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Machine learning in the prediction of in-hospital mortality in patients with first acute myocardial infarction

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ABSTRACT

Background: Persistent efforts are required to further reduce the in-hospital mortality of patients suffering from acute myocardial infarction (AMI), even in the face of a global trend of declining AMI-related fatalities. We investigated deep machine learning models for in-hospital death prediction in patients on their first AMI.
Method: In this 2-center retrospective analysis, first AMI patients from Hospital I and Hospital II were included; 4783 patients from Hospital 1 were split in a 7:3 ratio between the training and testing sets. Data from 1053 AMI patients in Hospital II was used for further validation. 70 clinical information and laboratory examination parameters as predictive indicators were included. Logistic Regression Classifier (LR), Random Forests Classifier (RF), eXtreme Gradient Boosting (XGB), Support Vector Machine Classifier (SVM), Multilayer Perceptron (MLP), Gradient Boosting Machine (GBM), Bootstrapped Aggregation (Bagging) models with AMI patients were developed. The importance of selected variables was obtained through the Shapley Additive exPlanations (SHAP) method. The performance of each model was shown using the area under the receiver operating characteristic curve (AUROC) and the area under the precision-recall curve (Average Precision; AP). Result: The in-hospital mortality for AMI in the training, testing, and validation sets were 5.7 %, 5.6 %, and 6.0 %, respectively. The top 8 predictors were D-dimer, brain natriuretic peptide, cardiogenic shock, neutrophil, prothrombin time, blood urea nitrogen, cardiac arrest, and phosphorus. In the testing cohort, the models of LR, RF, XGB, SVM, MLP, GBM, and Bagging yielded AUROC values of 0.929, 0.931, 0.907, 0.868, 0.907, 0.923, and 0.932, respectively. Bagging has good predictive value and certain clinical value in external validation with AUROC 0.893.
Conclusion: In order to improve the forecasting accuracy of the risk of AMI patients, guide clinical nursing practice, and lower AMI inpatient mortality, this study looked into significant indicators and the optimal models for predicting AMI inpatient mortality.

1. Introduction

Even though acute myocardial infarction (AMI) mortality has declined as a result of medical breakthroughs, it is still the world's leading cause of death, contributing to almost one-third of all deaths [1]. Records show that the in-hospital mortality of AMI in the United States decreased from 10.4 % to 9.7 % between 2006 and 2014 [2]. According to a study, the in-hospital mortality rate of first AMI in New Jersey hospitals dropped from 16.9 % to 7.5 % between 1986 and 2007 [3]. In Thanh Hoa and Hai Phong in Vietnam, the in-hospital mortality of AMI was 6.8 % and 3.8 %, respectively [4]. The in-hospital mortality of AMI varies among the 3 concentrations of hospitals in China, with 3.1 % in province-concentration hospitals, 5.3 % in prefecture-concentration hospitals, and 10.2 % in county-concentration hospitals [5]. Reducing in-hospital mortality in AMI patients can be achieved through proactive implementation of relevant management measures and efficient monitoring and prediction.

The factors affecting the in-hospital mortality of AMI patients are complex and diverse. Research shows that AMI combined with heart failure is independently associated with in-hospital mortality [6]. Moreover, diabetes mellitus is associated with increased in-hospital mortality in AMI inpatients [7]. For AMI patients aged $\geq$ 80 years, advanced age is a poor prognostic factor that is associated with a much greater in-hospital mortality rate [8]. In addition, there are significant

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racial and gender disparities in the in-hospital mortality of AMI patients [9]. Using machine learning algorithms on medical data, numerous studies have created a variety of models to direct clinical work using medical datasets [10]. Rodriguez et al. constructed multivariable hierarchical logistic regression models to analyze hospitalizations, care patterns, and mortality of AMI patients through factors such as sex, age, and race/ethnicity [9]. Jiang et al. developed a predictive model using a gradient-boosting tree algorithm (LightGBM) based on multiple parameters obtained by septic and non-septic survivors within one year of their first ICU admission, revealing differences in mortality risk factors between the two groups during ICU readmission [11]. Additionally, several deep machine learning methods use medical data to create, assess, and contrast various machine learning models to determine the best course of action for establishing clinical protocols. Kitcharanant et al. developed and internally validated 7 machine learning models for predicting the 1-year mortality after fragility hip fracture in the elderly [12]. Moll et al. used multiple machine models to predict the all-cause mortality across two chronic obstructive pulmonary disease (COPD) cohorts [13]. Machine learning aims to more accurately identify patients at high risk and create tailored treatment regimens [14].

2. Methods

2.1. Study design and population

The mode development and reporting process used in this study comply with the guidelines for transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) [15]. This retrospective study included 5836 first AMI patients from two medical centers, including 4783 AMI patients admitted to Taizhou Hospital in Zhejiang Province (Hospital I) from December 20, 2011, to December 27, 2020, and 1053 AMI patients admitted to the Enze Hospital (Hospital II) from January 2, 2019, to July 9, 2023. The diagnosis of AMI conforms to the pertinent diagnostic criteria established by the Chinese Medical Association [16]. Hospital I and II adhered to the same diagnostic and inclusion criteria. Inclusion criteria: (1) First-time AMI, (2) Adults over 20 years old, (3) Hospitalized patients, (4) Complete clinical information. The inclusion and exclusion of AMI patients are depicted in Fig. 1. There were 5376 hospitalized patients with AMI in Hospital I; 5 minors, 198 non-first-time AMI patients, and 390 patients with missing clinical information were excluded. The study recruited 4783 AMI patients from Hospital I. There were a total of 1208 hospitalized AMI adults in Hospital II; 52 non-first-AMI patients and 103 patients with missing clinical information were excluded. This study ultimately recruited 1053 AMI patients from Hospital II. This study was approved by the Medical Ethics Committee of Taizhou Hospital in Zhejiang Province affiliated with Wenzhou Medical University (#K20230923) and Enze Hospital (#K20230814).

2.2. Data collection

Clinical information and laboratory test data of AMI patients were retrieved and recorded from electronic medical records. The survival or mortality of AMI patients while hospitalized is the subject of this investigation. Physicians specializing in cardiology, nephrology, pulmonary medicine, neurology, gastrointestinal medicine, and endocrinology were engaged in the identification of concurrent disorders. The relevant laboratory examination indicators and clinical information are included in Table 1. The results of the first laboratory examination of AMI patients admitted to the hospital were recorded. Blood samples were collected from fasting AMI patients and at rest from 6 a.m. to 7 a.m. The serum brain natriuretic peptide (BNP) was detected using an Abbott i2000 automatic chemiluminescence analyzer. A Beckman DxI 800 automated chemiluminescence analyzer was used to analyze the concentration of cardiac troponin I (cTnI) in serum. A Sysmex 2100D routine hematology analyzer was used to test routine blood examinations. Biochemical parameters were performed with a Beckman Coulter AU5800 analyzer. Blood coagulation function was detected by the STAGO automatic blood coagulation analyzer.

