Systematic Review of Risk Prediction Models for Heart Failure in Patients with Coronary Heart Disease (Postprint)

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Abstract

Background: Heart failure (HF) is a major chronic disease that poses a serious threat to global health, and coronary heart disease (CHD) represents the most common etiology of heart failure. The development of risk prediction models targeting risk factors for HF secondary to CHD can facilitate early identification and intervention among high-risk populations by healthcare professionals. Objective: To systematically evaluate risk prediction models for heart failure among Chinese patients with coronary heart disease, thereby providing a reference for the development, selection, and dissemination of related risk prediction models. Methods: A systematic search was conducted across CNKI, VIP, Wanfang Data, SinoMed, PubMed, Cochrane Library, Web of Science, and Embase for studies developing risk prediction models for heart failure in Chinese patients with coronary heart disease from database inception to October 2024. Two investigators independently screened the literature and extracted data. The Prediction model Risk Of Bias ASsessment Tool (PROBAST) was employed to assess the risk of bias and applicability of the included studies. Results: Twenty-seven articles were included, which reported the development of 64 risk prediction models. The area under the receiver operating characteristic curve (AUC) ranged from 0.511 to 0.989, with 63 models demonstrating an AUC>0.7, suggesting favorable overall predictive performance. PROBAST assessment revealed that all 27 included studies were at high risk of bias with low applicability. Age, left ventricular ejection fraction, diabetes history, hypertension history, NT-proBNP (N-terminal pro-B-type natriuretic peptide), and Gensini score were identified as important predictive factors incorporated in the models. Conclusion: The stability and generalizability of current risk prediction models for heart failure in Chinese patients with coronary heart disease require further validation through prospective, large-scale studies. Future model development should strictly adhere to PROBAST guidelines in study design and

implementation to develop high-quality prediction models with strong generalizability.

Full Text

Systematic Review of Risk Prediction Models for Heart Failure in Patients with Coronary Heart Disease

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Abstract

Background
Heart failure (HF) is a major chronic disease that poses a serious threat to global health, with coronary heart disease (CHD) being its most common cause. Developing risk prediction models for HF in CHD patients based on relevant risk factors can help healthcare professionals identify high-risk populations early and implement timely interventions.

Objective
To systematically evaluate risk prediction models for HF in Chinese CHD patients, providing a reference for the development, selection, and dissemination of relevant predictive models.

Methods
We searched CNKI, VIP, Wanfang Data, SinoMed, PubMed, Cochrane Library, Web of Science, and Embase for studies on risk prediction models for HF in CHD patients, with a search timeframe from database inception to October 2024. Two reviewers independently screened literature and extracted data, using the Prediction Model Risk of Bias Assessment Tool (PROBAST) to evaluate the risk of bias and applicability of included studies.

Results
A total of 27 studies were included, reporting the development of 64 risk prediction models. The area under the receiver operating characteristic curve (AUC) ranged from 0.511 to 0.989, with 63 models achieving an AUC > 0.7, indicating good overall predictive performance. However, PROBAST assessment revealed that all 27 studies had a high risk of bias and low applicability. Key predictive factors included age, left ventricular ejection fraction, diabetes history, hypertension history, NT-proBNP (N-terminal pro-B-type natriuretic peptide), and Gensini score.

Conclusion
Current risk prediction models for HF in Chinese CHD patients require further validation through prospective, large-sample studies to establish stability and generalizability. Future model development should strictly adhere to PROBAST guidelines to ensure the design and implementation of high-quality, generalizable predictive models.

Keywords: coronary heart disease; heart failure; risk prediction model; systematic review

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Introduction

Heart failure is the end-stage manifestation of multiple cardiovascular disease risk factors and has become a major global public health problem due to its high prevalence, mortality, rehospitalization rate, and heavy economic burden. The China Cardiovascular Health and Disease Report 2023 indicates that the total number of HF patients in China is expected to reach 8.9 million, with a one-year mortality rate as high as 13.7%. Coronary heart disease is the leading cause of HF, accounting for 54.6% of HF cases. Percutaneous coronary intervention (PCI) is the primary treatment for CHD, yet some patients still develop HF despite receiving PCI. A study of 1,232 CHD patients undergoing PCI showed that approximately 6.3% developed HF after the procedure. Therefore, early identification and intervention of risk factors for HF in CHD patients is of significant clinical importance for improving patient prognosis and reducing HF risk.

