Machine Learning-based in-hospital Mortality Prediction Models for Patients With Acute Coronary Syndrome

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Abstract

Background

The purpose of this study is to identify the risk factors of in-hospital mortality in patients with acute coronary syndrome (ACS) and to evaluate the performance of traditional regression and machine learning prediction models.

Methods

The data of ACS patients who entered the emergency department of Fujian Provincial Hospital from January 1, 2017 to March 31, 2020 for chest pain were retrospectively collected. The study used univariate and multivariate logistic regression analysis to identify risk factors for in-hospital mortality of ACS patients. The traditional regression and machine learning algorithms were used to develop predictive models, and the sensitivity, specificity, and receiver operating characteristic curve were used to evaluate the performance of each model.

Results

A total of 7810 ACS patients were included in the study, and the in-hospital mortality rate was 1.75%. Multivariate logistic regression analysis found that age and levels of D-dimer, cardiac troponin I, N-terminal pro-B-type natriuretic peptide (NT-proBNP), lactate dehydrogenase (LDH), high-density lipoprotein (HDL) cholesterol, and calcium channel blockers were independent predictors of in-hospital mortality. The study found that the area under the receiver operating characteristic curve of the models developed by logistic regression, gradient boosting decision tree (GBDT), random forest, and support vector machine (SVM) for predicting the risk of in-hospital mortality were 0.963, 0.960, 0.963, and 0.959, respectively. Feature importance evaluation found that NT-proBNP, LDH, and HDL cholesterol were top three variables that contribute the most to the prediction performance of the GBDT model and random forest model.

Conclusions

The predictive model developed using logistic regression, GBDT, random forest, and SVM algorithms can be used to predict the risk of in-hospital death of ACS patients. Based on our findings, we recommend that clinicians focus on monitoring the changes of NT-proBNP, LDH, and HDL cholesterol, as this may improve the clinical outcomes of ACS patients.

Background

Acute coronary syndrome (ACS) is the unstable and progressive stage of coronary heart disease, defined as ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina (UA) [1–3]. The most common symptom of ACS is chest pain, which is also one of the most common reasons for visiting the emergency room, accounting for 6% of the visits and 27% of medical admissions[4]. Even if ACS patients receive timely percutaneous coronary intervention and/or appropriate antiplatelet drugs,

their prognoses are still poor[2, 5]. ACS is associated with high morbidity and mortality and causes approximately 7 million deaths annually in the Asia-Pacific region[6, 7]. Many ACS patients die during hospitalization[8, 9]. Even with medical intervention, the mortality risk within 1 year after the diagnosis of ACS remains about 5%[10–12]. Because appropriate management can significantly improve the prognosis of the patients, it is very important to identify ACS patients and their risk of disease progression promptly and accurately. Predicting the mortality risk of ACS patients may help develop appropriate treatment strategies for patients[5, 13].

The Global Registry of Acute Coronary Events (GRACE) and Thrombolysis In Myocardial Infarction risk scores are the most popular mortality risk prediction tools of ACS[14–16]. Although these risk assessment tools have been developed and validated, their use in daily practice is still limited. Other cardiovascular disease (CVD) risk prediction models were developed based on machine learning, such as random forest (RF), neural network, and support vector machine (SVM) to solve the limitations of traditional regression-based CVD prediction models[17–19]. However, there are few studies on machine learning models for predicting mortality risk of ACS patients. The purpose of this study is to build predictive models of in-hospital mortality risk of ACS patients based on traditional regression and machine learning algorithms and to evaluate the predictive efficacy of the models.

Methods

Patient and study design

Patients who were admitted to the Chest Pain Center (Emergency Department), Fujian Provincial Hospital from January 1, 2017 to March 31, 2020 due to chest pain were included in the retrospective cohort study. The inclusion criteria included age ≥ 18 years, admission to the hospital with a diagnosis of ACS (STEMI, NSTEMI, or UA), and complete outcome information (cure, improvement, or death) of the patient at the time of the last discharge. Exclusion criteria included pregnant women; patients with malignant tumors, end-stage renal disease, severe liver disease, or blood disease; and patients with non-cardiogenic chest pain. The study was approved by the Ethical Committee of Fujian Provincial Hospital. The informed consent requirement was waived since the study only involved the use of past clinical data.