2.3. Establishment and evaluation of Machine learning algorithms

Patients from Hospital I were stratified using random sampling techniques and were allocated to training and testing datasets in a 7:3 ratio. Additionally, data from Hospital II was used for external validation. (Fig. 1). According to the method proposed by Riley et al. [17], the sample size of the training set was estimated, assuming an event occurrence rate of 5.3 % [5], a total number of prediction parameters of

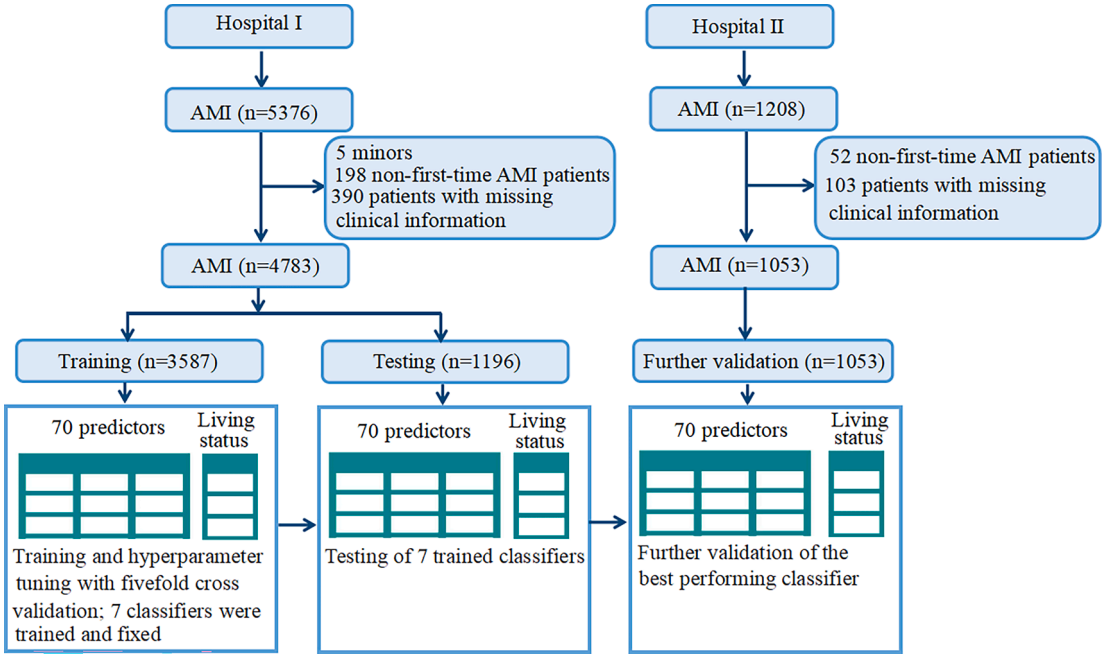

Fig. 1. Included and excluded AMI patients and the machine learning development process.

Table 1
Comparison of demographic and clinical characteristics between deaths and survivors of Hospital I / Hospital II.

