Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Development and external validation of a machine learning model for predicting enteral feeding intolerance in adult patients with severe burn injuries

Dan Sun
Affiliated Hospital of Jiangnan University
Minlie Yang
Affiliated Hospital of Jiangnan University
Huihong Wang
Affiliated Hospital of Jiangnan University
Hong Xu
Affiliated Hospital of Jiangnan University
Jianing Hua
huajianing@outlook.com
Affiliated Hospital of Jiangnan University

Article

Keywords: machine learning, feeding intolerance, severe burn, enteral nutrition

Posted Date: June 15th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9044709/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Enteral feeding intolerance (EFI) during enteral nutrition (EN) in adults with severe burn injuries warrants attention. In addition, there is a notable absence of reports from China on this topic. This study is the first to integrate EFI in adult patients with severe burn injuries into a machine-learning model for evaluation and validation.

Methods

This retrospective cohort study included 195 adults with severe burns. The modeling group comprised 155 eligible patients from the Department of Burns, Affiliated Hospital of Jiangnan University, and the validation group included 40 eligible patients from the Affiliated Hospital of Nantong University. We applied three machine learning algorithms: logistic regression, random forest, and support vector machine. The model performance was assessed using the area under the receiver operating characteristic curve (AUROC). SHapley Additive exPlanations (SHAP) values were used to interpret the model outputs and assess the feature importance.

Results

Among 195 adult patients with severe burn injuries, 96 (61.94%) were classified as having an EFI. RF achieved the best performance, with AUROC values of 0.992 (95% confidence interval (CI): 0.981–0.999) in the development cohort and 0.895 (95% CI: 0.783–0.997) in the validation cohort. The use of intestinal probiotics and white blood cell count within 24 h of admission were the most influential variables, followed by burn area, fasting blood glucose within 24 h of admission, and the number of underlying diseases.

Conclusion

The model highlights the key variables in the occurrence of EFI during EN through a SHAP-based interpretation. The use of intestinal probiotics, white blood cell count within 24 h of admission, burn area, fasting blood glucose within 24 h of admission, and the number of underlying diseases were significant contributing factors. Moreover, the final model may provide a basis for individualized EN management strategies for adult patients with severe burn injuries.

Introduction

Severe burn injuries trigger complex metabolic, immunological, and physiological responses that require immediate management, with effects lasting up to 2 years [1]. Nutritional support is essential to mitigate stress responses, hypermetabolism, and increased energy expenditure [2]. Early enteral nutrition (EN; initiated within 24 h post-admission) is widely recognized as the optimal nutritional support modality for major burn injuries requiring fluid resuscitation [3]. However, the gastrointestinal tract is often compromised in patients with severe burns, potentially leading to enteral feeding intolerance (EFI) during EN administration [4]. Trexler's [5] retrospective analysis of mechanically ventilated burn patients (> 20% total body surface area [TBSA]) found that 36.1% developed delayed defecation (> 6 days post-admission), which was associated with increased EFI rates; this was subsequently confirmed in Strang's prospective study [6]. EFI may necessitate the interruption or discontinuation of EN, adversely affecting the intensive care unit length of stay and mortality rates in patients with severe burns [4]. Balancing EN

with EFI has always been challenging in critical nutrition. Therefore, developing clinical prediction models to identify EFI risk could significantly improve the nutritional strategy formulation for patients with severe burns.

In a multicenter, large-sample study of critically ill mechanically ventilated patients, burn, gastrointestinal, and sepsis admission diagnoses were more likely to lead to the development of EFI than respiratory-related admission diagnoses [7]. Similarly, in a mixed retrospective prospective cohort study, Wang et al [8]. constructed a nomogram to predict the occurrence of EFI in critically ill patients. Their model incorporated several predictive factors, including the primary diagnosis, acute gastrointestinal injury grade, and APACHE II score. Nevertheless, existing studies mostly focus on critically ill patients, and it is difficult to directly apply these findings to patients with severe burns due to the obvious specificity of the etiological mechanism, clinical intervention, and prognosis. Therefore, it is essential to determine the factors affecting the occurrence of EFI in patients with severe burns and develop a predictive model.

Recent advances in machine learning (ML) techniques have shown superior performance in modeling complex nonlinear medical data compared with traditional statistical approaches [9]. ML algorithms have gradually been applied to predict EFI, and several ML prediction models have been developed to assess the incidence of EFI in critically ill patients [10, 11]. However, few studies have estimated the incidence of and risk factors for EFI in adult patients with severe burn injuries using real-world data. In this study, three ML algorithms were used: logistic regression (LR), random forest (RF), and support vector machine (SVM). We aimed to use retrospective clinical parameters to develop and externally validate methods for identifying EFI in adult patients with severe burn injuries and to determine the prevalence of EFI and its associated independent risk factors.

Methods

Illustration

The primary outcome was the occurrence of EFI. In this study, EFI was defined as the presence of symptoms such as vomiting, abdominal distension, constipation, high gastric residual volume (defined as gastric residual volume ≥ 250 mL/day), diarrhea (characterized by increased stool frequency > 3 times/day or liquid stool > 250g/day), gastrointestinal bleeding, and subjective discomfort [12]. Assessments based on medical records across enteral feeding were uniformly applied to both the development and validation cohorts. The diagnosis of EFI required the consent of at least two researchers.

Inclusion criteria

Inclusion criteria were (1) patients in the development dataset admitted to the Affiliated Hospital of Jiangnan University between November 2020 and November 2024, as well as those in the external validation dataset admitted to the Affiliated Hospital of Nantong University between November 2022 and November 2024; (2) complicated by major trauma or inhalation injury, a chemical burn, high-voltage electrical burn, and, any burn encompassing > 20% TBSA, excluding superficial burns (epidermal; first-degree burns); (3) patients aged over 18 years old, irrespective of sex.

