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Application of Machine Learning To Predict The Occurrence of Arrhythmia After Acute Myocardial Infarction

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Abstract

Background: Early identification of the occurrence of arrhythmia in patients with acute myocardial infarction plays an essential role in clinical decision-making. The present study attempted to use machine learning (ML) methods to build predictive models of arrhythmia after acute myocardial infarction (AMI).

Methods: A total of 2084 patients with acute myocardial infarction were enrolled in this study. The primary outcome is whether tachyarrhythmia occurred during admission containing atrial arrhythmia, ventricular arrhythmia, and supraventricular tachycardia. All data is randomly divided into training set (80%) and internal testing set (20%). Three machine learning algorithms (including decision tree, random forest, and artificial neural network) learn from the training set to build a model, use the testing set to evaluate the prediction performance, and compare it with the model built by the variable set involved GRACE risk score.

Results: Three ML models predict the occurrence of tachyarrhythmia after AMI. After variable selection, the artificial neural network (ANN) model achieves the highest accuracy of 0.654 (95% CI, 0.625–0.683). The area under the value of the curve (AUC) is 0.597 (95% CI, 0.568-0.626). The highest accuracy of the model built using the Grace variable set is 0.627 (95% CI, 0.598-0.656), and the AUC value is 0.574 (95% CI, 0.545-0.603).

Conclusions: We used advanced machine learning methods to build prediction models for tachyarrhythmia after AMI for the first time (especially the ANN model has the best performance). The current study can supplement the current AMI risk score, provide a reliable evaluation method for the clinic, and broaden the new horizons of ML and clinical research.

Trial registration: Clinical Trial Registry No.: ChiCTR2100041960.

Introduction:

Admittedly, acute myocardial infarction (AMI) is a clinically critical disease [1],which is often accompanied by various types of arrhythmia, leading to the deterioration of heart function and increased mortality [2–4]. As a result, identifying the risk factors of arrhythmia after AMI and predicting the occurrence of arrhythmia in AMI patients can arouse doctors' alertness and improve the prognosis of patients. In recent years, many studies have been concentrated on the risk factors of arrhythmia after AMI [5–9]. However, they are all limited to a single aspect and lack systematic risk assessment. The Global Registry of Acute Coronary Events (GRACE) risk score [1] is the most commonly used systematic assessment method for AMI patients while it is mainly used to predict mortality, and the accuracy of predicting arrhythmia may not remain high. Therefore, establishing a predictive model of arrhythmia after AMI exerts an essential role in assisting clinicians in decision-making. Traditional risk models are usually based on statistical methods, which can only linearly analyze several factors' relationship. Researchers will select variables in

advance to artificially cause the loss of potential risk factors. In terms of complex diseases such as acute myocardial infarction, it has higher requirements for dealing with multi-factor and multi-level interactions.

As the most critical subset of artificial intelligence, machine learning (ML) has gradually become an important research method in medicine [10–12]. Through simulating human learning activities, ML automatically obtains information from big clinical data for learning [13, 14],effectively avoiding the limitations of human factors and variables in traditional analysis. ML has been successfully applied in various cardiovascular field aspects, including disease prediction [15–19] and diagnostic classification [20–22]. In recent years, studies on ML and AMI have mainly concentrated on predicting patient mortality [23–26]while no exploration has been made on the prediction model of arrhythmias after AMI. As a result, this study intends to apply machine learning algorithms (including random forest, decision tree, and artificial neural network (ANN)) to establish a model to predict tachyarrhythmia after AMI and compare the performance with the model-based by GRACE risk variable set.

Methods:

Patient Cohort

We retrospectively studied patients with acute myocardial infarction diagnosed in the cardiac care unit of the First Affiliated Hospital of Harbin Medical University from January 2014 to January 2019. The guidelines define acute myocardial infarction as elevated Troponin I (TNI) (≥ 0.03μg/L) or elevated Troponin I (TNT) (≥ 42ng/L), accompanied by one of the following conditions: 1)Symptoms of myocardial ischemia; 2)New ischemic ECG changes:3)Development of pathological Q waves;4)Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology;5)Identification of a coronary thrombus by angiography: 1)Symptoms of myocardial ischemia; 2)New ischemic ECG changes:3)Development of pathological Q waves;4)Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology;5)Identification of a coronary thrombus by angiography.