	Hospital I			Hospital II		
	Total (n = 4783)	Deceased (n = 271)	Survived (n = 4512)	Total (n = 1053)	Deceased (n = 63)	Survived (n = 990)
Age (y)	66 ± 13	74 ± 12	65 ± 13▲▲▲	64 ± 15	74 ± 14	63 ± 14▲▲▲
WBC (109/l)	8.9 (7.0, 11.3)	12.5 (9.1, 16.5)	8.8 (6.9, 11.1)▲▲▲	9.0 (7.0, 11.6)	12.7 (10.1, 16.1)	8.8 (6.9, 11.3)▲▲▲
MONO (109/l)	0.6 (0.4, 0.7)	0.7 (0.5, 0.9)	0.6 (0.4, 0.7)▲▲▲	0.7 (0.5, 0.9)	0.8 (0.5, 1.1)	0.7 (0.5, 0.9)▲
RDW (%)	13.0 (12.6, 13.5)	13.6 (13.0, 14.2)	13.0 (12.5, 13.5)▲▲▲	13.0 (12.5, 13.7)	13.7 (12.9, 14.8)	13.0 (12.4, 13.6)▲▲▲
HCT (%)	0.39 ± 0.05	0.36 ± 0.06	0.40 ± 0.05▲▲▲	0.39 ± 0.06	0.33 ± 0.06	0.40 ± 0.06▲▲▲
LYM (109/l)	1.5 (1.1, 2.0)	1.2 (0.9, 1.6)	1.5 (1.2, 2.0)▲▲▲	1.5 (1.1, 2.0)	1.3 (0.9, 1.7)	1.5 (1.1, 2.0)▲▲
MCV (fl)	91 (89, 94)	92 (88, 95)	91 (89, 94)	91 (88, 94)	92 (87, 96)	91 (88, 94)
MCH (pg)	30.7 (29.7, 31.5)	30.6 (29.6, 31.4)	30.7 (29.7, 31.5)	30.6 (29.5, 31.6)	30.1 (29.0, 31.4)	30.7 (29.5, 31.7)
MCHC (g/l)	334 ± 10	331 ± 11	334 ± 10▲▲▲	334 ± 12	330 ± 13	335 ± 12▲▲
MPV (fl)	10.7 ± 1.3	10.7 ± 1.2	10.7 ± 1.1	10.5 ± 1.0	10.7 ± 1.1	10.5 ± 1.0
Baso (109/l)	0.00 (0.01, 0.02)	0.01 (0.00, 0.02)	0.01 (0.00, 0.02)▲▲▲	0.02 (0.01, 0.03)	0.02 (0.01, 0.04)	0.02 (0.01, 0.03)
Eos (109/l)	0.06 (0.01, 0.13)	0.00 (0.00, 0.03)	0.06 (0.02, 0.13)▲▲▲	0.06 (0.02, 0.12)	0.01 (0.00, 0.06)	0.06 (0.02, 0.13)▲▲▲
Hb (g/l)	131 ± 18	119 ± 21	132 ± 19▲▲▲	132 ± 21	110 ± 22	133 ± 20▲▲▲
PDW (%)	14.5 (12.4, 16.2)	15.3 (12.9, 16.3)	14.4 (12.4, 16.1)▲▲	12.0 (10.8, 13.5)	12.2 (11.1, 14.0)	12.0 (10.8, 13.5)
PLT (109/l)	208 (172, 247)	207 (165, 252)	208 (172, 247)	215 (179, 258)	194 (153, 257)	216 (181, 258)▲
PCT (%)	0.22 (0.19, 0.26)	0.22 (0.17, 0.27)	0.22 (0.19, 0.26)	0.22 (0.19, 0.27)	0.22 (0.17, 0.27)	0.22 (0.19, 0.27)
NEUT (109/l)	6.6 (4.7, 8.9)	10.4 (7.6, 14.4)	6.4 (4.6, 8.7)▲▲▲	6.6 (4.7, 9.0)	10.8 (7.9, 13.6)	6.5 (4.6, 8.8)▲▲▲
RBC (1012/l)	4.27 ± 0.61	3.89 ± 0.68	4.30 ± 0.60▲▲▲	4.35 ± 0.72	3.67 ± 0.77	4.39 ± 0.70▲▲▲
GGT (U/l)	28 (19, 46)	35 (20, 64)	27 (19, 45)▲▲▲	30 (21, 50)	35 (20, 67)	30 (21, 50)
ALB (g/l)	38.2 ± 4.0	34.6 ± 4.9	38.4 ± 3.9▲▲▲	37.2 ± 4.2	32.3 ± 5.1	37.5 ± 4.0▲▲▲
ALT (U/l)	36 (23, 61)	65 (31, 131)	36 (22, 58)▲▲▲	34 (20, 55)	65 (24, 240)	33 (20, 52)▲▲▲
CRP (mg/l)	8.7 (3.4, 24.1)	30.7 (10.1, 98.3)	8.2 (3.3, 22.1)▲▲▲	7.4 (3.0, 21.9)	41.4 (17.0, 96.2)	7.0 (2.9, 19.1)▲▲▲
LDL-C (mmol/l)	2.53 (2.01, 3.11)	2.25 (1.65, 3.02)	2.54 (2.04, 3.11)▲▲▲	2.73 (2.18, 3.33)	2.27 (1.62, 2.74)	2.77 (2.22, 3.35)▲▲▲
Ca (mmol/l)	2.16 ± 0.13	2.10 ± 0.16	2.17 ± 0.12▲▲▲	2.18 ± 0.12	2.09 ± 0.16	2.19 ± 0.11▲▲▲
TG (mmol/l)	1.39 (0.99, 2.02)	1.19 (0.92, 1.77)	1.40 (1.00, 2.03)▲▲▲	1.49 (1.00, 2.15)	1.32 (0.79, 1.77)	1.52 (1.01, 2.18)▲▲
HDL-C (mmol/l)	1.14 ± 0.26	1.16 ± 0.30	1.14 ± 0.25	1.04 (0.91, 1.21)	0.96 (0.86, 1.27)	1.04 (0.9, 1.21)
CK (U/l)	642 (172, 1864)	1009 (287, 3204)	635 (168, 1819)▲▲▲	495 (169, 1645)	1024 (198, 3939)	487 (167, 1600)▲
Cr (μmol/l)	77 (65, 93)	105 (77, 156)	76 (65, 91)▲▲▲	79 (66, 97)	117 (90, 175)	77 (65, 94)▲▲▲
K (mmol/l)	3.99 ± 0.37	4.18 ± 0.64	3.98 ± 0.35▲▲▲	3.99 (3.80, 4.22)	4.13 (3.91, 4.62)	3.99 (3.79, 4.20)▲▲
ALP (U/l)	86 (72, 102)	87 (72, 107)	86 (72, 102)	80 (68, 96)	88 (72, 106)	79 (68, 95)▲
P (mmol/l)	1.02 (0.87, 1.16)	1.18 (0.94, 1.52)	1.01 (0.87, 1.15)▲▲▲	1.02 (0.89, 1.16)	1.19 (0.88, 1.64)	1.02 (0.89, 1.15)▲▲▲
CL (mmol/l)	104 (102, 106)	99 (103, 105)	104 (102, 106)▲▲▲	105 ± 4	105 ± 4	105 ± 3
Mg (mmol/l)	0.87 (0.82, 0.94)	0.86 (0.80, 1.00)	0.87 (0.82, 0.94)	0.82 (0.77, 0.88)	0.82 (0.75, 0.90)	0.82 (0.77, 0.88)
Na (mmol/l)	140 (138, 142)	140 (137, 143)	140 (138, 142)	140 (138, 142)	141 (138, 144)	140 (138, 141)▲▲
BUN (mmol/l)	5.76 (4.50, 7.53)	9.10 (6.32, 12.84)	5.65 (4.44, 7.33)▲▲▲	5.65 (4.44, 7.58)	9.81 (6.88, 14.88)	5.56 (4.37, 7.20)▲▲▲
UA (μmol/l)	342 (275, 420)	410 (332, 540)	339 (273, 416)▲▲▲	387 ± 127	462 ± 171	382 ± 122▲▲▲
GLU (mmol/l)	6.20 (5.30, 7.92)	8.41 (6.60, 11.41)	6.13 (5.29, 7.70)▲▲▲	6.07 (5.24, 8.12)	7.14 (5.57, 10.07)	6.03 (5.21, 7.95)▲▲
PA (mg/dl)	22.3 ± 6.4	16.9 ± 6.0	22.6 ± 6.3▲▲▲	22.8 ± 6.3	17.3 ± 6.3	23.1 ± 6.2▲▲▲
LDH (U/l)	436 (252, 749)	715 (431, 1224)	425 (247, 728)▲▲▲	387 (250, 684)	645 (365, 2109)	380 (242, 661)▲▲▲
AST (U/l)	102 (40, 238)	246 (73, 524)	98 (39, 228)▲▲▲	82 (37, 202)	256 (42, 808)	78 (36, 187)▲▲▲
ADA (U/l)	8 (7, 10)	10 (8, 13)	8 (7, 10)▲▲▲	10 (8, 13)	15 (11, 25)	10 (8, 13)▲▲▲
APOAI (g/l)	1.29 ± 0.26	1.18 ± 0.31	1.29 ± 0.26▲▲▲	1.19 ± 0.25	1.03 ± 0.30	1.20 ± 0.30▲▲▲
APOB (g/l)	0.98 ± 0.28	0.89 ± 0.21	0.99 ± 0.28▲▲▲	0.87 (0.70, 1.08)	0.67 (0.51, 0.90)	0.88 (0.72, 1.09)▲▲▲
TC (mmol/l)	4.49 (3.78, 5.21)	4.13 (3.34, 5.01)	4.49 (3.81, 5.22)▲▲▲	4.58 (3.85, 5.42)	3.88 (3.00, 4.88)	4.61 (3.87, 5.45)▲▲▲
TBil (μmol/l)	13.0 (9.5, 17.8)	15.0 (10.2, 21.1)	12.9 (9.5, 17.6)▲▲▲	15.4 (11.6, 20.4)	14.8 (11.0, 20.5)	15.5 (11.7, 20.38)
TBA (μmol/l)	3.0 (1.7, 5.4)	2.40 (1.35, 5.20)	3.10 (1.70, 5.42)▲▲	2.5 (1.5, 4.4)	2.0 (0.9, 5.1)	2.5 (1.5, 4.3)
TP (g/l)	64 ± 6	62 ± 8	64 ± 6▲▲▲	63 ± 6	60 ± 1	64 ± 6▲▲▲
PT (S)	13.8 (13.3, 14.4)	14.9 (13.9, 16.5)	13.8 (13.3, 14.3)▲▲▲	12.8 (12.2, 13.5)	14.4 (13.3, 16.5)	12.8 (12.2, 13.4)▲▲▲
APTT (S)	41.7 (38.0, 46.9)	46.2 (39.6, 64.9)	41.5 (37.9, 46.5)▲▲▲	36.8 (31.2, 42.3)	41.7 (37.1, 51.0)	36.5 (30.9, 41.9)▲▲▲
FIB (g/l)	3.88 (3.25, 4.78)	4.38 (3.33, 5.85)	3.87 (3.25, 4.73)▲▲▲	3.42 (2.85, 4.13)	4.01 (3.06, 4.61)	3.38 (2.83, 4.09)▲▲▲
TT (S)	17.0 (16.0, 19.2)	17.6 (15.9, 26.1)	17.0 (16.0,19.1)▲▲	18.3 (17.2, 20.2)	19.0 (17.7, 33.3)	18.2 (17.2, 20.0)▲▲
DD (mg/l)	0.42 (0.27, 0.81)	1.54 (0.79, 4.38)	0.41 (0.26, 0.74)▲▲▲	0.40 (0.23, 0.90)	2.39 (1.10, 8.18)	0.38 (0.23, 0.78)▲▲▲
cTnI (ng/mL)	16.9 (3.6, 54.4)	35.6 (11.4, 78.0)	16.1 (3.3, 53.2)▲▲▲	9.08 (2.15, 39.4)	24.3 (4.08, 69.0)	9.0 (2.0, 37.7)
BNP (pg/mL)	258 (118, 580)	1038 (436, 2493)	243 (114, 533)▲▲▲	280 (117, 679)	1900 (367, 3623)	264 (113, 630)▲▲▲
Sex, n (%)						
Male	3513 (73.4)	149 (55.0)	3364 (74.6)▲▲▲	794 (75.4)	37 (58.7)	757 (76.5)▲▲
Female	1270 (26.6)	122 (45.0)	1148 (25.4)	259 (24.6)	26 (41.3)	233 (23.5)
STEMI, n (%)						
Yes	3665 (76.6)	242 (89.3)	3423 (75.9)▲▲▲	921 (87.5)	59 (93.7)	862 (87.1)
No	1118 (23.4)	29 (10.7)	1089 (24.1)	132 (12.5)	4 (6.3)	128 (12.9)
Atrial fibrillation, n (%)						
Yes	372 (7.8)	50 (18.5)	322 (7.1)▲▲▲	78 (7.4)	13 (20.6)	65 (6.6)▲▲▲
No	4411 (92.2)	221 (81.5)	4190 (92.9)	975 (92.6)	50 (79.4)	925 (93.4)
Heart failure, n (%)						
Yes	72 (1.5)	21 (7.7)	51 (1.1)▲▲▲	133 (12.6)	33 (52.4)	100 (10.1)▲▲▲
No	4711 (98.5)	250 (92.3)	4461 (98.9)	920 (87.4)	30 (47.6)	890 (89.9)
Cardiac arrest, n (%)						
Yes	56 (1.2)	39 (14.4)	17 (0.4)▲▲▲	13 (1.2)	8 (12.7)	5 (0.5)▲▲▲
No	4727 (98.8)	232 (85.6)	4495 (99.6)	1040 (98.8)	55 (87.3)	985 (99.5)
Cardiogenic shock, n (%)						
Yes	148 (3.1)	87 (32.1)	61 (1.4)▲▲	32 (3.0)	18 (28.6)	14 (1.4)▲▲▲
No	4635 (96.9)	184 (67.9)	4451 (98.6)	1021 (97.0)	45 (71.4)	976 (98.6)
Arrhythmias, n (%)						

