Am J Transl Res 2026;18(4):2908-2918
www.ajtr.org /ISSN:1943-8141/AJTR0170829

Original Article

Construction and validation of a prognostic nomogram for predicting in-hospital mortality of patients with acute chlorfenapyr poisoning

Yuan Xie[1*], Yanxing Lan[1*], Zongming Xu[2], Yaowu Chen[3], Guoyun Shi[3], Fenshuang Zheng[1]

[1]Department of Emergency Medicine, The Affiliated Hospital of Yunnan University, Kunming, Yunnan, China; [2]Department of Emergency Medicine, Yunnan Provincial Emergency Medical Center, Kunming, Yunnan, China; [3]Department of Emergency Medicine, People's Hospital of Lijiang, Lijiang, Yunnan, China. [*]Equal contributors and co-first authors.

Received December 18, 2025; Accepted February 12, 2026; Epub April 15, 2026; Published April 30, 2026

Abstract: Objectives: To identify key risk factors for in-hospital mortality in patients with acute chlorfenapyr poisoning and to develop a clinically applicable nomogram to predict in-hospital mortality in this population. Methods: This retrospective study analyzed 130 patients, who were assigned to training (n=91) and validation (n=39) cohorts. The training cohort included 53 survivors and 38 non-survivors, with 30-day mortality as the endpoint. Univariate analysis was used to identify factors associated with mortality. Candidate variables were screened using LASSO regression, followed by multivariate logistic regression to identify independent risk factors. A nomogram was constructed based on these predictive factors, and its discriminative power, calibration, and clinical applicability were evaluated. The performance of the nomogram was validated in an external validation cohort. Results: The mortality rate was 41.8% in the training cohort and 38.5% in the validation cohort. Among the nine candidate variables screened by LASSO regression, multivariate analysis identified four independent predictors: ATP-cytochrome C utilization (OR 78.57, 95% CI 1.81-3412), procalcitonin (OR 65.76, 95% CI 1.04-4175), administered dose (OR 1.08, 95% CI 1.02-1.14), and alanine aminotransferase (ALT) (OR 1.09, 95% CI 1.02-1.17). The predictive model demonstrated excellent discriminative power, with a C-index of 0.988 in the training group and 0.849 in the validation group. The calibration was good (P=0.771 and P=0.942), and decision curve analysis confirmed its significant clinical applicability. Conclusion: We developed and validated a practical nomogram that accurately predicts the risk of in-hospital mortality in patients with acute chlorfenapyr poisoning, which may aid in early risk stratification and clinical decision-making.

Keywords: Acute chlorfenapyr poisoning, nomogram, prediction model, risk factors

Introduction

Acute pesticide poisoning remains a major global health problem, causing significant morbidity and mortality each year [1]. Chlorfenapyr is a novel pyrrole insecticide whose metabolite, trolopyril, strongly dissociates mitochondrial oxidative phosphorylation, leading to impaired adenosine triphosphate (ATP) synthesis, cellular energy depletion, and multiple organ failure [2-4]. Clinically, chlorfenapyr poisoning has an incubation period of several days to two weeks, followed by nonspecific biochemical abnormalities such as high fever, sweating, elevated creatine kinase, increased liver enzymes, and elevated lactate levels [5, 6]. The clinical management of acute chlorfenapyr poisoning is challenging, primarily due to its rapid progression and the lack of a specific antidote [7-9]. Currently, risk stratification for these patients relies on clinical judgment and nonspecific biochemical markers [10]. Although it is generally believed that factors such as intake and certain laboratory parameters affect prognosis, there is currently no comprehensive and quantitative assessment tool [11]. Therefore, identifying reliable independent prognostic factors is crucial for early intervention and improving clinical

https://doi.org/10.62347/OURV6602

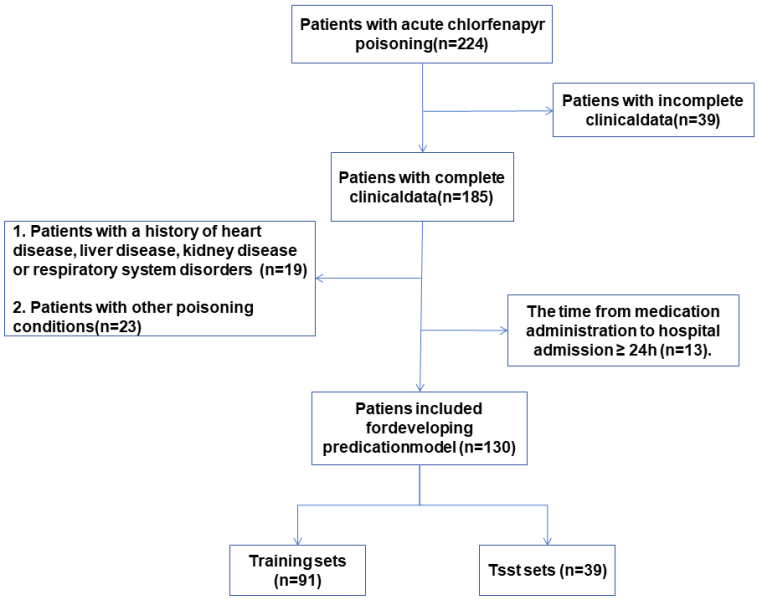

Figure 1. This study presents a flowchart for patient screening.

outcomes. Furthermore, a user-friendly predictive model that integrates these factors can significantly aid bedside decision-making.

Previous studies on acute chlorfenapyr poisoning have identified several outcome determinants, including the dose ingested, the timing of specific treatment initiation, the occurrence of multiple organ dysfunction syndrome (MODS), and characteristic abnormalities in hematological parameters [12, 13]. However, few studies have evaluated the applicability of predictive models that integrate these clinical and laboratory parameters into personalized mortality risk prediction.