All patients received three-dimensional echocardiography, coronary angiography, and 24-hour dynamic electrocardiogram within 24 hours of admission. Outcome events were defined as whether or not tachyarrhythmia occurred. Arrhythmic events include: atrial arrhythmia (atrial fibrillation, atrial flutter, and frequent atrial premature), ventricular arrhythmia (ventricular tachycardia, ventricular flutter, ventricular fibrillation, and frequent premature ventricular), supraventricular tachycardia.

variable selection

We selected the risk factors for tachyarrhythmia after AMI identified in the previous study and added some new risk factors as candidate variables, including demographics, baseline characteristics of admission, laboratory characteristics, echocardiographic parameters, and angiography features, a total of 45 variables(Table 1). We graded continuous variables and converted them into ordered categorical variables（see Additional file 1）. First, we feed all the variables into machine learning to build the

prediction model. Considering that too many parameters would lead to overfitting, we selected the top 15 variables using the information gain method to establish the ML model after feature selection further.

Table 1
Variables for machine learning

Category	Variables
Demographics and medical history	Age, sex, smoker, drinker, Pre-hypertension, Pre-diabetes mellitus, Prior MI, Prior CI,Prior HF, Prior CHD
Baseline characteristics of admission	SBP, DBP, HR, Killip, NYHA
Laboratory characteristics	Pro-BNP, CRP, Total cholesterol, Triglyceride, HDL, LDL, Cr, K+, TNI, CK-MB, UGLU, DDP
Findings on ECG	P-R, QTc, BBB (LAFB, LPFB, LBBB, RBBB)
Echocardiographic Parameters	LVEF, FS, E/A, Dt, LVEDD, IVST, LVPWT, LA, RA, PA, Vpa, Vao, ventricular wall motion
Angiographic Characteristics	LAD, LCX, RCA, LM, LAD + LCX, LAD + RCA, RCA + LCX, Triple vessels

MI indicates myocardial infarction; CI, cerebral infarction; HF, heart failure; CHD, coronary heart disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR,heart rate; pro-BNP, pro-B-type natriuretic peptide; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; DDP,D dimer; Cr, creatinine; TNI, Troponin I; CK-MB, creatine Kinase Isoenzyme; UGLU, urine glucose; P-R, PR interval; QTc, QTc interval; BBB, bundle-branch-block; LAFB, left anterior branch block; LPFB, left posterior branch block; LBBB, left bundle branch block; RBBB, right bundle branch block; LVEF, left ventricular ejection fraction; FS, fraction shortening; E/A, mitral valve peak velocity early diastolic filling(E wave) to peak velocity of late diastolic filling(A wave) ratio; Dt, E deceleration time; LVEDD, left ventricular end-diastolic diameter; IVST, interventricular septum thickness; LVPWT, left ventricular posterior wall thickness; LA, left atrium diameter; RA, right atrium diameter; PA, pulmonary artery internal dimension; Vpa, Pulmonary peak flow rate; Vao, Peak aortic velocity; LAD, left anterior descending; LCX, left circumflex artery; RCA, right coronary artery; LM, left main coronary artery.

Supervised ML approach

We applied three supervised machine learning algorithms (Decision Tree, Random Forest, ANN) to predict tachyarrhythmia after AMI. All models were cross-validated ten times. We chose 80% as the training set and 20% as the testing set (Fig. 1). To evaluate the ML model's clinical significance, we input the GRACE risk score variables into three ML algorithms for training to build the GRACE variable set model. All ML prediction model's performance was evaluated using accuracy, specificity, false-negative rate, false-positive rate, and the area under the curve (AUC). The ML techniques were implemented in the open-source Python 3.7 environment.

Statistical analysis

Descriptive analyses and comparisons between clinically defined groups were performed using SPSS 25.0 (IBM, Inc, Chicago, IL, USA). Continuous variables are presented as mean ± SD or median (25th and 75th percentiles) and categorical variables as number and percentage. Baseline characteristics of groups were compared using unpaired t test or Mann-Whitney's U-test for continuous variables and by chi-square test for categorical variables. A probability value of less than 0.05 was considered statistically significant.

