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Canada acute coronary syndrome risk score predicts no-/slow-reflow in ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention

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ABSTRACT

Background: The no-/slow-reflow phenomenon following primary percutaneous coronary intervention (PCI) in patients with ST-elevation myocardial infarction (STEMI)is associated with poor prognosis. The early identification of high-risk patients with no-/slow-reflow is critical. This study aimed to evaluate the predictive ability of the Canada Acute Coronary Syndrome (C-ACS) risk score for no-/slow-reflow in these patients.

Methods: Patients with STEMI who underwent primary PCI were consecutively enrolled and divided into three groups based on their C-ACS scores: 0, 1, and ≥2. The C-ACS score was computed using the four clinical variables evaluated at admission (one point for each): age ≥75 years, heart rate >100 beats/min, systolic blood pressure <100 mmHg, and Killip class >1. No-/slow-reflow was defined as thrombolysis in a myocardial infarction flow grade of 0–2 after primary PCI. The predictive ability of the C-ACS score for no-/slow-reflow was evaluated using a receiver operating characteristic curve.

Results: A total of 834 patients were enrolled, of whom 109 (13.1 %) developed no-/slow-reflow. The incidence of no-/slow-reflow increased from the C-ACS 0 group to the C-ACS ≥2 group (6.1 % vs 17.7 % vs 34.3 %, respectively, $p < 0.001$). After multivariable adjustment, the C-ACS score was an independent predictor of no-/slow-reflow (odd ratio 2.623, 95 % confidence interval 1.948–3.532, $p < 0.001$). Furthermore, the C-ACS score showed good discrimination for no-/slow-reflow (area under the curve 0.707, 95 % confidence interval 0.653–0.762, $p < 0.001$). Further subgroup analyses indicated a significant interaction between the C-ACS score and patient sex (p for interaction = 0.011). The independent association between the C-ACS score and no-/slow-reflow was only observed in male patients (odd ratio 3.061, 95 % confidence interval 1.931–4.852, $p < 0.001$). During a median follow-up duration of 4.3 years, the C-ACS score was

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independently associated with major adverse cardiovascular events independent of the occurrence of no-/slow-reflow (p for interaction = 0.212).
Conclusion: The C-ACS risk score could independently predict the no-/slow-reflow in patients with STEMI undergoing primary PCI, particularly in male patients.

Abbreviations

PCI	Percutaneous coronary intervention
STEMI	ST-elevation myocardial infarction
C-ACS	Canada Acute Coronary Syndrome
TIMI	Thrombolysis in myocardial infarction
LVEF	Left ventricular ejection fraction
MACEs	Major adverse cardiovascular events

1. Introduction

Primary percutaneous coronary intervention (PCI) is routinely performed for ST-elevation myocardial infarction (STEMI) to salvage the jeopardized myocardium, improve cardiac performance, and reduce mortality and complication rates [1,2]. However, some patients do not achieve adequate myocardial tissue reperfusion after revovering infarct-related arterial blood flow, a condition known as the no-/slow-reflow phenomenon [3,4]. The no-/slow-reflow phenomenon limits the benefits of primary PCI and significantly increases the risk of short- and long-term poor outcomes [3,4].

There is no agreement on managing no-/slow-reflow [5–7], and early identification of high-risk patients for the no-/slow-reflow phenomenon and further guidance and modification of interventional strategies are essential. Many clinical variables, biochemical parameters, and angiographic morphological features, such as decreased left ventricular ejection fraction, fibrinogen, C-reactive protein, C-reactive protein to albumin ratio, and high thrombus burden, have previously been identified as potential risk factors for no-/slow-reflow [8–11]. Furthermore, several risk-scoring systems have been reported to predict the no-/slow-reflow [12–15]. However, most of these risk factors or risk scoring systems may not be available immediately before primary PCI, limiting their use in critical and emergency conditions.

The Canada Acute Coronary Syndrome (C-ACS) risk score is a well-established and validated risk score used to stratify patients with acute coronary syndromes [16]. It includes only four clinical variables available at first medical contact: age, Killip class, systolic blood pressure, and heart rate. Thus, the C-ACS risk score is easy to memorize and calculate and can save time in risk stratification in critical and emergency conditions [16]. Recent studies have demonstrated that the C-ACS score can predict contrast-induced nephropathy and infection in STEMI patients undergoing primary PCI, further broadening the use of the C-ACS risk score in such patients [17,18]. Although the four C-ACS risk score variables have been shown to increase the risk of no-/slow-reflow [9,10,15], the predictive ability of the C-ACS risk score for no-/slow-reflow remains unclear. In this study, we investigated the predictive ability of the C-ACS score for no-/slow-reflow and clinical outcomes in patients with STEMI treated with primary PCI.