Exclusion criteria

The exclusion criteria were (1) incomplete clinical data, (2) discharge or death within 72 h after injury, (3) interruption of EN due to changes in condition or unstable circulatory system, and (4) immune or metabolic diseases.

Data collection

Data were extracted from electronic medical records, including medical records, nursing reports, and laboratory results. The dataset includes the following parameters: age, body mass index, number of underlying diseases, length of hospital stay, TBSA, number of antibiotics, modified early warning score, use of mechanical ventilation on the day of admission, use of intestinal probiotics, use of sedative and analgesic agents, and laboratory test indexes (white blood cell-count, C-reactive protein, serum albumin, fasting blood glucose) within 24 h after admission.

This retrospective cohort study was approved by the Medical Ethics Committee of Affiliated Hospital of Jiangnan University (LS2024037), and written informed consent was waived. All procedures were conducted in accordance with the Declaration of Helsinki. All data were fully anonymized to safeguard privacy and confidentiality. Data from electronic medical records were de-identified to ensure patient anonymity.

Model development

Patients with severe burns who were admitted to the Affiliated Hospital of Jiangnan University between November 2020 and November 2024 were selected for model development. Internal validation of the model was performed using the bootstrap resampling technique with 1000 iterations. Significant variables identified by univariate analysis were included as predictors in the model. Three ML algorithms (LR, RF, and SVM) were applied to construct the prediction model.

Model external validation

Validation was conducted on another clinical center dataset of patients with severe burns admitted to the Affiliated Hospital of Nantong University between November 2022 and November 2024. Various validation metrics, such as the AUROC, sensitivity, accuracy, precision, specificity, and F1 score, were employed to assess model performance. Generally, higher values of these metrics indicate superior model performance. The contribution of each input variable to the model output is determined using the Shapley value [13]. To address the opacity of ML algorithms and enhance clinical interpretability, we used SHAP to elucidate the predictions generated by the most effective model. The explanatory analysis primarily used the RF model, which was selected because of its strong compatibility with the SHAP method [14]. Global SHAP values are visualized in a bar chart format to illustrate the average importance of each feature.

Sample size

This study adopted a LR-based event per variable (EPV) method to determine the sample size [15]. A pilot study was conducted to screen for risk factors of EFI among 50 adult patients with severe burn injuries. The model included six covariates, and the incidence of EFI was 60.61%. An EPV value of 10 was selected to ensure the robustness of the regression analysis results. Accounting for a potential 10–20% loss to follow-up, the calculated sample size ranged from 112 to 125 participants.

Statistical analysis

Multiple imputations were used to handle the missing values under the assumption that they were missing at random. Normally distributed continuous variables were presented as means ± standard error, while non-normally distributed continuous variables were expressed as medians with interquartile ranges M (Q1, Q3). Categorical variables are reported as n (%). Comparisons of continuous variables were performed using the *t* test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. Categorical variables were compared using the chi-square (χ^2) test. Multivariate LR was used to analyze the data and identify independent risk factors associated with EFI. The variables identified through the univariate analysis were further evaluated using multivariate LR analysis to determine the final set of predictor variables. All ML algorithms were implemented in R 4.4.0, and statistical analyses were conducted using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, N.Y., USA). All statistical tests were conducted using a two-tailed approach, and a p-value < 0.05 was considered to indicate statistical significance.

Results

In total, 241 patient records were collected (Fig. 1). Among them, 17 patients were discharged or died within 72 h post-injury, and EN was discontinued in 29 patients because of changes in their clinical condition or other contributing factors. Ultimately, 195 patients were included in this study.

Descriptive statistics

In total, 195 participants were enrolled in this study. The baseline characteristics, including general demographic data, disease severity, and laboratory parameters, are summarized in Table 1. The overall mean age of the cohort was 49.77 ± 14.50 years, comprising 157 males (80.51%) and 38 females (19.49%). Among them, 96 developed feeding intolerance, whereas 59 showed no evidence of feeding intolerance. Univariate analysis revealed statistically significant differences in age, burn area, number of underlying diseases, number of antibiotics, fasting blood glucose within 24 h of admission, use of intestinal probiotics, use of sedatives or analgesics, and white blood cell count within 24 h of admission.

Table 1
Baseline characteristics of patients with severe burn injuries for the development and validation cohort