The nomogram feature provides an intuitive interface for visualizing complex statistical models containing multiple prognostic variables. By integrating various predictive factors into a single model, it enables a comprehensive assessment of the patient's condition [14]. This graphical tool allows attending physicians to quickly estimate the probability of adverse outcomes upon patient admission. Therefore, morphographs are a promising predictive tool in clinical toxicology [15-17]. Identifying reliable prognostic indicators is a prerequisite for early triage and targeted treatment. Therefore, this study aimed to identify independent risk factors associated with in-hospital mortality in patients with acute chlorfenapyr poisoning. Subsequently, we attempted to develop and validate a novel nomogram model that can intuitively quantify individual mortality risk, thereby facilitating early risk stratification and personalized patient management.

Materials and methods

Experimental design and participants

We retrospectively analyzed the clinical data of 130 patients with acute chlorfenapyr poisoning who visited the Emergency Department of the Affiliated Hospital of Yunnan University from April 2018 to December 2023 (**Figure 1**). The diagnosis of acute chlorfenapyr poisoning was based on the following criteria: (1) a clear history of oral chlorfenapyr exposure; (2) the presence of consistent clinical manifestations (early gastrointestinal symptoms, such as nausea and vomiting, and/or characteristic delayed manifestations, including profuse sweating, high fever, rhabdomyolysis, or progressive neurological deterioration); (3) exclusion of other common causes (acute infection, cerebrovascular accident, or other poisoning); (4) a 24-hour inclusion window was selected based on the biphasic characteristics of acute chlorfenapyr poisoning. Early nonspecific symptoms usually appear within 6 hours, while the critical delay period that determines prognosis usually begins 5-7 days after exposure. This window allows us to study patients in the early delay period to achieve early prediction. Exclusion criteria: Patients with a history of severe chronic organ dysfunction that could independently affect prognosis, including: stage 3b or higher chronic kidney disease (estimated glomerular filtration rate <45 mL/min/1.73 m^2); chronic heart disease (New York Heart Association class III/IV or left ventricular ejection fraction <40%); decompensated chronic liver disease (Child-Pugh class B or C); severe chronic respiratory disease (Global Initiative for Chronic Obstructive Pulmonary Disease class 3 or 4, or requiring long-term oxygen therapy); incomplete data, other poisoning conditions, time from exposure to the toxic sub-

stance to admission time exceeding 24 hours; pregnant patients.

Eligible patients were divided into the training group (91 cases) and the validation group (39 cases). The study endpoint was patient death within 30 days, with patients assigned to the survival group (n=53) and the death group (n=38) accordingly. In the validation group, there were 26 survivors and 13 deaths, and the estimated ingested dose ranged from 20 to 140 milliliters. This study was approved by the Ethics Committee of the Affiliated Hospital of Yunnan University, and no written informed consent form was required.

Treatment protocol

All patients received standardized management including gastric lavage, catharsis, fluid replacement, diuresis, gastrointestinal mucosal protection, antioxidant therapy, high-dose glucocorticoid therapy, organ protection, and nutritional support. Patients underwent hemoperfusion as soon as possible to remove the lipophilic chlorfenapyr and its metabolites (330-IIJaFron, Zhuhai). This procedure was performed using an HA type neutral macroporous resin adsorption column. On the day of admission, each hemoperfusion session lasted 8 hours, followed by 6 hours daily thereafter. With systemic heparin anticoagulation, the blood flow rate was maintained at approximately 180-200 mL/min. The concentration of chlorfenapyr in urine was monitored using the sodium hydrosulfite colorimetric method. A 10 mL sample of urine was collected from the patient, 2 mL of sodium hydroxide was added and shaken well, followed by the addition of 50 mg of sodium hydrosulfite. The color change of the urine was observed and compared with a standard colorimetric card to determine the concentration of chlorfenapyr in the urine; a darker color indicated a higher concentration.

Data collection

Within 24 hours of patient admission, researchers systematically extracted anonymized clinical data from electronic medical records. This dataset detailed various patient variables, including: time parameters (time from exposure to admission and total treatment duration); demographic characteristics (sex, age); vital signs; estimated intake dose (estimated intake dose was obtained through structured clinical assessment, including obtaining medical history from patients or witnesses, examining the original containers available, and correlating the reported intake with the severity of the patient's initial clinical and laboratory examinations; the final dose estimate was jointly confirmed by two attending physicians); and numerous laboratory parameters. Laboratory assessments included systemic inflammatory markers: lactate, procalcitonin, complete blood count and differential, C-reactive protein (CRP); liver function indicators: gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin fraction; renal function and muscle injury indicators: creatinine, urea, creatine kinase (CK), myoglobin, creatine kinase isoenzyme MB (CK-MB); comprehensive coagulation profiles: fibrinogen degradation products (FDP), activated partial thromboplastin time (APTT), thrombin time (TT), D-dimer, prothrombin time (PT); arterial blood gas analysis, and other hematological parameters. In addition, clinical manifestations (fever, sweating) were recorded. Crucially, we documented three primary therapeutic interventions: methylprednisolone administration, blood purification (including hemoperfusion), and ATP cytochrome C therapy. All treatments were systematically coded as binary variables (yes/no) based on their implementation during the acute phase.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range, IQR) based on their distribution. The normality of the distribution of all continuous variables was assessed using the Shapiro-Wilk test, with a p-value >0.10 as the criterion for conformity to a normal distribution. Therefore, normally distributed variables were expressed as mean ± standard deviation and compared using Student's t-test; non-normally distributed variables were expressed as median (IQR) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies (percentages) and compared using the χ^2 test or Fisher's exact test as appropriate. Variable selection was performed using LASSO regression, and 10-fold cross-validation was used to prevent overfitting. The optimal regularization parameter (λ) was selected