2. Methods

2.1. Study population

Patients with STEMI who underwent primary PCI between January 2015 and December 2019 were consecutively enrolled at China-Japan Friendship Hospital. The STEMI was diagnosed by the presence of typical chest pain with typical ST-segment elevation on an electrocardiogram, consisting of $\geq$2 mm in at least 2 contiguous precordial leads ($\geq$1 mm in at least 2 contiguous limb leads) or documented new or presumed new left bundle branch block. Patients with a pain-to-balloon period >24 h, history of coronary artery bypass grafting, history of coronary stent implantation, treatment without dual antiplatelet therapy, left main disease requiring coronary artery bypass grafting, missing detailed data, or death during hospitalization were excluded from the present study. Patients who were not followed up after discharge were also excluded. The remaining 834 patients were included in the analysis (Fig. S1). This study was conducted in compliance with the principles of the Declaration of Helsinki. The study protocol was approved by the China-Japan Friendship Hospital Ethics Committee, and informed consent was waived because of the retrospective study design. The present study was subject to the STROBE statement and referred to the broader EQUATOR guidelines [19].

2.2. Procedure

A loading dose of aspirin 300 mg and either clopidogrel 300–600 mg or ticagrelor 180 mg were administered before the procedure. Coronary angiography and PCI were performed using standard clinical techniques [20]. The use of thrombectomy, intracoronary

Table 1
Baseline characteristics stratified by the Canada Acute Coronary Syndrome risk score.

Variable	C-ACS 0 (n = 489)	C-ACS 1 (n = 237)	C-ACS ≥2 (n = 108)	*P* value
Age, years				
Mean (SD), y	55.4 (10.2)	65.2 (13.6)	72.1 (12.3)	<.001
≥75 y, No. (%)	0 (0)	77 (32.5)	66 (61.1)	<.001
Female gender, No. (%)	69 (14.1)	65 (27.4)	46 (42.6)	<.001
Medical history and risk factors, No. (%)				
Current smoker	287 (58.7)	100 (42.2)	37 (34.3)	<.001
Hypertension	235 (48.1)	138 (58.2)	58 (53.7)	.033
Diabetes mellitus	111 (22.7)	67 (28.3)	36 (33.3)	.040
Hyperlipidemia	130 (26.6)	62 (26.2)	27 (25.0)	.943
Prior stroke	40 (8.2)	36 (15.2)	16 (14.8)	.007
Systolic blood pressure				
Mean (SD), mmHg	125.1 (17.0)	120.5 (19.8)	111.7 (22.4)	<.001
<100 mmHg, No. (%)	0 (0)	16 (6.8)	31 (28.7)	<.001
Diastolic blood pressure, mmHg	77.2 (11.8)	71.4 (12.1)	67.1 (13.4)	<.001
Heart rate				
Mean (SD), beats/min	76.2 (12.0)	81.3 (15.2)	87.3 (21.1)	<.001
>100 beats/min, No. (%)	0 (0)	26 (11.0)	31 (28.7)	<.001
Absence of pre-infarction angina, No. (%)	303 (62.0)	162 (68.4)	78 (72.2)	.060
Total ischaemic time, Median (IQR), h	5.6 (3.5, 10.2)	5.4 (3.5, 9.7)	5.5 (3.8, 8.9)	.959
Killip class, No. (%)				<.001
I	489 (100.0)	119 (50.2)	15 (13.9)	
II	0 (0)	59 (24.9)	39 (36.1)	
III	0 (0)	12 (5.1)	11 (10.2)	
IV	0 (0)	47 (19.8)	43 (39.8)	
Killip class >1, No. (%)	0 (0)	118 (49.8)	93 (86.1)	<.001
Laboratory test				
Hemoglobin, g/L	141.3 (15.9)	133.6 (19.0)	125.8 (18.5)	<.001
eGFR, mL/min/1.73 m^2	97.7 (25.8)	83.8 (30.8)	77.1 (30.2)	<.001
Total cholesterol, mmol	4.8 (1.1)	4.7 (1.3)	4.6 (1.4)	<.001
Triglycerides, mmol/L	2.0 (1.6)	1.6 (1.2)	1.5 (0.8)	.080
HDL-C, mmol/L	1.0 (0.3)	1.0 (0.3)	1.0 (0.4)	.054
LDL-C, mmol/L	3.4 (6.6)	3.0 (1.0)	2.9 (1.0)	.420
D-dimer, mg/L	0.4 (0.5)	1.1 (2.6)	1.4 (2.3)	<.001
Fibrinogen, g/L	3.5 (0.9)	3.7 (1.2)	4.1 (1.4)	<.001
Peak TnT or TnI >10-fold higher than the upper limit of normal), No. (%)	279 (57.1)	136 (57.4)	67 (62.0)	.630
LVEF, %	59.9 (9.0)	55.7 (10.4)	53.3 (10.1)	<.001
Culprit vessel, No. (%)				.057
LAD	229 (46.8)	127 (53.6)	61 (56.5)	
LCX	62 (12.7)	21 (8.9)	5 (4.6)	
RCA	198 (40.5)	89 (37.6)	42 (38.9)	
Multivessel disease, No. (%)	319 (65.2)	146 (61.6)	80 (74.1)	.078
Initial TIMI flow grade, No. (%)				.640
0	308 (63.0)	163 (68.8)	73 (67.7)	
1	60 (12.3)	25 (10.5)	9 (8.3)	
2	81 (16.6)	32 (13.5)	15 (13.9)	
3	40 (8.2)	17 (7.2)	11 (10.2)	
TIMI thrombus score ≥4, No. (%)	89 (18.2)	62 (26.2)	31 (28.7)	.009
Gensini Score, Median. (IQR)	50.0 (37.0, 80.0)	57.0 (39.0, 82.0)	56.5 (42.0, 84.0)	.015
Intracoronary administration of GP IIb/IIIa receptor inhibitor	160 (32.7)	86 (36.3)	40 (37.0)	.518
Number of stents, Median. (IQR)	1.0 (1.0, 1.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	.608
Stent length, Median. (IQR), mm	24.5 (19.3, 30.0)	26.0 (20.0, 30.0)	22.8 (18.0, 30.0)	.024
Stent diameter, Median. (IQR), mm	3.0 (2.6, 3.5)	3.0 (2.5, 3.3)	3.0 (2.8, 3.5)	.539
Moderate or severe calcification, No. (%)	37 (7.6)	24 (10.1)	19 (17.6)	.006
After stent TIMI flow grade, No. (%)				<.001
1	6 (1.2)	9 (3.8)	4 (3.7)	
2	24 (4.9)	33 (13.9)	33 (30.6)	
3	459 (93.9)	195 (82.3)	71 (65.7)	
Medication, No. (%)				
$P2Y_{12}$ receptor inhibitor				.087
Clopidogrel	329 (67.3)	172 (72.6)	83 (76.9)	
Ticagrelor	160 (32.7)	65 (27.4)	26 (23.1)	
ACEI/ARB	422 (86.3)	170 (71.7)	68 (63.0)	<.001
β-blocker	461 (94.3)	217 (91.6)	96 (88.9)	0.100
CCB	21 (4.3)	6 (2.5)	3 (2.8)	.501
Statins	476 (97.3)	234 (98.7)	105 (97.2)	.456

