

Prediction models for no-reflow phenomenon after PCI in acute coronary syndrome patients: A systematic review

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ABSTRACT

Objective: To comprehensively evaluate existing prediction models for the no-reflow phenomenon (NRP) after percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS).

Methods: A systematic search was conducted across PubMed, Web of Science, Embase, Cochrane Library, Scopus, China National Knowledge Infrastructure (CNKI), Wanfang Database, Weipu (VIP), and the Chinese Biomedical Literature Service System (Sinomed) up until May 28, 2024, to identify studies on prediction models for the NRP in ACS patients after PCI. A qualitative synthesis was performed to assess study characteristics and model features.

Results: A total of 3738 studies were retrieved, and 21 studies involving 25 prediction models were finally included. The reported incidence of NRP ranged from 3.58 % to 33.3 %. Most models were developed using logistic regression, with area under the curve (AUC) ranged from 0.637 to 0.958. Frequently reported predictors across models included Killip classification, symptom-to-balloon time, total ischemic time, and pre-PCI TIMI thrombus grade, among others. All included studies were assessed as having a high risk of bias (ROB), mainly due to inappropriate data sources and methodological limitations in the analysis domain.

Conclusions: Current prediction models for NRP after PCI in ACS patients exhibit high ROB and have not been adequately validated. Currently, no suitable prediction models are recommended for clinical decision-making. Future research should adopt more rigorous methodologies and emphasize multicenter external validation to enhance model reliability and applicability.

1. Introduction

Cardiovascular disease is a major global health problem, accounting for approximately one-third of all deaths worldwide [1]. Among them, acute coronary syndrome (ACS) is one of the most common critical cardiovascular emergencies, encompassing ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA). ACS progresses rapidly from the onset of symptoms such as chest pain to malignant arrhythmias, shock, or even cardiac arrest, resulting in high mortality rates [2]. Percutaneous coronary intervention (PCI) is a mechanical method used to open occluded coronary arteries and restore myocardial blood flow. It is the preferred reperfusion strategy for STEMI patients [3], significantly improving short-term and long-term outcomes for ACS patients [4].

However, in approximately 10 % to 30 % of STEMI patients, myocardial tissue is not effectively reperfused after successful PCI, resulting in the no-reflow phenomenon (NRP) [5]. This condition is driven by complex mechanisms, including endothelial dysfunction, ischemic injury, reperfusion injury, and distal thromboembolism [6]. NRP after PCI in ACS patients may lead to severe complications and poor prognosis. Studies have shown that patients with NRP have a higher incidence of heart failure and all-cause mortality [7]. Long-term studies have also found that NRP is a strong predictor of 5-year mortality [8].

Considering the serious consequences of NRP, more attention should be paid to its prevention. Developing and validating effective prediction models is crucial for early identification of high-risk individuals and effective management. Although several prediction models have been developed, their quality and performance have not been systematically

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evaluated, and it remains unclear which models are suitable for clinical practice. Therefore, it is essential to thoroughly evaluate the quality and performance of existing prediction models.

In this study, we conducted a systematic review of prediction models for NRP after PCI in ACS patients. We aimed to evaluate the potential of these models for early identification of NRP, examine methodological limitation, and summarize commonly reported predictors. The findings may inform the design and validation of future predictive models in this field.

2. Methods

This study was registered in PROSPERO (Registration ID: CRD42024550274).

2.1. Search strategy

A systematic search was conducted across multiple English and Chinese databases, including PubMed, Web of Science, Embase, Cochrane Library, Scopus, China National Knowledge Infrastructure (CNKI), Wanfang Database, Weipu (VIP), and the Chinese Biomedical Literature Service System (Sinomed). A combination of subject terms and free-text terms was used for the search strategy. The search focused primarily on computer-based retrieval, supplemented by manual searches of references and citations from the included studies. The search period spanned from the inception of the databases to May 28, 2024 (Supplement 1). The following keywords were used: Acute Coronary Syndromes, ACS, Myocardial Infarction, myocardial infarct*, MI, AMI, STEMI, NSTEMI, unstable angina, Percutaneous Coronary Intervention, PCI, no-flow phenomenon, no-reflow, slow-flow, slow-flow phenomenon, Prediction model, Risk Prediction, predict*.

