Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Risk Factors and Prediction Model for ICU-Acquired Weakness in Severe Acute Pancreatitis: A Retrospective Cohort Study

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Objective: To investigate the incidence and independent risk factors of intensive care unit-acquired weakness (ICU-AW) in patients with severe acute pancreatitis (SAP) and to develop and validate a corresponding risk prediction model.

Methods: In this retrospective study, 277 SAP patients admitted to the ICU between January 2020 and March 2024 were enrolled. ICU-AW was diagnosed using the Medical Research Council sum score (MRC-SS), with a score <48 defining the condition. Patients were randomly split into a modeling cohort (70%) for model development and a validation cohort (30%) for internal validation. Univariate and multivariate logistic regression analyses were employed to identify factors associated with ICU-AW. A nomogram was constructed based on independent predictors identified from the multivariate analysis. The model's performance was assessed by the area under the receiver operating characteristic curve (AUC) and the Hosmer-Lemeshow (H-L) test.

Results: The incidence of ICU-AW was 38.6% (107/277) among the enrolled SAP patients. Multivariate analysis identified age ≥51 years (OR=5.83), APACHE II score ≥14 (OR=11.19), ICU length of stay ≥7 days (OR=12.61), use of neuromuscular blocking agents (OR=3.34), D-lactate ≥41.69 mg/L (OR=2.92), and presence of nutritional risk (OR=5.34) as independent risk factors for ICU-AW. Early rehabilitation care was a significant protective factor (OR=0.18). The prediction nomogram incorporating these seven factors demonstrated excellent discrimination, with an AUC of 0.922 (95% CI: 0.884–0.959) in the modeling cohort and 0.918 (95% CI: 0.873–0.963) in the validation cohort. The H-L test indicated good calibration in both cohorts (P=0.903 and P=1.000, respectively).

Conclusion: ICU-AW is a common complication in SAP patients. We developed a nomogram that effectively integrates readily available clinical variables (age, disease severity, ICU stay, medication use, D-lactate, nutritional status, and rehabilitation care) to individually predict the risk of ICU-AW. This model may assist clinicians in early identification of high-risk patients and facilitate targeted preventive strategies.

Keywords: severe acute pancreatitis, intensive care unit, ICU-acquired weakness, risk prediction model, nomogram

Introduction

Acute pancreatitis (AP) is one of the most common causes of acute abdominal pain and can occur at any age. It is an acute chemical inflammatory condition caused by the premature activation of pancreatic enzymes, resulting in auto-digestion of the pancreas and surrounding tissues. Severe acute pancreatitis (SAP) accounts for approximately 20% of all AP cases and is characterized by pancreatic hemorrhage and necrosis, often complicated by infection, peritonitis, and shock. SAP is associated with a high risk of complications and mortality, frequently requiring admission to the intensive care unit (ICU) for comprehensive management.[1]

ICU-acquired weakness (ICU-AW) is a common complication in critically ill patients and significantly impairs their quality of life. Clinically, ICU-AW—also known as ICU-acquired neuromuscular dysfunction—is primarily characterized by diffuse and symmetrical limb weakness, decreased muscle strength, reduced reflexes, and muscle atrophy.[2] Studies[3] have shown that the incidence of ICU-AW ranges from 24% to 55% in critically ill patients with ICU stays longer than 7 days.

https://doi.org/10.2147/JIR.S534421
Received: 6 May 2025
Accepted: 11 December 2025
Published: 20 January 2026

Clinical observations[4] have linked ICU-AW to prolonged mechanical ventilation, difficulties in weaning, extended ICU stays, and increased mortality. Additionally, other research[5] indicates that ICU-AW not only affects short-term prognosis but also contributes to long-term physical impairment, reduced quality of life, and even lifelong disability.

While ICU-AW is a recognized challenge in general critical care populations, patients with SAP may represent a uniquely high-risk subgroup. The pathophysiology of SAP creates a "perfect storm" of risk factors for neuromuscular dysfunction. This includes a profound and sustained systemic inflammatory response (SIRS), which can directly promote muscle catabolism and mitochondrial dysfunction.[6] Furthermore, SAP is characterized by significant hypermetabolism and hypercatabolism, often compounded by mandated fasting, leading to rapid muscle wasting.[7] The frequent development of multi-organ failure, particularly acute kidney injury and respiratory failure requiring prolonged mechanical ventilation, exacerbates immobilization and increases exposure to medications like neuromuscular blocking agents and sedatives, which are known contributors to ICU-AW.[8] The common complication of intra-abdominal hypertension in SAP can also impair intestinal barrier function, potentially leading to increased translocation of bacterial products and metabolites like D-lactate, which may further contribute to systemic toxicity and muscle injury.[9]

