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Early prognostication of critical patients with spinal cord injury：a machine learning study with 1485 cases

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Ethics approval and consent to participate:

This study protocol, which relies on two deidentified public database, was deemed exempt by the Institutional Review Board of our institution.

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Abstract

Study Design:

A retrospective case-series.

Objective:

The study aims to use machine-learning (ML) to predict the discharge destination of spinal cord injury (SCI) patients in the intensive care unit (ICU).

Summary of Background Data:

Prognostication following SCI is vital, especially for critical patients who need intensive care.

Methods:

Clinical data of patients diagnosed with SCI were extracted from a publicly available ICU database. The firstly recorded data of the included patients were used to develop a total of 98 ML classifiers, seeking to predict discharge destination (e.g. death, further medical care, home). The micro-average area under the curve (AUC) was the main indicator to assess discrimination. The best average-AUC classifier and the best death-sensitivity classifier were integrated into an ensemble classifier. The discrimination of the ensemble classifier was compared with top death-sensitivity classifiers and top average-AUC classifiers. Additionally, prediction consistency and clinical utility were also assessed.

Results:

A total of 1485 SCI patients were included. The ensemble classifier had a micro-average AUC of 0.851, which was only slightly inferior to the best average-AUC classifier (P=0.10) The best average-AUC classifier death sensitivity was much lower than that of the ensemble classifier. The ensemble classifier had a death sensitivity of 0.452, which was inferior to top 8 death-sensitivity classifiers, whose micro-average AUC were inferior to the ensemble classifier (P<0.05). Additionally, the ensemble classifier demonstrated a

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comparable Brier score and superior Net benefit in the decision curve analysis, when compared to the performance of the origin classifiers.

Conclusions:

The ensemble classifier shows an overall superior performance in predicting discharge destination considering discrimination ability, prediction consistency and clinical utility. This classifier system may aid in the clinical management of critical SCI patients in the early phase following injury.

Keywords:

Spinal cord injury; Machine learning; Intensive care unit; Critical care; prognostication

Level of Evidence:

3

Key points

1. A total of 98 initial machine-learning classifiers were successfully developed to predict a three-class discharge destination of critical patients with spinal cord injury.

2. The EmbeddingLSVC_lightGBM was the best average-AUC classifier and the MIC_lightGBM was the best death-sensitivity classifier.

3. An ensemble classifier was originated from the best average-AUC classifier and the best death-sensitivity classifier.

4. The ensemble classifier showed an overall superior performance in terms of discrimination ability, prediction consistency and clinical utility.

5. The ensemble classifier was associated with high applicability and interpretability.

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Introduction

The annual incidence of spinal cord injury (SCI) in industrialized countries ranges from 11.5 to 53.4/million[1]. With a prevalence of 583 per million[2], SCI results in a sizable economic burden to patients and society. More importantly, critical SCI patients may suffer from a higher mortality due to renal failure, respiratory failure, hemodynamic instability, sepsis from urinary tract infection, as well as life-threatening autonomic dys-reflexia[3-6].

Prognostication plays an important part in clinical practice, which can contribute to decision-making for clinical management and assist communication with the patients and their families. For critical patients in the intensive care unit (ICU), discharge destination may be one of the most important concerns[7,8]. SCI patients with severe complications may die in the hospital, and surviving patients may need further medical care (FMC) like long-term professional nursing and rehabilitation[3]. Thus, accurate prognostication is vital for critical SCI patients, although this may be challenging due to the heterogenous nature of SCI and substantial clinical variation[9].

Recently, the utility of machine learning (ML) has been shown in the fields of clinical and translational medicine[10-13]. ML is capable of identifying non-linear relationships between variables and predicting multi-class outcomes.[14]. However, different ML algorithms may show various prediction performance in diverse application scenarios, so an ensemble strategy can combine the merits of several selected ML classifiers[15]. The feasibility of ML for prognostication has been widely appreciated[16-18], and many studies have adopted ML to predict hospital discharge[19-21]. Knowledge of this outcome at the time of admission can optimize patient care [22], and initiation of care pathways, particularly around concerns for in-hospital mortality[23]. Therefore, we sought to develop ML classifiers using an ensemble strategy to enable the early prediction of discharge destination (e.g. death, FMC, home) among SCI patients who require intensive care admission.

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Methods

The ethical approval for this retrospective case-series study, which relies on two deidentified public databases, was obtained from the Institutional Review Board of our institutions. All clinical data in the current study were extracted from the Medical Information Mart for Intensive Care (MIMIC Database)[24] and the eICU Collaborative Research Database (eICU Database)[25]. The inclusion criteria of the study were: 1) diagnosis of spinal cord injury and at least one admission to the ICU; 2) clinical variables including demographics information, vital signs, laboratory tests, and intervention information; 3) from the MIMIC-III/IV database (2001-2019) or the eICU Database (2014-2015). The exclusion criteria were: 1) Subsequent admissions for ICU care; 2) Overlapping data between the MIMIC-III Database (2001-2012) and the MIMIC-IV Database (2008-2019); 3) Clinical variables with missing data over 70%.