Data are expressed as the mean value ± standard deviation, median with 25th and 75th or number (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; C-ACS, Canada Acute Coronary Syndrome risk score; CCB, calcium-channel blocker; PPIs, proton pump inhibitors; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LAD, left anterior descending; LCX, left

circumflex; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

vasodilator, or glycoprotein IIb/IIIa inhibitor was at the direction of interventional cardiologists. Blood flow in the infarct-related artery was evaluated using the thrombolysis in myocardial infarction (TIMI) flow scale [21]. TIMI thrombus scale was used to determine the thrombus burden [22]. The occurrence of no-/slow-reflow was assessed using angiography immediately after the PCI. Two interventional cardiologists, blinded to the individuals' clinical data, evaluated the pre- and post-PCI TIMI flow grades.

2.3. Data extraction

Information on demographic data, clinical characteristics, procedure details, and medications was gathered from medical records. Comorbidities were defined as self-reported or the use of relevant medications. Laboratory parameters collected within 24 h of admission included troponin I/T, lipids, serum creatinine, electrolyte, and blood count. Left ventricular ejection fraction (LVEF) was measured by ultrasonic cardiography using the Simpson's biplane method. The C-ACS risk score ranged from 0 to 4, with 1 point assigned for each of the following clinical parameters assessed at admission [16]: age $\geq$75 years, heart rate >100 beats/min, systolic blood pressure <100 mmHg, and Killip class >1.

2.4. Clinical outcomes and follow-up

The primary outcome of interest was no-/slow-reflow, which was defined as anterograde TIMI flow grade 0 to 2 in the culprit coronary artery despite successful dilatation revealed by the final angiogram [1]. The secondary outcomes of interest were major adverse cardiovascular events (MACEs), including all-cause death, ischemic stroke, or nonfatal myocardial infarction, during the follow-up period. For the present study, follow-up information was gathered via telephone interviews or outpatient clinics until December 2021. Myocardial infarction was defined according to the fourth universal definition [23], presenting with ischemic symptoms complicated by ST-segment changes on electrocardiography or elevated cardiac troponin levels. Ischemic stroke was defined as a new focal neurological deficit based on computed tomography or magnetic resonance imaging.