At present, there is no specific treatment for ICU-AW, making early identification and targeted prevention of risk factors essential for improving patient outcomes. While several studies[10] have analyzed the risk factors for ICU-AW and developed predictive models in mixed ICU populations, the unique and synergistic risk profile in SAP patients has not been sufficiently explored. General models may fail to capture the specific contributions of SAP-specific factors, such as the intensity of the pancreatic inflammatory cascade or the metabolic consequences of pancreatic necrosis. Based on this gap, the present study aimed to investigate the incidence and risk factors of ICU-AW specifically in the SAP population, and to construct a risk prediction model tailored to this high-risk group. The results are reported as follows.

Materials and Methods

This study was approved by the Medical Ethics Committee of Air Force Medical University (Approval No.: SAPJH2421) and was conducted in strict accordance with the ethical guidelines of the Declaration of Helsinki. All participants and their family members were fully informed about the study and signed the corresponding informed consent forms.

Study Population and Design

A total of 277 patients diagnosed with severe acute pancreatitis (SAP) and admitted to the intensive care unit (ICU) of our hospital between January 2020 and March 2024 were enrolled in this retrospective observational study.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows:Age ≥ 18 years; Diagnosis of SAP based on the revised Atlanta classification,[8] characterized by persistent organ failure (≥48 hours) involving one or more systems; First-time ICU admission with no prior history of ICU treatment; Duration of mechanical ventilation ≥ 2 days; ICU stay ≥ 3 days to ensure adequate observation period for ICU-AW development; Complete and analyzable medical records.

Exclusion criteria included: Preexisting neuromuscular disorders (eg, traumatic brain injury, spinal cord injury, cerebrovascular disease, brain tumors, or Guillain-Barré syndrome); Diagnosed psychiatric disorders; Inability to cooperate with muscle strength assessment using the Medical Research Council sum score (MRC-SS);Patients in a coma or with impaired consciousness throughout ICU stay.

Patients were categorized into ICU-AW (n=107) and non-ICU-AW (n=170) groups based on MRC-SS assessment during their ICU stay.

Diagnostic Criteria for ICU-AW

ICU-acquired weakness (ICU-AW) was diagnosed using the Medical Research Council sum score (MRC-SS),[9] which assesses six muscle groups bilaterally: shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion. Prior to MRC-SS assessment, patients' consciousness and cooperation were evaluated using a standardized command protocol (eg, "open your eyes," "squeeze my hand," "stick out your tongue"). Only patients who successfully performed ≥4 commands proceeded to MRC-SS evaluation. Each muscle group was scored from 0 (no contraction) to 5

(normal strength), with a total score range of 0–60. ICU-AW was defined as an MRC-SS score <48. The lowest MRC-SS score recorded during the ICU stay was used for diagnosis. Patients with preexisting neuromuscular disorders were excluded to ensure that weakness was acquired during ICU stay.

Clinical Data Collection

Data were prospectively collected using a standardized electronic case report form to minimize missing data. The following variables were recorded:

Demographic characteristics: sex, age, body mass index (BMI);

Personal habits: smoking status (current, former, never), alcohol consumption (non-drinker, drinker, hazardous drinking, harmful drinking);

Disease severity scores: APACHE II (calculated using worst physiological values within first 24 hours of ICU admission), CT severity index (CTSI);

Laboratory parameters (worst values within first 24 hours): C-reactive protein (CRP), procalcitonin (PCT), white blood cell count (WBC), electrolytes (Na^+, K^+, Ca^{2+}), alanine aminotransferase (ALT), aspartate aminotransferase (AST), D-dimer, serum amylase, lipase, urinary amylase, blood glucose, arterial pH, PO_2, D-lactate;

Clinical management: duration of mechanical ventilation, ICU length of stay, use of vasoactive agents, aminoglycosides, sedatives/analgesics, neuromuscular blocking agents (NMBAs);

Nutritional and rehabilitation factors: nutritional risk (NRS-2002 score ≥3), nutritional support route (enteral, parenteral, combined), early rehabilitation care (initiated within 48 hours of ICU admission, including passive/active limb exercises and cardiopulmonary training).

D-lactate levels were available for all enrolled patients. Missing data for other variables were <5%, and multiple imputation was not performed due to the low proportion of missingness.