Definition and variables

In-hospital mortality was defined as all-cause death during hospitalization. The variables collected include demographic characteristics, comorbidities, thrombolytic therapy, laboratory test data, and physical examination data. They were obtained from the patients' electronic medical records, hospital information system, laboratory information management system, and clinical data repository.

Construction of prediction model of in-hospital mortality risk for ACS patients

To develop the mortality prediction model of ACS patients, we employed four machine learning algorithms, including logistic regression (LR), gradient boosting decision tree (GBDT), random forest (RF), and SVM. As a linear model, LR was employed as the baseline model. SVM is a classical machine learning algorithm and makes prediction by means of learning the boundary hyperplane in the feature space between positive and negative samples. GBDT and RF are both ensemble methods based on the decision tree model, a flow chart with rules learned from data. In brief, GBDT builds an ensemble of decision trees with each tree trying to fit residual errors of all previous trees in a gradient descent manner, while RF builds an ensemble of decision trees in parallel and hence reduces the prediction error of a single decision tree.

First, the researchers divided the data into training and testing sets according to 7:3 ratio. The training data set was used for statistical analysis, feature selectin and model training, while the independent testing data set was used to evaluate the trained models. Second, we performed univariate analysis and chose the most eligible variables for model development. The preprocessing procedure also included mean value imputation, scaling and one-hot encoding. Third, in order to reduce over-fitting and improve model accuracy, we split the training data set in a cross-validation scheme and tuned the hyperparameters of each machine learning model to optimize the cross-validation performance. The optimal hyperparameters were then used to fit all training data to obtain the final models. Finally, we calculated a series of metrics to evaluate model evaluation using the independent test set, including the areas under the receiver operating characteristic (AUROC) curves, sensitivity, and specificity.

All machine learning models were developed using Python language (3.7). LR, RF and SVM were implemented using Python library scikit-learn (0.23.2), while GBDT was implemented using Python library Xgboost (1.2.1).

Statistical analysis

Continuous variables were summarized as median and interquartile range, and categorical variables were expressed by frequency and percentage. Comparisons between training and testing sets for continuous variables and categorical variables were conducted by Mann-Whitney U test and Chi-squared test or Fisher's exact test, respectively. Logistic regression analysis was used to analyze the potential risk factors of in-hospital mortality of ACS patient. The variables with a statistical significance ($P < 0.05$) in the univariate logistic regression analysis were included in the multivariate analysis. To assess the predictive performance for in-hospital mortality, logistic regression, random forest, SVM, and GBDT models were constructed using the training set and then evaluated with the testing set. ROC curves were plotted, and the area under the curve (AUC, 95% CI) with associated *P* values was calculated. In addition, sensitivity and specificity for various models were also derived by maximizing the Youden index. Furthermore, top 10 features of importance from the GBDT and random forest models were determined.

Results

Patients and outcomes

A total of 7810 patients were included in the study, including 910 STEMI patients, 1896 NSTEMI patients, and 5004 UA patients. The mortality rate was 1.75% (137/7810). A total of 5478 patients (97 deceased and 5391 survivors) were assigned into the training set and 2322 cases into the testing set (40 deceased and 2282 survivors). Clinical characteristics of patients in the mortality and non-mortality groups in the training and testing sets were showed in *Supplemental Table 1*.

Comparison of baseline characteristics of the patients in the training and testing sets

We compared the baseline characteristics of the patients in the training and testing sets. The results showed that there were no significant differences in the baseline characteristics of patients in the training and testing sets (Table 1).