(*continued on next page*)

Table 1 (*continued*)

	Hospital I			Hospital II		
	Total (n = 4783)	Deceased (n = 271)	Survived (n = 4512)	Total (n = 1053)	Deceased (n = 63)	Survived (n = 990)
Yes	323 (6.8)	31 (11.4)	292 (6.5)▲▲▲	147 (14.0)	9 (14.3)	138 (13.9)
No	4460 (93.2)	240 (88.6)	4220 (93.5)	906 (86.0)	54 (85.7)	852 (86.1)
Pulmonary infection, n (%)						
Yes	457 (9.6)	67 (24.7)	390 (8.6)▲▲▲	145 (13.8)	31 (49.2)	114 (11.5)▲▲▲
No	4326 (90.4)	204 (75.3)	4122 (91.4)	908 (86.2)	32 (50.8)	876 (88.5)
COPD, n (%)						
Yes	150 (3.1)	14 (5.2)	136 (3.0)▲	92 (8.7)	9 (14.3)	83 (8.4)
No	4633 (96.9)	257 (94.8)	4376 (97.0)	961 (91.3)	54 (85.7)	907 (91.6)
Renal dysfunction, n (%)						
Yes	461 (9.6)	113 (41.7)	348 (7.7)▲▲▲	168 (16.0)	20 (31.7)	148 (14.9)▲▲▲
No	4322 (90.4)	158 (58.3)	4164 (92.3)	885 (84.0)	43 (68.3)	842 (85.1)
Stroke, n (%)						
Yes	512 (10.7)	55 (20.3)	457 (10.1)▲▲▲	122 (11.6)	12 (19.0)	110 (11.1)
No	4271 (89.3)	216 (79.7)	4055 (89.9)	931 (88.4)	51 (81.0)	880 (88.9)
Diabetes, n (%)						
Yes	1246 (26.1)	76 (28.0)	1170 (25.9)	369 (35.0)	27 (42.9)	342 (34.5)
No	3537 (73.9)	195 (72.0)	3342 (74.1)	684 (65.0)	36 (57.1)	648 (65.5)
Hypertension, n (%)						
Yes	2568 (53.7)	150 (55.4)	2418 (53.6)	602 (57.2)	38 (60.3)	564 (57.0)
No	2215 (46.3)	121 (44.6)	2094 (46.4)	451 (42.8)	25 (39.7)	426 (43.0)
Fatty liver						
Yes	697 (14.6)	6 (2.2)	691 (15.3)▲▲▲	223 (21.2)	1 (1.6)	222 (22.4)▲▲▲
No	4086 (85.4)	265 (97.8)	3821 (84.7)	830 (78.8)	62 (98.4)	768 (77.6)
Abnormal LFTs, n (%)						
Yes	316 (6.6)	41 (15.1)	275 (6.1)▲▲▲	18 (1.7)	1 (1.6)	17 (1.7)
No	4467 (93.4)	230 (84.9)	4237 (93.9)	1035 (98.3)	62 (98.4)	973 (98.3)
Hyperlipidemia, n (%)						
Yes	126 (2.6)	3 (1.1)	123 (2.7)	182 (17.3)	1 (1.6)	181 (18.3)▲▲
No	4657 (97.4)	268 (98.9)	4389 (97.3)	871 (82.7)	62 (98.4)	809 (81.7)

Notes: ▲Means a P value < 0.05; ▲▲Means a P value < 0.01; ▲▲▲Means a P value < 0.001.

*__Abbreviations__: no. (%), number; White blood cell count, WBC; Monocytes, MONO; Red blood cell volume distribution width, RDW; Hematocrit, HCT; Lymphocyte, LYM; Mean corpusular volume, MCV; Mean corpusular hemoglobin, MCH; Mean corpusular hemoglobin concerntration, MCHC; Mean platelet volume, MPV; Basophil, Baso; Eosinophil, Eos; Hemoglobin, Hb; Platelet distribution width, PDW; Platelet count, PLT; Plateletocrit, PCT; Neutrophil, NEUT; Red blood cell, RBC; γ-glutamyl transpeptidase, GGT; Albumin, ALB; Alanine aminotransferase, ALT; C-reactive protein, CRP; Low-density lipoprotein cholesterol, LDL-C; Calcium, Ca; Triglycerides, TG; High-density lipoprotein cholesterol, HDL-C; Creatine kinase, CK; Creatinine, Cr; Potassium, K; Alkaline phosphatase, ALP; Phosphorus, P; Chlorine, CL; Magnesium, Mg; Sodium, Na; Blood urea nitrogen, BUN; Uric acid, UA; Glucose, GLU; Prealbumin, PA; Lactate dehydrogenase, LDH; Aspartate aminotransferase, AST; Adenosine deaminase, ADA; Apolipoprotein AI, APOAI; Apolipoprotein B, APOB; Total cholesterol, TC; Total bilirubin, TBil; Total bile acid, TBA; Total protein, TP; Prothrombin time, PT; Activated partial thromboplastin time, APTT; Fibrinogen, FIB; Thrombin time, TT; D-Dimer, DD; Cardiac troponin I, cTnI; Brain natriuretic peptide, BNP; ST-segment elevation myocardial infarction, STEMI; Chronic obstructive pulmonary disease, COPD; Liver function tests, LFTs.

100, a shrinkage factor of 0.80, and the apparent R^2 Nagelkerke's optimism was 0.05. The sample size required for the training set in this study was 1061. However, the sample size of our training set reached 3587. All clinical information of the patients in this study was complete, and the missing laboratory test indicators ranged from 0.1 % to 12.9 %. The Scikit-learn's sklearn.imple.IterativeInput function was used to fill in missing values. The main function of this function is to estimate and fill in null values in the data based on BayesianRidge, thereby making the dataset complete and more consistent and boosting the performance of machine learning models. Gender, ST-segment elevation myocardial infarction (STEMI), atrial fibrillation, heart failure, cardiac arrest, cardiogenic shock, arrhythmias, pulmonary infection, COPD, renal dysfunction, stroke, diabetes, hypertension, fatty liver, abnormal liver function tests (LFTs), hyperlipidemia, and the patient's survival status (alive or dead) are binary variables. The Age, white blood cell count (WBC), monocytes (MONO), red blood cell volume distribution width (RDW), hematocrit (HCT), lymphocyte (LYM), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), basophil (Baso), eosinophil (Eos), hemoglobin (Hb), platelet distribution width (PDW), platelet count (PLT), plateletcrit (PCT), neutrophil (NEUT), red blood cell (RBC), γ-glutamyl transpeptidase (GGT), albumin (ALB), alanine aminotransferase (ALT), C-reactive protein (CRP), low-density lipoprotein cholesterol (LDL-C), calcium (Ca), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), creatine kinase (CK), creatinine (Cr), potassium (K), alkaline phosphatase (ALP), phosphorus (P), chlorine (CL), magnesium (Mg), sodium (Na), blood urea nitrogen (BUN), uric acid (UA), glucose (GLU), prealbumin (PA), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), adenosine deaminase (ADA), apolipoprotein AI (APOAI), apolipoprotein B (APOB), total cholesterol (TC), total bilirubin (TBil), total bile acid (TBA), total protein (TP), prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (FIB), thrombin time (TT), D-Dimer (DD), cTnI, BNP were used as the continuous variables. Using training group data to screen important variables for model through BorutaShap, 7 machine learning classifiers were trained based on the training set (3587 patients; Fig. 1): LR, RF, XGB, SVM, MLP, GBM, Bagging. In each model, manual parameter tuning, grid search, random search, and fivefold cross-validation executed utilizing the training dataset. Following this, an assessment was conducted on the performance of each model utilizing a testing dataset (1196 patients; Fig. 1). The evaluation indicators of all models included sensitivity, specificity, positive predictive value, negative predictive value, calibration plots, the area under the receiver operating characteristic curve (AUROC), and the area under the precision-recall curve (Average Precision; AP). Furthermore, the best-performing model was selected to ascertain the risk factors most related to in-hospital mortality interpreted by the Shapley Additive exPlanations (SHAP) method. The SHAP value visually conveyed each feature's contribution to in-hospital mortality. Moreover, data from Hospital II were used as external validation (1053 patients) to assess the prediction model's performance, and the AUROC was conducted to evaluate the clinical application and the consistency of the predictive probabilities.