Statistical Analysis

All statistical analyses were performed using SPSS software (version 23.0; IBM Corp., Armonk, NY, USA) and R software (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria). To develop and validate the prediction model, the entire cohort of 277 patients was randomly divided into two groups: a modeling group (n = 193, 70%) for model development and a validation group (n = 84, 30%) for internal validation. This 7:3 split was chosen to allocate a majority of the data for model building while retaining a sufficient sample size for robust validation. The randomization was performed using the random number generator function in R software.

Data are presented as follows: normally distributed continuous variables as mean ± standard deviation, non-normally distributed continuous variables as median (interquartile range), and categorical variables as frequencies (percentages). Group comparisons were performed using the Student's *t*-test (normal continuous data), Mann–Whitney *U*-test (non-normal continuous data), or Chi-square test (categorical variables), with Fisher's exact test applied where appropriate.

To facilitate the construction of the logistic regression model and the subsequent nomogram, continuous variables were dichotomized. The dichotomization was based on clinically established thresholds where available; otherwise, the median values observed in the study population were used as cut-off points. The specific cut-offs were as follows: Age (≥51 years), APACHE II score (≥14), Mechanical ventilation duration (≥5 days), ICU length of stay (≥7 days), CRP (>66.32 mg/L), PCT (≥6.43 ng/mL), WBC (≥18.25 $\times 10^9$/L), K^+ (≥4.69 mmol/L), Ca^{2+} (≥1.64 mmol/L), ALT (≥73.52 U/L), AST (≥86.57 U/L), D-dimer (≥3.12 mg/L), Serum amylase (≥763.24 U/L), Lipase (≥927.45 U/L), Urinary amylase (≥1648.19 U/L), Blood glucose (≥13.04 mmol/L), pH (≥7.28), PO_2 (≥72.07 mmHg), D-lactate (≥41.69 mg/L), and CTSI score (≥5).

The categorical variables were: Nutritional risk (yes), Early rehabilitation care (yes), NMBA use (yes), and Nutritional route (enteral, parenteral, combined).

Variables that achieved a significance level of $P < 0.05$ in the univariate analyses were entered into a multivariate binary logistic regression model. A backward stepwise selection procedure (with a removal criterion of $P > 0.05$) was employed to identify independent predictors of ICU-AW and to build a parsimonious final model. Based on the coefficients of the final model, a nomogram was constructed to visualize the prediction model and facilitate individual risk calculation.

The model's discriminatory power was assessed by the area under the receiver operating characteristic (ROC) curve (AUC). Calibration, which reflects the agreement between predicted probabilities and observed outcomes, was evaluated using the Hosmer-Lemeshow (H-L) goodness-of-fit test and graphically represented by a calibration plot. A two-tailed P-value of less than 0.05 was considered statistically significant for all analyses.

Results

Incidence of ICU-AW in SAP Patients

Among 277 SAP patients, the median lowest MRC-SS score was 50 (range: 41–57). A total of 107 patients (38.6%) had MRC-SS scores <48 and were diagnosed with ICU-AW.

Univariate Analysis of Factors Influencing ICU-AW

Univariate analysis revealed significant differences between ICU-AW and non-ICU-AW groups in age, sex, smoking, alcohol consumption, APACHE II score, mechanical ventilation duration, ICU stay, CRP, PCT, WBC, K^+, Ca^{2+}, ALT, AST, D-dimer, serum amylase, lipase, urinary amylase, blood glucose, pH, PO_2, D-lactate, CTSI score, nutritional risk, early rehabilitation care, NMBA use, and nutritional route (all $P < 0.05$). No significant differences were found in BMI, Na^+, vasoactive drug use, aminoglycosides, or sedative/analgesic use ($P > 0.05$). Detailed results are presented in Table 1.