Results:

Patient Characteristics

Excluding patients with incomplete data records and prior arrhythmias, the study included 2084 patients with AMI, of whom 1224 had no arrhythmias and 860 had tachyarrhythmia (611 men and 249 women). Table 2 and Table 3 summarizes the differences in demographics, baseline characteristics of admission, laboratory characteristics, echocardiographic parameters, and angiography features between the two groups. Details on all 45 features are available in Additional file 2.

Table 2
Comparison of basic characteristics between the two groups

	arrhythmia		
Characteristics	**No(n = 1224)**	**Yes(n = 860)**	P value
Demographics and history			
Age,years	57.97 ± 11.38	61.68 ± 10.81	<0.001**
Sex(male), n (%)	942(76.96)	611(71.05)	0.002**
Prior MI, n (%)	86(7.03)	81(9.42)	0.048*
Prior CI, n (%)	115(9.40)	109(12.69)	0.017*
Prior CHD, n (%)	47(3.84)	48(5.58)	0.061
At admission			
Heart rate,beats/min	75(66,86)	72 (62,85)	<0.001**
SBP,mmHg	130(117 ~ 150)	127(112 ~ 144)	<0.001**
DBP,mmHg	83.84 ± 15.86	79.59 ± 16.68	<0.001**
Laboratory values			
Pro-BNP(pg/mL)	1003.5(420.0,2207.0)	1202.0(482.0,2641.5)	0.003**
k+(mmol/L)	4.16(3.9,4.4)	4.18(3.9,4.5)	0.698
TNI(ug/L)	19.810(1.1,50.0)	30.785(2.0,54.0)	0.001**
CK-MB(ug/L)	74.0(25.4,161.6)	91.5(33.7,190.6)	0.001**
TG(mmol/L)	1.95 ± 1.15	1.82 ± 1.10	0.014*
Cr(umol/L)	75.88 ± 37.08	79.88 ± 42.88	0.027*
DD-P(mg/L)	0.66 ± 3.01	0.87 ± 3.35	0.129
Findings on ECG			
BBB,n(%)			<0.001**
LAFB,n(%)	214(17.48)	175(20.35)	
LBBB,n(%)	22(1.80)	19(2.21)	
LPFB,n(%)	49(4.00)	35(4.07)	
RBBB,n(%)	25(2.04)	51(5.93)	
LAFB + RBBB,n(%)	13(1.06)	27(3.14)	

	arrhythmia		
P-R(ms)	0.16(0.14,0.17)	0.16(0.15,0.19)	0.006
Q-Tc(ms)	439(418,462)	442(418,469)	0.014*

Table 3
Comparison of basic characteristics between the two groups

	arrhythmia		
Characteristics	**No(n = 1224)**	**Yes(n = 860)**	P value
Findings on ECG			
BBB,n(%)			0.001**
LAFB,n(%)	214(17.48)	175(20.35)	
LBBB,n(%)	22(1.80)	19(2.21)	
LPFB,n(%)	49(4.00)	35(4.07)	
RBBB,n(%)	25(2.04)	51(5.93)	
LAFB + RBBB,n(%)	13(1.06)	27(3.14)	
P-R(ms)	0.16(0.14,0.17)	0.16(0.15,0.19)	0.006
Q-Tc(ms)	439(418,462)	442(418,469)	0.014*
Echocardiographic			
LVEF(%)	52.28 ± 9.04	51.17 ± 9.20	0.006**
RA(up and down),mm	44.0(42.0,46.0)	45.0(42.0,46.0)	0.006**
RA(right and left),mm	34.0(32.0,35.0)	34.0(32.0,36.0)	0.003**
ventricular wall motion abnormal,n(%)			0.001**
≥ 2 walls	270(22.06)	213(24.77)	
Anterior	430(35.13)	217(25.23)	
Apex	19(1.55)	3(0.35)	
Anteroseptal	19(1.55)	2(0.23)	
Posterior	148(12.09)	135(15.70)	
Inferior	297(24.26)	268(31.16)	
Angiographic			
Lesions vessels ,n(%)			0.001**

	arrhythmia	
LAD	262(21.41)	95(11.05)
LCX	46(3.76)	20(2.33)
RCA	78(6.37)	112(13.02)
LM	38(3.10)	35(4.07)
LAD + LCX	158(12.91)	64(7.44)
LAD + RCA	198(16.18)	166(19.30)
RCA + LCX	66(5.39)	60(6.98)
Triple vessels	378(30.88)	308(35.81)

