International Journal of General Medicine

Dovepress
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ORIGINAL RESEARCH

Development and Internal Validation of a Clinical Prediction Model for Refeeding Syndrome in Adult Intensive Care Unit Patients: A Retrospective Observational Study

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Objective: Refeeding syndrome (RFS) is a potentially life-threatening complication during nutritional rehabilitation in malnourished patients, especially those in intensive care units (ICUs). This study aimed to develop and internally validate a clinical prediction model for assessing the risk of RFS in adult ICU patients.

Methods: This retrospective observational study was conducted at Beijing Jishuitan Hospital from January 2022 to November 2023. Adult ICU patients at high risk for RFS, identified by nutritional assessment, were included. RFS was defined as a >10% decrease in serum phosphorus, potassium, or magnesium within 5 days after refeeding. Demographic, clinical, and biochemical data were collected from electronic medical records. For the biochemical data, the baseline (the day before refeeding), peak (highest measurements during the first five days after refeeding), and latest value (the fifth day after refeeding) value were analyzed. Univariable and multivariable logistic regression, with stepwise selection, identified independent predictors. Model performance was evaluated by receiver operating characteristic (ROC) curve analysis (area under the curve, AUC), calibration plots, and decision curve analysis (DCA), with internal validation performed using bootstrap resampling.

Results: A total of 132 ICU patients were included (RFS group, n=86; non-RFS group, n=46). Baseline characteristics, illness severity scores, and comorbidities, were generally comparable between groups. Multivariable analysis showed that higher peak urine epithelial cell count (OR=1.145, 95% CI: 1.023–1.282), lower baseline total bilirubin (OR=0.969, 95% CI: 0.940–1.000), lower peak potassium (OR=0.383, 95% CI: 0.147–0.995), and lower latest relative lymphocyte count (OR=0.946, 95% CI: 0.897–0.997) were independently associated with RFS risk. The model demonstrated good discrimination (AUC=0.78, 95% CI: 0.69–0.87) and calibration. DCA indicated clinical utility across a range of risk thresholds.

Conclusion: This internally validated model accurately predicts RFS risk in high-risk adult ICU patients, potentially improving early identification and individualized nutritional management. Further external validation is needed before wider clinical application.

Keywords: refeeding syndrome, intensive care unit, nomogram, prediction, decision curve analysis

Introduction

Refeeding syndrome (RFS) is a potentially fatal complication of clinical nutritional therapy that can occur when nutrition is reintroduced to malnourished patients, posing a particular risk in intensive care unit (ICU) patients experiencing high metabolic stress.[1,2] ICU patients are especially vulnerable due to both compromised nutritional status and the metabolic complexities of critical illness.[3] RFS is characterized by abnormal glucose and lipid metabolism and rapid electrolyte shifts when patients transition from a catabolic to an anabolic state following refeeding, especially after prolonged starvation.[1] The reintroduction of carbohydrates triggers insulin secretion, which drives phosphate, potassium, and magnesium into cells, resulting in potentially severe serum depletion.[4] This electrolyte imbalance can lead to complications such as cardiac failure, respiratory distress, and neurological issues.[5] Among critically ill patients receiving

Received: 5 June 2025
Accepted: 8 October 2025
Published: 14 October 2025

nutritional support, the incidence of RFS has been reported to range from 17.1% to 59%.[6] RFS may worsen prognosis, increasing the need for mechanical ventilation, susceptibility to infections, length of hospital stay, medical costs, and delays in recovery.[7] Furthermore, RFS is an independent risk factor for 6-month mortality in neurocritically ill patients, with mortality rates reported from 26% to 100%.[8,9] Early identification and timely intervention are therefore crucial to optimizing outcomes in this population.[10,11]

Despite its clinical importance, RFS is frequently underrecognized because of its non-specific clinical manifestations and incomplete risk factor assessment, and there is limited literature on effective prediction models for its onset. Developing a predictive model for RFS in ICU settings is thus of critical importance, as it would enable early identification and proactive management of high-risk patients. The American Society for Parenteral and Enteral Nutrition (ASPEN) defines RFS as a reduction in any combination of serum phosphate, potassium, or magnesium levels, often accompanied by manifestations of thiamine deficiency, appearing soon after the initiation of nutritional support in individuals with prolonged malnutrition.[12] However, electrolyte reductions may also occur due to other causes, such as diuretic or insulin use, complicating the diagnosis.[13] Several risk screening tools, such as the NRS-2002 and the Walmsley Score, have been proposed but lack specificity for the dynamic ICU context and often do not incorporate real-time biochemical markers.[14,15] Case studies have highlighted these models' limitations, including missed RFS cases and the need for frequent adjustments, which reduce their practicality in critical care.[16–18] Recent systematic reviews have summarized RFS risk factors in adults, but have not proposed practical predictive models for clinical use.[19]