Table 1 Univariate Analysis of Factors Influencing ICU-AW in SAP Patient

Variable	ICU-AW (n=107)	Non-ICU-AW (n=170)	t/χ2	P
Age (±s, years)	54.37±8.64	47.05±10.36	6.085	<0.001
Gender [Male/Female, n (%)]	80 (74.77) /27 (25.23)	106 (60.92) /64 (36.78)	4.587	0.032
BMI (±s, kg/m^2)	25.03±3.46	24.85±2.91	0.875	0.122
Smoking [Non-smoker/Former smoker/Smoker, n (%)]	34 (31.78) /26 (24.30) /47 (43.93)	80 (45.98) /49 (28.16) /41 (23.56)	12.333	0.002
Alcohol Consumption [Non-drinker/Drinker/Risky drinking/ Harmful drinking, n (%)]	13 (12.15) /24 (22.43) /35 (32.71) /35 (32.71)	53 (30.46) /48 (27.59) /43 (24.71) /26 (14.94)	21.157	<0.001
APACHE II Score (±s)	17.32±4.13	12.08±3.44	3.92	<0.001
Mechanical Ventilation Duration (±s, days)	5.73±2.05	4.13±1.85	4.075	<0.001
ICU Length of Stay (±s, days)	8.47±2.45	6.85±1.47	5.192	<0.001
CRP (±s, mg/L)	70.43±9.14	59.92±14.72	10.698	<0.001
PCT (±s, ng/mL)	7.54±2.36	5.86±1.74	7.211	<0.001
WBC (±s, $\times 10^9$/L)	19.03±4.54	17.02±3.87	5.387	<0.001
Sodium (Na^+) (±s, mmol/L)	133.61±6.24	135.07±6.08	0.42	0.508
Potassium (K^+) (±s, mmol/L)	4.82±0.63	4.47±0.54	2.406	0.027
Calcium (Ca^{2+}) (±s, mmol/L)	1.57±0.43	1.79±0.53	2.972	0.009
ALT (±s, U/L)	83.45±23.54	68.23±19.07	11.387	<0.001
AST (±s, U/L)	91.49±30.46	70.38±18.51	7.116	<0.001
D-Dimer (±s, mg/L)	3.47±0.85	2.83±0.64	2.587	0.021
Serum Amylase (±s, U/L)	787.58±183.15	705.32±137.46	6.392	<0.001
Lipase (±s, U/L)	1032.47±305.82	846.75±218.69	14.305	<0.001
Urine Amylase (±s, U/L)	1785.93±418.67	1437.05±385.96	10.427	<0.001
Blood Glucose (±s, mmol/L)	13.57±4.18	12.45±3.52	2.205	0.043
pH (±s)	7.23±0.20	7.31±0.16	2.239	0.039
PO_2 (±s, mmHg)	68.67±20.32	74.54±22.36	2.671	0.023
D-Lactic Acid (±s, mg/L)	50.48±16.32	39.05±11.46	8.29	<0.001
CTSI Score (points)	5.87±1.54	4.38±1.27	5.867	<0.001
Nutritional Risk [Yes/No, n (%)]	57 (53.27) /50 (46.73)	40 (22.99) /130 (74.71)	25.527	<0.001
Early Rehabilitation Nursing [Yes/No, n (%)]	28 (26.17) /79 (73.83)	86 (49.43) /84 (48.28)	16.17	<0.001
Vasoactive Drugs [Yes/No, n (%)]	30 (28.04) /77 (71.96)	56 (32.18) /114 (65.52)	0.738	0.39
Aminoglycosides [Yes/No, n (%)]	33 (30.84) /74 (69.16)	42 (24.14) /128 (73.56)	1.252	0.263
Analgesic and Sedative Drugs [Yes/No, n (%)]	91 (85.05) /16 (14.95)	133 (76.44) /37 (21.26)	1.969	0.161
Neuromuscular Blocking Agents [Yes/No, n (%)]	60 (56.07) /47 (43.93)	65 (37.36) /105 (60.34)	8.44	0.004
Nutrition Route [Enteral/Parenteral/Combined, n (%)]	31 (28.97) /33 (30.84) /43 (40.19)	58 (33.33) /25 (14.37) /87 (50.00)	10.396	0.006

Multivariate Logistic Regression Analysis

Multivariable logistic regression identified several independent risk factors for ICU-acquired weakness, including age ≥51 years (OR = 5.83, 95% CI: 2.28–14.87), APACHE II score ≥14 (OR = 11.19, 95% CI: 4.27–29.35), ICU stay ≥7 days (OR = 12.61, 95% CI: 3.54–44.87), D-lactate ≥41.69 mg/L (OR = 2.92, 95% CI: 1.19–7.13), nutritional risk (OR = 5.34, 95% CI: 2.15–13.24), and the use of neuromuscular blocking agents (OR = 3.34, 95% CI: 1.36–8.23). Early rehabilitation care served as a protective factor (OR = 0.18, 95% CI: 0.07–0.45). Detailed regression results are presented in Table 2.

Risk Prediction Model for ICU-AW in SAP Patients

Comparison of Clinical Features Between Modeling and Validation Groups

As described in the Methods, patients were allocated to modeling (n=193) and validation (n=84) groups. The baseline clinical characteristics were well-balanced between these two groups, with no statistically significant differences observed in any of the collected variables (all P > 0.05, Table 3). This confirms the success of the randomization process and ensures the comparability of the two datasets for model development and validation.