Clinical prediction models have become an important auxiliary tool that integrates multidimensional variables such as clinical data and test results to predict the probability of specific outcome events. However, due to substantial differences in healthcare levels and racial characteristics between countries, risk prediction models developed in European and American populations cannot be directly applied to Chinese populations. Consequently, developing risk prediction tools suitable for Chinese CHD patients and evaluating the applicability of existing models in Chinese populations has become an important research direction. This study aims to systematically evaluate the quality and clinical applicability of risk prediction models for HF in Chinese CHD patients, providing a basis for personalized management of CHD patients by clinical healthcare professionals.

Methods

1.1 Literature Search

We searched eight databases including CNKI, Wanfang Data, VIP, SinoMed, PubMed, Cochrane Library, Web of Science, and Embase for studies on risk prediction models for HF in CHD patients, with a search timeframe from database

inception to October 2024. We used a combination of subject headings and free-text terms. Chinese search terms included: "heart failure," "coronary heart disease," "myocardial infarction," "acute coronary syndrome," "risk prediction," "prediction model," and "predictive factors." English search terms included: "Coronary Heart Disease," "Myocardial Infarction," "Acute coronary syndrome," "Heart Failure," "cardiac failure," "Prediction Model," and "Risk Prediction." The search strategies for CNKI and PubMed are shown in Table 1 .

1.2 Inclusion and Exclusion Criteria

1.2.1 Inclusion Criteria: (1) Study population: Chinese patients with acute myocardial infarction (AMI) or CHD confirmed by coronary angiography or coronary CT angiography (CCTA); (2) Study objective: to develop or validate a risk prediction model for HF in CHD patients; (3) Outcome: confirmed HF diagnosis; (4) Model containing at least two variables; (5) Study design: cohort study, case-control study, or cross-sectional study.

1.2.2 Exclusion Criteria: (1) Studies with incomplete data or unavailable full text; (2) Conference abstracts, animal experiments, reviews, or methodological literature; (3) Studies analyzing only risk factors without constructing a prediction model; (4) Studies with sample size < 100.

1.3 Literature Screening and Data Extraction

We used EndNote X9 to remove duplicates from retrieved literature. Two reviewers independently screened titles and abstracts, then reviewed full texts for final selection. Disagreements were resolved through discussion with a third reviewer. Data were extracted using the Critical Appraisal and Data Extraction for Systematic Reviews of Prediction Modelling Studies (CHARMS) checklist and entered into Excel spreadsheets.

1.4 Risk of Bias and Applicability Assessment

Two reviewers independently assessed the risk of bias and applicability of included studies using the PROBAST tool, which evaluates 20 items across four domains (participants, predictors, outcome, statistical analysis) for risk of bias, and three domains (participants, predictors, outcome) for applicability. Each domain could be rated as "high risk," "low risk," or "unclear."

Results

2.1 Literature Search

We retrieved 5,180 relevant articles and supplemented 75 articles through other sources. After removing duplicates, 4,554 articles remained. After title and abstract screening, 4,448 articles were excluded, and after full-text review, 79

articles were excluded, resulting in the final inclusion of 27 studies [12-38]. The literature screening process is detailed in Figure 1 [Figure 1: see original paper].

2.2 Characteristics of Included Studies

The 27 included studies were published between 2019 and 2024, comprising 22 Chinese and 5 English articles. Three studies [17,21-22] were prospective, 19 [12-14,16,18,20-31,33,35-38] were retrospective, and 5 [15-16,19,32,34] were case-control studies. Data sources included clinical records and electronic medical record databases, with maximum follow-up of 7.3 years and outcome event rates ranging from 3.54% to 48.94%. Basic characteristics are shown in Table 2 .

Nineteen studies [13-14,17-20,22-26,28,30-31,33-36,38] were approved by institutional ethics committees, while eight [12,15-16,21,27,29,32,37] did not report ethics approval. Nine studies [13-14,16,20-22,25,28,37] converted continuous variables to categorical variables, six [12,23,30,32-33,36] partially converted continuous variables, and 12 [15,17-19,24,26-27,29,31,34-35,38] maintained continuous variables as continuous. Conversion criteria included clinical significance [12,16,21,33], optimal cut-off points from ROC curves [13,20,22,25,28], and distribution characteristics of the study population [32,37]. Three studies [15,26,33] reported specific missing sample sizes and deleted subjects with missing data, two [18,31] imputed missing data, and two [23-24] used combined multiple imputation and deletion methods without reporting specific missing sample sizes. Candidate variables ranged from 14 to 72, with total sample sizes from 120 to 44,772 cases, as shown in Table 3 .