Given these gaps, there remains a need for a reliable, clinically applicable predictive model for RFS tailored to adult ICU patients. Therefore, the present study aimed to establish a prediction model for RFS in ICU patients, providing clinicians with a tool to anticipate and mitigate the risk of RFS and potentially reduce its associated morbidity and mortality.

Materials and Methods

Study Design and Patients

This retrospective observational study was conducted in the Intensive Care Unit (ICU) of Beijing Jishuitan Hospital, Capital Medical University, from January 2022 to November 2023. The protocol was approved by the hospital's ethics committee (approval #Jilun [K2023] No. [354]-00) and conformed to the Declaration of Helsinki. The requirement for individual informed consent was waived by the Ethics Committee due to the retrospective nature of the study, the use of previously collected data, no direct contact with patients, and minimal risk to participants. All patient data were anonymized prior to analysis, and confidentiality was strictly maintained in accordance with institutional and ethical guidelines.

Adult patients (aged ≥18 years) admitted to the ICU during the study period were considered eligible if they were evaluated as being at high risk for refeeding syndrome (RFS) based on nutritional assessments.[11,20] Patients were excluded if they received palliative care or had incomplete data. The sample size was not calculated a priori, but the final sample provided at least 10 events per variable (EPV) for multivariable model development, which is considered sufficient for this retrospective study.

Data Collection and Definitions

All data were obtained retrospectively from electronic medical records. Collected variables included demographic information (age, sex, body weight, and body mass index [BMI, kg/m²]), medical history (including comorbidities such as diabetes and alcohol abuse), and medication records (use of insulin, sedatives/analgesics, proton pump inhibitors, probiotics, lipid-lowering drugs, laxatives, and diuretics such as furosemide). For each medication, usage was documented both before refeeding and after refeeding to capture changes in pharmacologic management during the study period. Nutritional and treatment-related data included the number of fasting days prior to refeeding (recorded as days) and daily protein intake (grams per day).

Clinical presentation at ICU admission was assessed using standardized scoring systems, including the Nutritional Risk Screening (NRS-2002),[14] Acute Physiology and Chronic Health Evaluation II (APACHE II),[21] Sequential Organ

Failure Assessment (SOFA),[22] and Glasgow Coma Scale (GCS).[23] Nutritional and treatment-related data included the number of fasting days prior to refeeding and protein intake. The total hospital cost was defined as the sum of all direct medical expenses incurred during the hospital stay, as recorded in the hospital billing system, and is reported in Chinese Yuan (CNY). The length of hospital stay was defined as the total number of days from ICU admission to hospital discharge or death. In-hospital mortality was defined as death from any cause occurring during the hospital admission.

Key laboratory and biochemical data included procalcitonin, creatine kinase-MB, myoglobin, aspartate aminotransferase, creatinine, uric acid, carbon dioxide combining power, platelet count, fibrinogen, urine urobilinogen, urine bilirubin, γ-glutamyl transferase, absolute and relative lymphocyte counts, relative neutrophil count, and relative basophil count. Urine routine tests included measurements such as urine epithelial cell count and urine conductivity. All blood and urine samples were collected at a standardized time (6:00 am) daily during ICU stay. For each patient, "baseline" values were defined as those measured on the last day of fasting (the day before refeeding); "peak" values were the highest measurements recorded during the first five days after initiation of refeeding; and "latest" values referred to the last measurement within this five-day observation period. These definitions were applied consistently to all relevant biochemical parameters. These markers were selected based on their potential to predict the occurrence of RFS, which was the primary outcome in this study.

The outcomes assessed in this study included total hospital cost (in Chinese Yuan), the length of ICU and overall hospital stay (in days), and clinical outcomes such as in-hospital mortality and the occurrence of complications during the ICU stay.