Table 1. Baseline data of the two groups in the training set

Risk factors	Survivors (n=53)	Non-survivors (n=38)	t/U/χ^2	P
Age (year)	44.49 ± 11.35	44.87 ± 8.55	T-test	0.863
Male Sex, n (%)	31 (58.5)	18 (47.4)	Fisher's Exact	0.394
Dosage, mg	45.00 (30.00-60.00)	120.00 (100.00-120.00)	Mann-Whitney U	<0.001
Medication to hospital admission time (h)	9.00 (6.00-11.00)	9.00 (6.00-12.75)	Mann-Whitney U	0.512
ATP Cytochrome C Use, n (%)	20 (37.7)	23 (60.5)	Fisher's Exact	0.036
Blood Purification, n (%)	26 (49.1)	25 (65.8)	Fisher's Exact	0.137
Methylprednisolone Use, n (%)	26 (49.1)	12 (31.6)	Fisher's Exact	0.132
White Blood Cell Count, $\times 10^9$/L	20.79 ± 6.00	22.13 ± 7.61	t=-0.94	0.3501
Procalcitonin, ng/mL	1.24 (1.09-1.57)	1.65 (1.38-2.10)	Mann-Whitney U	<0.001
Lactate, mmol/L	1.43 ± 0.77	2.32 ± 0.94	t=-5.13	<0.001
ALT, U/L	50.88 (30.54-69.24)	89.44 (61.98-116.22)	Mann-Whitney U	<0.001
AST, U/L	74.03 (45.43-107.19)	109.47 (81.53-188.35)	Mann-Whitney U	<0.001
Creatinine, μmol/L	67.95 ± 13.62	79.21 ± 12.68	t=-4.00	<0.001
CK, U/L	172.25 (128.47-233.43)	220.32 (146.01-342.56)	Mann-Whitney U	0.019
Myoglobin, ng/mL	162.34 (158.36-168.45)	168.54 (163.48-168.78)	Mann-Whitney U	0.004
APTT, s	33.15 (29.32-36.34)	34.00 (28.93-37.19)	Mann-Whitney U	0.281
Partial Pressure of Oxygen, mmHg	83.34 (77.59-91.67)	78.78 (68.35-85.32)	Mann-Whitney U	0.008

Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; APTT, activated partial thromboplastin time.

according to the "one standard error" rule, which determines the simplest model by selecting the largest λ value (whose cross-validation mean squared error falls within one standard error of the minimum error), corresponding to the lambda.1se value in the analysis. This LASSO procedure was applied independently to the five imputed datasets generated by multiple imputation. Candidate predictors for the final multivariate model were defined as consistency variables with at least three non-zero coefficients across the five imputed datasets. Variables selected through the above procedure were incorporated into a multivariate logistic regression to identify independent risk factors. Results were presented as odds ratios (OR) and their 95% confidence intervals (CI). A nomogram prediction model was constructed based on the final independent predictors. Model performance was evaluated on both the training and validation sets by discrimination (area under the receiver operating characteristic curve, C-index), calibration (calibration curve with Hosmer-Lemeshow test), and clinical applicability (decision curve analysis and clinical impact curve). All analyses were performed using R version 4.2.1 (R Foundation for Statistical Computation), and a two-sided *P*-value <0.05 was considered statistically significant.

Results

General data of the two groups in the training set

There were no significant differences between survivors and non-survivors in terms of age, sex, white blood cell count, time to hospitalization, methylprednisolone use, or APTT in the training set (all P>0.05) (**Table 1**). In contrast, non-survivors were characterized by significantly higher doses of medication (120.0 mg vs. 45.0 mg, P<0.001) and more frequent need for APT (60.5% vs. 37.7%, P=0.036). Furthermore, they had significantly elevated levels of procalcitonin, lactate, ALT, AST, creatinine, CK, and myoglobin, and lower partial pressure of oxygen (all P<0.05). In addition, univariate logistic regression analysis of the entire cohort, training set, and validation set is detailed in Supplementary Tables 1, 2, 3, 4.

Model development

This study used LASSO regression to identify 9 potential risk factors. The results showed that CK, AST, procalcitonin, ALT, direct bilirubin, ATP Cytochrome C, creatinine, dosage, and myoglobin were factors associated with mortality in patients with acute chlorfenapyr poisoning (**Figure 2A**). The optimal λ value was deter-

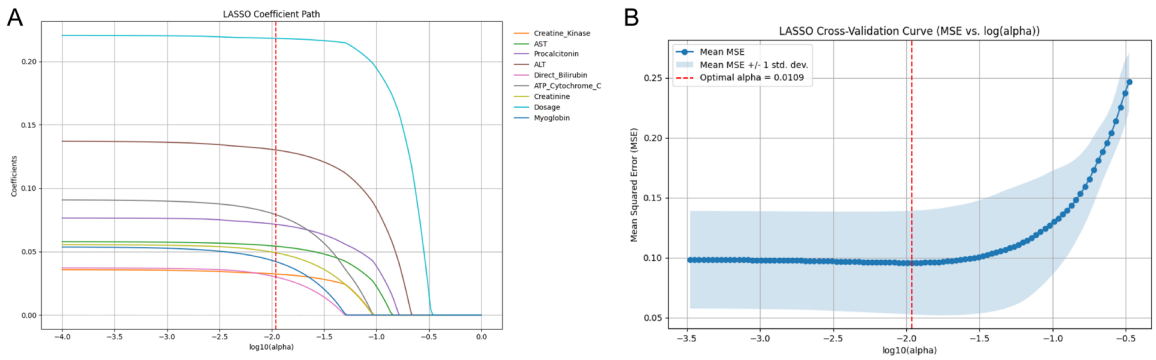

Figure 2. Results of LASSO regression analysis. A. LASSO regression coefficient path; B. Results of LASSO regression cross-validation.