The 27 studies reported 64 prediction models. Eighteen [13,16-20,22,25-26,28-30,32-35,37-38] used logistic regression (LR), while three [12,14,21] used Cox proportional hazards regression. Candidate variable selection methods included: univariate analysis [20,24,27,30,32,36]; univariate followed by multivariate analysis [12,14-15,17,19,21-23,25,28,33,37-38]; least absolute shrinkage and selection operator (LASSO) analysis [16,29]; LASSO followed by multivariate analysis [13,26,29,34-35]; and univariate followed by LASSO analysis [18]. All models reported discrimination, with 13 [18,22-24,27,29,31-38] using AUC, six [14,16-17,20-21,28] using C-index, and eight [12-13,15,18-19,25-26,30] using both. AUC ranged from 0.511 to 0.989, and C-index from 0.720 to 0.953. Twenty-two studies [12-21,23-30,33,35-36,38] reported calibration methods, including Hosmer-Lemeshow (H-L) goodness-of-fit test and calibration curves, as shown in Table 4 .

Twenty-one studies [12-19,22-27,29-31,33-36] reported model validation, with 13 [15-16,19,22-23,25-27,29-30,34-36] conducting internal validation only (using bootstrap, cross-validation, or random split methods), three [12,17,33] conducting external validation only (temporal, spatial, or combined temporal-spatial validation), and five [13-14,18,24,31] conducting both internal and external validation, as shown in Table 5 . The included models comprised 4-13 predictors, as shown in Figure 2 [Figure 2: see original paper]. Twenty-one studies [12-

23,25-26,28,30,32-35,38] presented models as nomograms, four [24,27,36-37] as regression equations, one [29] used both, and one [31] did not describe the presentation format.

2.6 Risk of Bias and Applicability Assessment

2.6.1 Risk of Bias Assessment: According to PROBAST criteria, all 27 studies were rated as high risk of bias. (1) Participants domain: Five studies [15-16,19,32,34] were high risk due to case-control design, and one [29] was unclear due to unspecified inclusion/exclusion criteria. (2) Predictors domain: Five studies [15-16,19,32,34] were high risk because predictors were assessed with knowledge of the outcome; 16 [12-14,20,23-28,30,33,35-38] were unclear; and 19 [12-14,16,18,20-31,33,35-38] did not report whether predictors were assessed with outcome knowledge. (3) Outcome domain: 17 studies [13,15,17,19-20,22-23,25-30,32-33,37-38] were high risk: 11 [15,17,19-20,22-23,25-26,29-30,32,37-38] had outcome definitions that included predictors; nine [13,15,19-20,23-24,27-28,33] had too short intervals between predictor assessment and outcome determination; six [12,16,18,21,31,34] were unclear, with five [12,15,20-21,31] not reporting diagnostic criteria for outcomes and six [16,18,29,31-32,34] not reporting time intervals between predictor assessment and outcome. (4) Statistical analysis domain: 22 studies [12,14-15,17,20-28,30-38] were high risk: 14 [14-15,20-22,26-28,30,32,35-38] had events per variable (EPV) < 20; five [14,23,30,33,36] had unclear rationale for converting continuous variables to categorical; three [15,26,33] used deletion for missing data; seven [20,25-26,28,30,32,36] used univariate analysis for variable selection; nine [15,22,24,28,31-32,34,36-37] did not report calibration methods or used only H-L test; 12 [12,17,20-21,23,27-28,31-33,37-38] did not conduct internal validation or used random split methods. Five studies [13,16,18-19,29] had unclear risk: 20 [12-14,16-17,19-22,25,27-30,32,34-38] did not report missing data or handling methods; no studies reported data complexity. See Figure 3 [Figure 3: see original paper].