Data extraction steps are depicted in **supplemental material** (**Supplemental Digital Content 1,** http://links.lww.com/BRS/C284**; Supplemental Digital Content 2,** http://links.lww.com/BRS/C285**)**. Demographic information included ethnicity, gender, age, and body mass index (BMI). Vital signs included respiration rate, heart rate, systolic and diastolic blood pressure, mean arterial pressure. Laboratory data consisted of white blood cell (WBC) count, red blood cell (RBC), platelet count, basophils, eosinophils, neutrophils, lymphocyte, monocyte, red blood cell distribution width (RDW), hemoglobin, hematocrit, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), partial pressure of oxygen (PO2), partial pressure of carbon dioxide (PCO2), fraction of inspiration oxygen (FiO2), potential of hydrogen (PH), bicarbonate, lactate, base excess (BE), anion gap, potassium, sodium, calcium, magnesium, chloride, phosphate, blood urea nitrogen (BUN), creatinine, albumin, and blood glucose. Medicine usage and treatment incorporated mechanical ventilation, morphine sulfate, cefazolin, potassium chloride (KCl), glucocorticoid, dopamine, dobutamine, epinephrine and norepinephrine. Missing data (<70%) were processed by different methods of imputation (Python package of scikit-learn 1.2.2) according to the variable type[26]. Predictive mean matching, logistic regression, and polynomial regression were used for continuous, binary and categorical features, respectively.

To develop ML classifiers via supervised learning, we randomly divided the included data into sub-datasets (training: validation: testing= 6:2: 2) with Python package of pandas 2.0.3. All training went through 3-time repeated 5-fold cross-validation with the training dataset, and all developed classifiers underwent independent testing using the testing dataset.

Seven common feature selection methods were conducted to identify useful variables for training ML classifiers. The feature selection methods included maximal information coefficient (MIC), recursive feature

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elimination (RFE), embedding linear supported vector classifier (embedding LSVC), embedding logistic regressor (embedding LR), embedding tree, embedding random forest (RF), and minimal-redundancy-maximal-relevance (mRMR).

The selected features were then used to train fourteen ML algorithms, namely logistic regression, linear discriminant analysis (LDA), support vector machine (SVM), K-Nearest Neighbor (KNN), Gaussian Naïve Bayes (NB), decision tree, extra tree, random forest (RF), bagging, adaptive boosting (AdaBoost), gradient boosting decision tree (GBDT), light gradient boosting model (lightGBM), extreme gradient boosting (XGBoost), and multilayer perceptron (MLP). As a result, a total of 98 prediction classifiers from 7×14 combinations were initially developed, and the early predictions of the discharge destination were trained with the firstly recorded data.

The prediction of all ML classifiers were conducted for a three-class outcome (e.g. death, FMC, home). The micro-average area under the curve (AUC) of the receiver operating characteristic (ROC) was the primary indicator to assess all ML classifiers. The sensitivity, specificity and precision (positive predictive value) of all predicted categories were also used to assess the discrimination of all ML classifiers. The best average-AUC classifier and the best death-sensitivity classifier in independent testing were combined into an ensemble classifier (**Figure 1A**). Additionally, the prediction consistency and the clinical utility of all classifiers were assessed with the calibration curve and decision curve analysis (DCA), respectively. The comparisons across the 98 ML classifiers and the ensemble classifier included the discrimination ability, the prediction consistency and the clinical utility (**Figure 1B**). To improve the interpretability of the ensemble classifiers, the included clinical predictors were rated by feature importance[27,28].

Categorical variables were expressed as count (percentage), and the chi-square test or Kruskal-Wallis method was used for statistical tests. Continuous variables were described as mean (standard deviations), and group differences were tested by one-way analysis of variance (ANOVA). AUC comparisons between different ML classifiers were assessed with the Delong test. All data was analyzed using Python 3.8. Two-

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sided P values of < 0.05 were considered statistically significant.

Results

We initially identified 1599 ICU admissions for 839 SCI patients from the MIMIC-III-IV database and 760 patients from the eICU database. After merging the two datasets and excluding patients with missing outcome (discharge destination), we were able to consider 1485 patients in our study cohort. Baseline characteristics of included patients for the early prediction are shown in **Table 1**, and other clinical variables are summarized in **Table 2**. In total, 67 variables were included. The data distributions of the MIMIC-III-IV database and the eICU database are summarized in supplemental **Table S1** (**Supplemental Digital Content 1,** http://links.lww.com/BRS/C284), and the percentage of missing values ranged from 0 to 60.5% (**Supplemental Digital Content 1**; **Table S2,** http://links.lww.com/BRS/C284).

The micro-average AUCs and the death sensitivity of all the initial 98 classifiers in the independent testing are shown as a matrix (**Figure 2A-B**). Among the initial 98 classifiers, the EmbeddingLSVC_lightGBM had the highest micro-average AUC (0.859) and the MIC_lightGBM demonstrated the best death sensitivity (0.613) in independent testing. Thus, the EmbeddingLSVC_lightGBM (the best average-AUC classifier) and the MIC_lightGBM (the best death-sensitivity classifier) were used as the two origin classifiers to create an ensemble classifier.