2.2. Inclusion and exclusion criteria

Inclusion criteria included the following: (1) study population was adult patients diagnosed with ACS; (2) study content focused on developing and/or validating prediction models for NRP after PCI; (3) NRP was used as outcome indicator; (4) study types were cohort studies, case-control studies, or cross-sectional surveys; (5) ≥ 2 variables of the prediction model; and (6) language of publication was Chinese or English.

Exclusion criteria included: (1) unavailability of full text, (2) duplicate publications, and (3) conference abstracts, reviews, and dissertations.

2.3. Study selection and screening

NoteExpress 3.4.0 software was used to remove duplicate studies. Two independent authors screened studies according to the inclusion and exclusion criteria. Obviously non-compliant studies were excluded by reading titles and abstracts. Remaining studies were then reviewed in full to identify suitable literature. Additionally, the reference lists and citations of the selected studies were examined to identify other potentially relevant studies. A third researcher would be consulted in cases of disagreement, and consensus would be reached through discussion.

2.4. Data extraction

Two independent authors extracted data and performed cross-checks. Data were extracted using standardized forms based on the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modeling Studies (CHARMS) checklist [9]. Extracted basic characteristics of included studies were as follows: first author, publication year, study aim, study design, participant, data source, sample size, number of outcome events, number of candidate variables, events

per variable (EPV), and incidence of NRP. Extracted model characteristics included methods for handling continuous variables and missing data, predictor selection methods, model development method and validation method, performance measurement, model presentation, and variables included in the final model. Disagreements were resolved by consulting a third author to reach a consensus.

2.5. Methodological quality assessment

Two independent authors assessed risk of bias (ROB) and applicability of included studies using the Prediction Model Risk of Bias Assessment Tool (PROBAST) [10]. ROB assessment consisted of 20 signaling questions in four domains, including study population, predictors, outcomes, and statistical analyses. Each question offers three response options: yes/possibly yes, no/possibly no, or no information. A domain was considered to have a low ROB when all questions were answered “yes/probably yes”. If any question was answered “no/probably no”, the domain was considered to have a high ROB. When a question was answered “no information” while other questions were answered “yes/no”, ROB of the domain was unclear. If any domain was rated as high ROB, the overall judgement was high ROB. If a domain was unclear ROB while other domains were low risk, the overall judgement was unclear ROB. The overall judgement was low ROB only if all domains were low ROB. Applicability was assessed from the first three domains in a similar way to the ROB assessment. Discordance was resolved by discussion and consulting a third author.

2.6. Statistical analysis

A descriptive analysis was conducted on the basic characteristics of the included studies and their respective prediction models. In addition to the main analysis, we conducted an exploratory meta-analysis of individual predictor effects based on adjusted odds ratios from multivariable logistic regression models across studies. Given the substantial heterogeneity in model structures and predictor definitions, results are provided in the Supplementary Materials (Supplement 2 and Supplement 3) and should be interpreted with caution.

3. Results

3.1. Study selection

A total of 3738 studies were retrieved. After 1907 duplicate studies were removed, 1831 studies were screened by reading titles and abstracts. Subsequently, 36 full-text articles were thoroughly reviewed, and 21 studies were ultimately included in this study. Fig. 1 shows the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flowchart of literature search and selection.

3.2. Characteristics of included studies

Twenty-one studies were published between 2015 and 2024, including 13 (61.9 %) in English and 8 (38.1 %) in Chinese (Table 1). Sixteen studies (76.2 %) were conducted in China, while the remaining five studies (23.8 %) were conducted in Pakistan, Australia, Serbia, Turkey, and Russia. Fifteen studies (71.4 %) were retrospective, five (23.8 %) were prospective, and one (4.8 %) was a cross-sectional study. Three studies (14.3 %) were multicenter, while the others (85.7 %) were single-center studies. Regarding the study population, 15 studies (71.4 %) focused on STEMI patients, four (19.0 %) on AMI patients, and two (9.5 %) on ACS patients. The sample sizes ranged from 46 to 440,256, and the reported incidence of NRP ranged from 3.58 % to 33.3 %.