2.4. Statistical analysis

To compare baseline parameters between survived and deceased, the Independent Sample *t*-test was used when the data was normally distributed and expressed as mean standard deviation. A Mann–Whitney *U* test was used when the data was not normally distributed and expressed as p50% (p25%, p75%). The differences between categorical variables were compared using the Chi-Squared test. The above statistical analysis was conducted using SPSS (version 24.0). The differences in parameters in the training, testing, and validation sets in Table 2 and the BorutaShap algorithms were conducted by R (version 4.1.3, Austria). The machine learning algorithms, SHAP, the receiver operating characteristic curve (ROC), and the precision-recall (P-R) curve were implemented via Python (version 3.9.12). A two-tailed P value < 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

The data for this study was garnered from a total of 5836 AMI patients from two centers (Hospital I and Hospital II). The exclusion and inclusion processes are depicted in Fig. 1 and in the Methods section. The in-hospital mortality of Hospital I was 5.7 %. The basic information about the two hospitals and the baseline characteristics of the in-hospital death and survival groups are listed in Table 1; the 70 variables in Table 1 will be used for subsequent variable screening. Hospital I (n = 4783) in this study was divided into training (n = 3587) and testing (n = 1196) sets, while hospital II served as the external validation (n = 1053) set. The prevalence of mortality was 5.7 % in the training population, 5.6 % in the testing population, and 6.0 % in the further validation population. There was no statistically significant difference between these three groups of AMI patients regarding hospitalization mortality ($P = 0.917$, Table 2).

Table 2
The in-hospital mortality of AMI patients and 8 important indicators screened by the BorutaShap algorithm in the Training, Testing, and Validation sets.

Variables	Training (n = 3587)	Testing (n = 1196)	Validation (n = 1053)	*P* Value
DD (mg/l)	0.44 (0.28, 0.88)	0.45 (0.27, 0.89)	0.44 (0.24, 1.00)	NS
BNP (pg/ml)	260 (117, 598)	277 (127, 610)	385 (157, 793)	< 0.001
BUN (mmol/l)	5.77 (4.50, 7.53)	5.74 (4.54, 7.5)	5.71 (4.45, 7.59)	NS
NEUT (109/l)	6.6 (4.7, 8.9)	6.5 (4.7, 8.9)	6.6 (4.7, 9.0)	NS
PT (S)	13.8 (13.3, 14.4)	13.8 (13.3, 14.4)	12.8 (12.2, 13.4)	< 0.001
P (mmol/l)	1.02 (0.88, 1.16)	1.02 (0.88, 1.17)	1.02 (0.89, 1.16)	NS
Cardiac arrest, n (%)				NS
Yes	42 (1.2)	14 (1.2)	13 (1.2)	
No	3545 (98.8)	1182 (98.8)	1040 (98.8)	
Cardiogenic shock, n (%)				NS
Yes	110 (3.1)	38 (3.2)	32 (3.0)	
No	3477 (96.9)	1158 (96.8)	1021 (97.0)	
Death, n (%)				NS
Yes	204 (5.7)	67 (5.6)	63 (6.0)	
No	3383 (94.3)	1129 (94.4)	990 (94.0)	

Notes: The laboratory indicators are represented by P_{50} (P_{25}, P_{75}).
*__Abbreviations__: no. (%), number; Neutrophil, NEUT; Phosphorus, P; Blood urea nitrogen, BUN; Prothrombin time, PT; D-Dimer, DD; Brain natriuretic peptide, BNP; No significance, NS.

3.2. Feature selection

This study used training data to screen model variables using the BorutaShap algorithm; the screening of 70 variables for this study is shown in Fig. 2. According to the Z-value and clinical significance of variables, the top 8 variables most relevant to the AMI in-hospital mortality variable are DD, Cardiogenic shock, BNP, BUN, Cardiac arrest, NEUT, PT, and P. The baseline situation of these 8 variables in the training, testing, and validation groups is listed in Table 2. These 8 variables were selected for the machine learning model development process.

3.3. Machine learning model development and evaluation

Seven machine learning models were generated to predict the in-hospital mortality in AMI patients. All the 7 models performed well in the training set, the AUROCs were LR model = 0.922, RF model = 0.957, XGB model = 0.965, SVM model = 0.827, MLP model = 0.918, GBM model = 0.958, Bagging model = 0.959. Regarding the testing dataset, the performance evaluation of these 7 algorithms is detailed in Table 3 and Fig. 3. Fig.s 3A and 3B showcase the discrimination performance of these machine learning models via ROC and precision-recall curves in the test set. All models achieved high AUROCs (between 0.884 and 0.932), high sensitivities (between 0.821 and 0.896), high specificities (between 0.833 and 0.876), and high NPVs (between 0.988 and 0.993). The AP of all models lies between 0.48 and 0.63.

3.4. Machine learning model selection

It can be inferred from Table 3 and Fig. 3 that the Bagging model exhibits the highest AUC (0.932 [95 %CI: 0.918, 0.946]) in the testing set, with a sensitivity of 0.881 (95 %CI: 0.806, 0.955), a specificity of 0.864 (95 %CI: 0.844, 0.884), and a negative predictive value of 0.992 (95 %CI: 0.986, 0.997). The Bagging also has the highest AP (0.63). Therefore, the Bagging algorithm was selected for model construction.

3.5. Visualization by SHAP

The SHAP algorithm was used to visually display the importance of each factor in predicting in-hospital mortality using the Bagging model. Fig. 4A depicts the feature importance graph, displaying the 8 most important variables related to in-hospital mortality in descending order. The average absolute value of SHAP 8 indicators is 0.0273, 0.0141, 0.0119, 0.0111, 0.0109, 0.0079, 0.0079, and 0.0069, respectively. DD has the strongest predictive power, followed by BNP and Cardiogenic shock. Fig. 4B shows the graph plots and the SHAP values of each feature for each sample, one point per sample. Each row in the Fig. represents a feature, with the horizontal axis representing the SHAP value. The color represents the feature value, indicating whether the feature is high (red) or low (blue). The DD has a risk impact on in-hospital mortality. A single-sample feature influence map is also depicted in Fig. 5. In this Fig., the features are represented as forces (arrows) that push the predicted results (black bars with bold numbers above) towards the positive or negative direction. The length of the arrow is proportional to its Shapley value. The color of the arrow corresponds to the positive or negative influence of the feature.

