scientific reports

OPEN



Interpretable machine learning for predicting sepsis risk in emergency triage patients

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The study aimed to develop and validate a sepsis prediction model using structured electronic medical records (sEMR) and machine learning (ML) methods in emergency triage. The goal was to enhance early sepsis screening by integrating comprehensive triage information beyond vital signs. This retrospective cohort study utilized data from the MIMIC-IV database. Two models were developed: Model 1 based on vital signs alone, and Model 2 incorporating vital signs, demographic characteristics, medical history, and chief complaints. Eight ML algorithms were employed, and model performance was evaluated using metrics such as AUC, F1 Score, and calibration curves. SHapley Additive exPlanations (SHAP) and Local Interpretable Model-agnostic Explanations (LIME) methods were used to enhance model interpretability. The study included 189,617 patients, with 5.95% diagnosed with sepsis. Model 2 consistently outperformed Model 1 across most algorithms. In Model 2, Gradient Boosting achieved the highest AUC of 0.83, followed by Extra Tree, Random Forest, and Support Vector Machine (all 0.82). The SHAP method provided more comprehensible explanations for the Gradient Boosting algorithm. Modeling with comprehensive triage information using sEMR and ML methods was more effective in predicting sepsis at triage compared to using vital signs alone. Interpretable ML enhanced model transparency and provided sepsis prediction probabilities, offering a feasible approach for early sepsis screening and aiding healthcare professionals in making informed decisions during the triage process.

Keywords Sepsis, Triage, Emergency, Interpretable machine learning, Warning mode

Despite global advances in sepsis management, early identification and treatment of sepsis remain critical challenges in emergency medicine, with persistently high morbidity and mortality rates. The 2021 American College of Emergency Physicians consensus statement emphasizes the importance of early recognition and intervention in suspected sepsis cases¹. Emergency departments present a unique opportunity for early detection and intervention, as they are often the first point of contact for patients with severe infections. Timely implementation of goal-directed therapy in this setting can significantly improve patient outcomes. However, current approaches face significant limitations in reliably achieving early identification.

The urgency of early sepsis detection is underscored by a 7.6% decrease in survival for each hour of delayed treatment^{2,3}. The 2018 Surviving Sepsis Campaign Bundle mandates critical interventions, including antibiotic administration and blood culture collection, within one hour of presentation⁴. However, achieving this target remains challenging due to difficulties in early identification. Epidemiological studies reveal that 86% of sepsis diagnoses occur at hospital admission^{5,6}, with 75–80% of treatments initiated in emergency departments^{7,8}. These findings highlight the critical role of triage in sepsis identification and the pressing need for reliable early warning tools that can be implemented at the initial point of patient contact.

Traditional scoring systems such as NEWS, MEWS, and qSOFA have played valuable roles in clinical decisionmaking, particularly in mitigating cognitive biases as demonstrated in recent studies⁹. However, these systems have shown limited effectiveness in sepsis prediction^{10–15}, with qSOFA demonstrating particular weakness compared to NEWS and MEWS for early detection^{16–19}. The Third International Consensus Definitions for Sepsis and the 2021 Sepsis Guidelines acknowledge these limitations^{20,21}, recommending more comprehensive screening approaches for high-risk patients. While these scoring systems provide structured evaluation frameworks and reduce clinical judgment biases, their reliance on vital signs alone limits their utility as standalone tools for sepsis screening. Recent advances in healthcare technology, particularly in machine learning, offer the potential to retain the benefits of standardized assessment while significantly improving predictive accuracy.

Modern healthcare infrastructure, particularly structured electronic medical records (sEMR), enables the integration of comprehensive patient data—including vital signs, demographics, medical history, and chief

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complaints—into advanced analytical systems^{22,23}. Machine learning (ML) models leveraging this rich data have demonstrated superior performance in critical illness prediction compared to traditional approaches^{22,24,25}. Although the application of machine learning in sepsis prediction is an active area of research, most existing studies focus on inpatient or ICU patients rather than triage-stage data. Additionally, its "black box" nature and lack of interpretability remain significant barriers to clinical adoption²⁶. Addressing these challenges is essential to ensuring that ML models provide actionable insights and are trusted by healthcare professionals.

This study aims to develop an interpretable ML framework that leverages comprehensive triage data to enhance sepsis prediction while ensuring clinical transparency. By incorporating SHapley Additive exPlanations (SHAP) and Local Interpretable Model-agnostic Explanations (LIME)²⁷, the model not only improves predictive accuracy but also provides actionable insights into sepsis risk factors, empowering clinicians to make informed and timely decisions during critical triage processes.