3.3. Basic features of prediction model

Table 2 summarizes the basic characteristics of the prediction

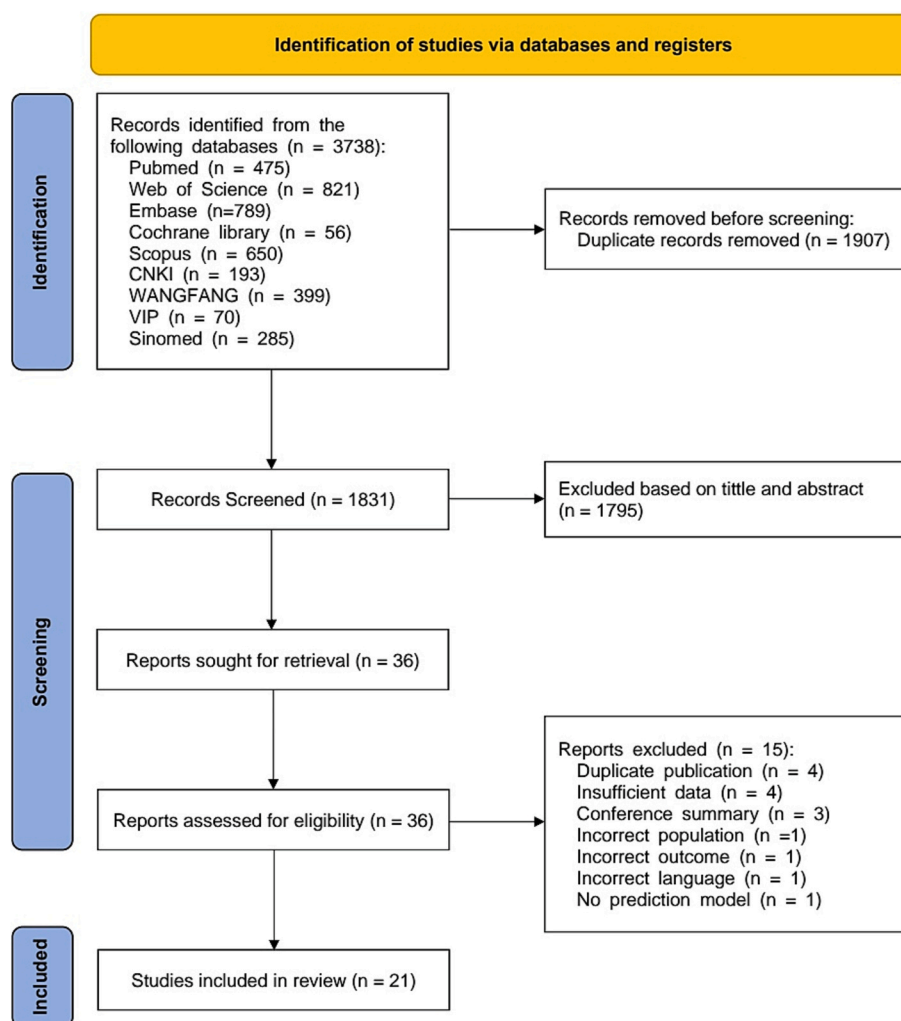


Fig. 1. PRISMA flowchart of literature search and selection.

models. A total of 25 prediction models were developed across the 21 included studies. Of these, 9 (36.0 %) were presented as risk scores, 7 (28.0 %) as nomograms, 5 (20.0 %) as machine learning models, and 4 (16.0 %) as formulas. Most models were developed using logistic regression. Among the five (20.0 %) machine learning-based models, the applied algorithms included artificial neural networks (ANNs), random forest (RF), support vector machine (SVM), and decision tree (CTREE).