Refeeding syndrome was diagnosed if (1) at least one of serum phosphorus, potassium, or magnesium levels decreased by >10% from baseline (with 10–20% defined as mild, 20–30% as moderate, and >30% as severe), (2) the baseline was defined as the value on the last day of fasting, and (3) the decrease occurred within five days after the start of nutritional support.[12] The diagnostic criteria and cut-off values were based on the ASPEN consensus recommendations.[12]

Statistical Analysis

Statistical analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as mean ± standard deviation (SD) or median and interquartile range (IQR), depending on their distribution (assessed using the Kolmogorov–Smirnov test), and were compared using Student's *t*-test or the Mann–Whitney *U*-test. Categorical variables were presented as counts (n) and percentages (%) and compared using the chi-squared test. Variables with $P < 0.20$ (clinical) or $P < 0.05$ (biochemical) in univariable analyses were entered into the multivariable logistic regression model. Bidirectional stepwise regression was performed to select predictors, minimizing the Akaike information criterion (AIC). Multicollinearity was assessed using the variance inflation factor (VIF), with variables showing VIF > 5 excluded from the final model. Model performance was evaluated by receiver operating characteristic (ROC) curve analysis (area under the curve, AUC), calibration plots, and decision curve analysis (DCA). Internal validation was performed using bootstrap resampling with 1000 iterations. A two-sided P-value < 0.05 was considered statistically significant.

Results

Characteristics of the Participants

A total of 132 patients at high risk for refeeding syndrome (RFS) were included in this study: 86 developed RFS and 46 did not. The mean age was 64.7 ± 17.4 years in the RFS group and 61.6 ± 18.0 years in the non-RFS group; 59.3% and 67.4% were male, respectively. Baseline demographic and clinical features, including comorbidities and illness severity scores, were generally similar between groups (all $P > 0.05$; Table 1). Although the observed proportion of alcohol abuse differed between groups (8.1% vs 21.7%), the difference was not statistically significant ($p = 0.051$). Clinical outcomes assessed included hospital stay (length of stay), cost, and in-hospital mortality.

Table 1 Baseline Characteristics of Study Participants

Variable	Non-RFS (n=46)	RFS (n=86)	p-value
A. Demographics			
Age (years), mean ± SD	61.61 ± 18.00	64.66 ± 17.38	0.299
Sex			0.469
Male, n (%)	31 (67.4%)	51 (59.3%)	
Female, n (%)	15 (32.6%)	35 (40.7%)	
Weight (kg), mean ± SD	66.37 ± 13.56	65.06 ± 13.82	0.380
BMI (kg/m²), mean ± SD	23.38 ± 3.76	23.21 ± 3.85	0.604
B. Clinical Outcomes			
Hospital Stay (days), mean ± SD	17.98 ± 12.35	17.53 ± 9.84	0.935
Cost (CNY), mean ± SD	122,719.36 ± 77,529.64	106,199.98 ± 91,823.95	0.118
In-hospital mortality, n (%)	1 (2.2%)	3 (3.5%)	1.000
C. Medical History			
History of Diabetes, n (%)	11 (23.9%)	22 (25.6%)	1.000
History of Alcohol Abuse, n (%)	10 (21.7%)	7 (8.1%)	0.051
Comorbidities (excl. diabetes), n (%)	29 (63.0%)	49 (57.0%)	0.624
D. Nutrition & Medication			
Fasting Days, mean ± SD	4.30 ± 5.83	3.24 ± 4.09	0.094
Protein Intake (g/day), mean ± SD	0.89 ± 0.31	0.86 ± 0.35	0.616
Insulin Dose (units/day), mean ± SD	239.26 ± 295.57	247.42 ± 428.26	0.450
Before Refeeding			
Sedatives & Analgesics, n (%)	33 (71.7%)	59 (68.6%)	0.861
Proton Pump Inhibitors, n (%)	26 (56.5%)	46 (53.5%)	0.881
Probiotics, n (%)	3 (6.5%)	7 (8.1%)	1.000
Lipid-lowering Drugs, n (%)	7 (15.2%)	16 (18.6%)	0.804
Laxatives, n (%)	6 (13.0%)	16 (18.6%)	0.567
Diuretics (eg, furosemide), n (%)	8 (17.4%)	18 (20.9%)	0.797
After Refeeding			
Sedatives & Analgesics, n (%)	37 (80.4%)	74 (86.0%)	0.555
Proton Pump Inhibitors, n (%)	43 (93.5%)	74 (86.0%)	0.320
Probiotics, n (%)	16 (34.8%)	32 (37.2%)	0.931
Lipid-lowering Drugs, n (%)	9 (19.6%)	21 (24.4%)	0.677
Laxatives, n (%)	13 (28.3%)	24 (27.9%)	1.000
E. Severity Scores			
NRS Score, mean ± SD	3.30 ± 1.24	3.41 ± 1.27	0.643
APACHE II Score, mean ± SD	16.37 ± 5.19	15.12 ± 6.62	0.059
SOFA Score, mean ± SD	6.09 ± 2.99	5.38 ± 2.88	0.170
GCS Score, mean ± SD	13.54 ± 2.56	13.44 ± 3.05	0.669

Abbreviations: BMI, body mass index; NRS, Nutritional Risk Screening; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale.