Table 2 Multivariate Logistic Regression Analysis of Factors Influencing ICU-AW in SAP Patients

Variable	β	SE	Waldχ2	P	OR	95% CI
Age						
< 51 years					1.000 (Reference)	
≥ 51 years	1.763	0.478	13.603	<0.001	5.829	2.284~14.872
APACHE						
< 14 points					1.000 (Reference)	
≥ 14 points	2.415	0.492	24.094	<0.001	11.190	4.266~29.351
ICU Length of Stay						
< 7 days					1.000 (Reference)	
≥ 7 days	2.534	0.648	15.292	<0.001	12.609	3.543~44.874
D-lactate						
< 41.69 mg/L					1.000 (Reference)	
≥ 41.69 mg/L	1.071	0.456	5.516	0.019	2.917	1.194~7.130
Nutritional Risk						
No					1.000 (Reference)	
Yes	1.675	0.463	13.088	<0.001	5.339	2.153~13.243
Neuromuscular Blockade Drugs						
No					1.000 (Reference)	
Yes	1.206	0.460	6.874	0.009	3.341	1.355~8.234
Early Rehabilitation Care						
No					1.000 (Reference)	
Yes	−1.715	0.465	13.603	<0.001	0.180	0.072~0.448

Table 3 Risk Prediction Model for ICU-AW in SAP Patients

Clinical Variable	Validation Group (n = 84)	Modeling Group (n = 193)	t/χ^2	P
ICU-AW [Yes/No, n (%)]	47 (55.95) / 37 (44.05)	123 (63.73) / 70 (36.27)	1.494	0.222
Age (±s, years)	50.86 ± 7.82	49.67 ± 9.82	1.071	0.285
APACHE II (±s, points)	14.25 ± 4.96	13.99 ± 4.31	0.441	0.659
ICU Stay (±s, days)	7.61 ± 1.51	7.30 ± 1.71	1.42	0.157
D-lactate (±s, mg/L)	43.14 ± 14.17	43.16 ± 14.72	0.011	0.991
BMI (±s, kg/m^2)	24.66 ± 2.71	24.99 ± 3.19	0.856	0.393
Mechanical Ventilation Time (±s, days)	4.77 ± 1.98	4.80 ± 2.06	0.106	0.916
CRP (±s, mg/L)	65.19 ± 12.03	63.46 ± 14.25	0.974	0.331
PCT (±s, ng/mL)	6.84 ± 2.31	6.39 ± 2.02	1.618	0.107

(*Continued*)

https://doi.org/10.2147/JIR.S534421

Table 3 (Continued).

Clinical Variable	Validation Group (n = 84)	Modeling Group (n = 193)	t/χ^2	P
WBC (±s, $\times10^9$/L)	18.49 ± 4.35	18.01 ± 4.22	0.859	0.391
Na^+ (±s, mmol/L)	134.83 ± 6.55	134.44 ± 6.08	0.476	0.634
K^+ (±s, mmol/L)	4.61 ± 0.55	4.62 ± 0.56	0.145	0.885
Ca^{2+} (±s, mmol/L)	1.68 ± 0.49	1.73 ± 0.54	0.779	0.437
ALT (±s, U/L)	76.78 ± 21.06	72.94 ± 23.84	1.274	0.204
AST (±s, U/L)	81.30 ± 23.87	77.87 ± 25.74	1.041	0.299
D-Dimer (±s, mg/L)	3.02 ± 0.84	3.08 ± 0.73	0.576	0.565
Amylase (±s, U/L)	746.20 ± 162.74	733.49 ± 163.80	0.595	0.552
Lipase (±s, U/L)	910.44 ± 263.86	920.97 ± 268.24	0.302	0.763
Urinary Amylase (±s, U/L)	1613.39 ± 418.51	1560.01 ± 413.14	0.985	0.326
Blood Glucose (±s, mmol/L)	7.30 ± 0.15	7.28 ± 0.19	0.832	0.406
pH (±s)	69.50 ± 22.82	73.46 ± 20.87	1.408	0.16
CTSI Score (points)	4.96 ± 1.70	4.96 ± 1.64	0.021	0.983
Nutritional Risk [Yes/No, n (%)]	53 (63.10) / 31 (36.91)	127 (65.80) / 66 (34.20)	0.189	0.664
Early Rehabilitation Care [Yes/No, n (%)]	47 (55.95) / 37 (44.05)	116 (60.10) / 77 (39.90)	0.416	0.519
Neuromuscular Blockers [Yes/No, n (%)]	44 (52.38) / 40 (47.62)	108 (55.96) / 85 (44.04)	0.303	0.582
Gender [Male/Female, n (%)]	27 (32.14) / 57 (67.86)	64 (33.16) / 129 (66.84)	0.027	0.868
Smoking [Non-smoker/Ex-smoker/Smoker, n (%)]	37 (44.05) / 21 (25.00) / 26 (30.95)	79 (40.93) / 52 (26.94) / 62 (32.12)	0.245	0.885
Alcohol [Non-drinker/Drinker/Hazardous drinking, n (%)]	18 (21.43) / 20 (23.81) / 26 (30.95) / 20 (23.81)	48 (24.87) / 52 (26.94) / 52 (26.94) / 41 (21.24)	1.021	0.796
Vasopressors [Yes/No, n (%)]	60 (71.43) / 24 (28.57)	131 (67.88) / 62 (32.12)	0.345	0.557
Aminoglycosides [Yes/No, n (%)]	65 (77.38) / 19 (22.62)	137 (70.98) / 56 (29.02)	1.213	0.271
Analgesics and Sedatives [Yes/No, n (%)]	13 (15.48) / 71 (84.52)	40 (20.73) / 153 (79.28)	1.042	0.307
Nutritional Method [Enteral/Parenteral/Combined, n (%)]	29 (34.52) / 16 (19.04) / 39 (46.43)	60 (31.09) / 42 (21.76) / 91 (47.15)	0.427	0.808