Internal validation was performed in 8 studies (38.1 %), external validation in 1 study (4.8 %), and temporal validation in 3 studies (14.3 %), while 9 studies (42.9 %) did not conduct any form of validation. The reported AUC values for model development ranged from 0.637 to 0.958, with most models achieving an AUC > 0.7. Four validation studies reported AUCs ranging from 0.74 to 0.891.

Calibration assessment was reported in 13 studies (61.9 %), utilizing methods such as the Hosmer-Lemeshow goodness-of-fit test and calibration curves. Additionally, 10 studies (47.6 %) reported other performance metrics including sensitivity, specificity, positive predictive value, and negative predictive value, which contribute to a more comprehensive understanding of overall model performance. Three studies (14.3 %) evaluated the clinical utility of the prediction models using Decision Curve Analysis (DCA).

3.4. ROB and applicability assessment

All studies were evaluated to have a high ROB (Supplement 4), indicating methodological issues in development or validation of the

models.

Sixteen studies (76.2 %) were assessed as having a high risk of bias (ROB) in the participant domain, primarily due to the use of inappropriate or non-representative data sources. In the predictor domain, all studies were deemed to have a low ROB. In the outcome domain, five studies (23.8 %) were rated as having a high ROB because they included the TIMI blood flow grade as a predictor variable. Since TIMI flow grade is part of the outcome definition, this may lead to an overestimation of the association between TIMI flow and the NRP [32].

All studies were assessed as having a high risk of bias in the analysis domain. The most common concern was insufficient sample size. Among the model development studies, only one study (5.9 %) reported an events per variable (EPV) greater than 20, five studies (29.4 %) had EPV between 10 and 20, and the remaining 11 studies (64.7 %) had EPVs below 10. For model validation studies, only one study (25 %) included at least 100 outcome events.

In four studies (19.0 %), continuous variables were dichotomized or categorized, a practice that may reduce the predictive performance of models [33]. With regard to missing data, eight studies (38.1 %) applied complete case analysis, one study (4.8 %) excluded all cases with missing values, and nine studies (42.9 %) did not report how missing data were handled. Notably, Kumar et al. [13]. and Deng et al. [22]. excluded cases with more than 5 % missing data and used mean imputation, while Dowson et al. [15]. excluded cases missing post-PCI TIMI flow grade and applied multiple imputation. Fifteen studies (71.4 %) selected predictors based on univariate analysis, and two studies (9.5 %)

Table 1
Characteristics of the included studies.