Table 2. Risk factors for death in patients with acute chlorfenapyr poisoning

Factor	B	SE	Wald χ^2	P	OR	95% CI
Dosage	0.0792	0.0281	7.98	0.00473	1.08	[1.02-1.14]
ALT	0.0886	0.0344	6.65	0.00994	1.09	[1.02-1.17]
ATP Cytochrome C use	4.3641	1.9243	5.14	0.02333	78.57	[1.81-3412.01]
Procalcitonin	4.1861	2.1176	3.91	0.04806	65.76	[1.04-4175.48]
Direct Bilirubin	0.7125	0.4383	2.64	0.10406	2.04	[0.86-4.83]
Creatinine	0.0972	0.0621	2.45	0.11763	1.10	[0.98-1.24]
Myoglobin	0.1730	0.1234	1.97	0.16086	1.19	[0.93-1.52]
CK	0.0034	0.0061	0.31	0.57904	1.00	[0.99-1.01]
AST	0.0025	0.0092	0.07	0.78439	1.00	[0.98-1.02]

Note: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase.

mined through 10-fold cross-validation, and the point with the smallest cross-validation error was selected (**Figure 2B**) to enhance the generalizability of the model.

Construction of nomogram

Multivariate logistic regression analysis was performed on the initial nine candidate predictors, identifying four independent predictors of mortality (**Table 2**). Among the risk factors, the use of ATP cytochrome C (OR=78.57, P=0.023) and elevated procalcitonin (OR= 65.76, P=0.048) were most strongly associated with fatal outcomes. Furthermore, the intake dose (OR=1.08, P=0.005) and ALT levels (OR=1.09, P=0.010) were also significant independent risk factors, with increases in these values leading to a progressively higher risk of death. Given the extremely wide confidence intervals used for procalcitonin and the use of ATP-cytochrome C in the initial multivariate model (including 9 candidate variables, with an event ratio of 4.2 for each variable), we conducted a series of sensitivity analyses to investigate the stability of these estimates. First, univariate analysis confirmed a strong and precise association between both factors and mortality (procalcitonin: OR=8.45, 95% CI: 2.73-26.18, P<0.001; ATP-cytochrome C: OR= 2.53, 95% CI: 1.08-5.95, P=0.033). No influential outliers were detected in procalcitonin. To address potential overfitting, we refitted a simpler logistic regression model containing only the four most clinically and statistically relevant independent predictors: intake dose, ALT, use of ATP-cytochrome C, and procalcitonin. This increased the event-to-number ratio for each variable to 9.5. In this stable model, the association between procalcitonin and use of ATP-cytochrome C and mortality remained statistically significant (both P<0.05), and their 95% CIs narrowed significantly (the upper limit for procalcitonin decreased from 4175 to 103.75, and for ATP-cytochrome C from 3412 to 97.83). These results confirm that the wider CIs in the initial model were due to statistical instability

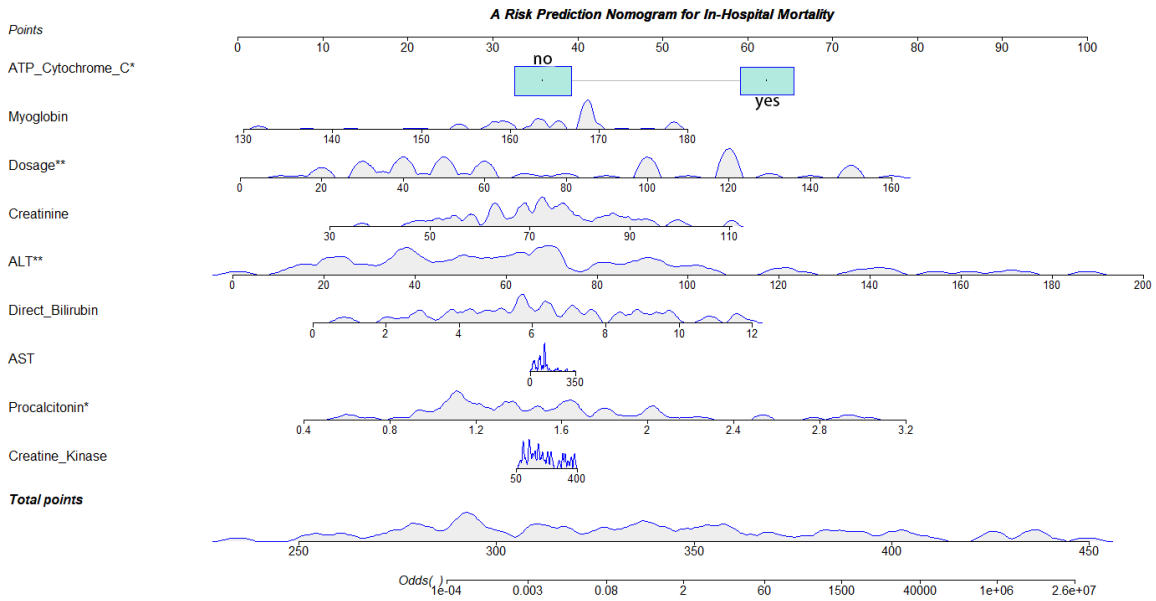

Figure 3. A nomogram for predicting the risk of in-hospital mortality in patients with acute chlorfenapyr poisoning. The model includes four independent predictors: CK, AST, Procalcitonin, ALT, Direct Bilirubin, ATP Cytochrome C, Creatinine, Dosage, and Myoglobin. The value of each variable corresponds to a specific position on the "point" scale. The sum of all points gives the "total score", which is projected downward onto the "mortality risk" axis to obtain the individual's predicted probability. The higher the total score, the greater the risk of mortality.

caused by model overcomplication, rather than instability of the predictors themselves.