Methods

Study design and data source

This was a retrospective cohort study designed according to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis statements²⁸. All data were obtained from the Medical Information Mart for Intensive Care IV (MIMIC-IV version 1.4) database, which contains the clinical information of patients in the emergency department, inpatient department, and intensive care unit of the Beth Israel Deaconess Medical Center, USA from 2008 to 2019. The database was developed by Massachusetts Institute of Technology's Computational Physiology Laboratory and was approved by the Institutional Review Committees of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. As the original data were anonymized and desensitized, the study was approved by the Hospital Ethics Committee. The data for this study were extracted by author ZL, who completed the examination of the training plan of the cooperative organization (Record ID 45797033).

Study population

Information on adult patients (age \geq 18 years) in the emergency department was extracted from the MIMIC-IV-ED database. To ensure the accuracy and completeness of the patient information, we excluded patients who had no hospitalization information.

Outcomes

The outcome of the prediction model in this study was sepsis, and the diagnosis of sepsis was based on the 2016 international guidelines sepsis 3.0 criteria². As the patients' visit time in the MIMIC-IV database was from 2008 to 2019, the data extraction of sepsis in this study was not based on the International Classification of Diseases (ICD) code, but the diagnostic criteria of sepsis 3.0. The MIMIC-IV codebase provides the extracted code of sepsis 3.0, which can be obtained directly.

Predictor variables

The predictors collected in Supplementary Materials Box1 were based on all possible outcomes-related indicators of a patient at the time of emergency triage, including vital signs, demographic characteristics, medical history, and chief complaints. For vital signs, we extracted information on the body temperature, heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and pain index. Regarding demographic characteristics, we extracted information on sex and age, and age was calculated by subtracting the date of birth from the date of hospitalization. The body mass index was not calculated because nearly 1/2 of the patients in the MIMIC database had missing height data, and in reality, most emergency departments could not obtain body mass index data during triage. For chronic diseases, we screened for common chronic diseases probably related to sepsis or having a poor prognosis according to clinical experience and guidelines^{29,30}. For free-text chief complaints, we employed natural language processing techniques to address issues of spelling errors and language inconsistencies. This involved using spell-checking and text normalization techniques. For complex or ambiguous texts that could not be automatically corrected, we conducted manual reviews and made appropriate adjustments based on the specific context. The suspected infection was defined as the presence of fever, cough, diarrhea, sore throat, chills, cellulitis, and an external abscess visible to the naked eye.

Missing and extreme values

Only complete data were analyzed in this study. Because of the relatively small number of missing values and large sample size in this study, we removed all missing values. Similarly, we removed the extreme values of the numerical variables based on the clinical situation, as shown in Fig. 1. To improve the accuracy of the model, we used a normalization method to scale all the variables and map the data to the [0,1] interval.

Statistical analysis

In this study, continuous variables were described using the median and interquartile range, and the Mann– Whitney U test was used to determine differences between groups. Categorical variables were described using frequencies and percentages, and group comparisons were made using the chi-square test or Fisher's exact test.

The data were randomly divided into a training set (80%) and test set (20%). We compared two models in our study: Model 1, which was based on vital signs alone, and Model 2, which included vital signs, demographic characteristics, medical history, and chief complaints. In our research, we selected eight widely-used and diverse machine learning algorithms based on their differing assumptions, learning mechanisms, and applicability to clinical prediction tasks:



Fig. 1. Flow Chart. *MIMIC* Medical Information Mart for Intensive Care, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *o2sat* oxygen saturation, *AUC* area under the receiver operating characteristic curve, *AUC-PR* area under the precision-recall curve, *PPV* positive predictive value, *NPV* negative predictive value, *SHAP* SHapley Additive exPlanations, *LIME* Local Interpretable Model-agnostic Explanations.

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- Logistic Regression (LR): Chosen as the baseline linear model due to its simplicity, interpretability, and frequent use in medical research.
- Decision Tree and Extra Tree: Tree-based models were included for their interpretability, ability to handle
 non-linear relationships, and complementary characteristics, with Extra Tree leveraging random splits for
 additional variability.
- Gradient Boosting and Random Forest: Modern ensemble learning methods known for their robustness, strong predictive performance, and effectiveness in handling large datasets with complex patterns.
- k-Nearest Neighbor (KNN) and Support Vector Machine (SVM): Non-linear algorithms were selected to evaluate their ability to capture local and non-linear relationships in the data.
- Naive Bayes: Included for its probabilistic framework and computational efficiency, providing a contrasting approach to tree-based and ensemble models.