Author (year)	Country/region	Study aim	Study design	Participants	Data source (study period)	Sample size	Number of outcome events	Number of candidate variables	EPV	Incidence of NRP (%)
Wang 2015 [11]	China	D	Prospective	STEMI	3 institutions	D:1776	367	32	11.47	20.66
Dai 2021 [12]	China	D	Prospective	STEMI	Registration database for 1 hospital (2009.01–2018.12)	D:2036	362	29	12.48	17.78
Kumar 2022 [13]	Pakistan	D	Cross-sectional study	STEMI	1 cardiac care center (2020.12–2021.06)	D:1711	493	29	17	28.81
Zhang 2021 [14]	China	D	Retrospective	AMI	Tangshan Gongren hospital (2019.01–2020.03)	D:327	55	21	2.62	16.82
Dawson 2024 [15]	Australia	D	Prospective	ACS	D: Multicenter Melbourne interventional group (MIG) PCI registry; (2005–2020) EV: British cardiovascular intervention society (BCIS) PCI registry (2006–2020)	D:30561 EV:440256	D:1249 EV: 41222	33	D:37.85	D:4.09 EV:9.36
STAJIC 2022 [16]	Serbia	D	Retrospective	STEMI	Clinical Hospital Center Zemun, (2012.01–2017.12)	D:1254	197	27	7.30	15.71
Yang 2020 [17]	China	D	Retrospective	STEMI	Tianjin chest Hospital (2010.01–2016.05)	1658	491	30	16.37	29.61
Dogan 2015 [18]	Turkey	D	Retrospective	STEMI	Dokuz Eylül University medical faculty (2009.01–2011.08)	173	45	47	0.96	26.01
Frolov 2021 [19]	Russian	D	Retrospective	AMI	City clinical hospital no.13 Nizhny Novgorod, Russia (2011–2020)	5621	201	17	11.82	3.58
Lou 2024 [20]	China	D	Retrospective	AMI	Xi'an Jiaotong university first affiliated hospital (2016.01–2021.12)	3041	325	–	–	10.69
Xiao 2019 [21]	China	D, EV	Prospective	STEMI	Second hospital of Hebei medical university, (2014.01–2016.12)	D:446 EV:99	D:127 EV:25	38	D:3.34	D:28.48 EV:25.25
Deng 2022 [22]	China	D	Retrospective	STEMI	Four National Chest Pain Center Alliance units In Nanning, Guangxi, China (2015.08–2019.12)	854	99	36	2.75	11.59
Liu 2022 [23]	China	D	Retrospective	STEMI	No. 904 Hospital of the Joint Logistics Support Unit of the Chinese People's Liberation Army (2018.02–2021.02)	443	80	45	1.78	18.06
Zhao 2021 [24]	China	D	Retrospective	STEMI	Qinghai Red Cross Hospital (2017.01–2020.06)	156	52	17	3.06	33.3
Wang 2024 [25]	China	D	Retrospective	STEMI	Nanyang City Center Hospital (2022.01–2024.01)	449	145	23	6.30	32.29
Li 2023 [26]	China	D	Retrospective	STEMI	Liuzhou People's Hospital (2015.01–2018.10)	585	64	28	2.29	10.94
Wang 2022 [27]	China	D	Prospective	ACS	Henan Chest Hospital (2018.04–2020.06)	165	37	11	3.36	22.42
Peng 2016 [28]	China	D, EV	Retrospective	STEMI	D: Baikouen international peace hospital (2009.01–2012.12) EV: Baikouen International Peace Hospital (2013.01–2013.12)	D:540 EV:94	D:170 EV:29	30	D:5.67	D:31.48 EV:30.85
Xie 2023 [29]	China	D	Retrospective	AMI	Wuhu First People's Hospital (2019.01–2022.12)	90	27	39	0.69	30
Shi 2023 [30]	China	D, EV	Retrospective	STEMI	D: Tianjin third center hospital (2018.01–2022.09) EV: Tianjin third center hospital (2022.10–2022.12)	D:237 EV:46	D:28 EV:6	29	D:0.97	D:11.81 EV:13.04
Dong 2022 [31]	China	D	Retrospective	STEMI	China-Japan Friendship Hospital (2018.01–2019.06)	280	86	14	6.14	30.7

ACS: acute coronary syndrome; AMI: acute myocardial infarction; D: Derivation; EPV: events per variable; EV: external validate; NRP: no-reflow phenomenon; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

did not report their predictor selection strategy. None of the studies mentioned the complexity of the data. One study (4.8 %) failed to report discrimination measures. Eight studies (38.1 %) did not report calibration performance, and two studies (9.5 %) reported calibration using only the Hosmer–Lemeshow test. Among the model development studies, nine studies (52.9 %) did not report whether internal validation was conducted, while seven studies (41.2 %) used a random split-sample approach.

In applicability assessment, all studies were assessed as low ROB in three domains of participants, predictors, and outcomes.

3.5. Predictors

The final prediction models included 3 to 9 predictors (Supplement 5), which could be classified into four categories: patient characteristics, clinical status, coronary features, and laboratory tests. The most common predictors were Killip classification, total ischemic time, pre-PCI TIMI thrombus grade, symptom-to-balloon time, and age.