2.6.2 Applicability Assessment: Seven studies [14,17,22,30,35-36,38] had good applicability, 13 [13,15,19-20,23-28,31,33,37] had low applicability, and seven [12,16,18,21,29,32,34] had unclear applicability risk. (1) Participants: Five studies [25-26,31,33,37] had high applicability risk, including one [26] limited to young/middle-aged patients, two [31,37] limited to elderly patients, one [25] limited to female patients, and one [33] limited to elderly patients (65-95 years) after hip fracture surgery. (2) Predictors: All studies had low applicability risk in the predictors domain. (3) Outcome: Nine studies [13,15,19-20,23-24,27-28,33] had high applicability risk due to overly short intervals between predictor assessment and outcome determination. Eight studies [12,16,18,21,29,31-32,34] had unclear applicability risk, with five [12,15,20-21,31] not using standard outcome definitions and six [16,18,29,31-32,34] not reporting time intervals between predictor assessment and outcome.

Discussion

3.1 Overall Good Predictive Performance with Logistic Regression as the Main Modeling Method

This study included 64 risk prediction models, with the earliest developed in 2019 and an increasing number of relevant studies in the past five years. One model had an AUC of 0.511; upon reviewing the original literature [15], we found it used all-subsets regression with only three predictors, and the omission of key variables may have resulted in insufficient explanation of data variability and low predictive ability. Excluding this model, the remaining 63 models had AUC/C-index values > 0.7, with 43 undergoing calibration, indicating good performance in predicting post-CHD HF.

Traditional modeling methods primarily use LR and Cox regression. With advances in artificial intelligence, machine learning has been increasingly applied in clinical medicine due to its powerful computational capabilities and high predictive accuracy on large datasets. In this study, six [15,23-24,27,31,36] compared LR with machine learning models. XU Qian [31] found LR outperformed machine learning models, while LI et al. [24] found that SVC (linear support vector classification), Ada Boost (adaptive boosting), RF (random forest), and DT (decision tree) performed better than LR. These differences may relate to data characteristics, sample size, and variable selection. LR demonstrates greater robustness with small sample sizes and linear relationships, with stronger interpretability suitable for scenarios requiring clinical explainability [39-40]. Machine learning models better capture complex patterns in high-dimensional, nonlinear datasets, making them suitable for complex clinical decision support systems [41]. Shapley Additive Explanations (SHAP) is a game theory-based interpretability method for allocating feature contributions to model predictions [42]. Future machine learning model development could combine SHAP analysis to assess feature contributions in models like XGBoost and RF to improve interpretability.

3.2 High Overall Risk of Bias and Low Applicability

The high risk of bias in included studies primarily stemmed from deficiencies in study design and statistical analysis methods. Heterogeneity across studies in populations, predictor definitions, and follow-up durations increased between-study variability. (1) Participants: Five case-control studies [15-16,19,32,34] were included, though PROBAST recommends randomized controlled trials or prospective cohort studies to improve reliability. Case-control studies cannot directly calculate absolute risk and are unsuitable for risk prediction model development. Additionally, since HF incidence varies across populations, models based on specific groups (e.g., young/middle-aged, female, or elderly post-hip fracture patients) may limit generalizability. (2) Predictors: Retrospective studies relying on existing data may suffer from missing information and selection bias. Prospective designs with standardized predictor definitions are recom-

mended to reduce bias. (3) Outcome: Seven studies [15,19,23-24,27-28,33] set predictor assessment and HF outcome determination intervals during hospitalization; however, HF can occur during hospitalization or after discharge in acute MI patients [43]. The vulnerable period for HF patients is considered the first three months after diagnosis [44]; thus, follow-up should cover the acute phase through at least three months post-discharge. (4) Statistical analysis: Fourteen studies [14-15,20-22,26-28,30,32,35-38] had insufficient sample sizes; PROBAST recommends EPV $\geq$ 20 to prevent overfitting [45]. When discretizing continuous variables, standard definitions or nonlinear fitting should be prioritized to minimize information loss. (5) Missing data: Direct deletion may affect model robustness; future studies should transparently report missing data and preferably use multiple imputation as recommended by PROBAST. Good prediction models require both internal and external validation; currently only five studies [13-14,18,24,31] conducted both, with TAN et al. [18] developing a model based on 44,772 subjects from seven hospitals in Chongqing showing good discrimination (AUC = 0.720) and robust multi-center validation, providing valuable reference for clinical screening.