3.6. External validation

We used AMI patients from Hospital II as an external validation dataset to verify the predictive accuracy of the selected Bagging model, Bagging had good predictive values with the AUROC of 0.893 (95 %CI: 0.874, 0.912), while the sensitivity and specificity were 0.888 and 0.841, respectively. In addition, based on the Bagging model, an application software program was developed for the 8 most important predictive factors to evaluate the risk of in-hospital mortality in AMI

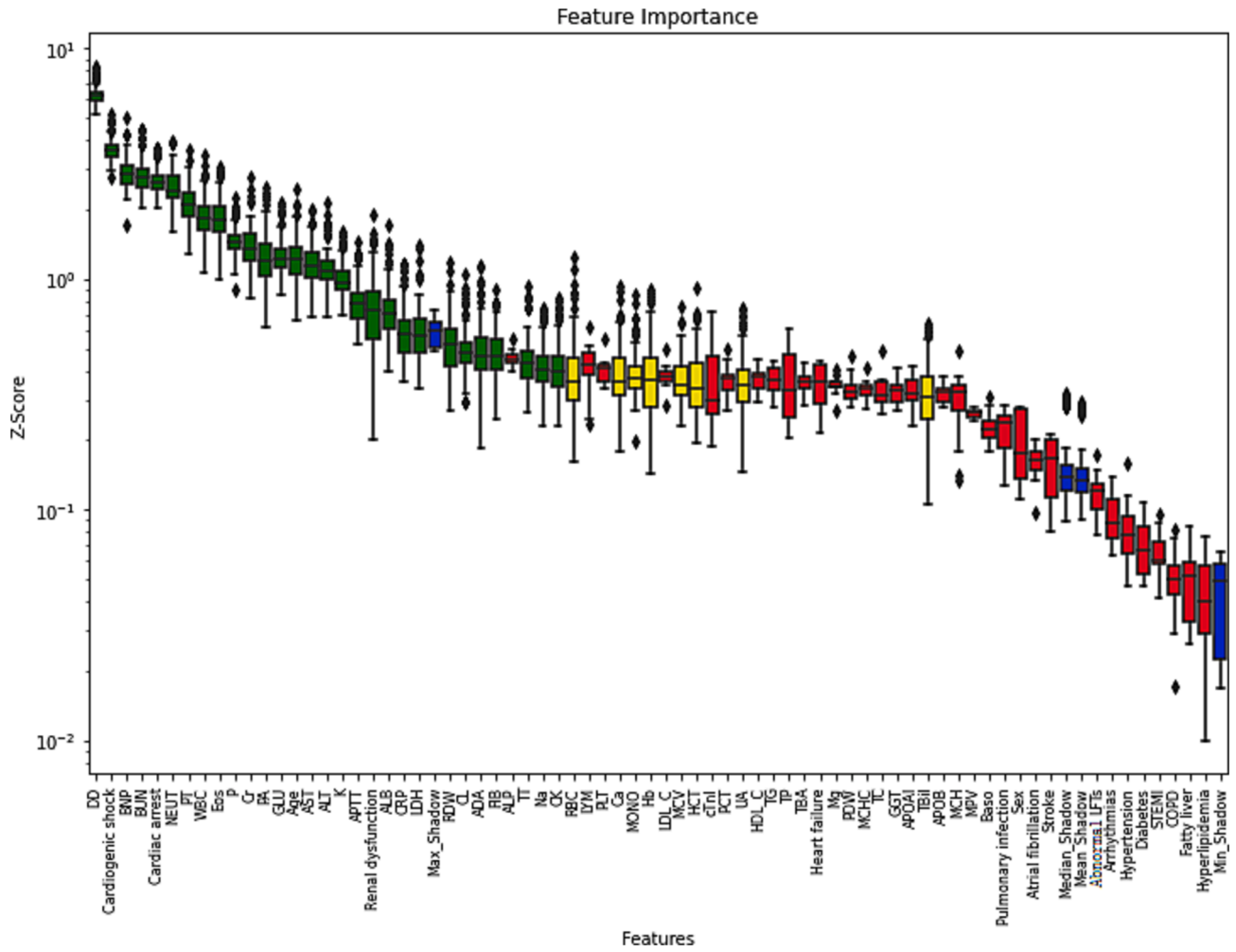

Fig. 2. The Borutashap algorithm was used for feature selection analysis. The horizontal axis displays the names of each variable, while the vertical axis displays the corresponding Z values of each variable. Each variable is arranged in descending order based on the Z value from left to right.

Table 3
Performance evaluation of each machine model based on the testing set.

Model	AUC (95 % CI)	Sensitivity (95 % CI)	Specificity (95 % CI)	PPV (95 % CI)	NPV (95 % CI)	Youden Index
LR	0.929 (0.914, 0.944)	0.896 (0.821, 0.955)	0.833 (0.811, 0.855)	0.241 (0.189, 0.293)	0.993 (0.987, 0.998)	0.728
RF	0.931 (0.917, 0.945)	0.881 (0.806, 0.955)	0.876 (0.857, 0.895)	0.296 (0.231, 0.362)	0.992 (0.986, 0.997)	0.757
XGB	0.916 (0.900, 0.932)	0.881 (0.806, 0.955)	0.865 (0.845, 0.885)	0.280 (0.223, 0.341)	0.992 (0.986, 0.997)	0.746
SVM	0.884 (0.866, 0.902)	0.821 (0.731, 0.910)	0.864 (0.844, 0.884)	0.264 (0.207, 0.327)	0.988 (0.981, 0.994)	0.685
MLP	0.907 (0.891, 0.923)	0.851 (0.761, 0.925)	0.848 (0.826, 0.869)	0.249 (0.192, 0.306)	0.990 (0.983, 0.996)	0.698
GBM	0.923 (0.908, 0.938)	0.881 (0.806, 0.955)	0.864 (0.844, 0.884)	0.277 (0.216, 0.338)	0.992 (0.986, 0.997)	0.744
Bagging	0.932 (0.918, 0.946)	0.881 (0.806, 0.955)	0.864 (0.844, 0.884)	0.277 (0.216, 0.338)	0.992 (0.986, 0.997)	0.744

Abbreviations: Confdence interval, CI; Logistic Regression Classifer, LR; Random Forests Classifer, RF; eXtreme Gradient Boosting, XGB; Support Vector Machine Classifer, SVM; Multilayer Perceptron, MLP; Gradient Boosting Machine, GBM; Bootstrapped Aggregation, Bagging; Positive predictive value, PPV; Negative predictive value, NPV.

patients. After admission, the chance of in-hospital mortality for each patient can be computed, with a predetermined threshold of 0.0648. (Fig. 6).

4. Discussion

We developed a predictive model for in-hospital mortality in patients with AMI by utilizing machine learning techniques and integrating laboratory data and clinical information. The most significant relevant factors for forecasting death in hospitals following AMI have been identified. The Bagging model has the highest AUROC among the seven machine models for prediction. The superiority of our model has been further proven through external evaluation.

