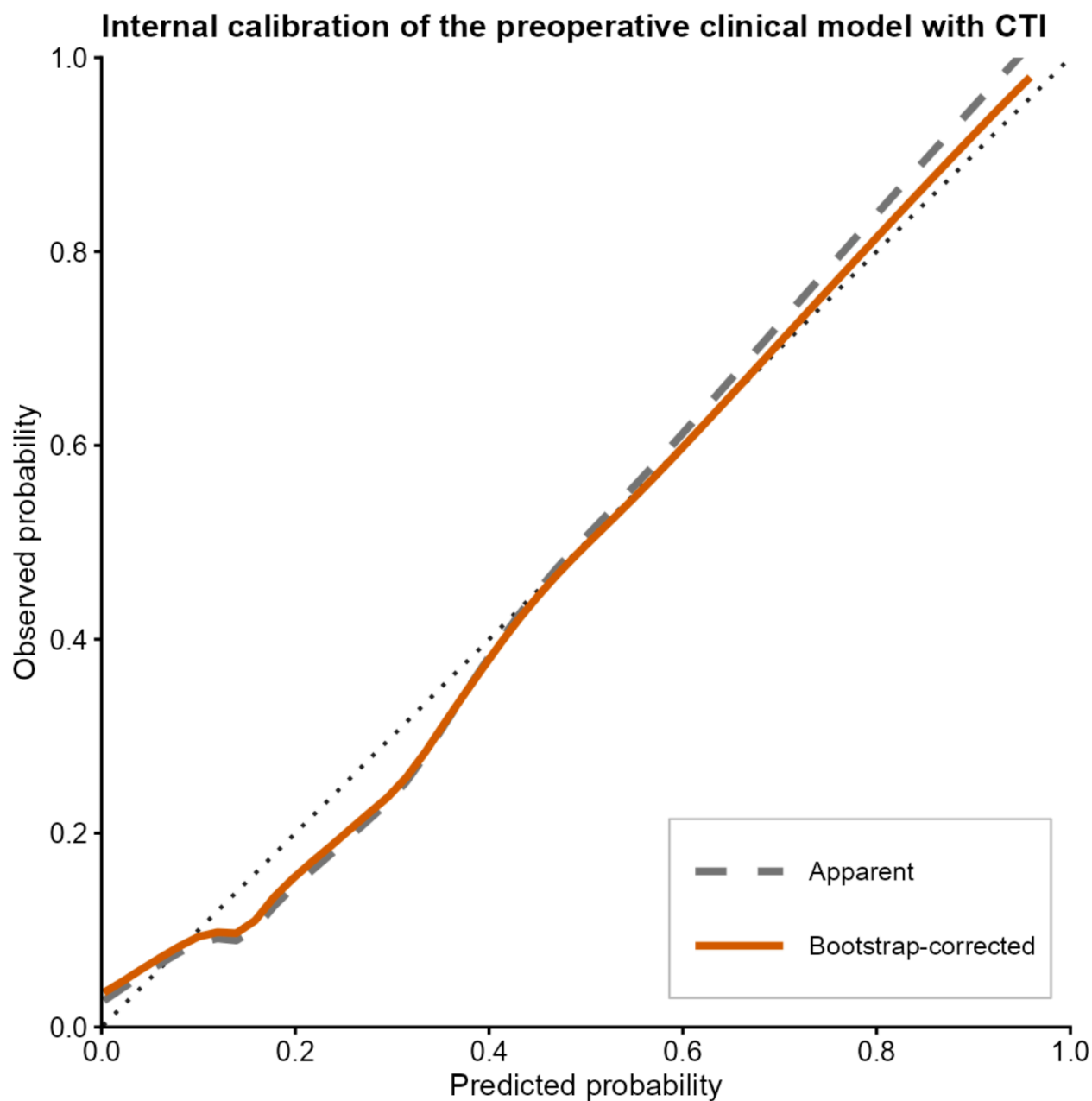


Figure 6

Bootstrap internal calibration of the extended model. The dotted diagonal indicates perfect agreement, the dashed curve shows apparent calibration, and the solid curve shows optimism-corrected calibration from 2,000 bootstrap resamples. The model included age, sex, STEMI, diabetes, hypertension, current smoking, eGFR, LVEF, and CTI (n = 429; 102 events). Internal validation does not replace external validation.