Variable		Development Cohort				Validation Cohort			
		Overall (n = 155)	EFI (n = 96)	Non-EFI(n = 59)	*P* value	Overall (n = 40)	EFI (n = 23)	Non-EFI(n = 17)	*P* value
Age (years), n (%)	18–34	19 (12.26)	8 (8.33)	11 (18.64)	0.007	0 (0.00)	0 (0.00)	0 (0.00)	0.687
	35–64	114 (73.55)	79 (82.29)	35 (59.32)		6 (15.00)	3 (50.00)	3 (50.00)	
	≥ 65	22 (14.19)	9 (9.38)	13 (22.04)		34 (85.00)	20 (58.82)	14 (41.18)	
BMI (kg/m^2), n (%)	< 18.5	3 (1.94)	2 (2.08)	1 (1.69)	0.229	5 (12.50)	4 (17.39)	1 (5.88)	0.481
	18.5–24	31 (20.00)	15 (15.63)	16 (27.12)		17 (42.50)	10 (43.48)	7 (41.18)	
	> 24	121 (78.06)	79 (82.29)	42 (71.19)		18 (45.00)	9 (39.13)	9 (52.94)	
Burn area (%TBSA), $\bar{x}\pm s$		61.56 ± 18.87	64.08 ± 19.04	57.44 ± 17.98	0.033	53.25 ± 24.85	62.65 ± 23.54	40.53 ± 21.07	0.004
Number of underlying diseases (n), median (IQR)		0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.00 (0.00, 0.00)	0.041	0.00 (0.00, 1.75)	1.00 (0.00, 2.00)	0.00 (0.00, 0.50)	0.047
Length of stay (d), median (IQR)		58.00 (37.00, 89.00)	62.50 (37.25, 94.50)	56.00 (36.00, 71.00)	0.127	37.00 (19.25, 67.75)	42.00 (29.00, 114.00)	30.00 (11.00, 48.50)	0.050
Number of antibiotics (n), median (IQR)		3.00 (3.00, 4.00)	4.00 (3.00, 4.00)	3.00 (2.00, 4.00)	< 0.001	4.00 (3.00, 5.75)	5.00 (4.00, 7.00)	3.00 (2.00, 4.50)	< 0.001
MEWS (scores), median (IQR)		4.00 (2.00, 5.00)	3.00 (2.00, 5.00)	4.00 (2.00, 4.00)	0.554	3.00 (2.00, 4.00)	3.00 (2.00, 4.00)	2.00 (2.00, 4.50)	0.310
Fasting blood glucose within 24h of admission (mmol/L), median (IQR)		8.20 (6.80, 10.30)	8.65 (7.23, 11.43)	7.20 (6.17, 8.56)	< 0.001	8.30 (7.10, 10.38)	9.10 (7.70, 12.50)	7.10 (6.10, 8.70)	0.002
Mechanical ventilation was performed on the day of admission, n (%)	Yes	119 (76.77)	72 (75.00)	47 (79.66)	0.505	24 (60.00)	14 (60.87)	10 (58.82)	0.896
	No	36 (23.23)	24 (25.00)	12 (20.34)		16 (40.00)	9 (39.13)	7 (41.18)	

Variable		Development Cohort				Validation Cohort			
		Overall (n = 155)	EFI (n = 96)	Non-EFI(n = 59)	*P* value	Overall (n = 40)	EFI (n = 23)	Non-EFI(n = 17)	*P* value
Use of intestinal probiotics, n (%)	Yes	48 (30.97)	16 (16.67)	32 (54.24)	< 0.001	14 (35.00)	3 (13.04)	11 (64.71)	< 0.001
	No	107 (69.03)	80 (83.33)	27 (45.76)		26 (65.00)	20 (86.96)	6 (35.29)	
Use of sedatives or analgesics, n (%)	Yes	142 (91.61)	92 (95.83)	50 (84.75)	0.034	38 (95.00)	22 (95.65)	16 (94.12)	0.826
	No	13 (8.39)	4 (4.17)	9 (15.25)		2 (5.00)	1 (4.35)	1 (5.88)	
White blood cell-count within 24 h of admission, n (%)	< 12.1×10^9/L	58 (37.42)	21 (21.88)	37 (62.71)	< 0.001	10 (25.00)	2 (8.70)	8 (47.06)	0.006
	≥ 12.1×10^9/L	97 (62.58)	75 (78.12)	22 (37.29)		30 (75.00)	21 (91.30)	9 (52.94)	
C-reactive protein within 24 h of admission, n (%)	< 13.5mg/L	27 (17.42)	18 (18.75)	9 (15.25)	0.577	7 (17.50)	2 (8.70)	5 (9.09)	0.088
	≥ 13.5mg/L	128 (82.58)	78 (81.25)	50 (84.75)		33 (82.50)	21 (91.30)	50 (90.91)	
Serum albumin within 24 h of admission, n (%)	≥ 35g/L	50 (32.26)	33 (34.38)	17 (28.81)	0.472	6 (15.00)	4 (17.39)	2 (11.76)	0.622
	< 35g/L	105 (67.74)	63 (65.62)	42 (71.19)		34 (85.00)	19 (82.61)	15 (88.24)	

BMI, body mass index; TBSA, total body surface area; IQR, interquartile range; MEWS, modified early warning score.

Feature selection

To identify significant predictors of the target variables, LR analysis was conducted, as shown in Table 2. Multivariate analysis revealed that the number of underlying diseases, use of intestinal probiotics, white blood cell count within 24 h of admission, fasting blood glucose within 24 h of admission, and burn area were significantly different between the groups ($P < 0.05$).

Table 2
Multivariate logistic regression analysis of predictors for EFI in the development cohort

Variable	*β*	Wald	Odds ratio (95%CI)	*P*-value
Number of underlying diseases	0.844	7.153	2.326 (1.253–4.318)	0.007
Use of intestinal probiotics	-2.476	20.835	0.084 (0.029–0.243)	< 0.001
White blood cell count within 24 h of admission	-2.221	18.165	0.109 (0.039–0.301)	< 0.001
Fasting blood glucose within 24 h of admission	0.195	5.778	1.215 (1.037–1.424)	0.016
Burn area	0.031	5.024	1.031 (1.004–1.060)	0.025

Model performance

Five predictive factors were incorporated, and three distinct machine-learning algorithms were employed to develop prediction models for EN feeding intolerance in patients with severe burns. Based on this, the stability and generalizability of the three predictive models were systematically validated in both the development and validation cohorts. Their discriminative performances are summarized in Table 3. The RF model demonstrated the highest performance, with an AUROC of 0.992 (95% CI 0.981–0.999) in the development cohort and 0.895 (95% CI 0.783–0.997) in the validation cohort, outperforming all other models (Figs. 2 and 3).