ML Analysis

Variable selection

ML extracted top-15 feature-ranking with the random forest for further modeling. The culprit lesion, heart rate, age, ventricular wall motion abnormal, bundle-branch-block, blood pressure, PR interval, D dimer, right atrium diameter, TNI, Killip classification, pro- Brain Natriuretic Peptide (BNP), urine glucose, and creatinine are highly predictive variables. The complete ML variables ranking is described in Additional file 3.

Model Evaluation and Comparison

We used three ML algorithms to construct the prediction models of tachyarrhythmia after AMI. Before feature selection, the ANN model had better prediction performance, with an accuracy of 0.646 and an AUC of 0.596 (95%CI, 0.567–0.652). After feature selection, the ANN model achieved the best prediction performance with an accuracy of 0.654 and an AUC of 0.597 (95%CI, 0.568–0.626), which was higher than the Grace variable set model with an accuracy of 0.627 and an AUC of 0.575 (95%CI, 0.545–0.603). Table 4 summarizes the other evaluation indicators of each model and Fig. 2 for the AUC curves of each model.

Table 4
Predictive performance of all machine learning models

Models	Accuracy	AUC	specificity	false negative rate	false positive rate
All features					
Decision Tree	0.6(95% CI,0.554–0.647)	0.524(95% CI,0.477–0.571)	0.963	0.915	0.037
Random Forest	0.624(95% CI,0.578–0.671)	0.564(95% CI,0.517–0.61)	0.869	0.755	0.131
Artificial Neural Network	0.646(95% CI,0.617–0.675)	0.596(95% CI,0.567–0.652)	0.861	0.665	0.139
Feature selection					
Decision Tree	0.622(95% CI,0.576–0.668)	0.554(95% CI,0.508–0.601)	0.963	0.915	0.037
Random Forest	0.615(95% CI,0.568–0.661)	0.556(95% CI,0.51–0.603)	0.913	0.802	0.087
Artificial Neural Network	**0.654(95% CI,0.625–0.683)**	0.597(95% CI,0.568–0.626)	0.922	0.755	0.078
Grace variable sets					
Decision Tree	0.608(95% CI,0.561–0.654)	0.524(95% CI,0.477–0.571)	0.973	0.927	0.027
Random Forest	0.598(95% CI,0.551–0.645)	0.520(95% CI,0.473–0.567)	0.966	0.904	0.034
Artificial Neural Network	0.627(95% CI,0.598–0.656)	0.575(95% CI,0.545–0.603)	0.892	0.778	0.108

Discussion:

As a clinically acute disease, AMI is often associated with arrhythmia, which complicates the patient's condition and increases the Incidence of adverse events (including stroke [27], higher use of pacemakers [2], re-infarction, cardiogenic shock, heart failure, asystole [5], and sudden cardiac death [28])At the same time, patients with arrhythmia have a significantly higher in-hospital mortality [2, 4, 27, 29], 30-day mortality [30, 31] and 1-year mortality[5] than those without arrhythmia. Therefore, it is essential to predict the

occurrence of arrhythmia after AMI as early as possible. To this end, a large number of studies have analyzed the risk factors for arrhythmia after AMI [5, 7–9, 30, 32–37], but there is no systematic risk model. Currently, AMI's clinical risk model is mainly the GRACE risk score recommended by the ACC/AHA guidelines [38]. Still, it is mainly used to assess patients' mortality and may not accurately predict the occurrence of arrhythmia. Besides, the model is constructed using traditional statistical methods and only linearly analyzes the relationship between a few factors,do not address the potential prognostic value of interactions between several unexpected weaker risk factors and the primary outcome. For complex diseases, multi-factor and multi-level interactions need to be analyzed. In this case, ML can provide a useful alternative when encountering a large number of potentially relevant variables when building a predictive model. In the cardiovascular field, ML has been used in medical image analysis [39–42]、disease classification and diagnosis [14, 17, 43, 44], and predictive model construction [19, 23, 26, 45, 46]. At present, researches related to ML and AMI were mainly devoted to the prediction of patient mortality [23, 47]、and the ML model of arrhythmia after AMI has not been explored. In this study, we sought to harness the power of big data analytics and ML to develop an ML-based prediction model for the occurrence of tachyarrhythmia after AMI.