Based on the above model, a nomogram was developed to individually predict the risk of in-hospital mortality in patients with acute chlorfenapyr poisoning (**Figure 3**). This graphical tool included nine independent predictors: procalcitonin, intake dose, ALT, ATP cytochrome C use, direct bilirubin, creatinine, myoglobin, CK, aspartate, and aminotransferase. To illustrate its application, a patient with procalcitonin at 2.0 ng/mL, an intake dose of 100 mg, ALT of 100 U/L, and requiring ATP cytochrome C therapy had a total score of approximately 103 points, corresponding to an estimated mortality risk of 80%. This nomogram is a practical bedside tool for rapid risk stratification.

Model evaluation

The model achieved a C-index of 0.988 in the training set and 0.849 in the validation set, demonstrating excellent discriminative power. This confirms its strong ability to differentiate patients with different prognoses (**Figure 4**). The calibration curves showed a highly consistent trend in both study groups, indicating that the model's predicted probabilities closely approximate actual outcomes. The Hosmer-Lemeshow test results were not statistically significant (P=0.771 in the training set; P= 0.942 in the validation set), statistically supporting this and indicating no significant deviation from a perfect fit (**Figure 5**).

Decision curve analysis showed that the nomogram had good clinical applicability in both cohorts (**Figure 6A** and **6B**). Furthermore, the clinical impact curves confirmed its accurate risk stratification ability, effectively identifying most non-survivors within a reasonable intervention threshold range (**Figure 6C** and **6D**). To determine the specific operational threshold for rapid clinical risk stratification, the optimal cutoff probability of the nomogram was determined by maximizing the Youden index on the ROC curve, which was 0.31. At this cutoff value, the model's sensitivity was 97.37% and its specificity was 90.57%. Patients were divided into a high-risk group (predicted probability ≥0.31) and a low-risk group (probability <0.31). The observed mortality rate was 88.10% in the high-risk group and 2.04% in the low-risk group, a highly statistically significant difference (χ^2=65.37, P<0.001).

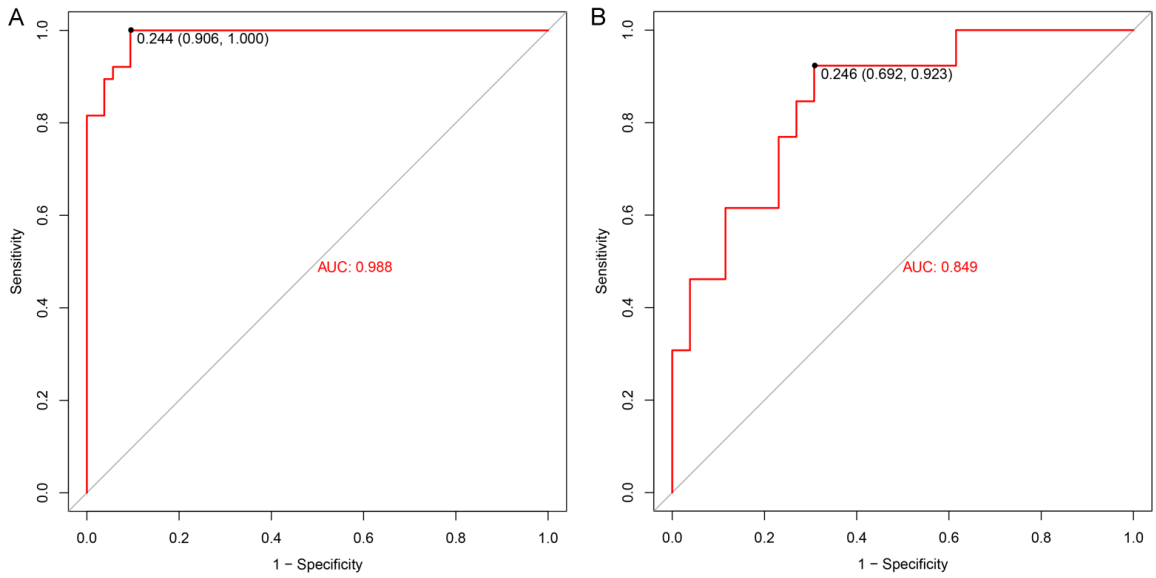

Figure 4. Receiver operating characteristic (ROC) curve of acute chlorfenapyr poisoning in the training (A) and validation (B) cohorts.