2.5. Statistical analysis

Patients were divided into three groups based on their C-ACS scores: 0, 1, and$\geq$2. Continuous variables with a normal distribution were presented as the mean $\pm$ standard deviation, while those with a non-normal distribution were expressed as the median and interquartile range. To compare continuous variables, we employed either the ANOVA test or the Kruskal-Wallis H test, as appropriate. Categorical variables were presented as numbers (percentage) and compared using Fisher's exact or the χ^2 test as appropriate. Univariable and multivariable logistic regression analyses were performed to identify the independent risk factors for no-/slow-reflow. To comprehensively evaluate the association between C-ACS risk score and no-/slow-reflow, a series of logistic regression models were constructed to adjust the relevant variables. Model 1 was unadjusted for a rough analysis; model 2 was adjusted for sex and medical history; model 3 was adjusted additionally for clinical manifestations and laboratory markers; and model 4 was adjusted additionally for angiographic details. Subgroup analyses in Model 4 were conducted to detect heterogeneity between the different groups stratified by sex, hypertension, diabetes mellitus, absence of pre-infarction angina, estimated glomerular filtration rate (eGFR), TIMI thrombus score $\geq$4, and multivessel disease. A receiver operating characteristic (ROC) curve was constructed to assess the predictive ability of the C-ACS score for no-/slow-reflow. PredIction of Angiographic NO-reflow (PIANO) score, a recently established scoring system specifically for angiographic no-/slow-reflow, was evaluated to confirm the predictive accuracy of the C-ACS score [12]. The PIANO score ranged from 0 to 14, with six clinical parameters as follows: age $\geq$70 years (2 points), absence of pre-infarction angina (3 points), total ischemic time $\geq$4 h (1 point), left anterior descending artery as the culprit artery (1 point), pre-PCI TIMI flow grade $\leq$1 (2 points) and pre-PCI TIMI thrombus score $\geq$4 (5 points). The area under the curve (AUC) between the C-ACS risk score and the PIANO score was compared using Delong's method. Kaplan-Meier curves and log-rank tests were used to discriminate groups' rates of all-cause death and MACEs. Univariable and multivariable Cox regression analyses were performed to evaluate the relationship between the C-ACS score and MACEs during the follow-up period. Significant variables identified in the univariate analysis model were entered into multivariate analysis model. Odds ratio (OR) or hazard ratio (HR) and the corresponding 95 % confidence interval (CI) were reported. A P value < 0.05 at a two-tailed test was considered statistically significant. Data were analyzed using SPSS (version 25.0; SPSS Inc., Chicago, IL, USA), R (version 4.2.0; R Development Core Team, Vienna, Austria), and GraphPad Prism (version 9.0.0; GraphPad Software Inc., CA, USA).

3. Results

3.1. Baseline characteristics

Overall, 834 patients were enrolled, with a mean age of 60.4 $\pm$ 13.1 years and 21.6 % of females. The clinical characteristics of the patients were summarized in Table 1. Patients were divided into three groups based on their C-ACS risk score: C-ACS 0 (n = 489), C-ACS 1 (n = 237), and C-ACS $\geq$2 (n = 108). Patients in the C-ACS $\geq$2 group were more likely to be older and female; have a history of hypertension, diabetes mellitus, and a previous stroke; and have a lower smoking rate. As the C-ACS risk score increased, patients had a

higher Killip class and lower LVEF. From the C-ACS 0 group to the C-ACS 2 group, there were positive trends in preprocedural D-dimer and fibrinogen levels and negative trends in preprocedural hemoglobin, eGFR, and total cholesterol. Furthermore, patients with higher C-ACS scores were less likely to receive angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. As for the angiographic findings, patients presented with a higher level of Gensini score as well as a higher rate of TIMI thrombus score ≥4 with C-ACS risk score increasing. Although the C-ACS ≥2 group showed the highest incidence of multivessel disease, the difference was not statistically significant.