Model Development and Validation

A nomogram was constructed incorporating seven predictors: age, APACHE II score, ICU length of stay, D-lactate, nutritional risk, NMBA use, and early rehabilitation care (Figure 1). The model demonstrated excellent discrimination, with AUCs of 0.922 (95% CI: 0.884–0.959) in the modeling group and 0.918 (95% CI: 0.873–0.963) in the validation group (Figure 2). The H-L test showed good calibration (modeling group: P=0.903; validation group: P=1.000). The calibration curve closely aligned with the ideal line (Figure 3).

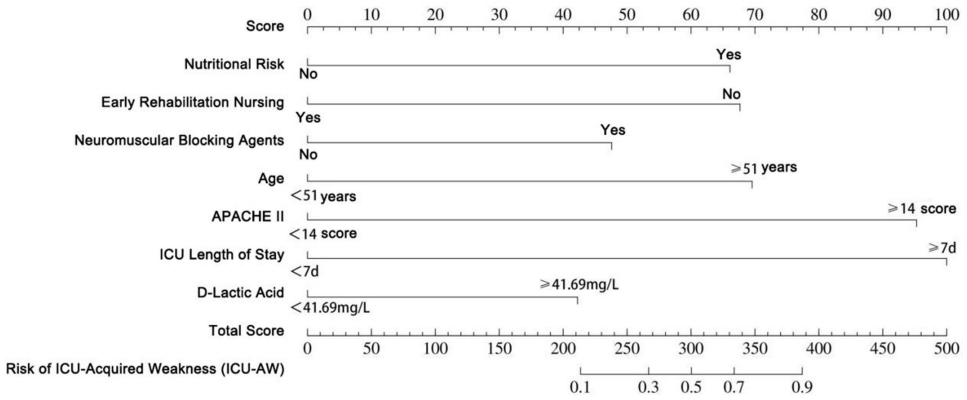

Figure 1 Nomogram for predicting ICU-AW risk in SAP patients.