Class imbalance can lead to overfitting and suboptimal performance in machine learning models. In this dataset, the majority class (non-septic patients) accounts for 94.05%, whereas the minority class (septic patients) represents only 5.95%. To investigate the impact of class imbalance handling on model performance, we used the LR algorithm as an example and compared the performance of three resampling methods (SMOTE, SMOTE Tomek, and RandomUnderSampler) with the original, non-resampled data in Models 1 and 2³¹. The model performance was evaluated using metrics including Precision, Sensitivity, and F1-Score, with a primary focus on improving the prediction ability for the minority class (septic patients). By adjusting the regularization parameters to control model complexity, we aimed to improve the model's generalization ability and performance. The performance of different algorithms on the test set was evaluated using several metrics: F1 Score, Accuracy, Sensitivity, Specificity, Area Under the Precision-Recall Curve (AUC-PR), Positive Predictive Value (PPV), Negative Predictive Value (NPV), Area Under the ROC Curve (AUC), Brier Score, calibration curves, and Decision Curve Analysis (DCA) curves.

Based on the characteristics of the algorithms, either SHAP or LIME methods were used for interpretation. In our study, SHAP was applied to the Gradient Boosting and Random Forest models due to its ability to provide comprehensive feature importance insights for tree-based models. LIME enables rapid interpretation of any model, providing quick insights into model predictions. However, it falls short in effectively capturing the overall model performance and the complex interactions between features. SHAP's slower computation speed in the context of Extra Tree and SVM limits its practical applicability in clinical settings.

Data extraction was conducted using Navicat Premium software (version 15.0), while statistical analysis and ML were carried out with R (version 4.1.3, The R Foundation for Statistical Computing, Vienna, Austria) and Python (version 3.8.5, Python Software Foundation). The main code and libraries used in the ML section of this study were detailed in the Supplementary Materials.

Results

Study population

This study included 189,617 patients: 178,343 (94.05%) non-septic patients and 10,824 (5.95%) septic patients (Table 1). Of the 171,584 patients without symptoms of infection, 9,095 (5.3%) were septic patients and of the 17,313 patients with symptoms of infection, 1,729 (10.0%) were septic patients (Supplementary Materials Table S1). In this study, most symptoms had a different proportion of septic patients (Supplementary Materials Table S1).

Impact of resampling on the data

The results showed that SMOTE, SMOTE Tomek, and RandomUnderSampler all significantly improved the Precision, Sensitivity, and F1-Score of the minority class compared to the original non-resampled data (Supplementary Materials Table S2), with their performances being relatively similar. Considering that the RandomUnderSampler relies solely on real data, it avoids the risk of overfitting associated with synthetic sample generation and requires fewer computational resources. Given the large-scale dataset and the need for multi-model analysis in this study, random undersampling was selected as the primary method to address class imbalance, achieving a balance between performance and computational efficiency.

Validation results of free-text preprocessing

To evaluate the performance of text preprocessing, we conducted validation on key steps of the workflow. For spell-checking, 500 randomly selected entries were manually reviewed, achieving a correction accuracy of 94.2% and a false positive rate of 4.5%, with most errors occurring in medical terms. For text normalization, a random sample of 300 entries showed a consistency improvement rate of 87.6%, with abbreviations such as "SOB" successfully standardized to "shortness of breath."

Performance of the models

Figure 2 showed a comparison of AUC values for sepsis prediction using two models across eight algorithms. Except for Naive Bayes, Model 2 showed a significant improvement over Model 1 in all cases (Table 2). In Model 2, the AUC values of the eight algorithms, listed from highest to lowest, were as follows: Gradient Boosting (0.83), Extra Tree (0.82), Random Forest (0.82), SVM (0.82), LR (0.79), KNN (0.76), Naive Bayes (0.74), and Decision Tree (0.65). The training set performance metrics of Model 2 were presented in the Supplementary Materials (Table S3). By comparing the performance metrics between the training and testing sets, we found that most algorithms demonstrated consistent performance without significant overfitting. Table 3 presents the overall performance, discrimination, and calibration metrics of different algorithms across the two models. We selected the four ML algorithms with the best AUC performance in Model 2—Gradient Boosting, Extra Tree, Random Forest, and SVM—for further comparison. The calibration curves showed good performance for all four algorithms (Fig. 3a), and the DCA curves demonstrated that Gradient Boosting slightly outperformed the other three algorithms (Fig. 3b). Table 4 showed that Gradient Boosting achieved the highest net benefit (0.47) at the 5% threshold, outperforming Extra Tree (0.41), Random Forest (0.44), and SVM (0.44), with a consistent advantage observed across clinically relevant thresholds.