The ensemble classifier had a micro-average AUC of 0.851, which was only slightly inferior to the best average-AUC classifier (*P* = 0.097). The death sensitivity of the best average-AUC was much lower than the ensemble classifier (**Table 3**). Similarly, the ensemble classifier had a death sensitivity of 0.452, which was only inferior to top 8 death-sensitivity classifiers. whose micro-average AUC was inferior to the ensemble classifier (*P* <0.001; **Table 4**). As such, the ensemble classifier had a superior overall discrimination over its origin classifiers.

For prediction consistency, the Brier score of the ensemble classifier was 0.145 (**Figure 3**), which was slightly lower than that (0.162) of the best average-AUC classifier, but higher than that (0.142) of the best death-sensitivity classifier. For clinical utility, however, the DCA demonstrated that the Net benefit of the ensemble classifier was superior to that of the best death-sensitivity classifier and slightly superior to that of the best average-AUC classifier (**Figure 4A**). The feature importance disclosed the top 10 predictors were

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‘mechanical ventilation’, ‘age’, ‘free Ca’, ‘cefazolin’, ‘albumin’, ‘sum-diagnosis’, ‘LOS before ICU admission’, ‘lymphocytes’, ‘arterial BP systolic’, and ‘Kcl’ (**Figure 4B**). Additionally, the micro-average AUCs of all classifiers during cross-validation can be found in supplemental **Fig S1** (**Supplemental Digital Content 1,** http://links.lww.com/BRS/C284), and the ROCs of the best average-AUC classifier and the best death-sensitivity classifier are shown in supplemental **Fig S2** (**Supplemental Digital Content 1,** http://links.lww.com/BRS/C284). The corresponding macro-AUCs of the early prediction models can be found in supplemental **Fig S3** (**Supplemental Digital Content 1,** http://links.lww.com/BRS/C284 and our website[29]. Original data can be obtained from the MIMIC-III[30] and MIMIC-IV[31] database, and the eICU database[32].

Discussion

The prognosis of critical SCI patients who require intensive care is important for clinical decisions and expectation management. We found that 1) a three-class discharge destination could be accurately predicted using numerous ML classifiers; 2) The best average-AUC classifier was the EmbeddingLSVC_lightGBM, and the best death-sensitivity classifier was the MIC_lightGBM; 3) The best average-AUC classifier and the best death-sensitivity classifier could be combined into an ensemble classifier; 4) The ensemble classifier showed an overall superior performance in terms of discrimination ability, prediction consistency and clinical utility.

There is a paucity of research on clinical outcomes among SCI patients who require intensive care[3,6,33-35]. The mortality rate of critical SCI patients was about 10% in the current study, but others have reported the mortality rate could reach as high as 38.5%[36]. For those who survive, most SCI patients need long-term rehabilitation and nursing support due to motor deficit, urinary incontinence and bowel dysfunction[33]. The percentage of critical SCI patients who need professional rehabilitation and nursing support (discharge to FMC) was about 50%, which was similar to other research[3]. Nearly one third of critical SCI patients were

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discharged home, which was higher than that reported in prior work[3].

Our ensemble classifier had a micro-average AUC of 0.851 (ranked top 2 among all 99 classifiers) and a sensitivity of death of 0.452 (ranked top 9 among all 99 classifiers), which demonstrated a competitive discrimination ability. We endeavored to improve the death sensitivity by combining the best average-AUC classifier with the best death-sensitivity classifier into an ensemble classifier, because in hospital death was much harder to judge in the early phase of clinical care. As in hospital death remains a major clinical concern, developing an ensemble classifier with a competitive overall AUC and a favorable death sensitivity would address the clinical need.

Several studies[37-39] have previously developed ML classifiers to predict the prognosis of SCI patients. For cervical SCI, Kalyani et al.[37] sought to prognosticate neurological recovery and found XGBoost was the optimal ML classifier with an AUC of 0.867. Similarly, Karabacak et al.[38] presented five ML classifiers to predict five outcomes for cervical SCI, with a wide variety of resultant AUCs. Among SCI patients in the ICU, Fan et al.[39] developed ML classifiers for prolonged hospital LOS and prolonged ICU-LOS with high accuracy based on AUC values. Similarly, we achieved high accuracy (micro-average AUCs: 0.851; AUC of in-hospital death: 0.833; AUC of FMC: 0.785; AUC of home: 0.823) in predicting the discharge destination of critical SCI patients. The major difference between the current study and prior work lies in the fact that the current study constructed a three-class prediction with a single ensemble classifier, which was optimized from nearly one hundred initial ML classifiers and possesses improved death sensitivity. Additionally, the ensemble classifier demonstrated a non-inferior Brier score and superior Net benefit in the DCA curve compared with its origin classifiers.

In order to identify valuable predictors from among dozens of clinical features, the introduction of appropriate feature selection is necessary[40-42], as superabundant predictors may lead to over-fitting[43]. A total of seven classic feature-selection methods were adopted in the current study, and the prediction performance of the initial 98 classifiers varied a great deal among different feature selection methods, similar to other

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investigations[44,45]. As for the predictors, it's not surprising that laboratory results like "free.Ca^{2+}", "Ca^{2+}", "albumin", "lymphocytes", "potassium", "GCS.total", "BUN", "blood glucose" "INR", "lactate" and basic characteristics or clinical signs like "age", "weight", "sum_diagnosis", "respiration", "systolic arterial blood pressure" contributed to the prognostication, as physicians may also consider these clinical features in their decision-making. However, the ensemble classifiers also used treatment information like "mechanical ventilation", "cefazolin", "KCl", "morphine sulfate" and lead time like "LOS before ICU admission", which were similar to other work[8,19,33].