Table 3
Performance of prediction models for predicting EFI

Model Name		Sensitivity	Precision	Accuracy	F1	Specificity	AUROC
LR	Develop	0.906	0.861	0.851	0.883	0.762	0.873
	Validate	0.565	0.928	0.725	0.702	0.941	0.916
SVM	Develop	0.885	0.841	0.825	0.862	0.728	0.892
	Validate	0.869	0.869	0.85	0.869	0.823	0.903
RF	Develop	0.979	0.949	0.954	0.964	0.915	0.992
	Validate	0.826	0.95	0.875	0.883	0.941	0.895

LR, logistic regression; RF, random forest; SVM, support vector machine; AUROC, area under the receiver operating characteristic curve.

Model explanation

Using the SHAP method, we performed a global interpretation of the RF model predictions and a local examination of the individual features to better understand the impact of the feature variables. An increased probability of patients achieving EFI was indicated by features with SHAP values > 0, corresponding to the positive predictions in the model. Global interpretation characterized the overall performance of the model, indicating that the use of intestinal probiotics and white blood cell count within 24 h of admission exhibited the strongest predictive significance, followed by burn area, fasting blood glucose within 24 h of admission, and the number of underlying diseases (Fig. 4A). The SHAP values were calculated and plotted (Fig. 4B). Positive SHAP values were observed for resilience, indicating a positive correlation. This indicates that patients who do not receive intestinal probiotics are at a higher risk of developing EFI, as are those presenting with an abnormal white blood cell count within 24 h of

admission, an extensive burn area, elevated fasting blood glucose within 24 h of admission, and a high number of underlying diseases, which collectively contribute to an increased likelihood of EFI.

Discussion

This study developed a high-resolution, calibration-validated predictive model to estimate the risk of EFI in patients with burn injuries. In the development and validation cohorts, the observed incidence of EFI was 61.94% and 57.50%, respectively. Considering the combined effects of critical illness, burn area, and infection, it is understandable that EFI occurs in more than half of the patients. The Aspen guidelines [16] report an EFI incidence of nearly 50% in critically ill adults, which is consistent with the findings of 14 multicenter observational studies by Alberda et al [17]. However, the specific incidence of EFI may vary owing to differences in definition, study design, and patient populations. Nevertheless, more attention should be given to the occurrence of EFI in adults with severe burn injuries. Accurately predicting the occurrence of EFI and taking targeted measures to address the five risk factors associated with EFI may improve the prognosis of patients with severe burns.

Interruption of early enteral feeding frequently results in insufficient energy and protein intake among patients in the intensive care unit [18, 19]. Evidence indicates that such interruptions are associated with an increased risk of malnutrition and higher in-hospital mortality rates [20]. Our study is the first to demonstrate the significance of white blood cell count within 24 h of admission as an indicator of EFI in adult patients with severe burn injuries. Several characteristics, including burn area and use of intestinal probiotics, have been extensively evaluated and identified as significant predictors of EFI [21, 22]. Additionally, fasting blood glucose within 24 h of admission and the number of underlying diseases have also been recognized as relevant predictors, albeit with smaller effect sizes. These findings underscore the clinical significance of ENI, particularly the value of evaluating white blood cell count within 24 h of admission as a predictive marker for ENI in patients with severe burn injuries. This observation suggests a significant association between the magnitude of the initial inflammatory response and gastrointestinal functional tolerance [23]. Excessive activation of the inflammatory cascade may predispose individuals to intestinal dysfunction, potentially involving alterations in neuronal density, impairment of intestinal barrier integrity, microbial dysbiosis, and aberrant activation of the innate immune system [24, 25].

Among the ML models used for predicting EFI, the RF model showed the best overall prediction performance, with an AUROC value of 0.992, which was significantly better than that of the other models. Compared to traditional LR, RF can effectively reduce the risk of overfitting, enhance the generalization ability of the model, and help analyze the contribution of data characteristics to model prediction through SHAP [26, 27]. Our model quantified the directional influence of these characteristics and identified the main predictors of intestinal probiotics and white blood cell count within 24 h of admission by integrating the SHAP interpretability framework. In addition to the burn area, which was considered a good predictor of EFI, fasting blood glucose within 24 h of admission and the number of underlying diseases were associated with EFI incidence. Hyperglycemia and its underlying diseases significantly contribute to the incidence of feeding intolerance through mechanisms involving intestinal barrier dysfunction, glycemic variability, and gut microbiota dysbiosis [28–30]. These factors collectively underscore the importance of managing blood glucose levels and addressing underlying conditions to improve feeding tolerance and clinical outcomes in affected patients [31, 32].

In the future, we aim to expand the sample size through a prospective, multicenter design to enhance the statistical power. Standardized assessment tools (such as laser Doppler imaging) should be used to objectively quantify burn depth and systematically collect clinical indicators that cannot be included because of missing data, such as vomiting before feeding and stability during the shock stage. Simultaneously, more dynamic laboratory parameters

reflecting inflammation and metabolic status could be added to comprehensively reveal the predictive factors and mechanisms of EFI.

Our study has some limitations. First, the statistical power may be limited because of the relatively small sample size. Second, the geographical distribution of the participants, who were predominantly from southern China, may constrain the generalizability of the findings to a broader Chinese population. Third, although burn depth is pathophysiologically plausible as a predictor of EFI, its inclusion in the analysis was precluded by substantial missing data and inconsistent clinical documentation (e.g., incomplete or clinically inaccurate burn depth assessments), which could introduce measurement bias. Similarly, other clinically relevant variables, including pre-feeding vomiting and hemodynamic stability during the shock phase, were excluded because of concerns about comparable data integrity.

Conclusion

This study used ML algorithms to examine patients' baseline information and nutritional characteristics across the overall population and various subgroups in a retrospective cohort dataset. The RF algorithms exhibited comparable performance in identifying EFI. The use of intestinal probiotics, white blood cell count within 24 h of admission, burn area, fasting blood glucose within 24 h of admission, and the number of underlying diseases were recognized as significant indicators of EFI risk. These models provide practical tools and potential interventions for the nutritional management of patients with high-risk EFI.