Univariable Analyses of the Factors Associated with the RFS

Table 2 summarizes the association of clinical and biochemical variables with RFS in univariable analysis. Variables significantly associated with RFS included higher peak urine epithelial cell count, lower baseline total bilirubin, lower peak potassium, and lower latest relative lymphocyte count, among others.

In the multivariable logistic regression analysis, the following variables were independently associated with RFS: peak urine epithelial cell count (odds ratio [OR] 1.145, 95% CI: 1.023–1.282, P = 0.019), baseline total bilirubin (OR 0.969, 95% CI: 0.940–1.000, P = 0.049), peak potassium (OR 0.383, 95% CI: 0.147–0.995, P = 0.049), latest relative lymphocyte count (OR 0.946, 95% CI: 0.897–0.997, P = 0.040), and baseline urine conductivity (OR 1.082, 95% CI: 0.997–1.174, P = 0.060) (Table 3). Predictors were selected using bidirectional stepwise regression based on statistical significance and clinical relevance.

Table 2 Biochemical Markers with Significant Differences in Univariable Analysis

Variable	Unit	Non-RFS (n=46)	RFS (n=86)	p-value
A. Blood Tests				
Procalcitonin - baseline, mean ± SD	ng/mL	9.70 ± 19.85	3.49 ± 7.68	0.018
Creatine Kinase-MB - baseline, mean ± SD	U/L	22.35 ± 51.34	10.64 ± 31.55	0.012
Myoglobin - baseline, mean ± SD	ng/mL	889.98 ± 1146.99	408.43 ± 748.32	0.002
Aspartate Aminotransferase - baseline, mean ± SD	U/L	173.18 ± 367.51	46.10 ± 67.32	0.024
Creatinine - baseline, mean ± SD	μmol/L	99.26 ± 56.15	86.16 ± 86.20	0.028
Uric Acid - baseline, mean ± SD	μmol/L	392.15 ± 192.77	321.22 ± 144.44	0.034
Carbon Dioxide Combining Power - baseline, mean ± SD	mmol/L	46.04 ± 12.95	51.33 ± 11.20	0.042
Platelet Count - baseline, mean ± SD	$\times 10^9$/L	181.57 ± 62.69	216.85 ± 111.09	0.049
Fibrinogen Quantification - peak, mean ± SD	mg/L	663.33 ± 184.23	607.15 ± 178.79	0.047
Gamma-Glutamyl Transferase - peak, mean ± SD	U/L	151.17 ± 174.51	104.24 ± 144.87	0.037
Absolute Lymphocyte Count - peak	$\times 10^9$/L	2.00 ± 0.98	1.78 ± 1.17	0.024
Creatinine - peak, mean ± SD	μmol/L	141.96 ± 128.36	112.92 ± 104.64	0.035
Absolute Lymphocyte Count - latest, mean ± SD	$\times 10^9$/L	1.32 ± 0.63	1.09 ± 0.55	0.034
Relative Neutrophil Count - latest, mean ± SD	%	71.06 ± 9.22	75.57 ± 11.21	0.008
Relative Lymphocyte Count - latest, mean ± SD	%	18.99 ± 8.57	14.95 ± 8.48	0.007
Relative Basophil Count - latest, mean ± SD	%	0.45 ± 0.26	0.38 ± 0.40	0.012
B. Urine Tests				
Urine Urobilinogen - peak, mean ± SD	mg/dL	0.85 ± 1.19	1.23 ± 1.21	0.040
Urine Bilirubin - peak, mean ± SD	mg/dL	0.57 ± 0.81	0.29 ± 0.63	0.028
Urine Bilirubin - latest, mean ± SD	mg/dL	0.15 ± 0.47	0.05 ± 0.30	0.041
Epithelial Cells - latest, mean ± SD	/HPF	3.27 ± 3.17	8.52 ± 19.71	0.031
Equivalent to Epithelial Cells - latest, mean ± SD	/HPF	0.59 ± 0.58	1.53 ± 3.55	0.030

Notes: Statistical analysis: Continuous variables are presented as mean ± SD and compared using the Student's *t*-test or Mann–Whitney *U*-test, as appropriate. Significance level: $p < 0.05$.
Abbreviations: SD, standard deviation; HPF, high power field.