We acknowledge several limitations. First, the dataset did not record severity of SCI (e.g. American Spinal Injury Association grade), which might also contribute to the prediction performance of ML classifiers. Second, the current study could not realize prediction of long-term outcomes of SCI patients who underwent intensive medical care, because the eICU database did not include adequate follow-up information. Third, the ensemble classifier requires validation in other clinical contexts. Last, our findings may not be universally applicable to other countries or regions, as the source data was restricted to the United States.

Conclusion

Our novel ensemble classifier shows an overall superior performance in predicting the discharge destination when accounting for discrimination ability, prediction consistency and clinical utility. This classifier system may aid in the clinical management of critical SCI patients in the early phase following injury, as well as resource allocation.

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Fig 1. Flow chart of the study design. A: development of prediction classifiers; B: prediction assessment and classifier comparisons.

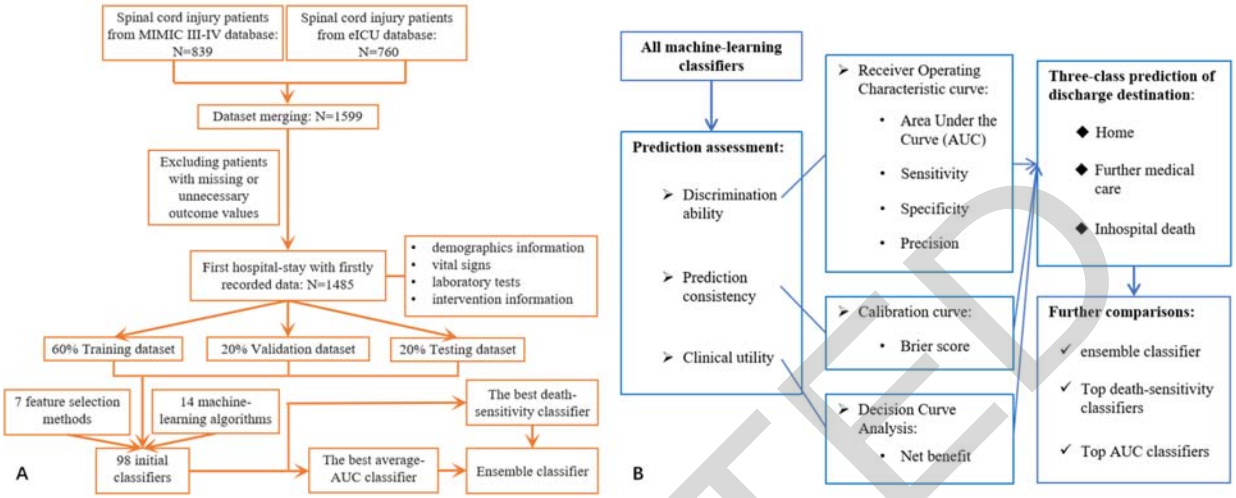

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Fig 2. Discrimination assessment of the initial 98 classifiers for discharge prediction. A: micro-average AUCs in the independent testings; B: death sensitivity in the independent testings; C: micro-average AUC of the ensemble classifier during cross-validation; D: the performance of the ensemble classifier during independent testing.