Feature importance and interpretation of the models

Figure 4 shows the feature importance for each of the top-performing four ML algorithms in Model 2. Using Case 1 as an example, we interpreted the predictions of the four algorithms and provided the probability of sepsis occurrence (Fig. 5). Generally, a probability of less than 20% indicates a low risk; 20%-50% suggests that observation might be appropriate; above 50% requires attention; and over 80% is highly suggestive of sepsis. The probabilities of sepsis predicted by the four algorithms were: Gradient Boosting (47%), Random Forest (50%), Extra Tree (46%), and SVM (64%). The explanations provided by the SHAP method were more comprehensible (Fig. 5).

Discussion

Our study found that modeling with more comprehensive triage information, rather than relying solely on vital signs, can more effectively predict sepsis at triage. The best-performing machine learning algorithm was Gradient Boosting, achieving an AUC of 0.83. The SHAP method enhanced the model's transparency through improved interpretability.

The 2016 sepsis guidelines recommend screening for infections or suspected infections². However, defining these terms is challenging, as early sepsis symptoms may not align with infection indicators. Our study found no international consensus, with definitions often based on physician experience. We identified suspected infections by symptoms like fever, cough, or visible abscesses. As shown in Table S1, 10% of patients with suspected symptoms and 5.3% without were septic. This suggests that screening based solely on suspected infections may miss cases. Early sepsis signs are often non-specific^{1,6–8,30}, with many cases lacking fever, especially in older or immunocompromised individuals. Approximately one-third of sepsis cases lack fever, presenting instead with symptoms like hypothermia or altered mental status³², and about 20% of septic shock patients show no early infection signs³⁰. Additionally, 20%-40% of suspected infections are non-infectious^{33,34}. Therefore, sepsis screening should encompass all patients, not just those with suspected infections.

Sepsis is highly heterogeneous, making early prediction, particularly during triage, quite challenging. Furthermore, traditional warning models are designed to predict critical illness rather than sepsis, highlighting the need for remodeling. Additionally, these models convert vital signs into categorical variables for ease of application, which can somewhat diminish predictive efficiency. We initially explored the maximum efficacy

Variable	Non-Sepsis (n = 178,343)	Sepsis (n = 10,824)	P-Value
Vital signs in triage	I		
Oxygen saturation (%)	98 (97, 100)	96 (95, 99.)	< 0.001
Heart rate (beats/min)	84 (73, 97)	93 (78, 110)	< 0.001
Respiratory rate (times/min)	17 (16, 18)	19 (16, 20)	< 0.001
Temperature range (°C)	36.7 (36.4, 37.0)	37.1 (36.5, 37.3)	< 0.001
Systolic blood pressure (mmHg)	133 (119, 150)	122 (105, 141)	< 0.001
Diastolic blood pressure (mmHg)	76 (66, 86)	69 (58, 80)	< 0.001
Pain index	3 (0, 7)	0 (0, 7)	< 0.001
Demographic characteristics			
Age (year)	58 (43, 71)	66 (54, 77)	< 0.001
Male [n (%)]	86,666 (48.6%)	5954 (55.0%)	< 0.001
Past history [n (%)]	<u>I</u>		
Smoke	34,322 (19.2%)	3158 (29.2%)	< 0.001
Chronic obstructive pulmonary disease	973 (0.5%)	176 (1.6%)	< 0.001
Chronic kidney diseases	24,897 (14.0%)	2808 (25.9%)	< 0.001
Chronic heart failure	5325 (3.0%)	824 (7.6%)	< 0.001
Coronary heart disease	30,818 (17.3%)	2950 (27.3%)	< 0.001
Tumor	5166 (2.9%)	462 (4.3%)	< 0.001
Hypertension	31,405 (17.6%)	1931 (17.8%)	0.541
Diabetes	45,305 (25.4%)	3939 (36.4%)	< 0.001
Cirrhosis	5701 (3.2%)	1056 (9.8%)	< 0.001
Chief complaints [n (%)]			
Fever	8597 (4.8%)	1302 (12.0%)	< 0.001
Chills	360 (0.2%)	42 (0.4%)	< 0.001
Tachycardia	1042 (0.6%)	175 (1.6%)	< 0.001
Weakness	8043 (4.5%)	704 (6.5%)	< 0.001
Diarrhea	2038 (1.1%)	116 (1.1%)	0.499
Dizziness	3900 (2.2%)	118 (1.1%)	< 0.001
Dyspepsia	12,855 (7.2%)	1372 (12.7%)	< 0.001
Headache	3476 (1.9%)	134 (1.2%)	< 0.001
Fatigue	763 (0.4%)	34 (0.3%)	0.076
Blood pressure low	1090 (0.6%)	485 (4.5%)	< 0.001
Blood pressure high	785 (0.4%)	18 (0.2%)	< 0.001
Lethargy	941 (0.5%)	229 (2.1%)	< 0.001
Jaundice	782 (0.4%)	126 (1.2%)	< 0.001
Syncope	3374 (1.9%)	112 (1.0%)	< 0.001
Abscess	756 (0.4%)	48 (0.4%)	0.761
Mantal altered	3665 (2.1%)	729 (6.7%)	< 0.001
Swelling	4346 (2.4%)	181 (1.7%)	< 0.001
Anxiety	1100 (0.6%)	6 (0.1%)	< 0.001
Palpitations	1503 (0.8%)	25 (0.2%)	< 0.001
Hemoptysis	429 (0.2%)	79 (0.7%)	< 0.001
Hematuria	1016 (0.6%)	62 (0.6%)	0.967
Nausea or vomiting	9767 (5.5%)	531 (4.9%)	0.011
Bradycardia	342 (0.2%)	22 (0.2%)	0.791
Cough	3524 (2.0%)	291 (2.7%)	< 0.001
Sore throat	761 (0.4%)	35 (0.3%)	0.107
Dysuria	806 (0.5%)	34 (0.3%)	0.036
Cellulitis	794 (0.4%)	27 (0.2%)	0.003
Hyperglycemia	1550 (0.9%)	134 (1.2%)	< 0.001
Hypoglycemia	503 (0.3%)	37 (0.3%)	0.258
Seizure	1841 (1.0%)	118 (1.1%)	0.564
Rash	715 (0.4%)	27 (0.2%)	0.014
Gastrointestinal bleeding	1261 (0.7%)	171 (1.6%)	< 0.001
Slurred speech	637 (0.4%)	35 (0.3%)	0.566
Continued	1		