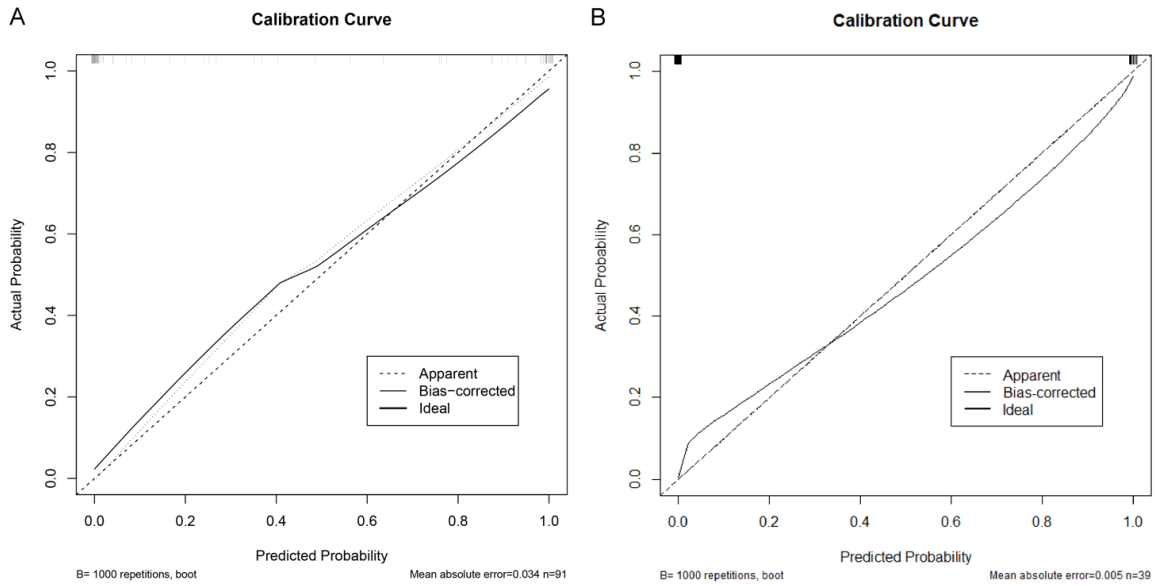

Figure 5. Calibration curve of acute chlorfenapyr poisoning in the training (A) and validation (B) set.

Discussion

Despite the high mortality rate of acute chlorfenapyr poisoning, accurate early prognosis remains a significant clinical challenge. Rapid progression to multiple organ failure underscores the urgent need for early risk stratification [10]. Therefore, we developed and validated a clinically applicable nomogram for accurately assessing mortality risk in hospitalized patients to facilitate timely intervention and optimize resource allocation.

Chlorfenapyr is a novel pyrethroid insecticide classified as a moderately hazardous compound [18]. In this study, the mortality rate in the non-survivor group was 41.8%. While this figure is lower than individual case reports, it highlights the lethal potential of this toxin. Notably, chlorfenapyr requires activation by

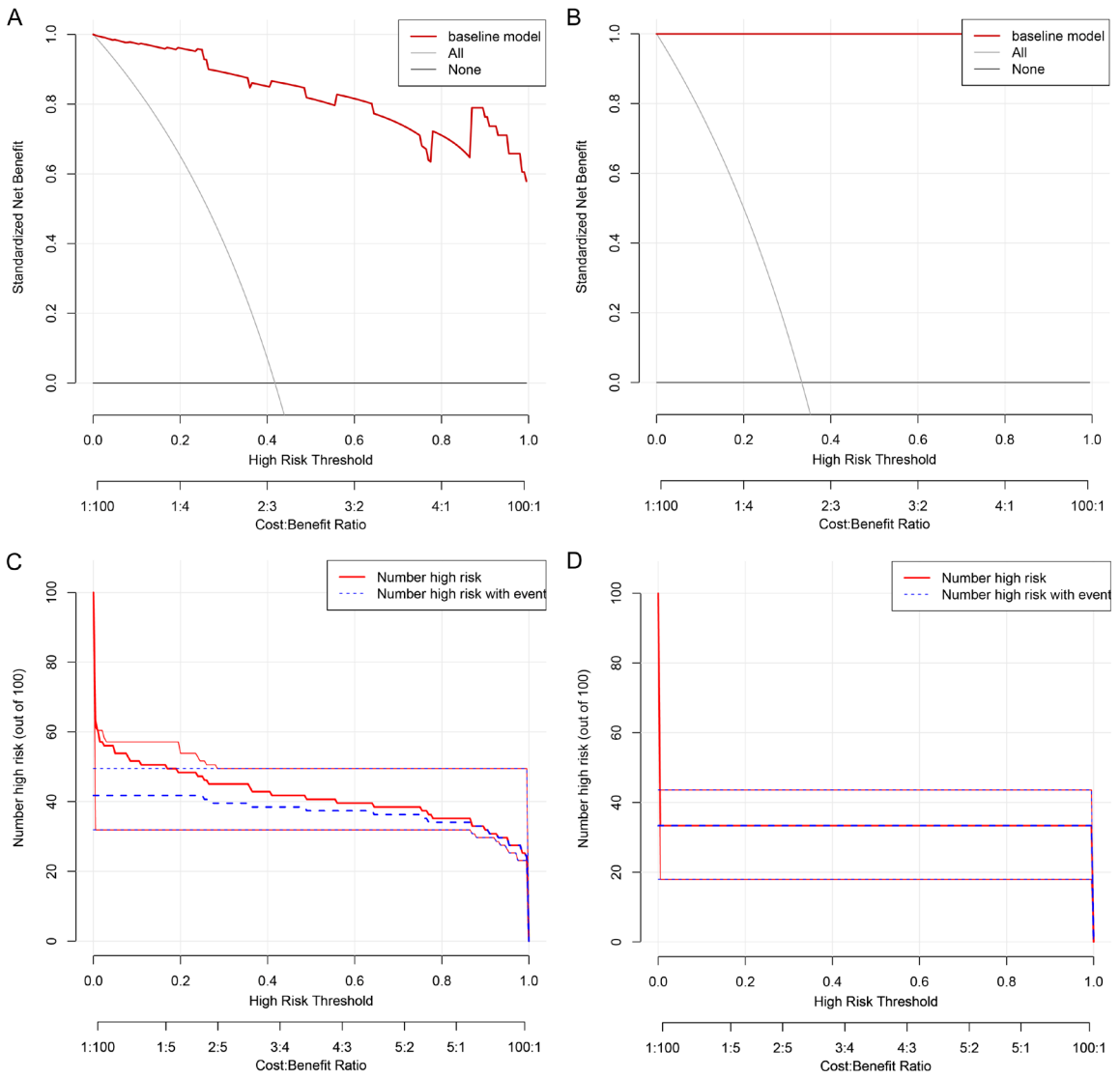

Figure 6. The nomogram decision curve analysis for the training group (A) and the validation group (B), as well as the clinical impact curves for the training group (C) and the validation group (D).