Declarations

Declaration of Interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding Statement

This study was supported by the National Natural Science Foundation of China [82472587] and the 2024 Wuxi Youth Science and Technology Talents Promotion Action [TJXD-2024-211].

Ethics approval

This study has been approved by the Medical Ethics Committee of the Affiliated Hospital of Jiangnan University as a retrospective study using documented anonymous clinical data and materials, and the ethics committee determined that written informed consent was waived. All procedures were conducted in accordance with the Declaration of Helsinki.

Data Availability Statement

All data supporting this study will be made available upon request to the corresponding author.

Acknowledgments

The authors thank the team from the Department of Burns of the Affiliated Hospital of Jiangnan University and the team from the Department of Burns of the Affiliated Hospital of Nantong University for their assistance in data

collection.

CRediT authorship contribution statement

Dan Sun: Data curation, Formal analysis, Methodology, Writing; **Minlie Yang**: Investigation, Methodology; **Huihong Wang**: Methodology, Supervision; **Hong Xu**: Validation, Visualization; **Jianing Hua**: Conceptualization, Methodology, Revision.

Patient consent for publication

Not applicable.

References

1. Grammatikopoulou MG, Theodoridis X, Gkiouras K, Stamouli EM, Mavrantoni ME, Dardavessis T, et al. AGREEing on guidelines for nutrition management of adult severe burn patients. JPEN J Parenter Enteral Nutr 2019;43:490-6. https://doi.org/10.1002/jpen.1452
2. Clark A, Imran J, Madni T, Wolf SE. Nutrition and metabolism in burn patients. Burns Trauma 2017;5:11. https://doi.org/10.1186/s41038-017-0076-x
3. Kurmis R, Nicholls C, Singer Y, Edgar DW, Wood FM, Gabbe BJ, et al. An investigation of early enteral nutrition provision in major burn patients in Australia and New Zealand. Nutr Diet 2022;79:582-9. https://doi.org/10.1111/1747-0080.12746
4. He QL, Gao SW, Qin Y, Huang RC, Chen CY, Zhou F, et al. Gastrointestinal dysfunction is associated with mortality in severe burn patients: a 10-year retrospective observational study from South China. Mil Med Res 2022;9:49. https://doi.org/10.1186/s40779-022-00403-1
5. Trexler ST, Lundy JB, Chung KK, Nitzschke SL, Burns CJ, Shields BA, et al. Prevalence and impact of late defecation in the critically ill, thermally injured adult patient. J Burn Care Res 2014;35:e224-9. https://doi.org/10.1097/BCR.0b013e31829b0057
6. Strang SG, Breederveld RS, Cleffken BI, Verhofstad MHJ, Van Waes OJF, Van Lieshout EMM. Prevalence of intra-abdominal hypertension and markers for associated complications among severe burn patients: a multicenter prospective cohort study (BURNIAH study). Eur J Trauma Emerg Surg 2022;48:1137-49. https://doi.org/10.1007/s00068-021-01623-1
7. Heyland DK, Ortiz A, Stoppe C, Patel JJ, Yeh DD, Dukes G, et al. Incidence, risk factors, and clinical consequence of enteral feeding intolerance in the mechanically ventilated critically ill: an analysis of a multicenter, multiyear database. Crit Care Med 2021;49:49-59. https://doi.org/10.1097/CCM.0000000000004712
8. Wang Y, Li Y, Wang H, Li H, Li Y, Zhang L, et al. Development and validation of a nomogram for predicting enteral feeding intolerance in critically ill patients (NOFI): mixed retrospective and prospective cohort study. Clin Nutr 2023;42:2293-2301. https://doi.org/10.1016/j.clnu.2023.10.003
9. Karako K, Tang W. Applications of and issues with machine learning in medicine: bridging the gap with explainable AI. Biosci Trends 2025;18:497-504. https://doi.org/10.5582/bst.2024.01342
10. Raphaeli O, Statlender L, Hajaj C, Bendavid I, Goldstein A, Robinson E, et al. Using machine-learning to assess the prognostic value of early enteral feeding intolerance in critically ill patients: a retrospective study. Nutrients 2023;15:2705. https://doi.org/10.3390/nu15122705