Variable	Non-Sepsis (n = 178,343)	Sepsis (n = 10,824)	P-Value
Gait unsteady	643 (0.4%)	23 (0.2%)	0.012
Wound	3375 (1.9%)	175 (1.6%)	0.040
Lightheaded	776 (0.4%)	29 (0.3%)	0.009
Fall	8521 (4.8%)	382 (3.5%)	< 0.001
Chest pain	15,331 (8.6%)	444 (4.1%)	< 0.001
Abdominal pain	24,282 (13.6%)	1224 (11.3%)	< 0.001
Back pain	4832 (2.7%)	180 (1.7%)	< 0.001
Flank pain	1880 (1.1%)	76 (0.7%)	< 0.001
Arm pain	962 (0.5%)	26 (0.2%)	< 0.001
Arthralgia pain	4505 (2.5%)	101 (0.9%)	< 0.001
Limb pain	4876 (2.7%)	150 (1.4%)	< 0.001

Table 1. The relationship between sepsis as an outcome and each variable.

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of predicting sepsis based on triage vital signs using the AUC value. The best-performing algorithm was Gradient Boosting, with an AUC of 0.76, compared to the traditional LR algorithm, which had an AUC of 0.72 (Fig. 2a,d). Previous studies have demonstrated that certain demographic characteristics and medical histories are risk factors for sepsis, such as age≥65 years, diabetes, chronic kidney disease, cirrhosis, and cancer^{30,35–37}. Additionally, some symptoms have been shown to correlate with the occurrence of sepsis^{29,32}. For instance, psychiatric symptoms are positively correlated^{37,38}, while abdominal pain and chest pain are negatively correlated³⁹. Demographic information, medical history, and chief complaints are structured data that can be obtained through sEMR during triage and analyzed using machine learning algorithms. In our Model 2, the best AUC value was 0.83 for Gradient Boosting, demonstrating a significant improvement over traditional models. While the improvement in AUC from 0.72 to 0.83 may appear modest, this enhancement represents a clinically meaningful advancement in sepsis prediction. Given that each hour of delayed treatment results in a 7.6% decrease in survival rate, even incremental improvements in early detection accuracy can translate to significant clinical benefits. Our model leverages existing electronic medical record infrastructure and readily available triage data, making implementation both feasible and cost-effective. Although traditional scoring systems (NEWS, MEWS, qSOFA) require minimal resources, their limited effectiveness in early sepsis detection may result in higher downstream costs due to delayed interventions. Furthermore, our model's interpretability features provide clear, actionable insights that support clinical decision-making, potentially improving workflow efficiency in emergency settings. These advantages justify the implementation of our improved model, as the potential benefits in patient outcomes outweigh the modest resource requirements.