cytochrome P450 enzymes in the liver to form its active metabolite, chlorphenamine N-acetyl-L-tyrosine [19]. This metabolite disrupts mitochondrial function by uncoupling oxidative phosphorylation, thereby impairing ATP synthesis and ultimately leading to multiple organ failure [20]. This mechanism explains the strong correlation between ATP cytochrome C utilization and mortality observed in our study, consistent with previous reports that mitochondrial dysfunction is a key determinant of lethality [21].

Our initial univariate analysis revealed distinct clinical characteristics between survivors and non-survivors. The non-survivors exhibited significantly higher toxicant exposures and more severe physical impairment. The significantly elevated intake doses observed in the non-survivors further confirm the established dose-response relationship in pesticide poisoning, a phenomenon consistently documented in toxicology studies [22]. Furthermore, significant elevations in multiple biomarkers collectively contributed to the pattern of multi-organ dysfunction. Elevated procalcitonin levels indicated a systemic inflammatory response [23, 24], while increased lactate levels reflected underlying tissue hypoxia and metabolic acidosis [25]. Elevated transaminases suggested liver dam-

age, while elevated creatinine indicated impaired renal function [26, 27]. Simultaneous elevations in creatine kinase and myoglobin are characteristic of rhabdomyolysis [28, 29]. These abnormal laboratory findings are consistent with progressive organ failure observed in severe toxicological presentations. More frequent use of ATP-cytochrome C therapy in non-survivors may represent a targeted therapeutic response to critically ill patients, particularly addressing the core mechanisms of mitochondrial dysfunction and cellular energy depletion [30, 31]. Consequently, its use serves as an indicator of clinically relevant disease severity.

Through multivariate analysis, we identified four independent predictors of mortality: ATP cytochrome C use, procalcitonin, intake dose, and ALT. The extremely high odds ratios associated with ATP cytochrome C use and elevated procalcitonin were particularly noteworthy. The strong correlation of ATP cytochrome C use primarily reflects bias due to clinical indication rather than direct treatment efficacy. This intervention was empirically used only in patients diagnosed with life-threatening mitochondrial dysfunction, as evidenced by their significantly higher baseline lactate and procalcitonin levels (**Table 1**). Therefore, it most accurately serves as a robust, clinically defined, comprehensive biomarker of extreme baseline disease severity. The strong correlation of procalcitonin underscores the crucial role of severe systemic inflammatory responses in the pathophysiology of fatal outcomes. The elevation of procalcitonin in chlorfenapyr poisoning is mechanistically related to its primary toxic effects. Inhibitors of mitochondrial oxidative phosphorylation produced by cyhalothrin metabolism disrupt cellular energy metabolism, leading to cellular stress, ATP depletion, and an increase in reactive oxygen species, potent activators of the innate immune system [32, 33]. This process triggers a severe systemic inflammatory response syndrome, characterized by the release of pro-inflammatory cytokines such as IL-6 and TNF-α, which are key inducers of procalcitonin synthesis in hepatocytes [34]. Furthermore, the resulting cellular energy crisis may impair the integrity of the intestinal barrier, potentially promoting bacterial or endotoxin translocation, another proven pathway leading to significant increases in procalcitonin [35]. Therefore, procalcitonin serves as a comprehensive biomarker reflecting the severe inflammatory phenotype driven by the fundamental mitochondrial toxicity of chlorfenapyr, and is a key driver of multi-organ failure. Furthermore, the intake dose confirms its role as a fundamental determinant of exposure severity. The inclusion of ALT, over other organ damage markers, underscores the specific susceptibility to liver injury and its prognostic importance in this poisoning. These predictive factors were incorporated into a clinically applicable nomogram. The model exhibits strong discriminative power. The C-index for the training set was 0.988, and for the validation set, it was 0.849. The calibration was satisfactory. These results demonstrate that the nomogram outperforms existing tools for predicting acute pesticide poisoning. By integrating these four readily available variables, the nomogram provides a practical quantitative method for risk stratification. Its high performance in both the training and validation cohorts confirmed its strong discriminative power, while the excellent calibration and significant net benefit observed in decision curve analysis confirmed that the model is not only statistically sound but also clinically applicable. This tool enables clinicians to shift from qualitative assessment to individualized mortality risk assessment, supporting more informed decisions regarding treatment intensity, resource allocation, and patient communication.

Limitations

This study has several limitations that warrant our attention. First, the retrospective, single-center study design may introduce selection and information bias. Second, although the sample size in this study is relatively large for this type of poisoning research, it is still relatively limited (n=130), which restricts the accuracy of some estimates (e.g., wide confidence intervals) and the generalizability of the model. Third, we did not formally compare it with commonly used severity scores (such as APACHE II) because our goal was to develop a poisoning-specific tool that utilizes key, pathophysiologically relevant variables not covered by the scores. Fourth, although baseline comparability was confirmed, we did not use propensity score matching to balance the training and validation sets. Fifth, due to the lack of systematic long-term follow-up data, the predictive

scope was limited to in-hospital mortality, an inherent limitation of retrospective study design. Finally, while internal validation showed good performance, external multicenter prospective validation was crucial for confirming its generalizability and exploring its added value when combined with conventional scores.