3.2. Canada acute coronary Syndrome risk score for No-/slow-reflow

A total of 109 patients (13.1 %) developed no-/slow-reflow. The incidence of no-/slow-reflow increased as the C-ACS score increased (6.1 % vs 17.7 % vs 34.3 %, respectively; $p < 0.001$) (Fig. 1A). Fig. 1 showed the association between C-ACS score and no-/slow-reflow in different adjusted models. In the rough analysis with no adjustment (Model 1, Fig. 1B), the C-ACS risk score was associated with an increased risk of no-/slow-reflow (OR 2.818, 95 % CI 2.176–3.650, $p < 0.001$). Model 2 was adjusted for sex and smoking status, with an adjusted OR of 2.996 (95 % CI 2.280–3.936, $p < 0.001$). Similar results were obtained when additionally adjusted for the absence of pre-infarction angina, hemoglobin, eGFR, fibrinogen, and peak troponin I/T. (Model 3, Fig. 1B; adjusted OR 2.685, 95 % CI 2.010–3.586, $p < 0.001$). In the fully adjusted model (Model 4, Fig. 1B), which was additionally adjusted for angiographic findings (including initial TIMI flow grade ≤1, TIMI thrombus score ≥4, and Gensini Score), the C-ACS score remained independently associated with no-/slow-reflow (adjusted OR 2.623, 95 % CI 1.948–3.532, $p < 0.001$). Other independent risk factors for no-/slow-reflow in Model 4 were the absence of pre-infarction angina, a peak troponin I/T > 10-fold higher than the upper limit of normal, and a TIMI thrombus score ≥4 (Table 2). In the ROC curve analysis, the C-ACS score showed a good ability to predict the risk of no-/slow-reflow (AUC 0.707, 95 % CI 0.653–0.762, $p < 0.001$; Fig. 2). Furthermore, an ROC curve was constructed for the PIANO score, as it is a recently established and validated scoring system for angiographic no-/slow-reflow. The predictive performance for no-/slow-reflow was comparable between the two scoring systems (AUC 0.717, 95 % CI 0.664–0.769, $p < 0.001$; Fig. 2). ($p = 0.767$).

Subgroup analyses stratified according to patient characteristics and comorbidities were performed to assess the robustness of the results (Fig. 3). A significant interaction was observed between C-ACS score and patient sex on the increased risk of no-/slow-reflow (p for interaction = 0.011). After full adjustment, the higher C-ACS score were independently associated with no-/slow-reflow in male patients (OR 3.061, 95 % CI 1.931–4.852, $p < 0.001$), whereas no significant association was detected in female patients (OR 1.537, 95 % CI 0.875–2.702, $p = 0.135$). Furthermore, the test for interactions was not statistically significant for hypertension, diabetes mellitus, absence of pre-infarction angina, eGFR, TIMI thrombus score ≥4, and multivessel disease (all p for interaction >0.05, Fig. 3).

3.3. Canada acute coronary Syndrome risk score for long-term clinical outcomes

The median follow-up duration was 4.3 years (interquartile range, 3.0–5.7 years). Overall, 52 (6.2 %) all-cause deaths and 132 (15.8 %) MACEs were reported. The incidence of all-cause death (1.8 % vs 9.3 % vs 19.4 %, respectively, $p < 0.001$) and MACEs (8.4 % vs 19.8 % vs 40.7 %, respectively, $p < 0.001$) increased from the C-ACS 0 group to C-ACS ≥2 group (Fig. S2). Cumulative long-term all-cause mortality and MACEs were significantly higher in patients with higher C-ACS score (both Log-rank $p < 0.001$; Fig. S3). Univariable and multivariable Cox regression analyses for MACEs were demonstrated in Table S1. After adjusting for other clinical risk determinants and no-/slow-reflow, the C-ACS score was associated with a significantly increased risk of MACEs (adjusted HR 1.619, 95 % CI 1.273–2.059, $p < 0.001$). Furthermore, there was no significant interaction between the C-ACS score and no-/slow-reflow (p