The differences in predicted sepsis probabilities among the algorithms (e.g., Gradient Boosting at 47% vs. SVM at 64%) can be attributed to the fundamental differences in their learning mechanisms and probability calibration. Tree-based models, such as Gradient Boosting and Random Forest, tend to provide more conservative and better-calibrated probability estimates due to ensemble smoothing, while SVM is more sensitive to features near decision boundaries, which can lead to higher or more variable probabilities. These discrepancies highlight the need for caution when interpreting probabilities, particularly in clinical settings. We compared eight common ML algorithms, and Gradient Boosting consistently performed the best across all metrics, including AUC and other model evaluation criteria. Gradient Boosting excels at capturing complex nonlinear interactions among diverse clinical features while reducing overfitting. Previous studies have consistently demonstrated that Gradient Boosting is among the best-performing algorithms for predicting critical illness and hospitalization rates across various clinical datasets and methodologies. For example, in a study predicting hospital mortality in ICU patients, Gradient Boosting exhibited superior performance compared to traditional scoring systems such as APACHE II, achieving an accuracy of 0.86 and an area under the ROC curve (AUC) of 0.81⁴⁰. Similarly, Gradient Boosting Decision Trees were successfully employed in a population-based study to predict unplanned hospitalizations, achieving promising AUC values ranging from 0.789 to 0.802⁴¹. In the context of emergency department triage, a Gradient Boosting model stood out by predicting early mortality with an AUC of 0.962, highlighting its effectiveness in identifying high-risk patients⁴². These findings collectively underscore the robustness of Gradient Boosting algorithms in healthcare predictive analytics, particularly in critical care settings. In our study, the preference for Gradient Boosting aligns with its well-documented strengths in handling complex, non-linear relationships and datasets with missing or imbalanced variables, both of which are common challenges in sepsis prediction. Compared to alternative algorithms, Gradient Boosting also provided better-calibrated probabilities and feature importance metrics (as analyzed using SHAP values), thereby enhancing interpretability and actionable insights for clinical settings. These findings collectively underscore the robustness and adaptability of Gradient Boosting in healthcare predictive analytics, particularly in critical care and emergency contexts where timely and accurate predictions are crucial. The DCA demonstrated that Gradient Boosting achieved the highest net benefit across clinically relevant thresholds, particularly at the 5% threshold where early sepsis detection is critical. Its higher net benefit at lower thresholds reflects an optimal balance between sensitivity and specificity, effectively capturing more true positives while minimizing false positives. This is especially important for early intervention, which can significantly improve patient outcomes. Although net benefit decreased as thresholds increased, Gradient Boosting consistently outperformed other models, highlighting its robustness and potential to enhance clinical decision-making in sepsis risk prediction.



Fig. 2. Comparison of ROC Curves of Different Algorithms on Two Models. (**a**) Logistic Regression; (**b**) Decision Tree; (**c**) Extra Tree; (**d**) Gradient Boosting; (**e**) k-Nearest Neighbor: (**f**) Naive Bayes; (**g**) Random Forest; (**h**) Support Vector Machine. *ROC* receiver operating characteristic curve, *AUC* area under the receiver operating characteristic curve.

The purpose of interpretability in ML is to enhance model transparency, thereby effectively assisting healthcare professionals in decision-making. SHAP and LIME both have their pros and cons in explaining machine learning models. SHAP is theoretically robust and fairly allocates contribution values to each feature, explaining the difference between an individual sample's predicted value and the model's average. However, it can be computationally intensive. LIME, while lacking a strong theoretical foundation and not guaranteeing fair attribution of predicted values to features, is versatile and applicable to most models without requiring specific types⁴³. In our study, the SHAP method provided explanations that were easier to understand and was highly compatible with the Gradient Boosting algorithm, eliminating concerns about computational speed. In scenarios where triage resources are limited, the high heterogeneity and atypical presentation of sepsis make early screening challenging yet highly valuable. We are the first to use interpretable ML to explore sepsis prediction based on more comprehensive triage information. By integrating sEMR with machine learning, we can quickly output sepsis prediction probabilities and explanations during triage, rather than just simple prediction outcomes. This approach offers feasibility for early sepsis screening and intervention in busy and resource-limited emergency settings. However, while our ML model demonstrates promising performance in sepsis prediction, its successful