Table 1
Patient characteristics in training and validation sets

		Training (n = 5488)	Testing (n = 2322)	P value
Age	Median (IQR)	68 (60,75)	68 (60,75)	0.707
Gender	Female	1399 (25.49%)	637 (27.43%)	0.074
	Male	4089 (74.51%)	1685 (72.57%)	
D-Dimer	Median (IQR)	0.330 (0.180,0.72)	0.350 (0.190,0.715)	0.302
cTnI	Median (IQR)	0.074 (0.011,0.497)	0.070 (0.010,0.448)	0.244
CK	Median (IQR)	83 (58,131)	85.5 (58,136)	0.277
NT-proBNP	Median (IQR)	243.1 (76,869.5)	245.1 (73.8,873.3)	0.873
LDH	Median (IQR)	179 (154,229)	181 (154,235)	0.126
HDL cholesterol	Median (IQR)	0.99 (0.820,1.180)	0.99 (0.820,1.190)	0.906
LDL cholesterol	Median (IQR)	2.370 (1.800,3.090)	2.370 (1.800,3.140)	0.809
Total cholesterol	Median (IQR)	3.83 (3.170,4.620)	3.830 (3.180,4.660)	0.846
Triglycerides	Median (IQR)	1.350 (1.000,1.910)	1.340 (1.010,1.870)	0.679
Hypertension	No	1610 (29.34%)	681 (29.33%)	0.994
	Yes	3878 (70.66%)	1641 (70.67%)	
Diabetes	No	3531 (64.34%)	1494 (64.34%)	> 0.999
	Yes	1957 (35.66%)	828 (35.66%)	
Clopidogrel	No	814 (14.83%)	338 (14.56%)	0.753
	Yes	4674 (85.17%)	1984 (85.44%)	

Note: cTnI: cardiac troponin I; CK: creatine kinase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LDH: lactate dehydrogenase; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol; ACEI: angiotensin converting enzyme inhibitor; PCI: percutaneous coronary intervention

		Training (n = 5488)	Testing (n = 2322)	P value
Beta-blockers	No	1419 (25.86%)	615 (26.49%)	0.562
	Yes	4069 (74.14%)	1707 (73.51%)	
Calcium channel blockers	No	3534 (64.4%)	1461 (62.92%)	0.215
	Yes	1954 (35.6%)	861 (37.08%)	
Statins	No	209 (3.81%)	97 (4.18%)	0.442
	Yes	5279 (96.19%)	2225 (95.82%)	
Low molecular weight heparin	No	2145 (39.09%)	955 (41.13%)	0.092
	Yes	3343 (60.91%)	1367 (58.87%)	
Ticagrelor	No	4341 (79.1%)	1857 (79.97%)	0.383
	Yes	1147 (20.9%)	465 (20.03%)	
Glycoprotein IIb/IIIa receptor antagonist	No	4692 (85.5%)	1989 (85.66%)	0.851
	Yes	796 (14.5%)	333 (14.34%)	
Angiotensin receptor antagonist	No	3798 (69.21%)	1567 (67.48%)	0.134
	Yes	1690 (30.79%)	755 (32.52%)	
ACEI	No	2617 (47.69%)	1093 (47.07%)	0.619
	Yes	2871 (52.31%)	1229 (52.93%)	
Aspirin	No	612 (11.15%)	275 (11.84%)	0.379
	Yes	4876 (88.85%)	2047 (88.16%)	
PCI	No	4983 (90.8%)	2115 (91.09%)	0.687
	Yes	505 (9.2%)	207 (8.91%)	
Thrombolysis with drugs	No	5484 (99.93%)	2321 (99.96%)	> 0.999
	Yes	4 (0.07%)	1 (0.04%)	

Note: cTnI: cardiac troponin I; CK: creatine kinase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LDH: lactate dehydrogenase; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol; ACEI: angiotensin converting enzyme inhibitor; PCI: percutaneous coronary intervention

Univariate and multivariate logistic analysis of risk factors

Univariate analysis found that age, D-dimer, cardiac troponin I (cTnI), creatine kinase (CK), N-terminal pro-B-type natriuretic peptide (NT-proBNP), lactate dehydrogenase (LDH), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, total cholesterol, triglycerides, clopidogrel, beta-blockers, calcium channel blockers, statins, ticagrelor, glycoprotein IIb/IIIa receptor antagonist, angiotensin receptor antagonist, angiotensin converting enzyme inhibitor, aspirin, and thrombolysis with drugs were significantly associated with in-hospital mortality of ACS patients (Table 2).