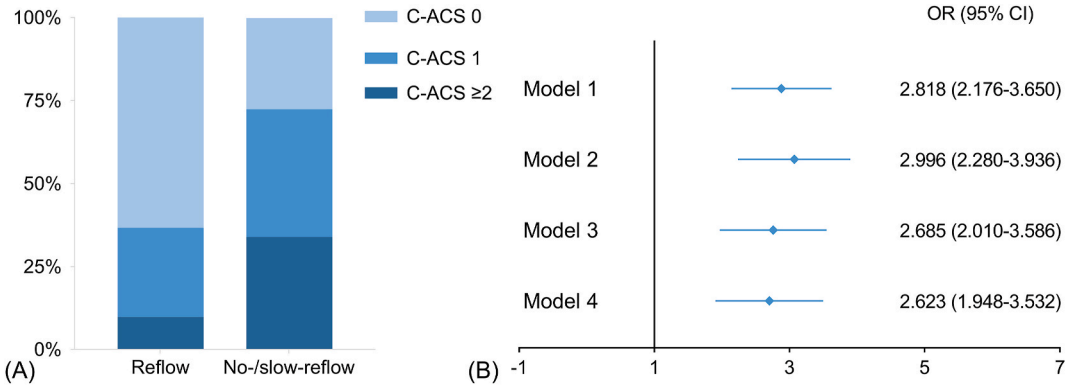

Fig. 1. Association of the Canada Acute Coronary Syndrome risk score and no-/slow-reflow.
(A) The proportion of the C-ACS risk score groups in reflow and no-/slow-reflow population. (B) The odds ratios (95 % confidence interval) of the C-ACS risk score for no-/slow-reflow in different models. Model 1 is an unadjusted model; Model 2 was adjusted for gender and smoking; Model 3 was additionally adjusted for the absence of pre-infarction angina, hemoglobin, estimated glomerular filtration, fibrinogen, and peak troponin I/T; Model 4 was additionally adjusted for initial TIMI flow grade ≤1, TIMI thrombus score ≥4, and Gensini Score. C-ACS, Canada Acute Coronary Syndrome risk score; CI, confidence interval; OR, odds ratios.

Table 2
Univariate and multivariate predictors for no-/slow-reflow.

	Univariable		Multivariable	
Variable	OR (95 % CI)	*P* Value	OR (95 % CI)	*P* Value
C-ACS score	2.818 (2.176–3.650)	<.001	2.623 (1.948–3.532)	<.001
Female gender	0.968 (0.591–1.584)	.896	0.552 (0.289–1.055)	.072
Current smoker	0.615 (0.408–0.926)	.020	0.687 (0.418–1.128)	.138
Absence of pre-infarction angina	1.326 (1.126–1.562)	.001	1.268 (1.063–1.512)	.008
Hemoglobin	0.988 (0.977–0.999)	.030	0.999 (0.984–1.013)	.842
eGFR	0.990 (0.983–0.997)	.006	1.000 (0.992–1.008)	.975
Fibrinogen	1.355 (1.151–1.595)	<.001	1.201 (0.996–1.447)	.055
Peak TnI or TnT >10-fold higher than the upper limit of normal)	2.608 (1.640–4.149)	<.001	2.538 (1.540–4.181)	<.001
TIMI thrombus score ≥4	3.313 (2.171–5.056)	<.001	1.233 (1.123–1.354)	<.001
Gensini Score	1.008 (1.001–1.015)	.029	1.005 (0.997–1.013)	.230

C-ACS, Canada Acute Coronary Syndrome risk score; CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio; TIMI, thrombolysis in myocardial infarction.

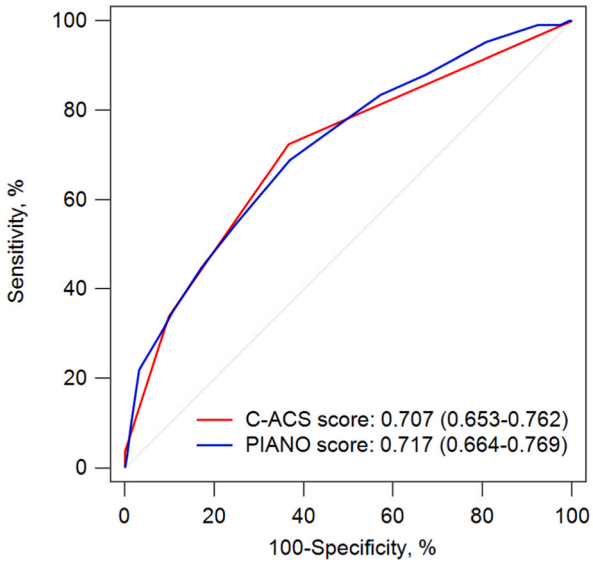

Fig. 2. Receiver operating characteristic curves for no-/slow-reflow.
C-ACS, Canada Acute Coronary Syndrome risk score; PIANO, the PredIction of Angiographic NO-reflow risk score.

for interaction = 0.212).

4. Discussion

The present study demonstrated that the C-ACS risk score was independently associated with an increased risk of no-/slow-reflow in patients with STEMI undergoing primary PCI, particularly in male patients. The ROC curves showed that the C-ACS score exhibited a good ability for predicting no-/slow-reflow in such patients. Furthermore, the C-ACS score was an independent predictor of long-term MACEs independent of no-/slow-reflow.