4. Discussion

This systematic review analyzed and synthesized the literature on prediction models for NRP in ACS patients after PCI. A total of 25 prediction models from 21 studies were evaluated. High-quality prediction models are crucial for stratifying no-reflow risk in ACS patients after PCI, facilitating targeted clinical decision-making and efficient allocation of medical resources. Seventeen models (68.0 %) reported an AUC above 0.7, indicating good discriminative ability. Four studies (19.0 %) conducted external validation, supporting the generalizability and potential application of models. However, three of these studies (75.0 %) had insufficient sample sizes, potentially biasing the performance evaluation. Most models were developed by logistic regression. Frolov et al. [19] and Deng et al. [22] used machine learning methods to construct their predictive models. Compared to traditional logistic regression, machine learning methods are better suited for analyzing large datasets, as they can incorporate more predictive factors, regardless of their statistical significance [34]. Nevertheless, there is ongoing debate about whether machine learning offers superior accuracy over traditional logistic regression [35]. According to the PROBAST checklist, all studies exhibited high ROB, highlighting the need for more rigorous research to develop reliable predictive models.

This study found several methodological issues in the development and/or validation of prediction models. Firstly, most studies used retrospective data, which may entail a higher ROB. Thus, it is recommended that future studies use high-quality prospective data sources. Secondly, inadequate sample size is a common problem. Generally, an EPV of less than 10 in model development studies may lead to overfitting or underfitting [9], whereas an EPV of 20 or more can reduce potential ROB [32]. For model validation studies, at least 100 outcome events are generally recommended to ensure stable estimation of performance measures and to minimize the risk of bias [36]. When developing prediction models using machine learning, larger sample sizes may be needed to ensure stable and generalizable performance [37]. However, some algorithms with embedded feature selection, such as penalized logistic regression, can handle moderate EPVs more robustly [38]. Therefore, EPV considerations should be interpreted in the context of model complexity and regularization strategies. Thirdly, univariate analysis fails to identify interactions between multiple variables, potentially overlooking significant predictors [32]. Variable selection should integrate relevant guidelines, literature, and clinical expertise. Fourthly, the direct exclusion of missing data can lead to bias in model performance and the relationship between predictors and outcomes [32]. Appropriate methods, such as multiple imputation, should be used

to handle missing data, and complete-case analysis should be avoided. Additionally, model development and validation studies should comprehensively report model performance metrics, including discrimination, calibration, and clinical utility and so on. Finally, there is a prevalent focus on model development rather than validation and updating. Future research should prioritize both internal and external validation of high-performing models to facilitate their early implementation in clinical practice.

Several predictors were frequently included across the final models, suggesting their potential relevance to the development of the NRP in ACS patients after PCI. These included age, Killip classification, symptom-to-balloon time, total ischemic time, pre-PCI TIMI thrombus grade, admission blood glucose, diabetes, D-dimer, leukocyte counts, and LAD as the culprit artery. The frequent inclusion of these predictors across models is consistent with their known pathophysiological relevance. For instance, advanced age is associated with endothelial dysfunction and arteriosclerosis [39]. High levels of D-dimer and leukocyte counts reflect a hypercoagulable state and inflammatory response [40,41], all contributing to increased NRP risk. Hyperglycemia can trigger metabolic disturbances and endothelial dysfunction, while promoting oxidative stress, inflammatory responses, and a pro-thrombotic state [42]. Studies have demonstrated a positive correlation between the duration of diabetes, preoperative blood glucose levels, and the incidence of the NRP [43]. Notably, 20 % to 50 % of myocardial infarction patients experience stress-induced hyperglycemia upon admission, with a higher likelihood of developing the NRP compared to those with normoglycemia [44]. Killip classification $\geq$ II indicates severe cardiac dysfunction, which may be associated with reduced coronary blood flow and increased microcirculatory resistance, thereby increasing the incidence of NRP [45]. Symptom-to-balloon time and total ischemic time indicate delayed medical intervention. Extended myocardial ischemia can cause distal capillary bed edema, myocardial cell swelling, and inflammatory cell occlusion of the lumen [46,47], thereby disrupting microcirculation and increasing the likelihood of NRP [48]. Patients with a high pre-PCI TIMI thrombus grade are more likely to experience NRP, possibly due to the fragmentation of large amounts of organized thrombus during PCI, leading to distal embolization. Thrombus fragments can also cause an inflammatory response and the aggregation of inflammatory cells, reducing coronary blood flow [49]. When LAD is culprit artery, the probability of NRP increases, possibly due to the larger area of myocardial damage caused by LAD occlusion [50]. Most of these predictors are objective and readily obtainable in clinical settings, which may support their utility in future prediction models.