https://doi.org/10.2147/JIR.S534421

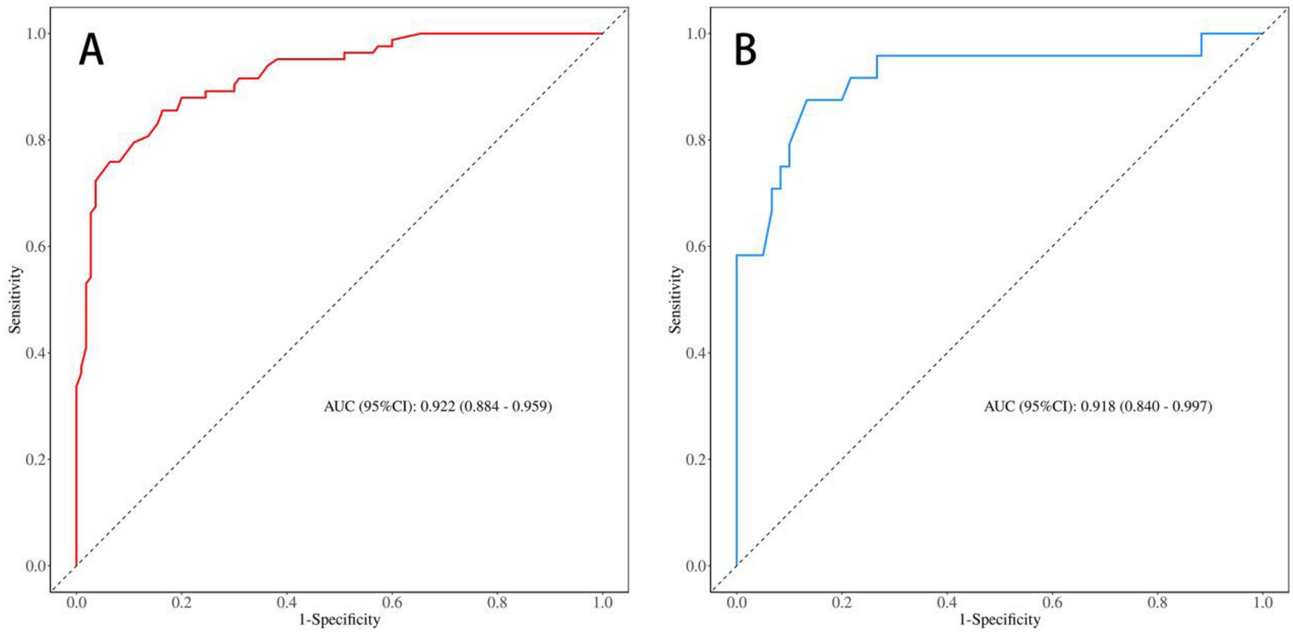

Figure 2 Receiver operating characteristic (ROC) curves of the prediction model. (**A**) ROC curve for the modeling cohort. (**B**) ROC curve for the validation cohort.

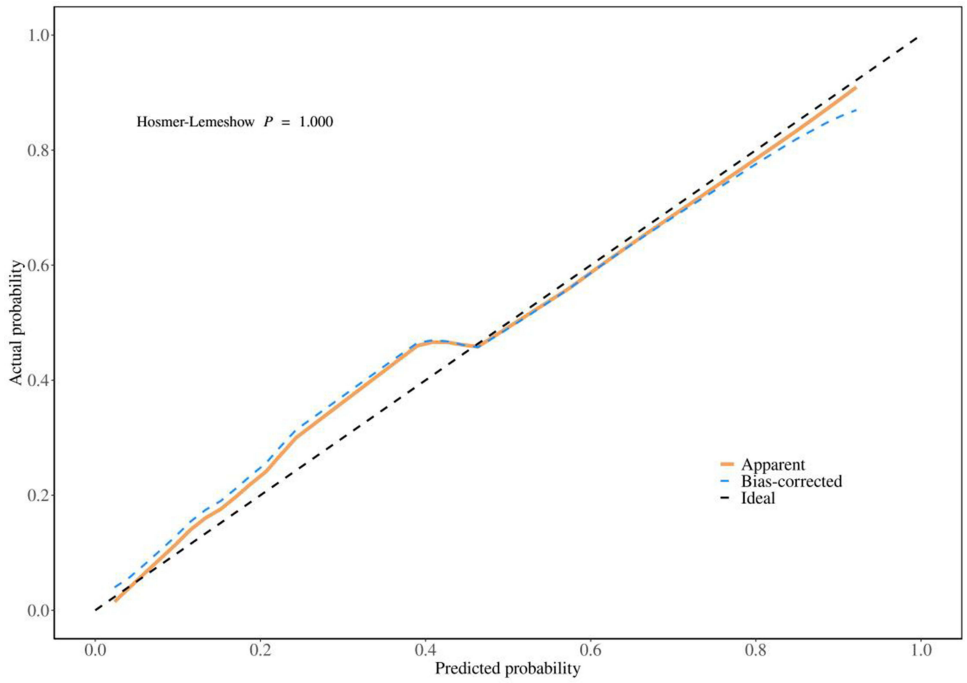

Figure 3 Calibration curve for the prediction model in the validation group.

Discussion

This single-center study identified a notably high incidence (38.6%) of ICU-AW among patients with severe acute pancreatitis. We further developed and validated a predictive nomogram based on seven independent factors, which demonstrated excellent performance. These findings underscore the substantial burden of ICU-AW in this specific patient population and provide a practical tool for early risk stratification.

The observed incidence in our cohort is consistent with the higher end of the range (25%-33%) reported in general critical care populations,[10,11] and appears elevated compared to rates reported in other studies of mixed ICU patients (22.5%[12] and 34.81%).[13] This suggests that SAP patients may represent a particularly vulnerable subgroup for the development of ICU-AW, likely due to the profound systemic inflammation, hypercatabolism, and frequent requirement for prolonged life-support interventions characteristic of the disease.