The incidence of no-/slow-reflow has been reported to range from 5 % to 50 % in patients with STEMI undergoing primary PCI [3,4]. The most practical and valuable method for detecting no-/slow-reflow is TIMI flow grade, also called angiographic no-/slow-reflow [1]. In the present study, no-/slow-reflow was documented in 109 (13.1 %) patients, which is consistent with recent studies [9,12]. The no-/slow-reflow phenomenon is related to reduced myocardial salvage, larger infarct sizes, and reduced global systolic function and further predicts adverse cardiovascular outcomes [3,4]. Thus, early identification with high-risk patients of no-/slow-reflow is critical, and further optimal preoperative preparations, interventional strategies, and close monitoring can be used to minimize the risk of no-/slow-reflow and its potential harm. Several risk scoring systems have been developed to predict no-/slow-reflow in patients with STEMI undergoing primary PCI in previous studies [12–15]. However, their applicability in clinical practice, however, remains limited. Some risk scores may be limited by unavailable parameters in emergencies, such as neutrophil count [14], plasma glucose level [14], and left ventricular ejection fraction [13], while others may be limited by the complexity of their calculation [13] or some unstable parameters [12]. Thus, a simple and time-saving risk score is required to identify high-risk patients for no-/slow-reflow in clinical practice.

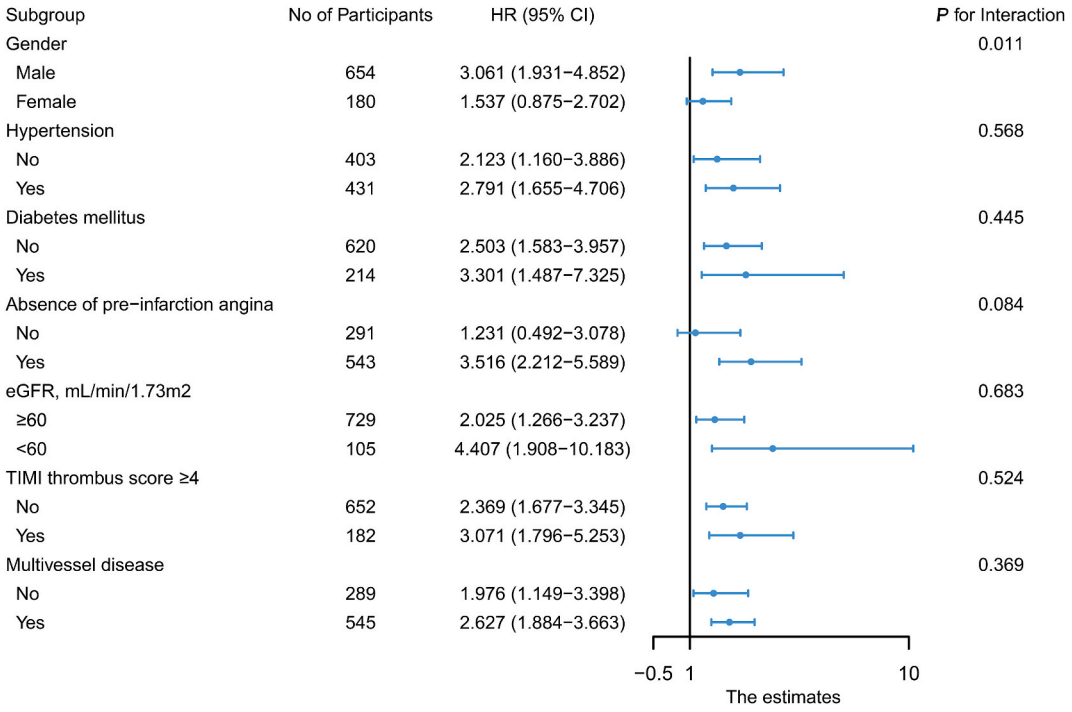

Fig. 3. Multivariable cox proportional hazard ratios for no-/slow-reflow in Subgroups stratified by patients' characteristics and comorbidities.