4.1. Limitations

This study has several potential limitations. First, only literature published in English or Chinese was included, which may have resulted in the omission of relevant studies in other languages. Second, most of the prediction models were developed or validated in China, potentially limiting the generalizability of the findings to other countries or regions. Third, due to the lack of multiple external validations for the same models, a quantitative synthesis of model performance metrics could not be performed. Finally, the exploratory meta-analysis of individual predictors was limited by substantial heterogeneity, which reduces the reliability of pooled estimates.

5. Conclusions

This study included 21 papers encompassing 25 prediction models. While most models demonstrated good discriminative ability, methodological and transparency issues led to all studies being assessed as high

Table 2
Characteristics of prediction model.

Author (year)	Continuous Variables	Missing Value Handling	Predictor selection	Model development Method	Validation method	AUC	Calibration	Other performance metrics	Model presentation
Wang 2015 [11]	Converted to categorical variables	–	Stepwise selection	LR	IV (random split)	0.800 (0.772,0.826)	–	SEN: 76.14 %, SPEC: 70.78, PPV: 43.8 %, NPV: 90.8 %	Risk score
Dai 2021 [12]	Remain unaltered	–	Univariate, LASSO→stepwise	LR	IV (random split)	D: 0.854 (0.831,0.877) EV: 0.817 (0.776,0.860)	D: H-L, brier score, calibration curves EV: Calibration curves	D: SEN: 77.6 % SPEC: 80.3 %	Risk score
Kumar 2022 [13]	Converted to categorical variables	Missing <5 %: Mean imputation; missing >5 %: Direct exclusion	Univariate → stepwise	LR	IV (random split)	0.775 (0.722,0.829)	H-L	SEN: 77.9 %, SPEC: 62.6 %, NPV: 87.3 %, PPV: 46.3 %	Risk score
Zhang 2021 [14]	Remain unaltered	Full case study	Univariate →MLR	LR	–	0.860	H-L, calibration curves	–	Nomogram
Dawson 2024 [15]	Converted to categorical variables	Exclude cases with missing TIMI flow post-PCI; multiple imputation	LASSO	LR	EV	D: 0.808 (0.804,0.812) EV: 0.741 (0.739,0.744)	D and EV: Brier score, calibration-in-the-large, slope	–	Risk score
STAJIC 2022 [16]	Remain unaltered	–	Univariate → stepwise	LR	IV (random split)	0.718 (0.654,0.783)	–	SEN: 60.00 %, SPEC: 69.05 %, PPV: 26.53 %, NPV: 90.26 %	Risk score
Yang 2020 [17]	Remain unaltered	–	Univariate → stepwise	LR	IV (random split)	0.637 (0.582, 0.692)	–	SPEC: 53.2 %, SEN: 66.7 %, PPV: 41.2 %, NPV: 76.4 %	Risk score
Dogan 2015 [18]	Remain unaltered	–	Univariate →MLR	LR	–	0.734 (0.654, 0.814)	–	–	Risk score
Frolov 2021 [19]	Remain unaltered	Direct exclusion	–	ANNs, LR	–	ANNs: 0.64 (0.61, 0.67) LR: 0.64 (0.61, 0.67)	–	ANNs: SEN: 39.4 %, SPEC: 90.6 %, PPV: 14.6 %, NPV: 97.4 %, F1-score: 21.3 % LR: SEN: 30.3 %, SPEC: 90.9 %, PPV: 11.9 %, NPV: 97 %, F1-score: 17.1 %	ANNs ; Formula
Lou 2024 [20]	Converted to categorical variables	–	Univariate →MLR	LR	IV (random split)	0.663 (0.604, 0.722)	Calibration curves	DCA	Nomogram
Xiao 2019 [21]	Remain unaltered	–	Univariate → stepwise	LR	Temporal validation	D: 0.925 (0.900, 0.949) EV: 0.939 (0.894, 0.984) RF: 0.7891 (0.7093,0.8688) SVM: 0.7488 (0.6613, 0.8363) ANNs: 0.681 (0.5767, 0.7854) CTREE: 0.6437 (0.5506, 0.7368)	D: Calibration curves EV: -	SEN: 81.1 % SPEC: 96 %	Nomogram
Deng 2022 [22]	Remain unaltered	Missing <5 %: Mean imputation; missing >5 %: Direct exclusion	–	RF, ANNs, SVM, CTREE	–	–	–	–	RF, SVM, ANNs, CTREE
Liu 2022 [23]	Remain unaltered	Full case study	Univariate →MLR	LR	IV (bootstrap)	0.706	Calibration curves	DCA	Nomogram
Zhao 2021 [24]	Remain unaltered	–	Univariate →MLR	LR	–	0.875	–	–	Risk score
Wang 2024 [25]	Remain unaltered	–	Univariate →MLR	LR	–	–	Calibration curves	DCA	Nomogram