3.3 Diverse but Common Predictive Factors

The 189 predictors from 27 studies concentrated on several high-frequency factors: age, left ventricular ejection fraction (LVEF), diabetes history, hypertension history, NT-proBNP level, and Gensini score. Age was the most frequent predictor; aging-related cardiomyocyte apoptosis, increased oxidative stress, and chronic low-grade inflammation lead to cardiac dysfunction and vascular microenvironment changes, triggering cardiovascular disease [46-47]. LVEF is a recognized indicator of myocardial contractility; reduced LVEF indicates insufficient cardiac output. Diabetes and hypertension are well-established risk factors for CHD and HF [48], promoting HF development through endothelial damage, oxidative stress, and immune system activation [49-51]. NT-proBNP directly reflects myocardial volume and pressure load changes; the Framingham Heart Study confirmed BNP/NT-proBNP' s value in predicting new-onset HF [52]. The Gensini score quantifies coronary lesion location, number, and stenosis severity to assess cardiac ischemia risk; higher scores indicate more severe coronary disease and increased ischemic risk [53].

International HF risk prediction studies include the Framingham Heart Study [54] and Health ABC Study [55], which developed early HF risk models for elderly populations with existing cardiovascular disease or high risk. The ARIC (Atherosclerosis Risk in Communities) risk score [56] built upon Framingham with a simplified model integrating age, sex, race, and NT-proBNP for primary care risk stratification. The PCP-HF study [57] developed and validated a 10-year HF risk formula based on 33,010 general population subjects from seven cohorts, using age, blood pressure, fasting glucose, BMI, cholesterol, smoking status, and QRS duration as main predictors. Notably, these studies emphasize racial differences in HF risk, highlighting the importance of optimizing models

for different populations. While Western studies provide important references, Chinese-specific models should be developed considering Chinese population characteristics to improve clinical feasibility and prediction accuracy.

3.4 Future Directions

Future development of HF risk prediction models for Chinese CHD populations should employ prospective, multi-center, large-sample cohort studies covering diverse regions and income groups, with strict inclusion/exclusion criteria to reduce population heterogeneity. Predictor selection should prioritize routinely available electronic medical record data, avoiding expensive or difficult-to-obtain indicators. Clinical expert input should be combined to unify predictor and outcome diagnostic standards, balancing data quality and cost-effectiveness. Model development could integrate traditional prediction models with machine learning algorithms, using SHAP analysis for feature contribution and decision tree visualization to optimize feature selection and improve medical interpretability. For clinical translation, models could be designed as scoring tables, online calculators, or integrated into electronic medical systems or mobile applications to enhance usability. Established models should undergo further clinical validation to assess their value, with dynamic updates to support personalized treatment and early intervention decisions.

This study has limitations: (1) Only Chinese and English literature was searched, potentially missing important predictors and limiting generalizability; (2) Included studies had heterogeneous populations and outcome diagnostic standards, and without quantitative analysis, evaluation results are somewhat limited; (3) Most included models were single-center, small-sample studies lacking both internal and external validation, affecting stability and generalizability.

In summary, this study included 27 articles reporting 64 CHD-HF risk prediction models with generally good predictive performance but high risk of bias. Among established models, TAN et al.'s [18] LR-based model and LI et al.'s [24] model combining LR with multiple machine learning algorithms demonstrated stable performance and rigorous validation, offering high quality for clinical reference. Future model development should strictly follow PROBAST guidelines, optimize predictor selection, improve validation procedures, and standardize statistical analysis to enhance model stability and generalizability, providing more reliable risk assessment and intervention decision support for clinical healthcare professionals.

Author Contributions

JIANG Xiaorui: conceptualization, statistical analysis, manuscript writing. JIANG Xiaorui and YAN Yuyao: literature screening, risk of bias and applicability assessment, data extraction and verification. WEI Jingjing and QIAO Lijie: manuscript revision and quality control. PENG Guangcao: manuscript

review.

Conflict of Interest: None declared.

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Tables and Figures

Search strategies of CNKI and PubMed
Basic characteristics of included studies
Construction of risk prediction models for HF complications in Chinese patients with CHD
Construction and performance evaluation of a risk prediction model for HF in Chinese patients with CHD
Validation and presentation of risk prediction models for HF complications in Chinese patients with CHD
[Figure 1: see original paper] Flowchart of literature screening
[Figure 2: see original paper] Network diagram of high frequency predictor
[Figure 3: see original paper] Risk of bias and applicability assessment

Note: Figure translations are in progress. See original paper for figures.