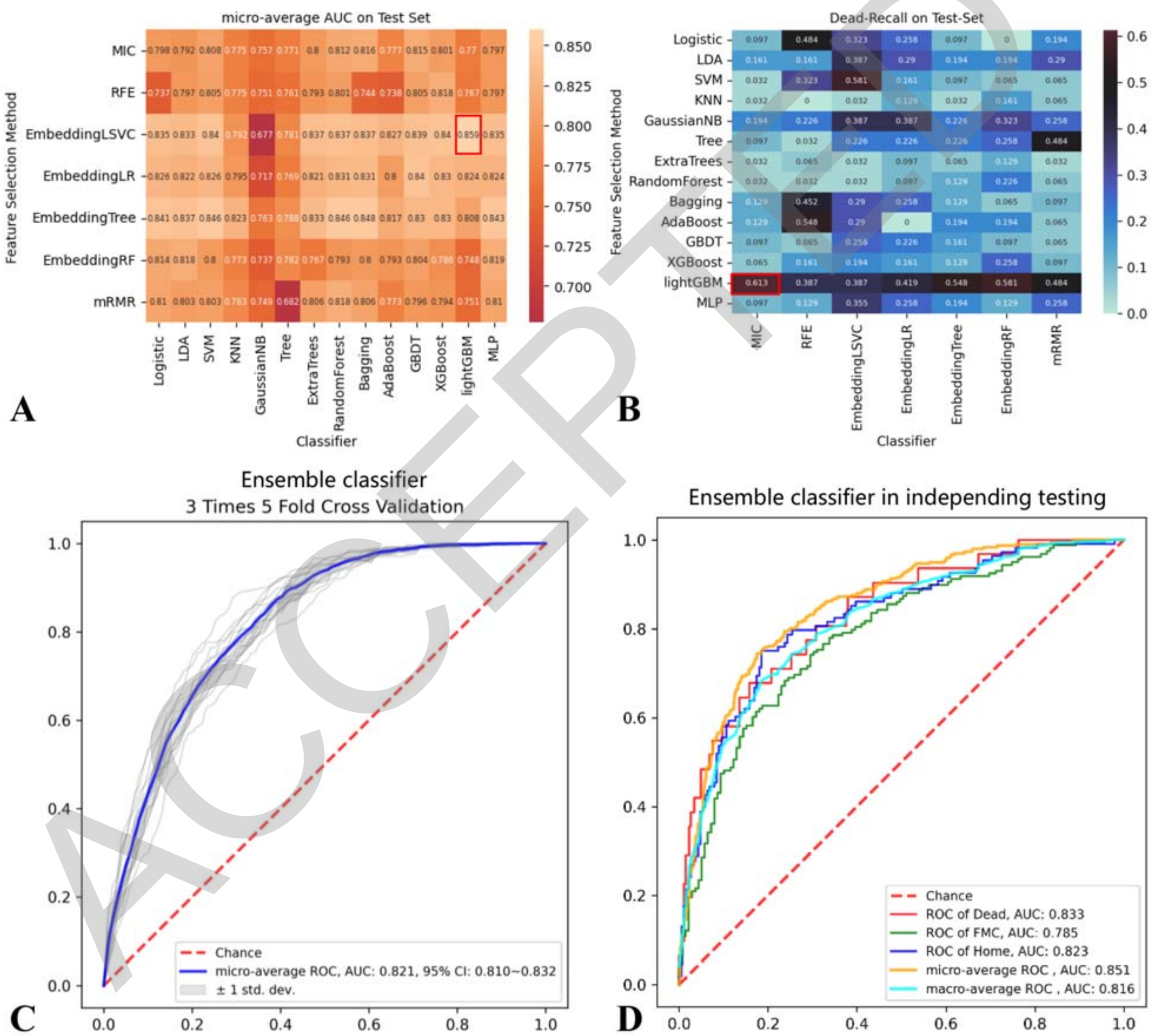

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Fig 3. Prediction consistency and clinical utility of the ensemble classifier and its origin classifiers. A: the confusion matrix of the MIC_lightBGM during independent testing; B: the confusion matrix of the EmbeddingLSVC_lightBGM during independent testing; C: the confusion matrix of the ensemble classifier during independent testing; D: calibration curve of the MIC_lightBGM during independent testing; B: calibration curve of the EmbeddingLSVC_lightBGM during independent testing; C: calibration curve of the ensemble classifier during independent testing.