Table 3 Multivariable Analysis of Predictive Variables for RFS

Variable	OR (95% CI)	p-value
Cost	1.000 (1.000, 1.000)	0.153
APACHE II Score	1.014 (0.927, 1.109)	0.760
SOFA Score	0.969 (0.810, 1.159)	0.729
History of alcohol abuse	0.504 (0.140, 1.813)	0.294
Fasting days	0.940 (0.858, 1.030)	0.187
Urine epithelial cells - peak	1.145 (1.023, 1.282)	0.019
Urine conductivity - baseline	1.082 (0.997, 1.174)	0.060
Aspartate aminotransferase - baseline	0.997 (0.992, 1.002)	0.229
Total bilirubin - baseline	0.969 (0.940, 1.000)	0.049
Uric acid - baseline	0.998 (0.995, 1.001)	0.106
Potassium - peak	0.383 (0.147, 0.995)	0.049
Relative lymphocyte count - latest	0.946 (0.897, 0.997)	0.040

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; CI, Confidence Interval.

Model Performance

A nomogram was constructed based on the significant predictors identified in the multivariable model (Table 3 and Figure 1). The model demonstrated good discrimination, with an area under the ROC curve (AUC) of 0.780 (95% CI: 0.695–0.865) (Figure 2). Calibration analysis showed that the predicted probabilities closely matched observed outcomes, with a mean absolute error of 0.021 (Figure 3). Decision curve analysis demonstrated a standardized net benefit above 0.6 for threshold probabilities between

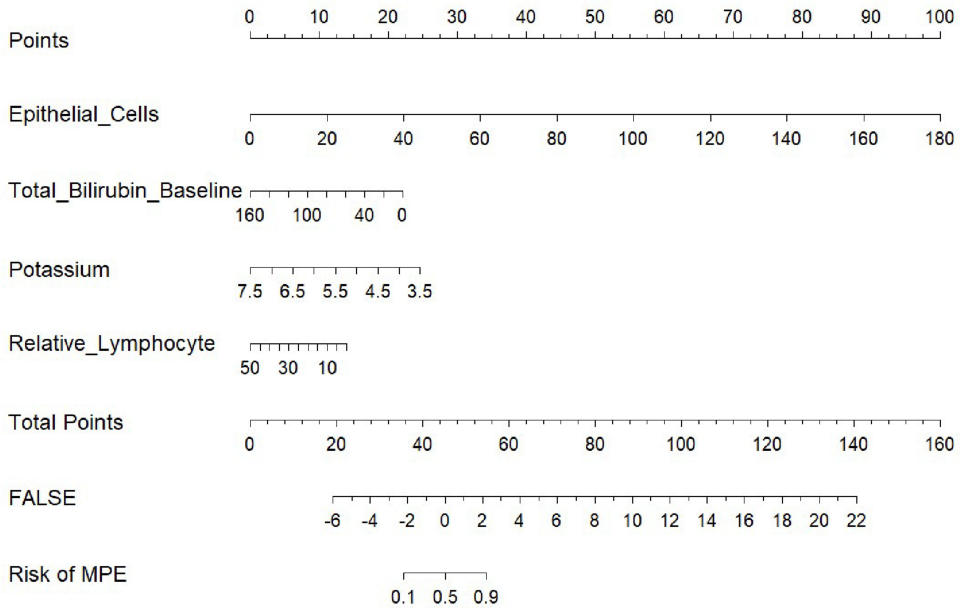

Figure 1 Nomogram for predicting the risk of refeeding syndrome (RFS) of ICU patients. The nomogram includes four predictors: urine epithelial cell count, baseline total bilirubin levels, potassium levels, and relative lymphocyte count. Each predictor corresponds to a point value on the "Points" scale. The total points are calculated by summing the points for all predictors, which are then aligned to the "Risk of RFS" scale to determine the overall risk. Higher total points indicate a higher risk of RFS.