Algorithm	Model 1 (AUC)	Model 2 (AUC)	DeLong Test (z)	p-value
LR	0.72	0.79	- 4.3391	< 0.001
Decision Tree	0.60	0.65	- 4.2912	< 0.001
Extra Trees	0.73	0.82	- 5.8787	< 0.001
Gradient Boosting	0.76	0.83	- 4.6764	< 0.001
KNN	0.68	0.76	- 4.9441	< 0.001
Naive Bayes	0.74	0.74	- 0.3877	0.698
Random Forest	0.74	0.82	- 5.9244	< 0.001
SVM	0.75	0.82	- 4.3505	< 0.001

Table 2. DeLong test-based comparison of AUC between model 1 and model 2 across different algorithms. LR Logistic Regression, KNN K-Nearest Neighbors, SVM Support Vector Machine, AUC area under the receiver operating characteristic curve.

	F1 Score	Accuracy	Sensitivity (Recall)	Specificity	AUC-PR	Precision (PPV)	NPV	Brier score
Model 1								
LR	0.66	0.67	0.63	0.71	0.73	0.68	0.66	0.21
Decision Tree	0.60	0.60	0.60	0.59	0.70	0.60	0.60	0.39
Extra Trees	0.66	0.68	0.65	0.70	0.73	0.68	0.67	0.20
Gradient Boosting	0.68	0.70	0.65	0.75	0.76	0.72	0.68	0.19
KNN	0.62	0.64	0.59	0.67	0.69	0.64	0.62	0.24
Naive Bayes	0.60	0.67	0.49	0.85	0.73	0.76	0.62	0.22
Random Forest	0.67	0.68	0.65	0.70	0.73	0.68	0.67	0.20
SVM	0.67	0.70	0.62	0.77	0.75	0.73	0.67	0.20
Model 2								
LR	0.72	0.73	0.71	0.73	0.79	0.72	0.72	0.18
Decision Tree	0.64	0.65	0.65	0.66	0.73	0.64	0.64	0.35
Extra Trees	0.74	0.75	0.74	0.76	0.80	0.75	0.74	0.17
Gradient Boosting	0.75	0.75	0.74	0.78	0.83	0.77	0.74	0.16
KNN	0.68	0.70	0.65	0.76	0.76	0.72	0.68	0.20
Naive Bayes	0.71	0.71	0.72	0.70	0.74	0.70	0.71	0.25
Random Forest	0.74	0.74	0.75	0.74	0.81	0.73	0.74	0.17
SVM	0.74	0.75	0.73	0.76	0.81	0.75	0.74	0.17

Table 3. Performance of different algorithms in models 1 and 2. LR Logistic Regression, KNN K-Nearest Neighbors, AUC area under the receiver operating characteristic curve, AUC-PR area under the precisionrecall curve, PPV positive predictive value, NPV negative predictive value, SVM Support Vector Machine. Model 1 utilizes vital signs for modeling, Model 2 incorporates vital signs, demographics, medical history, and chief complaints. Note: Sensitivity and Recall refer to the same metric and are used interchangeably in the table. Similarly, Precision is equivalent to PPV.

implementation in clinical practice still faces several challenges. Specifically, the integration of ML models into existing electronic medical record systems requires user-friendly interfaces to ensure predictions are presented in an intuitive and actionable format. Moreover, clinician education programs are essential to help healthcare professionals understand the model's capabilities and properly interpret its outputs. Thus, future work should prioritize developing interfaces that seamlessly integrate with existing workflows and establishing training protocols to support effective model deployment in emergency department settings.

This study has several limitations that merit discussion. Firstly, the chief complaint content is unstructured data, and even with the use of natural language processing techniques, inevitable errors and inconsistencies may arise, potentially limiting the model's accuracy and generalizability. Secondly, while the removal of missing and extreme values was implemented to improve data quality, this approach might have introduced bias or inadvertently excluded clinically significant outliers. Therefore, the application of advanced imputation techniques and sensitivity analyses in future studies could better evaluate the impact of these handling methods on model performance⁴⁴. Additionally, although eight widely-used machine learning algorithms were employed, the selection process in this study was not as systematic as it could have been. Hence, future research could adopt a more structured approach to algorithm selection, including the exploration of newer methods and conducting thorough preliminary assessments to identify the most appropriate algorithms for specific clinical prediction tasks. Furthermore, to address the variability in predicted probabilities among different algorithms, combining predictions from multiple models (e.g., ensemble averaging) or applying advanced probability calibration