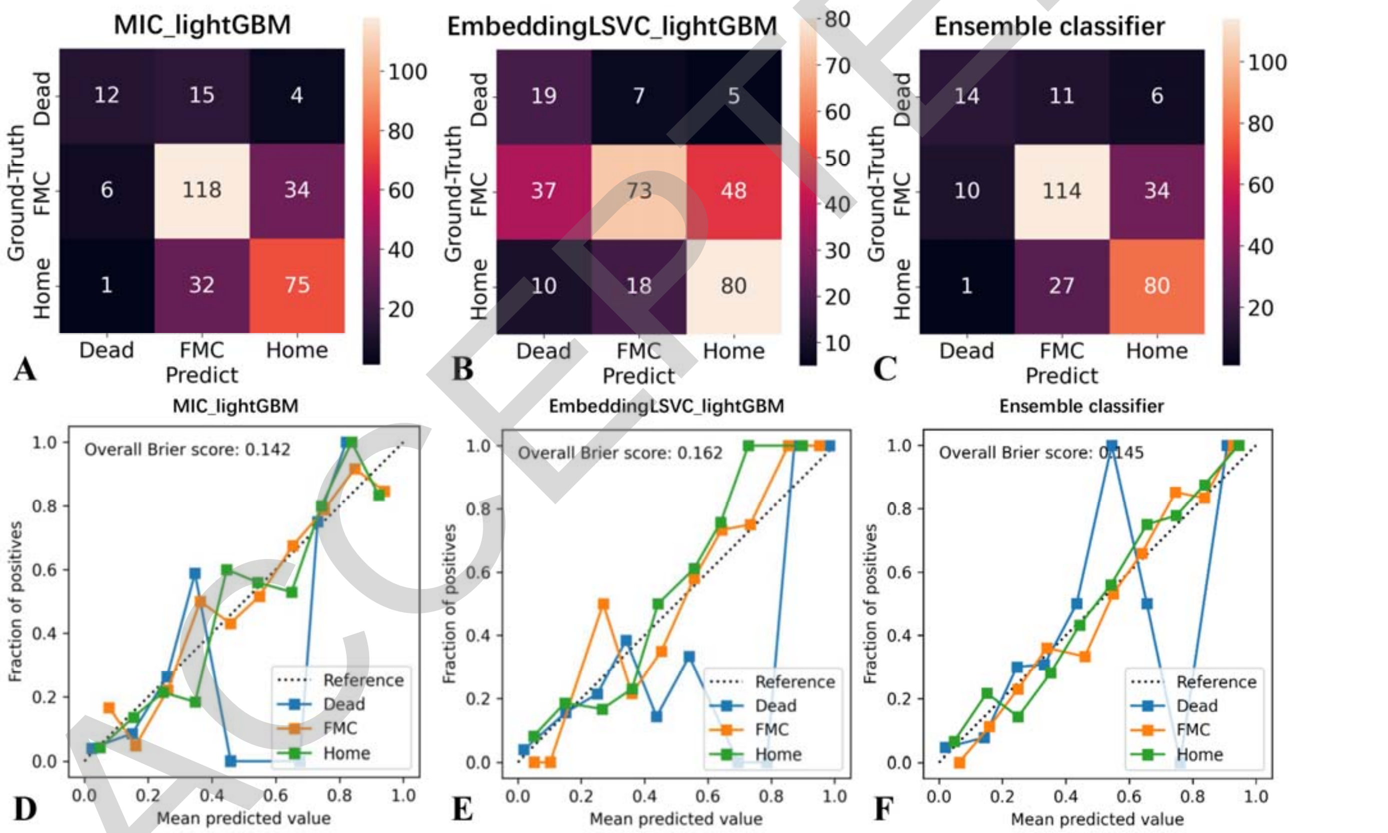

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Fig 4. Prediction consistency and interpretability of the ensemble classifier. A: decision curve analysis (DCA) of the ensemble classifier and its origin classifiers during independent testing; B: Top 20 predictors of the ensemble classifier.

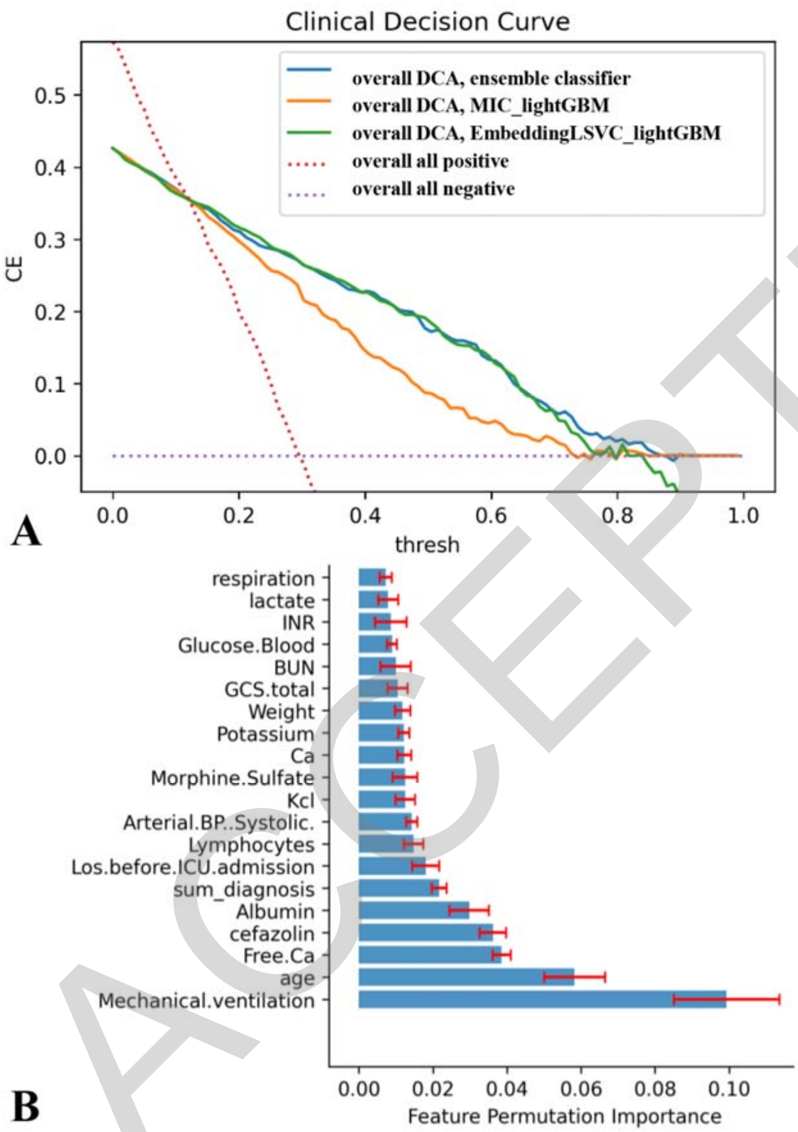

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Table 1. Basic characteristics of patients for discharge prediction.