11. Chen H, Han J, Li J, Xiong J, Wang D, Han M, et al. Risk prediction models for feeding intolerance in patients with enteral nutrition: a systematic review and meta-analysis. Front Nutr 2024;11:1522911. https://doi.org/10.3389/fnut.2024.1522911
12. Blaser AR, Deane AM, Preiser JC, Arabi YM, Jakob SM. Enteral feeding intolerance: updates in definitions and pathophysiology. Nutr Clin Pract 2021;36:40-9. https://doi.org/10.1002/ncp.10599
13. Nohara Y, Matsumoto K, Soejima H, Nakashima N. Explanation of machine learning models using shapley additive explanation and application for real data in hospital. Comput Methods Programs Biomed 2022;214:106584. https://doi.org/10.1016/j.cmpb.2021.106584
14. Scavuzzo CM, Scavuzzo JM, Campero MN, Anegagrie M, Aramendia AA, Benito A, et al. Feature importance: opening a soil-transmitted helminth machine learning model via SHAP. Infect Dis Model 2022;7:262-76. https://doi.org/10.1016/j.idm.2022.01.004
15. Peduzzi P, Concato J, Feinstein AR, Holford TR. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. J Clin Epidemiol 1995;48:1503-10. https://doi.org/10.1016/0895-4356(95)00048-8
16. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr 2016;40:159-211. https://doi.org/10.1177/0148607115621863
17. Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhaliwal R, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. Intensive Care Med 2009;35:1728-37. https://doi.org/10.1007/s00134-009-1567-4
18. van Nieuwkoop MM, Ramnarain D, Pouwels S. Enteral nutrition interruptions in the intensive care unit: a prospective study. Nutrition 2022;96:111580. https://doi.org/10.1016/j.nut.2021.111580
19. Zhou Z, Zhang J, Fan C, Wei Z, Wang Q, Liu C. Risk prediction models for enteral nutrition feeding intolerance in critically ill patients: an overview of systematic reviews. Front Nutr 2025;12:1662409. https://doi.org/10.3389/fnut.2025.1662409
20. Arabi YM, Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G, et al. Permissive underfeeding or standard enteral feeding in critically ill adults. N Engl J Med 2015;372: 2398-408. https://doi.org/10.1056/NEJMoa1502826
21. Lu G, Huang J, Yu J, Zhu Y, Cai L, Gu Z, et al. Influence of early post-burn enteral nutrition on clinical outcomes of patients with extensive burns. J Clin Biochem Nutr 2011;48:222-5. https://doi.org/10.3164/jcbn.10-91
22. Fleming D, Jiang Y, Opoku K, Saleh AA, Larumbe-Zabala E, Kesey JE, et al. Prophylactic probiotics in burn patients: risk versus reward. J Burn Care Res 2019;40:953-60. https://doi.org/10.1093/jbcr/irz132
23. Soares CLR, Wilairatana P, Silva LR, Moreira PS, Barbosa NM, da Silva PR, et al. Biochemical aspects of the inflammatory process: a narrative review. Biomed Pharmacother 2023;168:115764. https://doi.org/10.1016/j.biopha.2023.115764
24. Megha KB, Joseph X, Akhil V, Mohanan PV. Cascade of immune mechanism and consequences of inflammatory disorders. Phytomedicine 2021;91:153712. https://doi.org/10.1016/j.phymed.2021.153712
25. Zheng D, Liwinski T, Elinav E. Inflammasome activation and regulation: toward a better understanding of complex mechanisms. Cell Discov 2020;6:36. https://doi.org/10.1038/s41421-020-0167-x
26. Ali S, Akhlaq F, Imran AS, Kastrati Z, Daudpota SM, Moosa M. The enlightening role of explainable artificial intelligence in medical & healthcare domains: a systematic literature review. Comput Biol Med

2023;166:107555. https://doi.org/10.1016/j.compbiomed.2023.107555
27. Wu H, Liao B, Ji T, Ma K, Luo Y, Zhang S. Comparison between traditional logistic regression and machine learning for predicting mortality in adult sepsis patients. Front Med (Lausanne) 2024;11:1496869. https://doi.org/10.3389/fmed.2024.1496869
28. Blaser AR, Malbrain ML, Starkopf J, Fruhwald S, Jakob SM, De Waele J, et al. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM Working Group on Abdominal Problems. Intensive Care Med 2012;38:384-94. https://doi.org/10.1007/s00134-011-2459-y
29. Emgin Ö, Yavuz M, Şahin A, Güneş M, Eser M, Yavuz T, et al. The association between glycemic variability and mortality in critically ill patients: a multicenter prospective observational study. J Clin Med 2024;13:6939. https://doi.org/10.3390/jcm13226939
30. Tan F, Cao Y, Zheng L, Wang T, Zhao S, Chen J, et al. Diabetes exacerbated sepsis-induced intestinal injury by promoting M1 macrophage polarization via miR-3061/Snail1 signaling. Front Immunol 2022;13:922614. https://doi.org/10.3389/fimmu.2022.922614
31. Bohé J, Abidi H, Brunot V, Klich A, Klouche K, Sedillot N, et al. Individualised versus conventional glucose control in critically-ill patients: the CONTROLING study-a randomized clinical trial. Intensive Care Med 2021;47:1271-83. https://doi.org/10.1007/s00134-021-06526-8
32. Singer P, Blaser AR, Berger MM, Calder PC, Casaer M, Hiesmayr M, et al. ESPEN practical and partially revised guideline: clinical nutrition in the intensive care unit. Clin Nutr 2023;42:1671-89. https://doi.org/10.1016/j.clnu.2023.07.011