Table 2
Univariate and multivariate logistic analysis of risk factors for in-hospital mortality of ACS patients

	Unadjusted			Adjusted		
Variables	OR	95% CI	*P* value	OR	95% CI	*P* value
Age (Unit = 1)	1.190	(1.157,1.223)	< 0.001	1.143	(1.096,1.193)	< 0.001
Gender (Male vs Female)	1.243	(0.764,2.022)	0.382			
D-Dimer (Unit = 1)	1.322	(1.247,1.401)	< 0.001	1.101	(0.996,1.217)	0.061
cTnI (Unit = 1)	1.115	(1.080,1.152)	< 0.001	1.086	(1.044,1.131)	< 0.001
CK (Unit = 10)	1.006	(1.004,1.008)	< 0.001	1.004	(1.000,1.009)	0.045
NT-proBNP (Unit = 100)	1.016	(1.014,1.018)	< 0.001	1.012	(1.009,1.015)	< 0.001
LDH (Unit = 10)	1.018	(1.013,1.022)	< 0.001	1.020	(1.013,1.026)	< 0.001
HDL cholesterol (Unit = 0.1)	0.619	(0.568,0.675)	< 0.001	0.656	(0.572,0.753)	< 0.001
LDL cholesterol (Unit = 1)	0.280	(0.203,0.386)	< 0.001	0.507	(0.176,1.464)	0.209
Total cholesterol (Unit = 1)	0.351	(0.270,0.456)	< 0.001	1.794	(0.695,4.627)	0.227
Triglycerides (Unit = 1)	1.134	(1.014,1.270)	0.028	0.919	(0.679,1.242)	0.581
Hypertension (Yes vs No)	1.610	(0.981,2.643)	0.059	1.164	(0.468,2.897)	0.744
Diabetes (Yes vs No)	1.272	(0.846,1.913)	0.248			
Clopidogrel (Yes vs No)	0.421	(0.269,0.657)	< 0.001	0.396	(0.136,1.152)	0.089
Beta-blockers (Yes vs No)	0.190	(0.125,0.289)	< 0.001	0.668	(0.297,1.501)	0.329

Note: cTnI: cardiac troponin I; CK: creatine kinase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LDH: lactate dehydrogenase; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol; ACEI: angiotensin converting enzyme inhibitor; PCI: percutaneous coronary intervention; ACS: acute coronary syndrome

	Unadjusted			Adjusted		
Calcium channel blockers (Yes vs No)	0.557	(0.348,0.892)	0.015	0.350	(0.148,0.826)	0.017
Statins (Yes vs No)	0.188	(0.108,0.327)	< 0.001	2.824	(0.676,11.801)	0.155
Low molecular weight heparin (Yes vs No)	0.838	(0.558,1.256)	0.391			
Ticagrelor (Yes vs No)	0.382	(0.192,0.762)	0.006	0.464	(0.125,1.727)	0.252
Glycoprotein IIb/IIIa receptor antagonist (Yes vs No)	0.316	(0.128,0.780)	0.012	0.503	(0.082,3.105)	0.459
Angiotensin receptor antagonist (Yes vs No)	0.312	(0.170,0.573)	< 0.001	1.120	(0.410,3.056)	0.825
ACEI (Yes vs No)	0.294	(0.185,0.467)	< 0.001	0.987	(0.456,2.137)	0.974
Aspirin (Yes vs No)	0.142	(0.094,0.214)	< 0.001	1.077	(0.427,2.717)	0.875
PCI (Yes vs No)	0.420	(0.154,1.147)	0.091	0.294	(0.058,1.492)	0.14
Thrombolysis with drugs (Yes vs No)	18.725	(1.931,181.546)	0.011	0.542	(0.011,26.361)	0.758