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Table 2 (continued)

Author (year)	Continuous Variables	Missing Value Handling	Predictor selection	Model development Method	Validation method	AUC	Calibration	Other performance metrics	Model presentation
Li 2023 [26]	Remain unaltered	Full case study	Univariate →MLR	LR	–	0.687 (0.619, 0.754)	H-L	SEN: 82.8 %, SPEC: 50.7 %	Formula
Wang 2022 [27]	Remain unaltered	Full case study	Univariate →MLR	LR	–	0.899 (0.848, 0.951)	Calibration curves, H-L	–	Formula
Peng 2016 [28]	Some converted to categorical variables	Full case study	Univariate →MLR	LR	Temporal validation	D: 0.716 (0.671, 0.716) EV: 0.891 (0.822, 0.959)	D and EV: H-L	–	Risk score
Xie 2023 [29]	Some converted to categorical variables	Full case study	Lasso→MLR	LR	–	0.958	Calibration curves	SEN: 93.70 %, SPEC: 96.30 %	Nomogram
Shi 2023 [30]	Remain unaltered	Full case study	Univariate →MLR	LR	Temporal validation	D: 0.76 (0.61, 0.90) EV: 0.74 (0.57, 0.90)	–	D: SEN: 70.6 %, SPEC: 76.7 % EV: SEN: 100.0 %, SPEC: 52.5 %	Formula
Dong 2022 [31]	Some converted to categorical variables	Full case study	Univariate →MLR	LR	IV (bootstrap)	0.731 (0.668, 0.795)	Calibration curves, H-L	–	Nomogram

ANNs: artificial neural networks; AUC: area under the curve; D, derivation; DCA: decision curve analysis; EV: external validated; H-L: Hosmer–Lemeshow goodness of fit test; IV: internal validation; LR: logistic regression; MLR: multivariate logistic regression; NPV: negative predictive value; PPV: positive predictive value; SEN: sensitivity; SPEC: specificity; RF: random forest; SVM: support vector machine; CTREE: decision tree.

ROB. It suggests that the performance of these models might be over-estimated, casting doubt on their actual accuracy when applied to ACS patients. Furthermore, the lack of external validation for most models makes it difficult to ascertain their generalizability and stability. Therefore, no suitable prediction models have been recommended for clinical decision making. Future research should adhere to the PROBAST checklist to enhance the quality and transparency of studies. Moreover, concerns need to be placed on evaluating clinical utility of prediction models and multicenter, large-sample external validations should be conducted.

CRediT authorship contribution statement

Fang Li: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jin-jiang Zhang:** Writing – review & editing, Validation, Methodology, Conceptualization. **Gui-ji Ruan:** Writing – review & editing, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Yue-yun Zhan:** Writing – review & editing, Visualization, Investigation. **Ai-hua Qiu:** Writing – review & editing, Visualization, Investigation. **Meng-si Ye:** Writing – review & editing, Visualization, Investigation. **Qian-wen Xiang:** Writing – review & editing, Visualization, Investigation. **Hong-cheng Fang:** Writing – review & editing, Resources, Project administration, Methodology, Data curation, Conceptualization.

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Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2025.133603>.

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