Figures

Figure 1

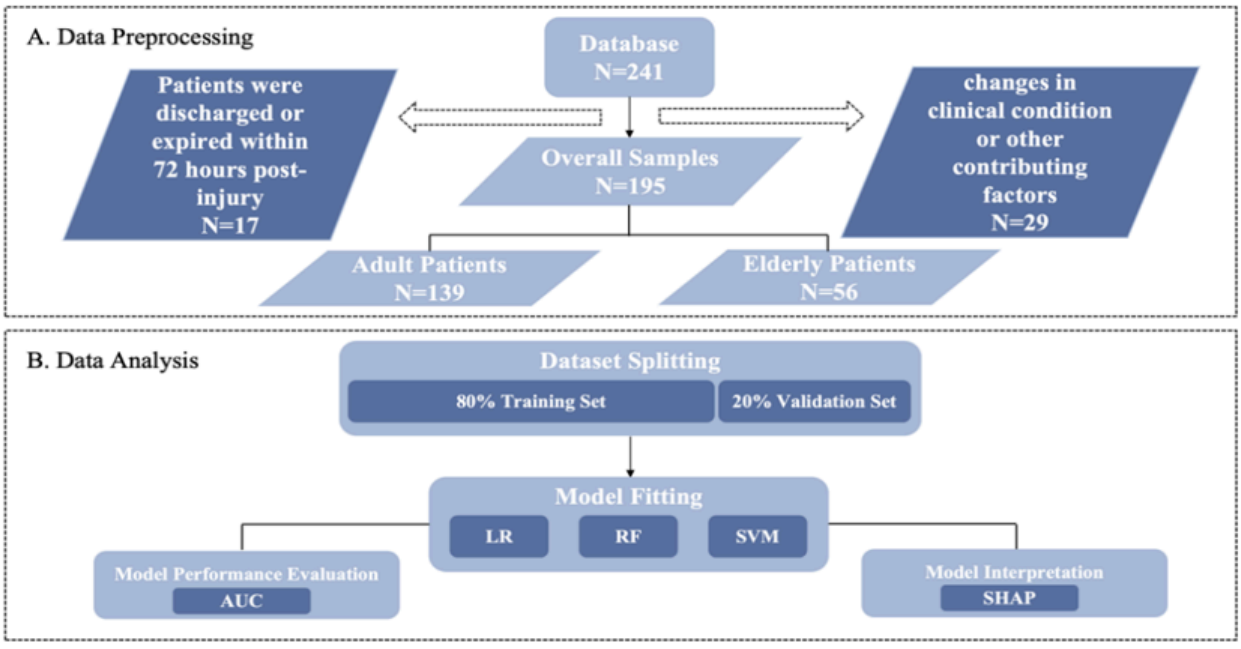


Figure 1

The process of constructing the machine learning model for enteral feeding intolerance in adult patients with severe burn injuries.

LR, logistic regression; RF, random forest; SVM, support vector machine; AUROC, area under the receiver operating characteristic curve; SHAP, Shapley Additive exPlanations.

Figure 2

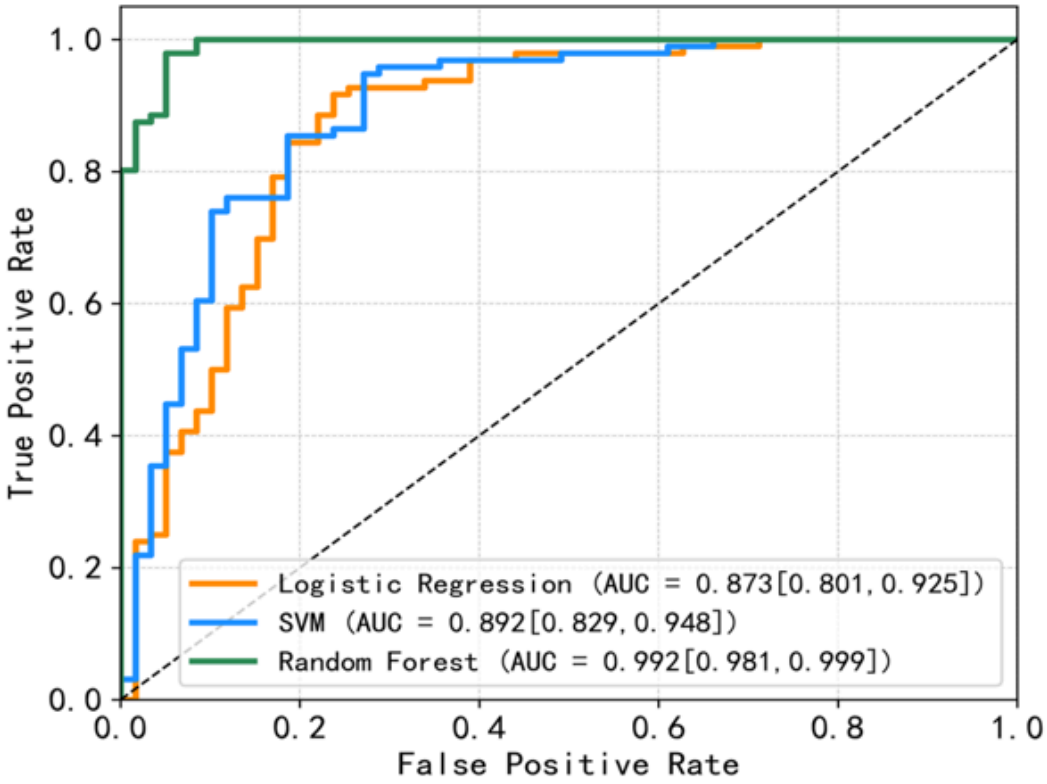


Figure 2

Receiver operating characteristic curve in the development cohort.

SVM, support vector machine; AUROC, area under the receiver operating characteristic curve