Note: cTnI: cardiac troponin I; CK: creatine kinase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LDH: lactate dehydrogenase; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol; ACEI: angiotensin converting enzyme inhibitor; PCI: percutaneous coronary intervention; ACS: acute coronary syndrome

After adjusting for confounding factors, the study found that age (OR = 1.143, 95%CI: 1.096,1.193; *P*< 0.001), cTnI (OR = 1.086, 95%CI: 1.044,1.131; *P*< 0.001), CK (OR = 1.004, 95%CI: 1.000,1.009; *P* = 0.045), NT-proBNP (OR = 1.012, 95%CI: 1.009,1.015; *P*< 0.001), and LDH (OR = 1.020, 95%CI: 1.013, 1.026; *P*< 0.001) were independently associated with increased risk of in-hospital mortality (Table 2). Moreover, calcium channel blockers (OR = 0.350, 95%CI: 0.148, 0.826; P = 0.017) and HDL cholesterol (OR = 0.656, 95%CI: 0.572,0.753; *P*< 0.001) were independently associated with decreased risk of in-hospital mortality (Table 2).

Predictive power analysis of in-hospital mortality risk prediction model (validation set)

The study found that AUCs of the models for predicting the risk of in-hospital mortality of ACS patients developed with logistic regression, GBDT, random forest, and SVM were 0.962 (95%CI: 0.930, 0.994), 0.960 (95%CI: 0.915, 1.000), 0.963 (95%CI: 0.915, 1.000), and 0.959 (95%CI: 0.916,1.000), respectively (Table 3). The sensitivities were 0.844, 0.938, 0.938, and 0.938 and the specificities were 0.965, 0.930, 0.945 and 0.929, respectively (Table 3, Fig. 1).

Table 3
Predictive power analysis of each model for predicting in-hospital mortality (validation set)

Models	AUC (95% CI)	*P* value	Sensitivity	Specificity
Logistic regression	0.962 (0.930, 0.994)	< 0.001	0.844	0.965
GBDT	0.960 (0.915, 1.000)	< 0.001	0.938	0.930
Random Forest	0.963 (0.915, 1.000)	< 0.001	0.938	0.945
SVM	0.959 (0.916,1.000)	< 0.001	0.938	0.929
GBDT: gradient boosting decision tree; SVM: support vector machine; AUC: area under curve				

Feature importance evaluation of the GBDT and random forest models

Feature importance analysis found that the top 10 variables contributing to the predictive performance of the GBDT model were NT-proBNP (0.180), LDH (0.153), HDL cholesterol (0.146), age (0.117), cTnI (0.108), CK (0.107), D-dimer (0.092), LDL cholesterol (0.084), beta-blockers (0.009), and aspirin (0.006). The top 10 variables contributing to the predictive performance of the random forest model were NT-proBNP (0.296), HDL cholesterol (0.179), LDH (0.139), age (0.115), cTnI (0.090), D-dimer (0.065), LDL cholesterol (0.065), CK (0.043), aspirin (0.004), and beta-blockers (0.003), respectively (Table 4).

Table 4
Feature importance evaluation of GBDT model and random forest model

GBDT		**Random Forest**	
Feature name	Feature importance (score)	Feature name	Feature importance (score)
NT-proBNP	0.180	NT-proBNP	0.296
LDH	0.153	HDL cholesterol	0.179
HDL cholesterol	0.146	LDH	0.139
Age	0.117	Age	0.115
cTnI	0.108	cTnI	0.090
CK	0.107	D-Dimer	0.065
D-Dimer	0.092	LDL cholesterol	0.065
LDL cholesterol	0.084	CK	0.043
Beta-blockers	0.009	Aspirin	0.004
Aspirin	0.006	Beta-blockers	0.003

Note: cTnI: cardiac troponin I; CK: creatine kinase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LDH: lactate dehydrogenase; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol; ACEI: angiotensin converting enzyme inhibitor; PCI: percutaneous coronary intervention; GBDT: gradient boosting decision tree