We applied 3 ML techniques (decision tree, random forest, ANN) to evaluate the risk of tachyarrhythmia after AMI. We found that the ANN algorithm's prediction ability in both the full variable model and after feature selection compared with other machine classifiers. After feature selection, the ANN model obtained the best prediction performance (accuracy of 0.654, AUC of 0.597). To evaluate our ML results clinically, we referred to the GRACE variables utilized in the models implemented in current AHA/ACC Guidelines, which are widely used for risk assessment in patients with AMI.

Our results show that the overall performance of ML was moderate, and therefore, it probably cannot yet replace diagnostic or risk estimations that further workup can provide. Nevertheless, when results were compared to those of utilizing the sets of variables considered in the Grace models, ML exhibited a higher performance for predicting the occurrence of tachyarrhythmia after AMI. Therefore, the ML-based prediction model can as a supplement to the current risk score.

Before ML, we included 45 variables based on the current AMI risk score [1,31,48–52] and the risk factors for tachyarrhythmia after AMI identified in previous studies [5–7,9,31–34,53–55]. We used the information gain method to select the top 15 highly predictive variables for the ML model construction to reduce the data dimension. Furthermore, Using ML feature-selection ranking, we found that certain risk factors that were not included in previous risk scores were significant predictors, such as angiographically determined lesion location, ultrasonic ventricular wall motion parameters abnormalities, right atrium diameter, and bundle-branch-block. These variables can be used as supplements to the current AMI risk score to assist clinicians in disease assessment.

Limitation:

The present study naturally carries the limitations of any observational study. However, this kind of largescale retrospective analysis is the main target of the data-driven approaches of ML. Second, this ML approach still needs further model training, validation, and optimization before clinical application. Patients in this study were enrolled from a single center that included only Chinese patients. Nevertheless, we compared the performance of advanced ML algorithms with the GRACE variable set model. The main finding of the current analysis was that ANN exhibited the highest prediction performance. ML-based prediction model could represent a great supplement in optimizing risk assessment and even clinical alerts of patients after AMI.

Conclusions:

In summary, we used advanced ML algorithms to select 15 clinical variables and construct a predictive model for the occurrence of tachyarrhythmia after AMI. This novel approach proved was better than that of the GRACE variable set model. Such findings could highlight the utility of using the ML approach to develop a more precise risk assessment in an era where the early estimation of tachyarrhythmia after AMI is critical to clinician decision-making.

List Of Abbreviations

ACC	American College of Cardiology
AHA	American Heart Association
AMI	Acute Myocardial Infarction
ANN	Artificial Neural Network
AUC	Area Under The Curve
BNP	Brain Natriuretic Peptide
GRACE	Global Registry of Acute Coronary Events
ML	Machine Learning
TNI	Troponin I
TNT	Troponin T

Declarations

Ethics approval and consent to participate: The Ethics Committee approved the study of the First Affiliated Hospital of Harbin Medical University, and the right to exempt informed consent was obtained. The Chinese Clinical Trial Registry approved this study (No.:ChiCTR2100041960).

Consent for publication: Not applicable.

Availability of data and materials: All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Suhuai Wang designed and experimented and participated in the data collection, and was a major contributor in writing the manuscript. CCJ and WSH collected data on patients with AMI, while ZLW and SSQ analyzed data on patients with post-AMI arrhythmias. LJJ and SL, as corresponding authors, guided the progress of the study throughout the process to ensure the authenticity of the data. All authors read and approved the final manuscript.

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Perspectives:

We established ML-based prediction models in a cohort of patients with AMI. The GRACE variable set model's comparable performance indicates ML approaches' potential value for evaluating complex and multifactorial diseases. There is no doubt that 2020 has been a great year, dominated by the COVID-19 pandemic. Under these difficult circumstances, most areas of cardiovascular research compromised due to national lockdowns. ML to extract and analyze large volumes of data remotely allowed cardiovascular medicine to continue its evolution. This study is only a small part of this booming field, providing new ideas for what will come to clinical practice in the coming years.