Variables		Training (including validation) dataset (n=1188)	Testing dataset (n=297)	p
discharge_destination (%)	Dead	120 (10.1)	31 (10.4)	0.951
	Further medical care	644 (54.2)	158 (53.2)	
	Home	424 (35.7)	108 (36.4)	
ethnicity (%)	African American	165 (13.9)	39 (13.1)	0.497
	Asian	28 (2.4)	10 (3.4)	
	Hispanic	66 (5.6)	14 (4.7)	
	Other	63 (5.3)	10 (3.4)	
	White	866 (72.9)	224 (75.4)	
age (years) (mean (SD))		55.89 (18.94)	56.88 (19.27)	0.421
gender (%)	Female	335 (28.2)	89 (30.0)	0.595
	Male	853 (71.8)	208 (70.0)	
Weight (Kg) (mean (SD))		83.53 (24.08)	84.78 (31.89)	0.455
Height (cm) (mean (SD))		172.92 (12.62)	172.22 (13.31)	0.401
BMI (kg/㎡) (mean (SD))		27.92 (7.42)	28.12 (7.87)	0.678
careunit (%)	CCU	115 (9.7)	32 (10.8)	0.436
	MICU/SICU	849 (71.5)	201 (67.7)	

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	NICU	224 (18.9)	64 (21.5)	
source.of.admission (%)	Emergency	842 (70.9)	213 (71.7)	0.423
	General care area/OR	216 (18.2)	46 (15.5)	
	Transfer	130 (10.9)	38 (12.8)	
LoS.before.ICU.admission (days) (mean (SD))		0.87 (2.74)	0.90 (2.47)	0.843

SD, standard deviation; Kg, kilogram; cm, centimeter; BMI, body mass index; CCU, Coronary Care Unit; ICU, Intensive Care Unit; MICU, Medical Intensive Care Unit; NICU, Neurological Intensive Care Unit; SICU, Surgical Intensive Care Unit; LoS, length of stay.

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Table 2. Laboratory examination and treatment of patients for discharge prediction.

Variables		Training dataset (n=1188)	Testing dataset (n=297)	p
sum_diagnosis (mean (SD))		11.56 (9.05)	10.61 (8.41)	0.1
Paralysis (%)	No	760 (64.0)	187 (63.0)	0.798
	Yes	428 (36.0)	110 (37.0)	
Mechanical.ventilation (%)	No	703 (59.2)	166 (55.9)	0.336
	Yes	485 (40.8)	131 (44.1)	
GCS.total (mean (SD))		12.20 (4.23)	12.42 (3.97)	0.402
HR (bpm) (mean (SD))		84.77 (21.24)	84.10 (19.93)	0.623
respiration (bpm) (mean (SD))		17.72 (7.47)	17.65 (8.09)	0.887
Arterial.BP..Diastolic. (mmHg) (mean (SD))		69.06 (17.96)	71.78 (20.51)	0.024
Arterial.BP..Systolic. (mmHg) (mean (SD))		127.34 (26.90)	128.43 (28.44)	0.535
Arterial.BP..mean. (mmHg) (mean (SD))		84.97 (20.21)	87.49 (21.71)	0.058
Potassium (mmol/L) (mean (SD))		4.09 (0.66)	4.02 (0.58)	0.108
Sodium (mmol/L) (mean (SD))		138.24 (4.46)	138.41 (5.01)	0.584
PO2 (mmHg) (mean (SD))		155.06 (102.40)	166.36 (104.65)	0.091
PT (seconds) (mean (SD))		14.16 (5.29)	14.24 (6.02)	0.821
PTT (seconds) (mean (SD))		30.72 (13.75)	31.16 (15.97)	0.63
Glucose.Blood (mg/dL) (mean (SD))		138.54 (105.10)	133.83 (52.54)	0.454
Hemoglobin (g/dL) (mean (SD))		12.04 (2.32)	12.26 (2.33)	0.142
RDW (%) (mean (SD))		14.28 (2.13)	14.44 (2.00)	0.253
BUN (mg/dL) (mean (SD))		19.52 (14.30)	19.86 (16.08)	0.721
WBC (K/uL) (mean (SD))		11.64 (6.26)	11.58 (6.91)	0.883
Platelets (K/uL) (mean (SD))		235.23 (105.96)	237.20 (120.26)	0.781
creatinine (mg/dL) (mean (SD))		1.05 (0.89)	1.01 (0.73)	0.567
bicarbonate (mmol/L) (mean (SD))		24.06 (4.34)	24.34 (4.13)	0.31
hematocrit (%) (mean (SD))		36.00 (6.53)	36.80 (6.39)	0.061
lactate (mmol/L) (mean (SD))		2.02 (1.52)	1.94 (1.37)	0.401
INR (mean (SD))		1.26 (0.58)	1.27 (0.70)	0.956