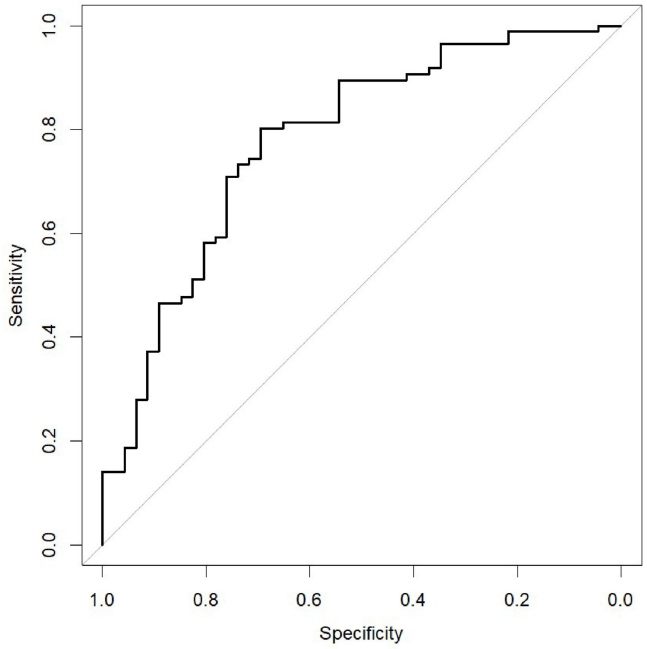

Figure 2 Receiver Operating Characteristic (ROC) curve for the nomogram model. The ROC curve illustrates the model's ability to discriminate between ICU patients with and without RFS. The area under the curve (AUC) is 0.7798, with a 95% confidence interval (CI) ranging from 0.6947 to 0.8650, as calculated by the DeLong method.

0.1 and 0.4, peaking at a threshold of 0.2, and remaining favorable up to a threshold of 0.8 (Figure 4). Internal validation with bootstrap resampling (1000 runs) yielded a mean AUC of 0.782 ± 0.044, and the bootstrap-corrected AUC was 0.765 (95% CI: 0.675–0.856) (Figure 5).

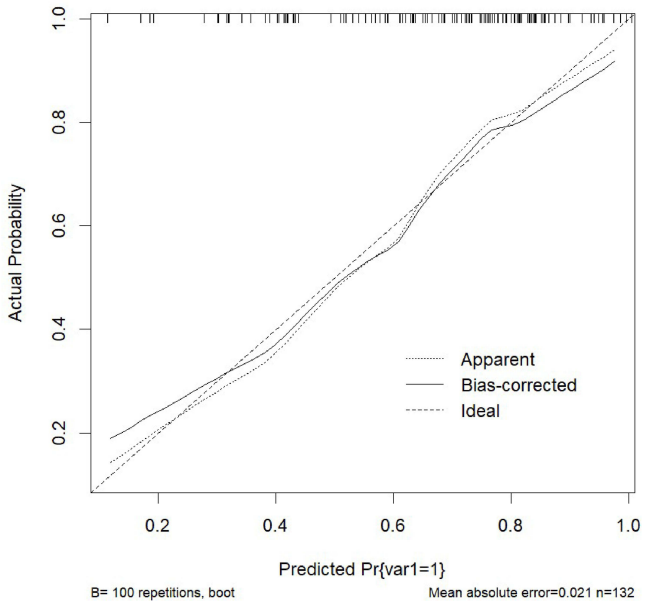

Figure 3 Calibration curve for the nomogram model. The calibration curve shows the agreement between the predicted probabilities and the observed outcomes for the risk of RFS. The "Apparent" line represents the initial model fit, the "Bias-corrected" line indicates the model performance after bootstrapping with 100 repetitions, and the "Ideal" line represents perfect calibration. The closeness of the "Bias-corrected" line to the "Ideal" line suggests good calibration of the model. The mean absolute error is 0.021, mean squared error is 0.00066, and the 0.9 quantile of absolute error is 0.038, indicating the accuracy of the model's predictions. The sample size (n) is 132.