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Figures

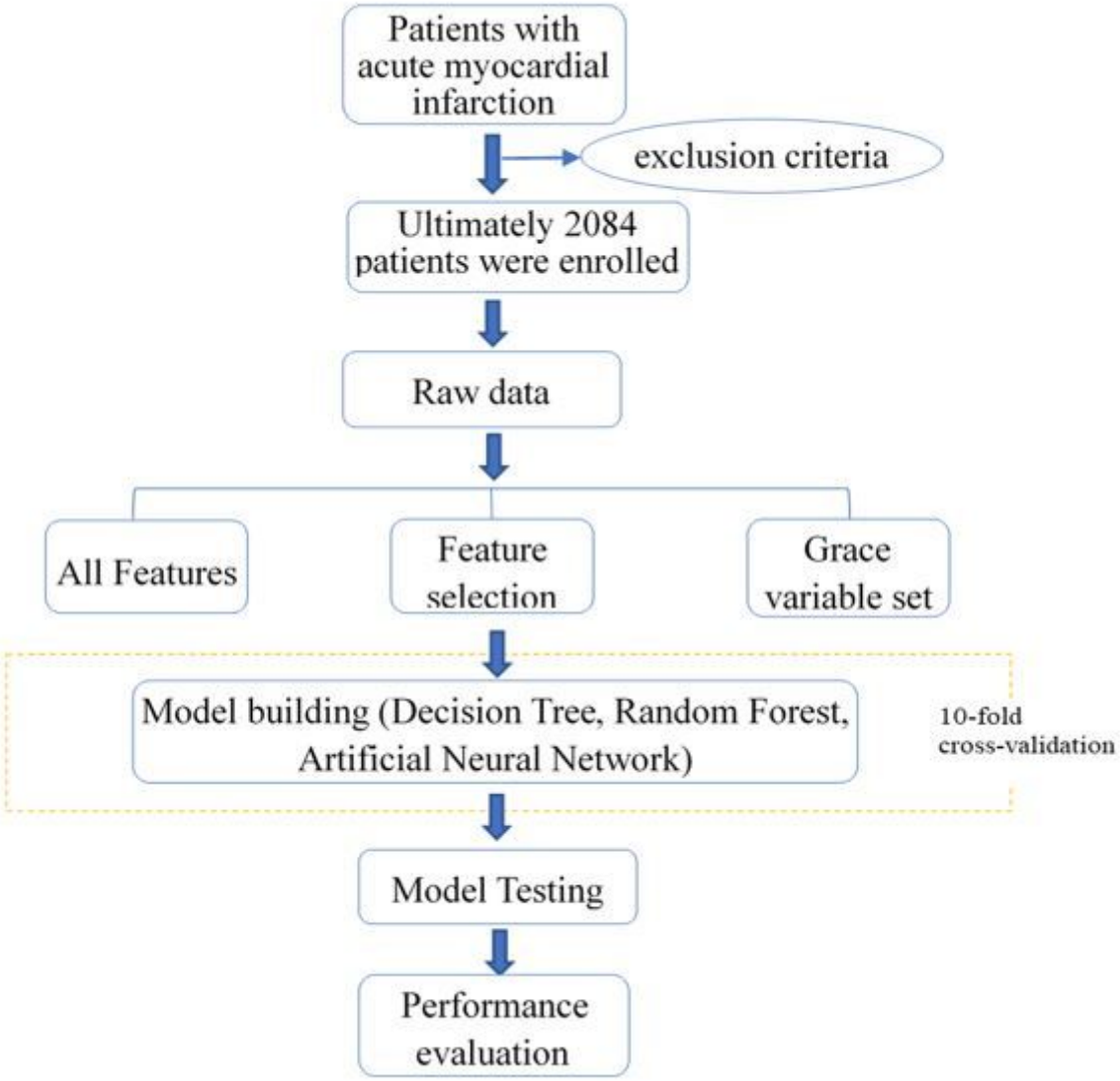

Figure 1

Flow diagram showing the process for evaluating the performance of ML methods.