Discussion

ACS is one of the main causes of death worldwide[20]. Predicting the mortality risk of ACS patients is helpful for disease management, prolonging the survival time of patients, and improving the quality of life of patients. In our study, the mortality rate was 1.75%, which was lower than that of the Asia-Pacific region; the mortality rate of ACS patients in the Asia-Pacific region during hospitalization was about 5% [21]. Multivariate logistic regression analysis found age, cTnI, CK, NT-proBNP and LDH were independently associated with increased risk of in-hospital mortality. Moreover, calcium channel blockers and HDL cholesterol were independently associated with decreased risk of in-hospital mortality. The study showed that the models developed using logistic regression, GBDT, random forest, and SVM algorithms can predict the risk of in-hospital mortality of ACS patients. We also found that NT-proBNP, LDH, and HDL cholesterol were top three variables that contribute the most to the prediction performance of GBDT model and random forest model.

We employed four machine learning algorithms to develop prediction models of mortality during hospitalization in ACS patients and compared their performances. The study found that prediction models constructed by logistic regression, GBDT, random forest, and SVM can effectively predict the risk of death for ACS patients in hospitals. Previous studies have found that the prediction performance of a

3-year mortality risk prediction model for ACS patients based on machine learning algorithms was better than the GRACE score (AUC: 0.768 vs. 0.701)[22]. Sherazi et al. found that a mortality risk prediction model based on machine learning algorithms can effectively predict the 1-year death risk of ACS patients[23]. Another study found that a prediction model based on machine learning algorithms can predict the 30-day mortality rate of post-ST-segment elevation myocardial infarction. The authors suggested that machine learning can be used for outcome prediction in complex cardiology settings[24].

The risk of mortality of ACS patients during hospitalization is affected by risk factors. We evaluated the contribution of variables to the predictive effect of the GBDT and random forest risk prediction model.

The top three variables that contributed the most to the prediction effect of GBDT and random forest models were the levels of NT-proBNP, LDH, and HDL cholesterol. It was consistent with previous research that has found that among patients with chronic heart failure, patients with increased levels of NT-proBNP had a poorer prognosis[25]. Furthermore, preoperative NT-proBNP can predict the in-hospital mortality and long-term survival of patients undergoing surgery for ACS[26]. Another study found that in non-ST elevation-acute coronary syndrome (NSTE-ACS) patients, NT-proBNP had a good predictive effect on 30-day mortality (AUC = 0.85)[27]. Moreover, elevated plasma LDH was associated with worse outcomes and increased risk of mortality in patients with several diseases[28–32]. Previous studies have shown that increased plasma LDH level was an independent predictor of the risk of mortality in patients with acute aortic syndromes[33]. Additionally, plasma LDH levels were associated with 28-day risk of death in patients with sepsis[34], and in patients with acute decompensated heart failure, plasma LDH may be an independent predictor of 90-day, 180-day, and 365-day all-cause mortality risk[35]. However, there were few studies conducted specifically with ACS patients. Our study found that LDH was related to the increased risk of mortality in patients with ACS and that it provided a considerable contribution to the predictive effect of the model. Previous studies have found that low levels of HDL and LDL cholesterol have been shown to be important predictors of in-hospital mortality[36–38]. A low early HDL cholesterol level should be regarded as an independent predictor of in-hospital mortality in ACS patients presenting to the cardiac care unit[38]. TRILOGY ACS Trial found that lower baseline HDL cholesterol was significantly associated with increased risk of cardiovascular death and all-cause death in ACS patients[39]. The findings of both of these studies are consistent with the results of our study.