The C-ACS risk score is a validated risk score for assessing short- and long-term mortality in acute coronary syndromes [16,24,25]. However, whether the C-ACS risk score can be used to predict no-/slow-reflow remains unclear. Our results demonstrated that the C-ACS score was independently associated with no-/slow-reflow, especially in male patients. The ROC curves showed that the C-ACS score had an excellent predictive ability for no-/slow-reflow. Advanced age is a well-known risk factor for angiographic no-/slow--reflow [3]. Aging increases the risk of vascular endothelial dysfunction and large elastic artery stiffness [26,27], which might increase the susceptibility to impaired coronary flow reserve and myocardial vulnerability to ischemia and reperfusion injury [28]. Furthermore, common comorbidities in older patients, such as hypertension, chronic kidney disease, and microvascular disease, may contribute to the occurrence of no-/slow-reflow [4]. Two other components of the C-ACS score, systolic heart rate and blood pressure, might directly reflect the hemodynamic status. Previous studies have found that unstable hemodynamics might decrease coronary and collateral blood flow and increase infarct size [29,30]. Furthermore, a reduction in blood flow can accelerate leukocyte aggregation, adhesion, and capture by capillaries, thus aggravating no-/slow-reflow [31]. Because the Killip class is a key indicator of heart function that is easy to use for most healthcare practitioners, it is included in several risk scores for no-/slow-reflow [13–15]. Systolic dysfunction is associated with reduced coronary blood flow and increased coronary microcirculation resistance, leading to poor myocardial perfusion [30]. Furthermore, patients with Killip class >1 are reported to experience a higher rate of distal embolization, which might increase the risk of no-/slow-reflow [32]. Therefore, the C-ACS risk score showed good discrimination for no-/slow--reflow. The present study also detected an independent association between C-ACS risk score and MACEs, consistent with the previous studies [17,18,25]. These results broaden the applicability of C-ACS risk score in the management of patients with STEMI. Furthermore, the C-ACS risk score may be useful for screening eligible patients for research activities concerning the management of no-/slow-reflow. Of note, the current guidelines recommend that risk assessment should be a continuous process. Thus, the repeated risk assessment should be performed once a more comprehensive evaluation has been performed, and combining them might have a beneficial cumulative effect.

Furthermore, we compared the predictive ability of the C-ACS risk score and a recently established scoring system specifically for angiographic no-/slow-reflow that included six clinical and angiographic parameters in its calculation, the PIANO score [12]. The present study validated the predictive ability of the PIANO score in predicting no-/slow-reflow (AUC 0.717, 95 % CI 0.664–0.769) and found no statistical difference between the C-ACS score and the PIANO score for predicting no-/slow-reflow ($p = 0.767$). Apart from its simplicity, the C-ACS score seems to exhibit good discriminative ability, similar to other scoring systems comprising demographic and angiographic variables (such as the PIANO score), which might be more practical for risk estimation in emergencies.

This study represents, to our knowledge, the first investigation to evaluate the association of C-ACS score with no-/slow-reflow in STEMI patients undergoing primary PCI. Our results demonstrated that the high C-ACS score was independently associated with an increased risk of no-/slow-reflow, especially in male patients. These findings suggest that patients with high C-ACS scores should consider preventive measures, including thrombus aspiration and intracoronary/intravenous glycoprotein IIb/IIIa receptor inhibitor injection, to prevent compromised coronary blood flow after PCI. However, it is important to acknowledge the retrospective nature of

our study, and further studies are warranted to validate the role of preventive interventions guided by the C-ACS score in mitigating the risk of no-reflow. This study has some limitations. First, this was a retrospective, single center study, which may have a potential risk of selection bias. The C-ACS score was evaluated only at admission; therefore, we were unable to determine whether changes in the C-ACS score over time were associated with no-/slow-reflow and other clinical outcomes in patients with STEMI undergoing primary PCI. Moreover, the participants in the present study were from a cohort of Chinese population. Thus, the validation of our findings in other populations is required. In addition, the Killip class evaluation is subjective, and its accuracy may largely depend on the examiner's expertise. However, the assessment of Killip class >1 requires only the presence of pulmonary rales and normal blood pressure, which is easy for most healthcare practitioners to perform. Finally, the no-/slow-reflow phenomenon was assessed using only TIMI flow grade. More robust data, provided by large sample trials using other sensitive and specific methods such as myocardial blush grade, contrast echocardiography, or cardiac magnetic resonance imaging to evaluate reperfusion success, will be necessary to confirm our findings.

5. Conclusion

The present study revealed that the C-ACS score was independently associated with no-/slow-reflow and other clinical outcomes in patients with STEMI undergoing primary PCI. Our results support the potential role of the C-ACS risk score in predicting no-/slow-reflow in such patients. Further multicenter and large-scale studies are required to corroborate these findings.

Ethics statement

This study was conducted in compliance with the principles of the Declaration of Helsinki. The study protocol was approved by the China-Japan Friendship Hospital Ethics Committee (No. 2021-15-K07), and informed consent was waived due to the retrospective study design.

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Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Enmin Xie: Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Qing Li:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Zixiang Ye:** Writing – original draft, Methodology, Data curation. **Ziyu Guo:** Validation, Methodology, Data curation, Conceptualization. **Yike Li:** Writing – original draft, Methodology, Data curation. **Nan Shen:** Resources, Methodology, Conceptualization. **Changan Yu:** Writing – original draft, Methodology, Data curation. **Yanxiang Gao:** Writing – review & editing, Writing – original draft, Data curation. **Jingang Zheng:** Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21276.

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