Our multivariate analysis confirmed several established risk factors for ICU-AW. Advanced age is a well-documented risk factor, a finding consistent with studies by Anastasopoulos[14,15] and Zhang et al,[12] which can be attributed to the physiological decline in muscle mass and function known as sarcopenia. Similarly, a higher illness severity, as reflected by the APACHE II score, is a logical contributor given its association with a more pronounced inflammatory and catabolic state. Furthermore, our findings align with previous research by Khalil et al[16] identifying longer ICU stay as a significant risk factor, potentially related to prolonged immobility and the cumulative burden of critical illness. While Elkalawy et al[17] identified duration of mechanical ventilation as an independent risk factor, this variable was not retained in our final model. This discrepancy may be explained by the collinearity between mechanical ventilation duration and overall ICU length of stay in our SAP cohort; when confounding was accounted for, the latter emerged as the more dominant predictor. The use of neuromuscular blocking agents was also confirmed as a significant risk factor, corroborating both international and domestic literature,[18,19] likely through their direct effects on muscle protein synthesis and excitability.

This study adds to the existing literature by identifying two particularly relevant risk factors in the context of SAP: elevated D-lactate levels and nutritional risk. SAP is characterized by impaired intestinal barrier function, which can lead to increased translocation of D-lactate from the gut into the systemic circulation. Concurrent systemic inflammation and potential tissue hypoperfusion further contribute to lactate accumulation. We hypothesize that this elevated D-lactate may impair muscle function by disrupting intracellular pH, calcium handling, and energy metabolism within myocytes. This concept is indirectly supported by the work of Levy et al,[20] who demonstrated that hyperlactatemia during septic shock could induce muscle weakness in animal models. Regarding nutritional risk, the mandatory initial fasting in SAP management places patients at high risk for a significant caloric and protein deficit. Our finding that nutritional risk (NRS-2002 $\geq$3) is a strong independent predictor highlights the critical role of metabolic stress and undernutrition in the pathogenesis of ICU-AW in this population. This implies that rigorous nutritional risk screening and the timely initiation of tailored nutritional support are not merely supportive but potentially essential strategies to mitigate muscle wasting in SAP patients.

A key and encouraging finding of our study is that early rehabilitation care emerged as a powerful protective factor, significantly reducing the odds of developing ICU-AW. This aligns with a growing body of evidence[21,22] advocating for early mobilization in critically ill patients. Our rehabilitation protocol, which incorporated both active/passive limb exercises and acupressure, is hypothesized to work through multiple mechanisms: preserving muscle mass and excitability, improving respiratory muscle function to facilitate weaning, and potentially modulating systemic inflammation. Although traditional practices and staffing constraints have sometimes limited the implementation of early mobilization in some settings,[23] our results provide strong support for its feasibility and efficacy in SAP patients. The inclusion of acupressure, targeting points such as Zusanli (ST36) and Fenglong (ST40), is a novel integrative approach suggested to stimulate muscle contraction, and its reported benefits[24,25] warrant further investigation in rigorous trials.

To translate these identified factors into a clinically usable tool, we constructed a nomogram prediction model. The model, incorporating age, APACHE II score, ICU length of stay, NMBA use, D-lactate, nutritional risk, and early rehabilitation care, demonstrated high discriminatory accuracy (AUC >0.9 in both modeling and validation sets) and excellent calibration. This suggests that the model has robust predictive ability and could assist clinicians in identifying SAP patients at the highest risk for ICU-AW upon ICU admission, enabling targeted preventive strategies.

Conclusion

In conclusion, this study confirms a high incidence of ICU-AW in patients with SAP and identifies a set of independent predictors. The risk factors include older age ($\geq$51 years), higher disease severity (APACHE II $\geq$14), prolonged ICU stay ($\geq$7 days), use of neuromuscular blocking agents, elevated D-lactate levels ($\geq$41.69 mg/L), and the presence of nutritional risk. Conversely, the implementation of early rehabilitation care was identified as a significant protective factor. The developed nomogram provides a validated visual tool for individualized risk prediction. The primary limitations of this

study are its single-center, retrospective design and the sample size, which, while sufficient for this analysis, necessitates future validation through large-scale, multi-center prospective studies.Furthermore, future research should aim to prospectively validate the nomogram and investigate the causal mechanisms linking D-lactate to muscle dysfunction, as well as the optimal composition and timing of rehabilitation bundles in this population.

Disclosure

The authors report no conflicts of interest in this work.

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