In addition to the above three important variables, age, cTnI, CK, D-dimer, LDL cholesterol, beta-blockers, and aspirin all had an important influence on the prediction effect of the model. These results were consistent with previous findings about these factors. Cardiac troponin I (cTnI) was a validated biomarker for diagnosis and risk stratification of patients with acute coronary syndrome[40]. The increase of high sensitivity-cTnI level in the stable phase after ACS event was an independent predictor of all-cause death and cardiovascular death in the ACS outpatient population[41]. In a stabilized phase of patients with non-ST-segment elevation ACS, cTnI levels exhibited a continuous and slight increase, and levels of cTnI elevated above 0.01 ug/L can predict the long-term mortality of patients[42]. EPICOR registry study found that old age was a risk factor for poor prognosis during the first two years after discharge in ACS patients[43]. As the age of ACS patients increases, the risk of poor prognosis increases, as even elderly

patients with good heart function had a higher risk of death[44]. The study found that compared with younger patients, elderly patients with ACS had a higher risk of comorbidities, hospitalization, and 6-month mortality[45]. The increased D-dimer level was found to be a predictor of a patient's adverse outcome[46]. Several studies have found that increased D-dimer levels were significantly associated with adverse outcomes and increased risk of mortality in ACS patients[47–49]. In addition, studies have found that increased levels of creatine kinase-MB can predict the risk of hospital death in elderly ACS patients[50]. European Society Of Cardiology guidelines recommend that patients with NSTEMI and STEMI receive optimal medical therapy, which includes aspirin, beta-blockers, and other drugs[2]. The study found that ACS patients receiving aspirin treatment before admission had a reduced 30-day mortality[51]. Real-world studies have found that receiving optimal medical therapy (including aspirin and beta- blockers) in patients with ACS after discharge can reduce their mortality risk[52].

In our research, we found an interesting result. Calcium channel blockers was significantly associated with a reduction in the risk of hospital death in ACS patients. This was inconsistent with some research results in western countries[53]. Several studies have found that calcium channel blockers had no advantages over other antihypertensive drugs in reducing the serious complications of hypertension, and calcium channel blockers increased the overall mortality risk and the adverse events risk in patients with coronary heart disease[54–56]. However, in the Japanese study, there was no significant difference in the incidence of cardiovascular death, reinfarction, uncontrolled unstable angina and nonfatal stroke in patients with post-acute myocardial infarction after receiving beta blockers and calcium antagonists[57]. Another Japanese retrospective study found that Calcium channel blockers (nifedipine-retard) did not increase the incidence of cardiac events in post-MI patients, and even prevent the risk of cardiac events in non-smokers under 50 years of age[58]. An Australian study found that calcium channel blockade was not associated with the excess risk of death in post-AMI patients[59].

Our research results suggested that preventing abnormally elevated levels of NT-proBNP, LDH, cTnI, and CK in patients with ACS, while preventing the level of HDL cholesterol in patients from falling below the normal range, may reduce the risk of in-hospital death in patients with ACS.

This study had several limitations. First, this was a retrospective study, and the results need to be verified by a prospective clinical trial. Second, our study was a single-center study; therefore, the results of the study limit the generalizability to apply to all ACS patients.

Conclusion

The predictive models developed using logistic regression, GBDT, random forest, and SVM algorithms can be used to predict the risk of in-hospital death for ACS patients. Based on our findings, we recommend that clinicians focus on monitoring the changes of NT-proBNP, LDH, and HDL cholesterol, as this may improve the clinical outcomes of ACS patients.

Abbreviations

ACS: acute coronary syndrome; STEMI : ST-segment elevation myocardial infarction; NSTEMI : non-STEMI; UA: unstable angina; LR: logistic regression; GBDT: gradient boosting decision tree; RF: random forest; SVM: support vector machine; cTnI: cardiac troponin I; CK: creatine kinase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LDH: lactate dehydrogenase; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol; ACEI: angiotensin converting enzyme inhibitor; PCI: percutaneous coronary intervention

Declarations

- Ethics approval and consent to participate

Our study was approved by the Ethical Committee of Fujian Provincial Hospital. The informed consent requirement was waived since the study only involved the use of past clinical data.

- Consent for publication

There are no details on individuals reported within the manuscript, consent for publication is not applicable in our study.