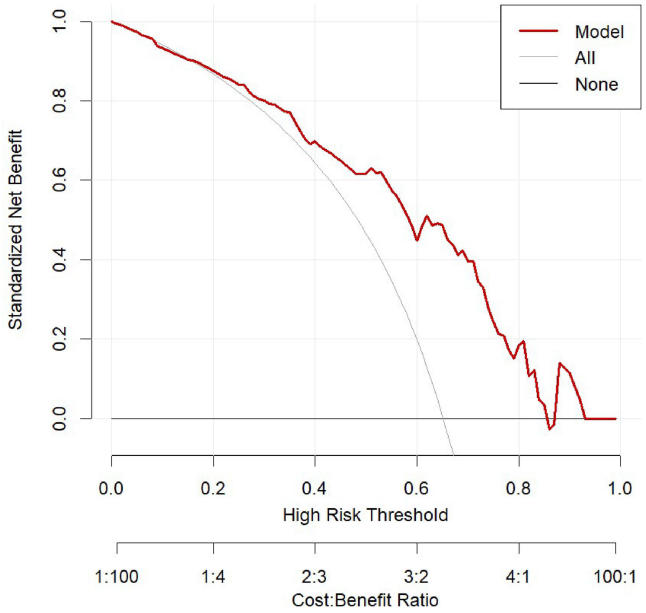

Figure 4 Decision curve analysis (DCA) for the nomogram model. The decision curve shows the standardized net benefit of using the nomogram model (red line) compared to two default strategies: diagnose all ICU patients (gray line) as RFS or diagnose no ICU patients (black line) as RFS across a range of high-risk thresholds. The x-axis represents the high-risk threshold probability, and the y-axis indicates the standardized net benefit. The results suggest that the nomogram model provides a higher net benefit than the "Treat All" or "Treat None" strategies at most threshold probabilities, indicating its clinical utility for guiding RFS in ICU patients. The curve emphasizes the benefit of using the model for personalized decision-making when the risk threshold is between 0.1 and 0.8.

Discussion

This study developed and internally validated a clinical prediction model for the risk of RFS in ICU patients. The resulting nomogram integrates routinely accessible clinical and biochemical indicators—specifically, urine epithelial cell count, baseline total bilirubin, peak potassium, and latest relative lymphocyte count. The model demonstrated good

https://doi.org/10.2147/IJGM.S544989

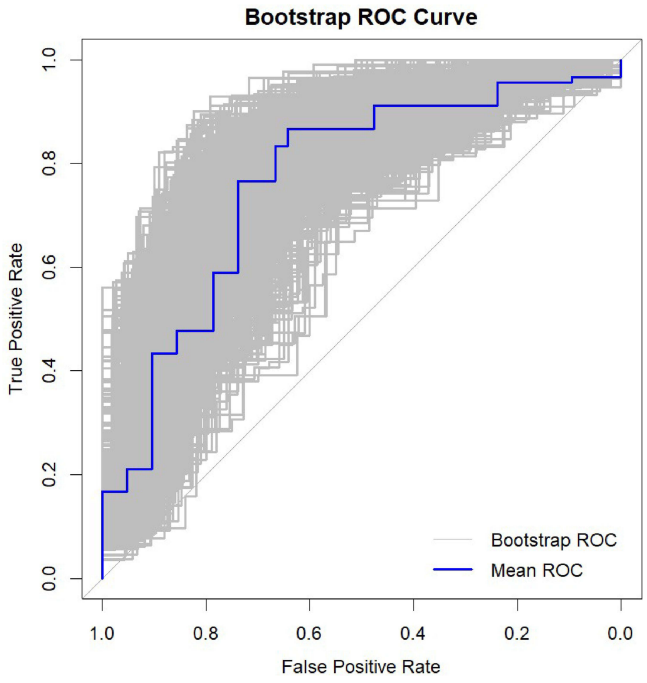

Figure 5 Bootstrap ROC Curve for Model Validation. This figure presents the bootstrap Receiver Operating Characteristic (ROC) curve used for validating the predictive performance of the nomogram-based risk model for RFS in ICU patients with adenomyosis. The blue line represents the mean ROC curve obtained from 1000 bootstrap samples, demonstrating the model's discriminatory ability. The gray lines represent the ROC curves from individual bootstrap samples, providing a visual representation of the model's stability across different samples. The area under the curve (AUC) for the mean ROC was 0.7653, with a 95% confidence interval (CI) of 0.6752 to 0.8555, indicating good discriminative power. The mean AUC from the bootstrap samples was 0.7821, with a standard deviation of 0.0442, further confirming the robustness and reliability of the model.

discrimination (AUC 0.78) and calibration, and decision curve analysis indicated meaningful clinical utility for risk stratification in this high-risk population.

To our knowledge, this is the first study to construct a comprehensive and practical prediction model specifically for RFS risk in a general ICU population. Previous models, such as those by Zhang et al,[24] Elnenaei et al,[25] and Goyale et al,[26] included variables like history of alcoholism, fasting duration, severity scores, and specialized biomarkers (eg, leptin, IGF-1), with reported AUCs ranging from 0.75 to 0.80. Recent machine learning approaches have achieved higher AUCs,[27] but often require complex data inputs or are not tailored to ICU populations. Our model, while comparable in performance (AUC 0.78), has the advantage of using parameters that are routinely monitored in ICU practice, improving its clinical applicability and potential for bedside use.