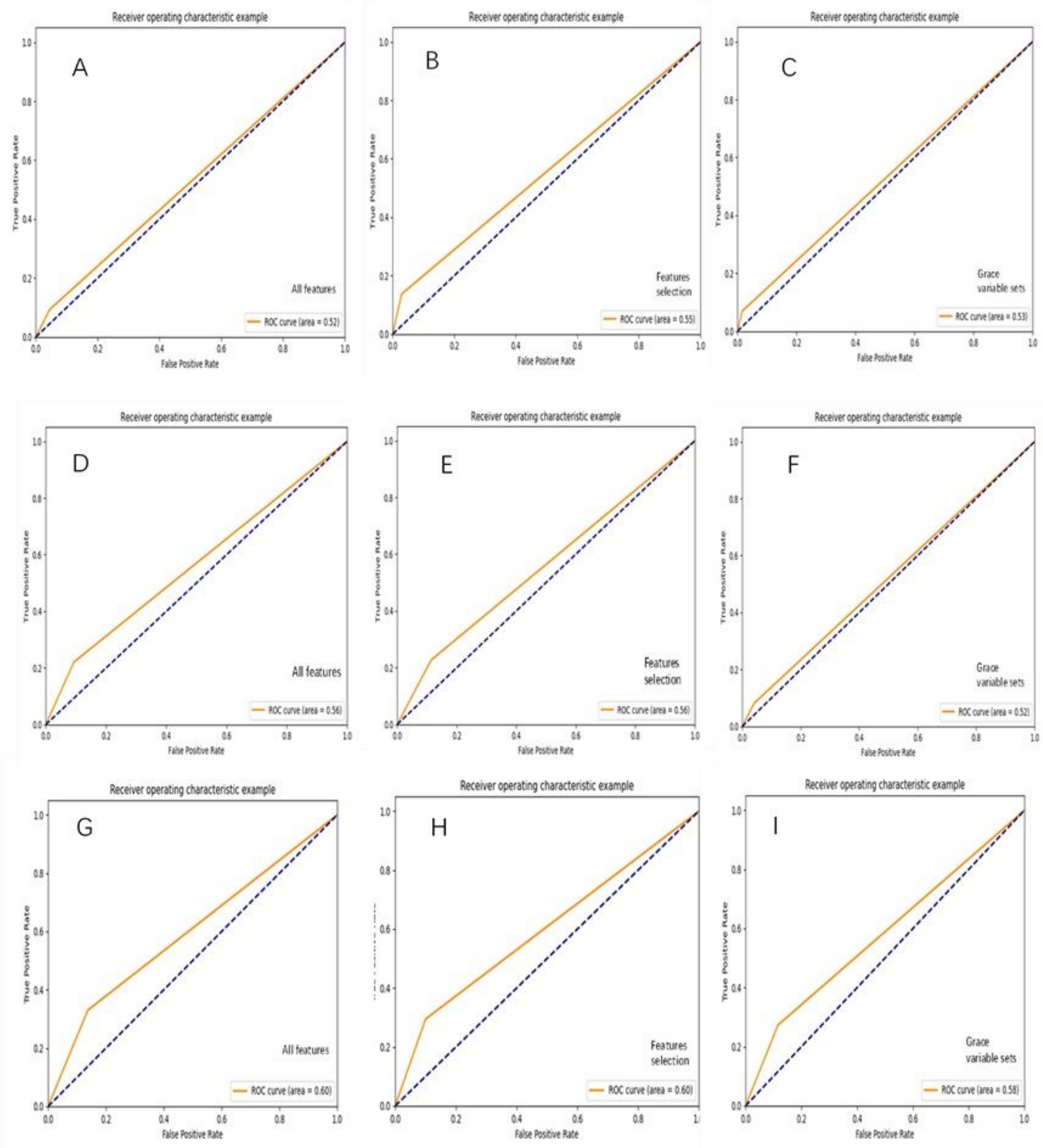

Figure 2

The AUC curves of all machine learning models:(A)decision tree-all feature models;(B)decision tree-feature selection model;(C)Decision Tree-GRACE model;(D) Random forest-all feature models;(E) Random Forest -feature selection model;(F) Random Forest-GRACE model;(G) ANN-all feature models;(H) ANN-feature selection model;(I) ANN-GRACE model.

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