- Availability of data and materials

All data generated or analysed 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

Jun Ke: responsible for research protocol, data collection and analysis

Yiwei Chen: responsible for the statistics and analysis of research data

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Zhiyong Wu: responsible for data collection and data review, and final pooling of data

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Yangpeng Lian: responsible for supervising the implementation of research and data quality control

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Figures

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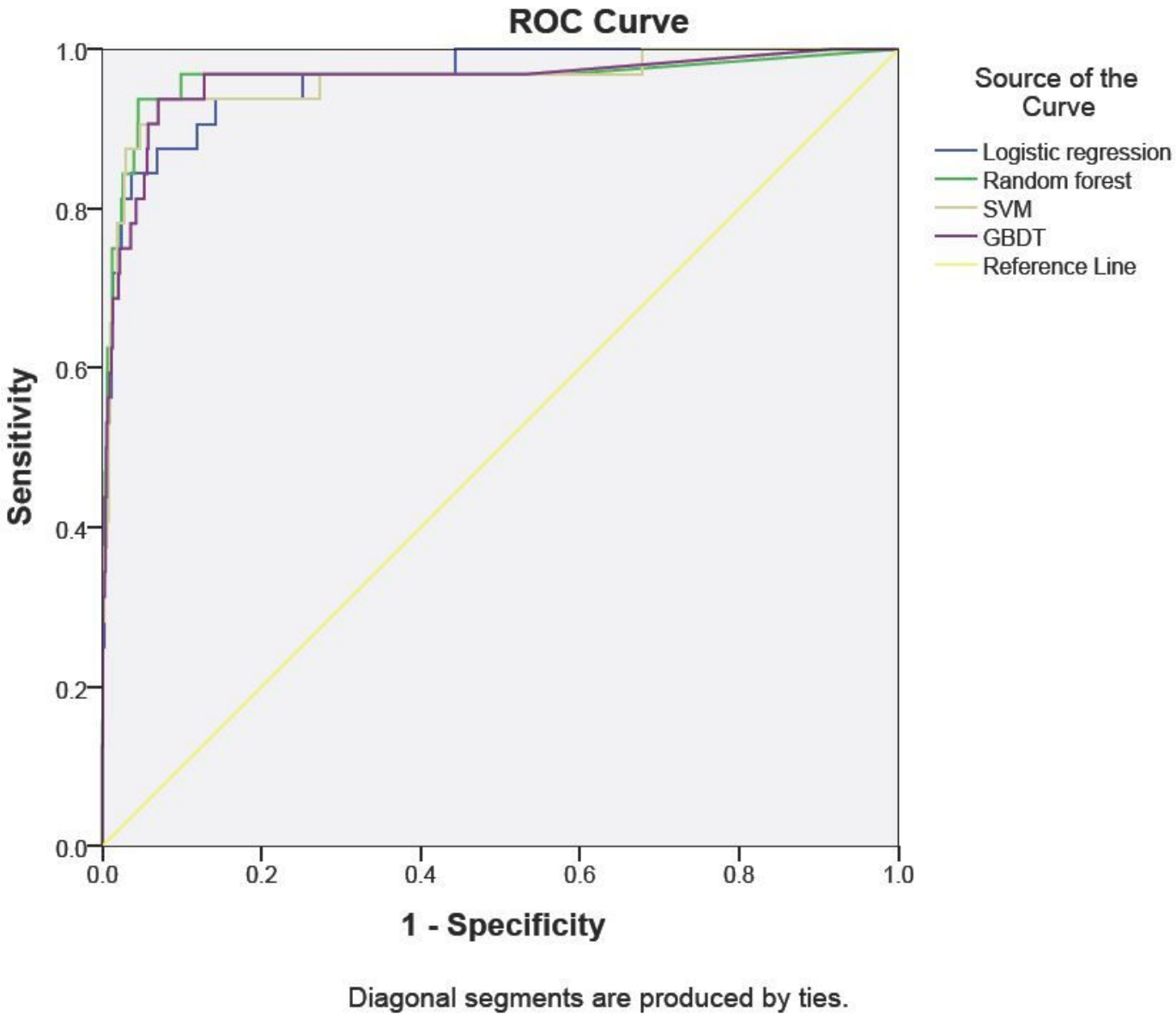

Figure 1

Receiver operating characteristic (ROC) analysis result of in-hospital mortality risk prediction model.

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