Fig. 3. Calibration Curves and Decision Curve Analysis Curves for the Four Best-Performing Algorithms in Model 2. (a) Calibration Curves; (b) Decision Curve Analysis Curves; *SVM* Support Vector Machine.

techniques could improve the consistency and reliability of the outputs. However, this study does not explore these strategies in detail, and future studies should focus on incorporating and validating such approaches to enhance the interpretability and usability of predictive models in real-world clinical applications. Lastly, while the study demonstrated promising results, further validation is essential in real-world clinical settings using prospective data and diverse patient cohorts. Moreover, practical implementation of the model may also be

Threshold (%)	Gradient boosting	Extra tree	Random forest	SVM
5	0.47	0.41	0.44	0.44
10	0.35	0.32	0.33	0.35
20	0.20	0.18	0.19	0.19

Table 4. Comparison of net benefits of different algorithms in DCA at various threshold probabilities in model2. SVM Support Vector Machine, DCA Decision Curve Analysis.







SHAP Explanation for Random Forest



Not Sepsis

age <= 49.00

cirrhosis <= 0.00

BP low <= 0.00

bradycardia <= 0.00

mantal_altered <=

0.13

0.12

0.00

0.08 CKD <= 0.00

0.08

CHF <= 0.00

Sepsis

heartrate > 103.00

numbness <= 0.00

0.08 chest pain <= 0.00

LIME Explanation for Gradient Boosting LIME Explanation for Random Forest **Not Sepsis** Sepsis Prediction probabilities Prediction probabilities cirrhosis <= 0.00 Not Sepsis 0.53 Not Sepsis 0.50 0.19 heartrate > 103.00 Sepsis 0.47 Sepsis 0.50 0.19 age <= 49.00 Value Value Feature Feature 0.16 aphasia <= 0.00 cirrhosis 0.00 0.14 28.00 age palpitations <= 0.00 28.00 0.00 age BP low <= 0.00 aphasia **BP** low 012 ellulitis <= 0.00 bradycardia RP IO mantal_altered 0.00 mantal altered <= CKD 0.00 0.10 $CKD \le 0.00$ mantal altered 0.00 0.09 CKD lethargy <= 0.00 СНЕ ethargy

LIME Explanation for Extra Trees Model



Fig. 5. Interpretation of Four Algorithms in Model 2. SHAP SHapley Additive exPlanations, LIME Local Interpretable Model-agnostic Explanations. In the SHAP method, f (X) represented the final prediction result, which equaled the baseline value E [f (X)] plus the sum of all variable SHAP values. The SHAP values quantified the quantity and direction of each variable's influence on predicting the outcome. Blue and red respectively represented decreases or increases in risk, with longer arrows indicating greater effects. The baseline value E[f(X)] was equivalent to the average risk in the dataset. The LIME method provided the overall prediction probability of the model and the prediction weight for each variable. Orange indicated an increase in risk, while blue indicated a decrease in risk.

influenced by factors such as existing workflows, resource availability, and other contextual considerations, which future studies should address to enhance the model's applicability and reliability.

Conclusion

This study provided a feasible approach for early sepsis screening at triage. Our findings indicated that modeling with more comprehensive triage information using sEMR and ML methods was more effective in predicting sepsis at triage compared to relying solely on vital signs. Interpretable ML enhanced transparency and provided sepsis prediction probabilities, aiding healthcare professionals in making informed medical decisions during the triage process.

Data availability

Publicly available datasets were analyzed in this study. These data can be found at https://mimic.mit.edu/. The datasets generated during and/or analysed during the current study are available in the figshare repository, "https://doi.org/10.6084/m9.figshare.26098048.v1".

Received: 4 July 2024; Accepted: 1 January 2025 Published online: 06 January 2025

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Acknowledgements

The authors would like to express their sincere gratitude to the MIMIC database for providing publicly available data, which has been instrumental in facilitating this research.

Author contributions

W.C. and Z.L. conceptualized the study. Z.L. and W.S. extracted and analyzed the data. Z.L. wrote the manuscript. T.L. and X.Z. verified the results. W.C. revised the manuscript. All the authors contributed to the article and approved the submitted version.

Funding

This research was supported by the Education Department of Liaoning Province, China [Grant No. LJ232410159024].

Declarations

Competing interests

The authors declare no competing interests.

Ethics declarations

The data for this study came from a public database. The study design was approved by the appropriate ethics review board. Informed consent was not necessary because the database used was anonymized.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/1 0.1038/s41598-025-85121-z.

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