Each of the predictors included in our model is supported by pathophysiologic rationale and/or previous evidence. Urine epithelial cell count reflects renal and urinary tract integrity; higher counts may indicate acute kidney stress or underlying infection, which are known to complicate nutritional interventions in the critically ill.[28,29] Baseline total bilirubin serves as a marker of hepatic function and nutritional status; elevated levels may reflect liver dysfunction or malnutrition, both of which predispose to metabolic complications during refeeding.[30,31] Serum potassium, a key electrolyte, is central to the pathogenesis of RFS: hypokalemia is a hallmark of the syndrome and is associated with adverse cardiac and neuromuscular outcomes if not promptly corrected.[32,33] Relative lymphocyte count is an indirect marker of immune competence and nutritional reserve; low lymphocyte counts are frequently observed in malnourished or critically ill patients and may signal an impaired ability to respond to metabolic stress.[34,35] While low lymphocyte counts are not specific to RFS, they are consistently associated with worse outcomes in malnutrition and critical illness.[31]

Strengths and Limitations

The strength of our model lies in its inclusion of dynamic, routinely measured variables that can adapt to the rapidly changing conditions typical of ICU patients. The use of robust statistical methods, including stepwise regression and

bootstrap validation, minimizes overfitting and supports the model's internal validity. By integrating multiple clinically relevant markers, our approach offers a more nuanced and individualized risk assessment for RFS, which could support earlier interventions and potentially improve patient outcomes.

Several limitations must be acknowledged. First, this was a single-center retrospective study, which may introduce selection bias and limit the generalizability of findings. The sample size, though adequate for model development and validation, may not capture the full diversity of ICU populations. Our model was derived and validated only in patients at high risk for RFS as defined by current nutritional screening criteria, and thus its applicability to broader ICU populations or to other clinical settings (eg, surgical, cardiac, or pediatric ICUs) remains to be established. Additionally, the model is based primarily on variables measured at baseline or within the first days of refeeding, and does not account for subsequent changes in clinical status or interventions. Further prospective, multicenter studies—including external validation across diverse ICU populations and healthcare systems—are needed to confirm the robustness and applicability of the model. The practical implementation of the nomogram may also require some adaptation and education for ICU teams.

Future research should consider incorporating additional dynamic and longitudinal variables, as well as advanced analytic methods such as machine learning, to further improve predictive accuracy and clinical utility. Ultimately, integrating such tools into ICU practice could enable real-time risk stratification, guide tailored nutritional interventions, and reduce the incidence and severity of RFS in critically ill patients.

Conclusions

In this retrospective study of ICU patients at risk for refeeding syndrome, we developed and internally validated a clinical prediction model incorporating routine clinical and biochemical indicators. The model demonstrated good discriminatory ability and calibration for identifying patients at higher risk of RFS. While our findings suggest this tool may help guide risk stratification and support clinical decision-making in the ICU, its application should be limited to similar high-risk populations until further prospective and multicenter validation is conducted. Ongoing research and refinement are necessary to optimize the model's utility and assess its potential to improve patient outcomes through timely, individualized interventions.

Abbreviation

RFS, Refeeding Syndrome; ICU, Intensive care unit; BMI, Body mass index; ASPEN, American Society for Parenteral and Enteral Nutrition; NRS, Nutritional Risk Screening; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; SD, Standard deviation; IQR, Interquartile range; AIC, Akaike Information Criterion; VIF, Variance Inflation Factor; MAE, Mean absolute error; MSE, Mean squared error; ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; CIs, Confidence intervals; DCA, Decision Curve Analysis.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Approval and Informed Consent

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Beijing Jishuitan Hospital, Capital Medical University (Jilun [K2023] No. [354] −00). The requirement for individual informed consent was waived by the Ethics Committee due to the retrospective nature of the study, the use of previously collected data, no direct contact with patients, and minimal risk to participants. All patient data were anonymized prior to analysis, and confidentiality was strictly maintained in accordance with institutional and ethical guidelines.

Funding

The study was supported by 2023 Guo Jia Lin Chuang Zhong Dian Zhuan Ke Jian She Projects.

Disclosure

The authors declare no conflicts of interest in this work.

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