Figure 3

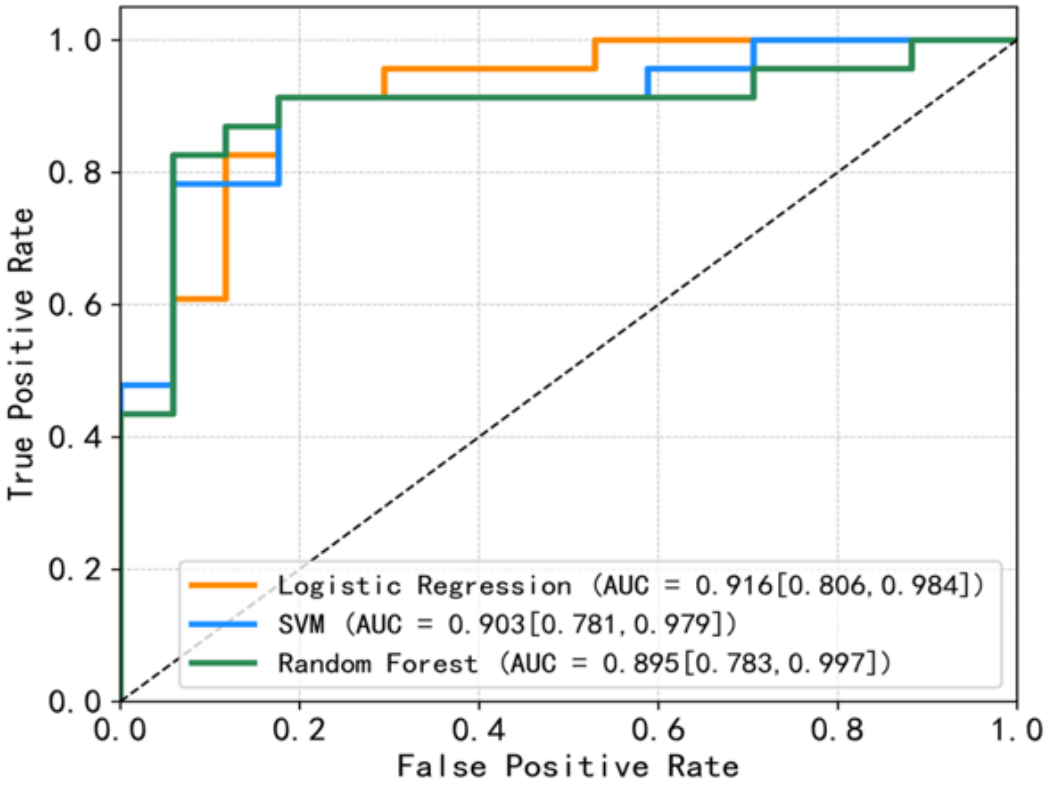


Figure 3

Receiver operating characteristic curve in the validation cohort.

SVM, support vector machine; AUROC, area under the receiver operating characteristic curve

Figure 4

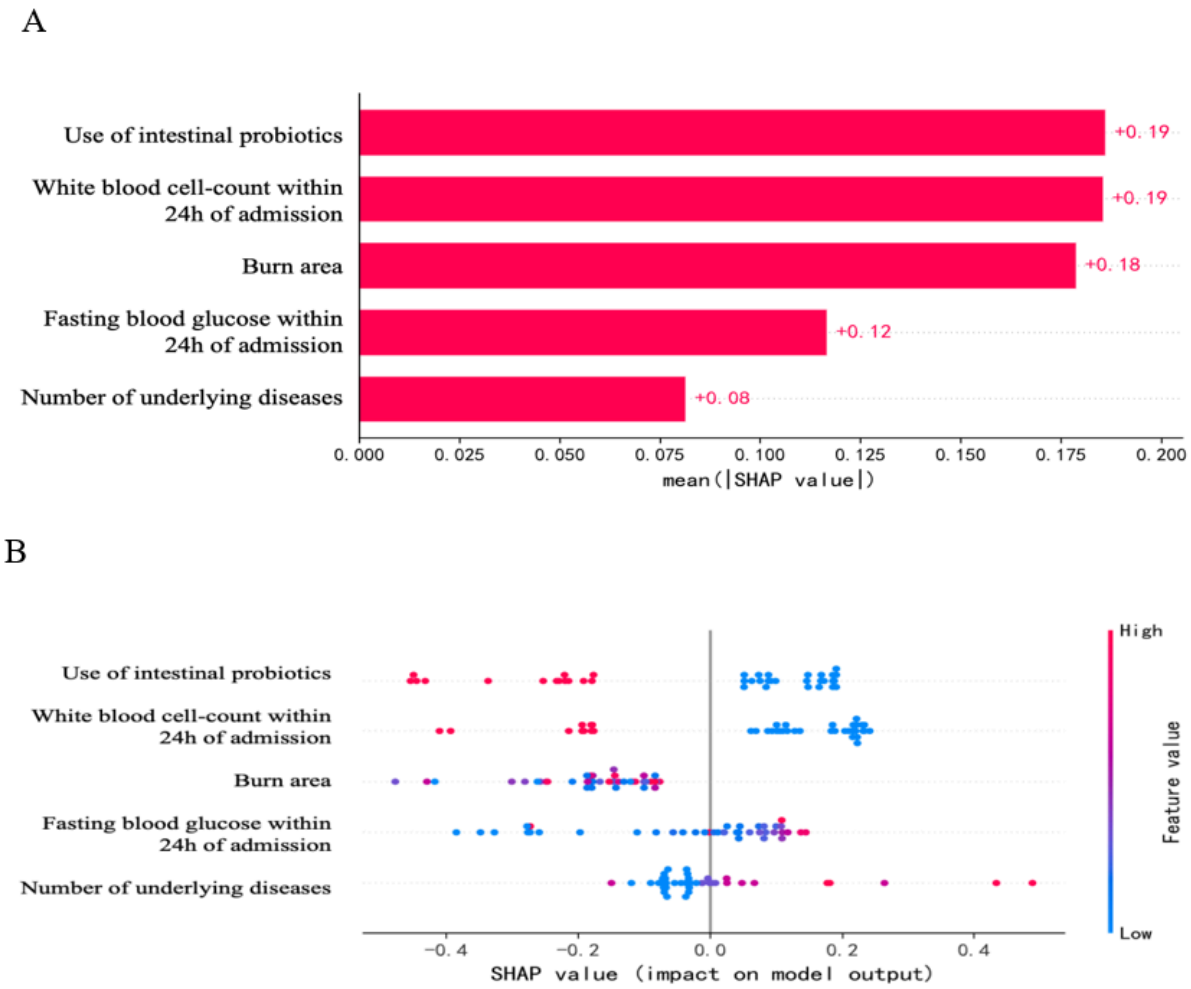


Figure 4

SHAP features for the RF model. (A) SHAP feature importance. (B) Beeswarm summary plot.

SHAP, SHapley Additive exPlanations; RF, random forest