Several studies are currently using machine learning to diagnose, differentiate, and forecast the short- and long-term fatality rates in AMI. Utilizing ferroptosis-related genes (FRGs) as indicators, Huang et al. created the optimal model for predicting early AMI using machine learning techniques, thereby identifying possible molecular targets for the optimal treatment of AMI [18]. Zhu et al. garnered 6 datasets from the Gene Expression Omnibus (GEO) database and used machine learning methods to identify immune-related genes and construct diagnostic models, which revealed that immune-related genes and immune cells are closely related to AMI [19]. Using machine learning, a study established a completely automated real-time system for

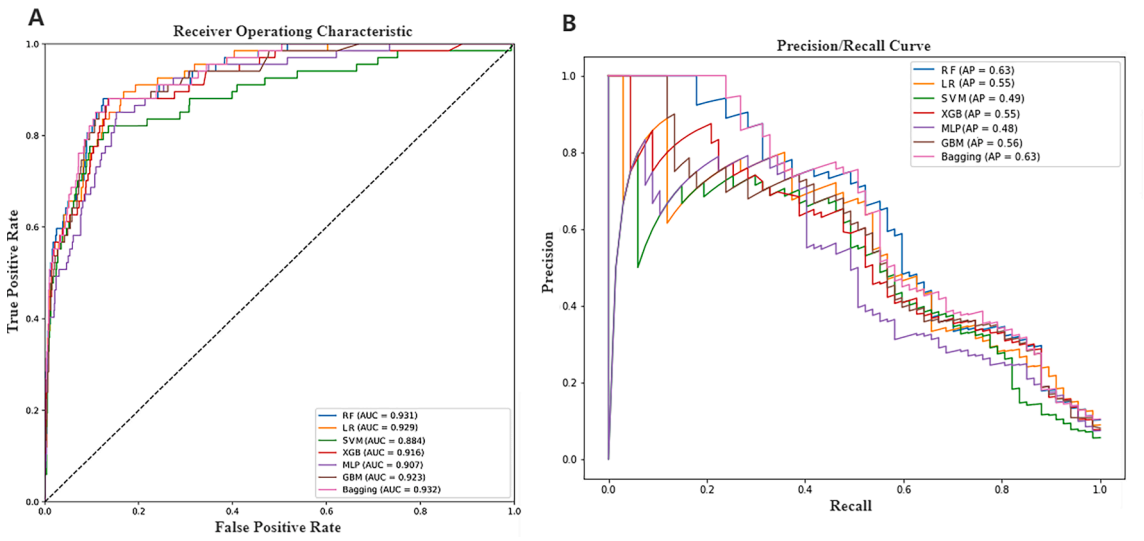

Fig. 3. Discrimination performance of seven machine learning models. A: ROC of seven machine learning models. B: P-R curves of seven machine learning models.

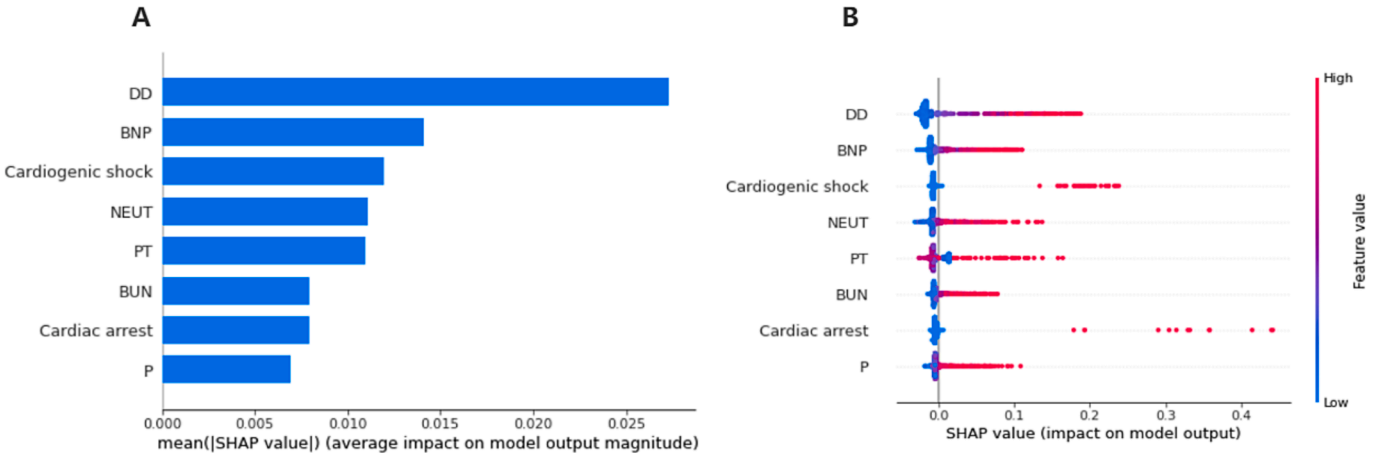

Fig. 4. SHAP analysis results. A: The bar chart ranks the importance of the top 8 important variables most related to AMI in-hospital mortality in the Bagging model. B: The impact of SHAP values on the in-hospital mortality of AMI inpatients in the Bagging model.

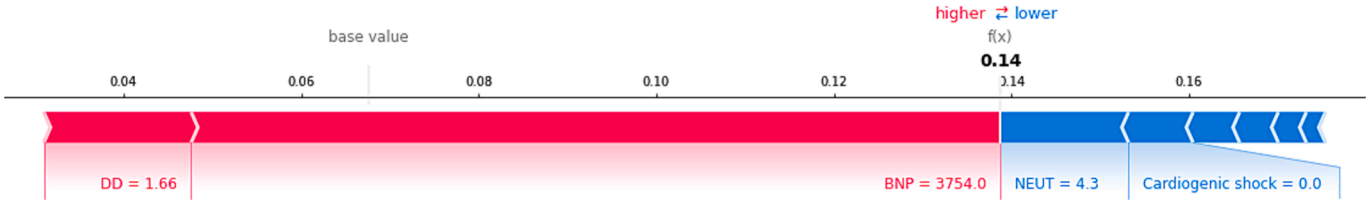

Fig. 5. Force plot of SHAP values for a single patient.

evaluating echocardiogram films, including Takotsubo syndrome (TTS) and AMI [20]. Cai et al. developed a machine learning prediction model for identifying acute kidney injury (AKI) in AMI patients using machine learning algorithms, which can be used to accurately identify AKI risk in AMI patients [21]. Zhao et al. used machine learning to predict bleeding after percutaneous coronary intervention (PCI) in AMI patients [22]. These machine learning methods can automatically select combinations of important features [22], enabling efficient and accurate evaluation and prediction of disease courses and providing better scientific guidance for clinical practice. A large nationally registered cohort study in the United States predicted AMI in-hospital mortality based on patient comorbidities, medical history, presentation characteristics, and initial laboratory values. The study developed and validated three machine learning models (XGBoost, a neural network, and a metaclassifier model.), suggesting that XGBoost and *meta*-classifier models are superior in identifying high-risk populations compared to logistic regression [23]. Three studies were conducted in a hospital in Portugal using various machine learning techniques to predict AMI in-hospital mortality. These three experiments used different numbers and types of variables, resulting in different optimal machine models, suggesting that there is no universal method for predicting AMI mortality [24]. These findings illustrate that in different conditions, such as variations in race and region, the included population, and factors, the conclusions produced from machine learning vary. On the one hand, machine learning