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BE (mmol/L) (mean (SD))		-0.82 (5.11)	-0.72 (5.66)	0.761
Basophils (%) (mean (SD))		0.32 (0.38)	0.37 (0.39)	0.02
Ca (mg/dL) (mean (SD))		8.53 (0.82)	8.67 (0.75)	0.008
Chloride (mmol/L) (mean (SD))		103.59 (5.53)	103.34 (5.58)	0.49
Free.Ca (mmol/L) (mean (SD))		0.95 (0.45)	0.92 (0.45)	0.251
Phosphate (mg/dL) (mean (SD))		3.35 (1.06)	3.34 (1.15)	0.783
Eosinophils (%) (mean (SD))		1.34 (1.81)	1.42 (1.70)	0.48
Lymphocytes (%) (mean (SD))		14.89 (10.60)	15.63 (11.30)	0.292
Magnesium (mg/dL) (mean (SD))		1.83 (0.33)	1.86 (0.34)	0.139
Monocytes (%) (mean (SD))		6.25 (3.32)	6.27 (3.00)	0.917
PCO2 (mmHg) (mean (SD))		42.66 (11.18)	42.74 (11.43)	0.909
RBC (m/uL) (mean (SD))		4.02 (0.76)	4.07 (0.77)	0.264
MCH (pg) (mean (SD))		29.89 (3.24)	30.07 (2.58)	0.375
MCHC (%) (mean (SD))		33.31 (1.83)	33.32 (1.43)	0.975
MCV (fL) (mean (SD))		89.65 (8.54)	90.39 (6.74)	0.165
PH (mean (SD))		7.37 (0.10)	7.37 (0.10)	0.78
Anion.Gap (mmol/L) (mean (SD))		13.00 (4.19)	13.00 (4.29)	0.993
CO2.Blood (mmol/L) (mean (SD))		26.11 (6.53)	26.44 (6.96)	0.441
Specific.Gravity (mean (SD))		1.02 (0.01)	1.02 (0.01)	0.931
Fio2 (%) (mean (SD))		55.78 (29.77)	55.83 (31.64)	0.981
Total.bilirubin (mg/dL) (mean (SD))		0.71 (0.88)	0.75 (1.17)	0.561
Albumin (g/dL) (mean (SD))		3.21 (0.71)	3.31 (0.69)	0.046
Morphine.Sulfate (%)	No	798 (67.2)	219 (73.7)	0.035
	Yes	390 (32.8)	78 (26.3)	
cefazolin (%)	No	851 (71.6)	220 (74.1)	0.443
	Yes	337 (28.4)	77 (25.9)	
Kcl (%)	No	566 (47.6)	151 (50.8)	0.357
	Yes	622 (52.4)	146 (49.2)	
glucocorticoid (%)	No	887 (74.7)	221 (74.4)	0.988
	Yes	301 (25.3)	76 (25.6)	
Dopamine (%)	No	1149 (96.7)	291 (98.0)	0.344

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	Yes	39 (3.3)	6 (2.0)	
Dobutamine (%)	No	1181 (99.4)	296 (99.7)	0.929
	Yes	7 (0.6)	1 (0.3)	
Epinephrine (%)	No	1156 (97.3)	284 (95.6)	0.185
	Yes	32 (2.7)	13 (4.4)	
Norepinephrine (%)	No	990 (83.3)	254 (85.5)	0.408
	Yes	198 (16.7)	43 (14.5)	

SD, standard deviation; mg, milligram; dL, deciliter; GCS, Glasgow Coma Scale; HR, heart rate; BPM, beat per minute; BP, blood pressure; PO2, partial pressure of oxygen; PT, prothrombin time; PTT, partial thromboplastin time; RDW, red blood cell distribution width; BUN, blood urea nitrogen; WBC, white blood cell; INR, international normalized ratio; BE, base excess; PCO2, partial pressure of carbon dioxide; RBC, red blood cell; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; PH, potential of hydrogen; FiO2, fraction of inspiration oxygen.

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Table 3. Category discrimination of the ensemble classifier and its origin classifiers.

Prediction category		EmbeddingLSVC_lightGBM	MIC_lightGBM	ensemble classifier
death	AUC	0.832	0.787	0.833
	sensitivity	0.387	0.613	0.452
	specificity	0.974	0.823	0.959
	precision	0.632	0.288	0.56
further medical care	AUC	0.777	0.695	0.785
	sensitivity	0.747	0.462	0.722
	specificity	0.662	0.82	0.727
	precision	0.715	0.745	0.750
home	AUC	0.822	0.784	0.823
	sensitivity	0.694	0.741	0.741
	specificity	0.799	0.72	0.788
	precision	0.644	0.602	0.667

EmbeddingLSVC, embedding linear supported vector classifier; lightGBM, light gradient boosting model; MIC, maximal information coefficient; AUC, area under the curve.

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Table 4. Top death-sensitivity classifiers over the ensemble classifier.

Ranking by death sensitivity	death sensitivity	micro-average AUC	AUC of death	AUC of FMC	AUC of home
MIC_lightGBM	0.613	0.77	0.787	0.695	0.784
EmbeddingLSVC-SVM	0.581	0.84	0.779	0.751	0.795
EmbeddingRF-lightGBM	0.581	0.748	0.777	0.631	0.756
EmbeddingTree-lightGBM	0.548	0.808	0.805	0.747	0.808
RFE-AdaBoost	0.548	0.738	0.736	0.649	0.732
mRMR-lightGBM	0.484	0.751	0.762	0.649	0.757
RFE-Logistic	0.484	0.737	0.767	0.674	0.723
mRMR-Tree	0.484	0.682	0.604	0.542	0.656
ensemble classifier	0.452	0.851	0.833	0.785	0.823

AUC, area under the curve, FMC, further medical care; MIC, maximal information coefficient; lightGBM, light gradient boosting model; EmbeddingLSVC, embedding linear supported vector classifier; SVM, support vector machine; EmbeddingRF, embedding random forest; RFE, recursive feature elimination; AdaBoost, adaptive boosting; mRMR, minimal-redundancy-maximal-relevance.

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