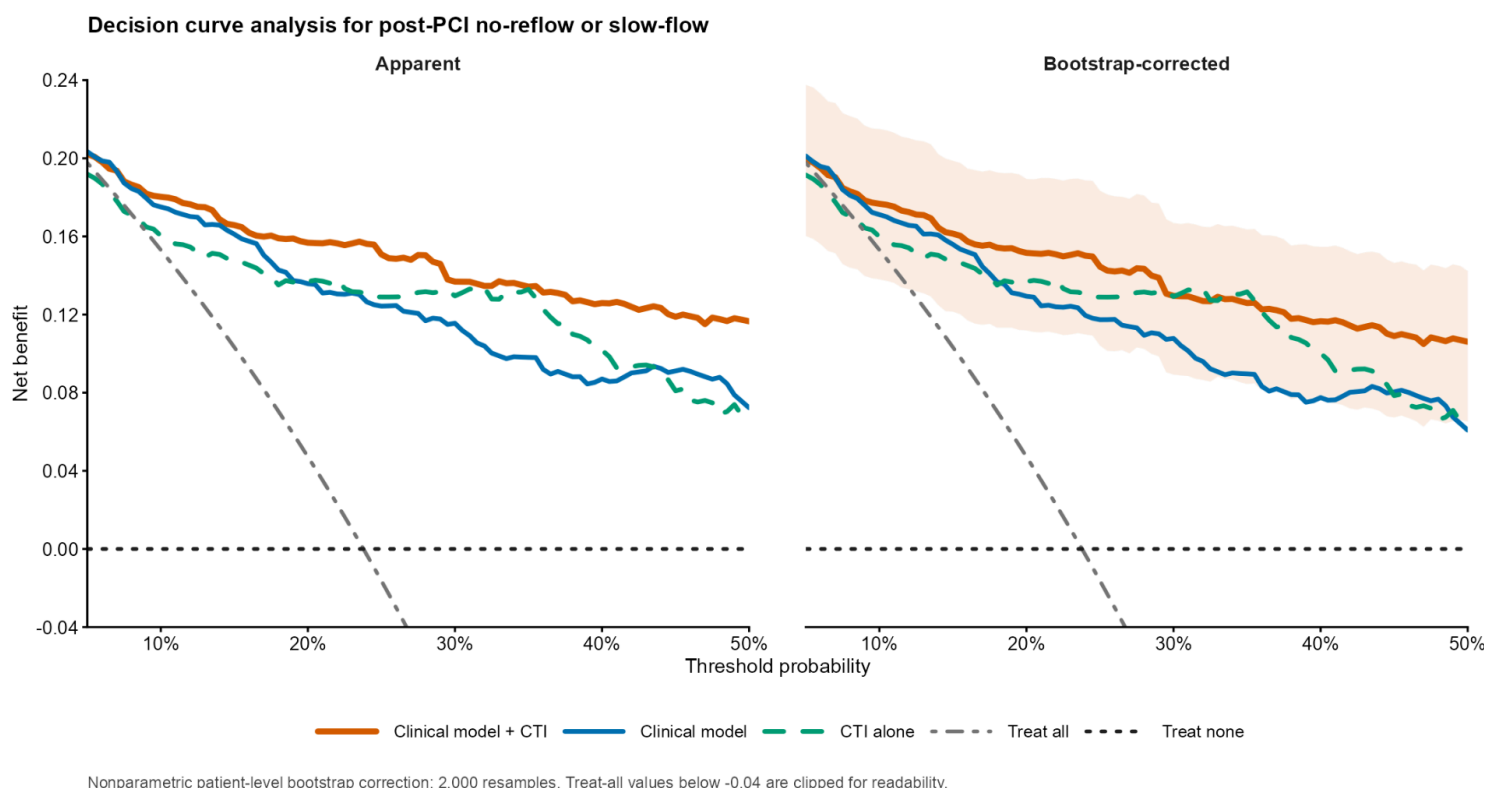


Figure 7

Decision curve analysis of pre-PCI models. The left panel shows apparent net benefit and the right panel shows optimism-corrected net benefit from 2,000 patient-level bootstrap resamples with model refitting. The display range from 0.05 to 0.50 is exploratory and does not define a clinical treatment threshold. Pointwise intervals were not adjusted for repeated assessment across thresholds.

Supplementary Files

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