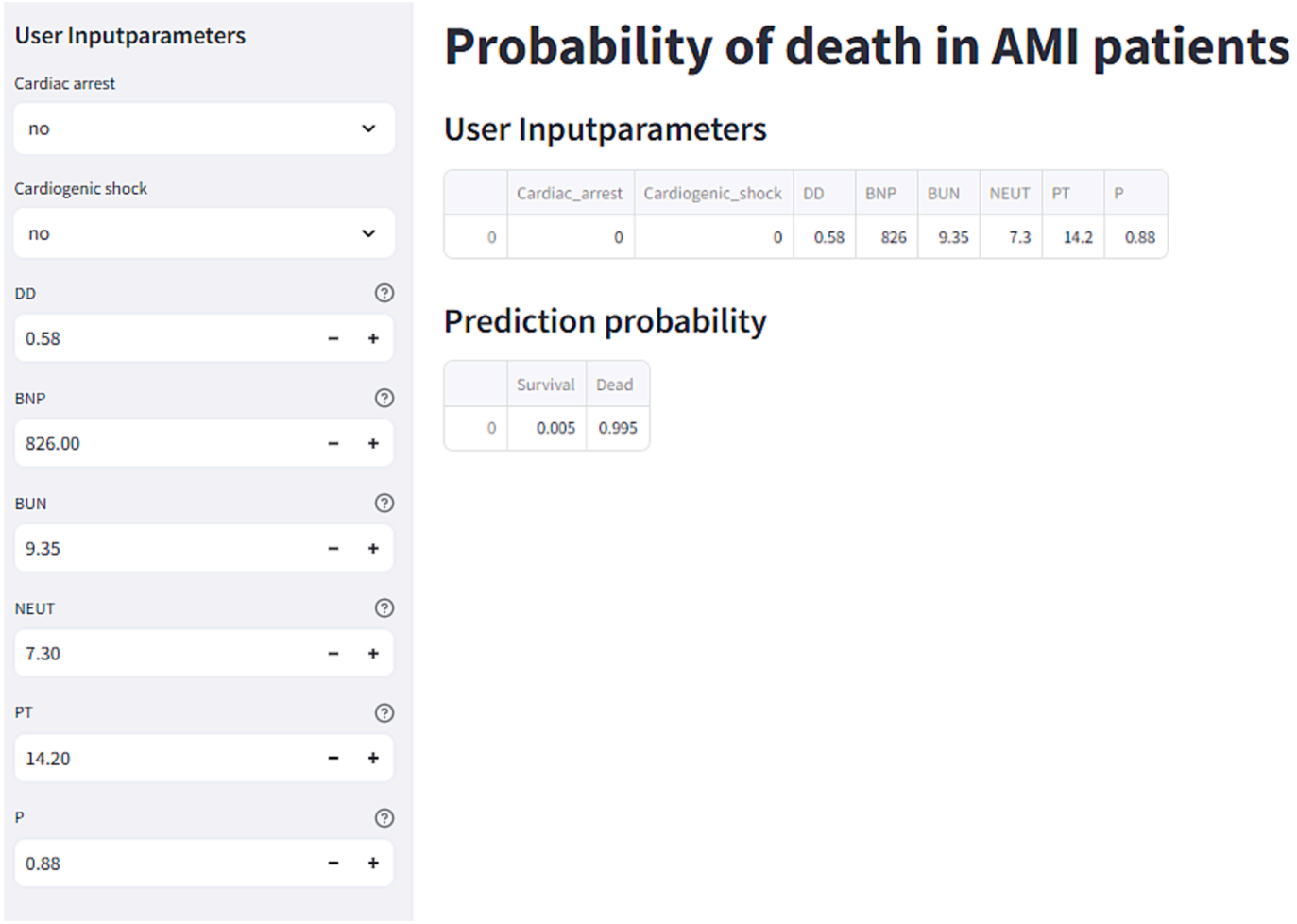

Fig. 6. An example of the application software for predicting in-hospital mortality risk in AMI patients.

can completely analyze the characteristic variables of diseases, while on the other, clinical doctors must be able to discern the actual condition. Therefore, research utilizing machine learning in healthcare will help to determine which data clustering and prediction methods are most beneficial and suited for clinical implementation [25].

This study screened 8 of the most important characteristic indicator variables from 70 variables, including Cardiac arrest, DD, BNP, Cardiogenic shock, BUN, NEUT, PT, and P. Cardiogenic shock and cardiac arrest are common complications of AMI, and studies have shown a correlation between cardiogenic shock and in-hospital mortality in AMI [26]. According to studies, AMI patients who experience cardiac arrest during hospitalization have a higher 30-day all-cause death rate [27]. Other studies have demonstrated that AMI exacerbated by cardiac arrest and cardiogenic shock is associated with a poor prognosis for long-term survival [28]. The role of BNP in the diagnosis and risk stratification of HF has been widely proven [29]. For AMI patients undergoing PCI, serum BNP concentrations are an independent risk factor for major adverse cardiovascular events (MACE) [30], and serum BNP is also considered an independent risk factor for in-hospital mortality in non-ST-elevation AMI patients [31]. Due to the fact that AMI is a severe cardiovascular disease caused by transient or persistent ischemia and hypoxia of the coronary artery, coagulation function is crucial to this process. Patients with chest pain diagnosed with AMI in the emergency department have increased D-dimer concentrations at the time of treatment. Increased D-dimer concentrations at admission are a major prognostic marker for adverse cardiovascular events and bleeding [32]. Other studies have shown that PT is an independent predictor of 2-year mortality in AMI patients, which may help identify AMI patients with high mortality rates [33]. High BUN concentrations can considerably predict poor prognosis in patients with acute decompensated heart failure and in-hospital mortality [34]. Moreover, BUN at admission is an independent predictor of long-term cardiovascular mortality in AMI patients, helping to identify high-risk patients [35]. Higher serum phosphorus independently increases the risk of in-hospital all-cause mortality and cardiac mortality following AMI [36]. A prediction model for hospitalization mortality in patients with severe acute myocardial infarction (AMI) in the coronary artery monitoring unit (CCU) identified WBC, RDW-CV, and NEUT percentage as the three most important predictors [37]. Other studies have shown that WBC, NEUT, eosinophil count, and eosinophil/white blood cell ratio can help predict the hospitalization mortality rate of AMI patients [38]. The aforementioned significant characteristic parameters are frequently detected items and clinically relevant indicators which is very conducive to clinical promotion and application.

Advantages: This study contained many factors, with a total of seventy clinical information and laboratory indicators. The eight chosen markers were the most prevalent in clinical practice, facilitating the clinical implementation and sharing of the study's findings. Secondly, 7 of the most classic machine models were compared, and the optimal method with efficient predictive ability was selected. Thirdly, this study involved two centers. Data from one of the centers was applied for external validation, and the validation results were excellent. This may be due to the fact that both hospitals are classified as Class A and Class 3 and employ comparable medical quality management approaches. The methods and time required to collect blood samples in the laboratory are identical, as are the testing instruments, check reagents, and operational

procedures. Limitations: First, this study's sample size is only 5836, which is significantly smaller than large-scale clinical trials conducted countrywide. Secondly, in Table 2, it can be inferred that there are variances in the concentrations of BNP and PT between the two centers, indicating a certain degree of heterogeneity in the data between the two centers. This may be due to different populations in the regions where the two hospitals are located and different processing methods for test result data in the two laboratories, such as threshold settings, quality control standards, etc. Moreover, there are disparities in death rates between hospitals of various concentrations in China. In this study, data from municipal tertiary hospitals was used. Additionally, both hospitals' data are from southern Chinese cities, which may introduce regional bias.

This study used 70 factors and 7 machine learning models to predict hospital mortality in AMI, and ultimately identified 8 most significant variables and the machine model Bagging. The overarching objective of these thorough assessments is to provide clinical practitioners with improved guidance, prioritize and attend to AMI patients who are at a heightened risk of mortality in the hospital, and ultimately decrease the in-hospital mortality rate among AMI patients.

5. Ethical approval and informed consent

This research did not affect the patients' health and privacy. All procedures performed in the studies involving human participants accorded with the ethical standards of the Medical Ethics Committee of Taizhou Hospital of Zhejiang Province (#K20230923) and Enze Hospital (#K20230814), and with the 1964 Helsinki Declaration and its later amendments, or other comparable ethical standards.

CRediT authorship contribution statement

Xiaoli Zhu: Writing – review & editing, Writing – original draft, Resources, Investigation, Data curation. **Bojian Xie:** Resources, Project administration, Formal analysis. **Yijun Chen:** Software, Methodology, Data curation. **Hanqian Zeng:** Validation, Resources, Project administration, Investigation, Formal analysis. **Jinxi Hu:** Writing – review & editing, Writing – original draft, Data curation.

Declaration of competing interest

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

Data availability

The authors do not have permission to share data.

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