Conclusions

This study identified four independent prognostic factors for in-hospital mortality in patients with acute chlorfenapyr poisoning: ingested dose, elevated ALT, ATP cytochrome C therapy requirement, and procalcitonin levels. A novel nomogram integrating these factors demonstrated excellent predictive performance, with a C-index of 0.988 in the training cohort and 0.849 in the external validation cohort, confirming its strong discriminative power. The model calibration curve and the Hosmer-Lemeshow test (which showed no significant difference) indicated excellent agreement between the predicted and observed mortality risks. In summary, we developed and validated a nomogram that accurately predicts in-hospital mortality risk in patients with acute chlorfenapyr poisoning using four readily available clinical parameters.

Disclosure of conflict of interest

None.

Address correspondence to: Fenshuang Zheng, Department of Ethics Committee, The Affiliated Hospital of Yunnan University, 176 Qingnian Road, Wuhua District, Kunming 650021, Yunnan, China. E-mail: 503002938@qq.com

References

[1] Boedeker W, Watts M, Clausing P and Marquez E. The global distribution of acute unintentional pesticide poisoning: estimations based on a systematic review. BMC Public Health 2020; 20: 1875.

[2] Shi M, Huang XY, Ren XY, Wei XY, Ma Y, Lin ZZ, Liu DT, Song L, Zhao TJ, Li G, Yao L, Zhu M, Zhang C, Xie C, Wu Y, Wu HM, Fan LP, Ou J, Zhan YH, Lin SY and Lin SC. AIDA directly connects sympathetic innervation to adaptive thermogenesis by UCP1. Nat Cell Biol 2021; 23: 268-277.

[3] Chien SC, Chien SC and Su YJ. A fatal case of chlorfenapyr poisoning and a review of the literature. J Int Med Res 2022; 50: 3000605221121965.

[4] Zhang S, Deng Y and Gao Y. Malignant hyperthermia-like syndrome in acute chlorfenapyr poisoning - a case report. Heliyon 2022; 8: e10051.

[5] Kang C, Kim DH, Kim SC and Kim DS. A patient fatality following the ingestion of a small amount of chlorfenapyr. J Emerg Trauma Shock 2014; 7: 239-241.

[6] Periasamy S, Deng JF and Liu MY. Who is the real killer? Chlorfenapyr or detergent micelle-chlorfenapyr complex? Xenobiotica 2017; 47: 833-835.

[7] Chung MJ, Mao YC, Hsu CT, Chung MC, Wang TJ, Yu TM, Liu PY, Fu PK and Hsieh CM. A fatal case of chlorfenapyr poisoning and the therapeutic implications of serum chlorfenapyr and tralopyril levels. Medicina (Kaunas) 2022; 58: 1630.

[8] Choi UT, Kang GH, Jang YS, Ahn HC, Seo JY and Sohn YD. Fatality from acute chlorfenapyr poisoning. Clin Toxicol (Phila) 2010; 48: 458-459.

[9] Tang S, Zhang S, Du H, Yang X, Yao Q, Peng A, Tang M and Cao Y. A rapid and sensitive LC-MS/MS method for the simultaneous determination of chlorfenapyr and its major metabolite tralopyril in human plasma: from method development, validation to clinical application. J Chromatogr B Analyt Technol Biomed Life Sci 2025; 1257: 124580.

[10] Cheng J, Chen Y, Wang W, Zhu X, Jiang Z, Liu P and Du L. Chlorfenapyr poisoning: mechanisms, clinical presentations, and treatment strategies. World J Emerg Med 2024; 15: 214-219.

[11] Comstock GT, Nguyen H, Bronstein A and Yip L. Chlorfenapyr poisoning: a systematic review. Clin Toxicol (Phila) 2024; 62: 412-424.

[12] Cheng Y, Zhao Y, Li H, Duan M, Li L, Zhou S, Tang Q, Xie W and Shi J. A clinical warning in the treatment of chlorfenapyr poisoning. Toxicol Rep 2024; 13: 101703.

[13] Wu B, Xue F, Lu M, Ma A and Fan L. Experience in the treatment of chlorfenapyr poisoning. J Toxicol Sci 2023; 48: 221-225.

[14] Jalali A, Alvarez-Iglesias A, Roshan D and Newell J. Visualising statistical models using dynamic nomograms. PLoS One 2019; 14: e0225253.

[15] Elgazzar FM, Afifi AM, Shama MAE, Askary AE and El-Sarnagawy GN. Development of a risk prediction nomogram for disposition of acute toxic exposure patients to intensive care unit. Basic Clin Pharmacol Toxicol 2021; 129: 256-267.

[16] Sharif AF, Kasemy ZA, Alshabibi RA, Almufleh SJ, Abousamak FW, Alfrayan AA, Alshehri M, Alemies RA, Almuhsen AS, AlNasser SN and Al-

Mulhim KA. Prognostic factors in acute poisoning with central nervous system xenobiotics: development of a nomogram predicting risk of intensive care unit admission. Toxicol Res (Camb) 2023; 12: 62-75.
[17] Lashin HI, Sobeeh FG and Sobh ZK. Development and validation of a nomogram for predicting mechanical ventilation need among acutely intoxicated patients with impaired consciousness. Hum Exp Toxicol 2024; 43: 9603271241267214.
[18] Zhao Y, Wang Q, Wang Y, Zhang Z, Wei Y, Liu F, Zhou C and Mu W. Chlorfenapyr, a potent alternative insecticide of phoxim to control bradysia odoriphaga (Diptera: Sciaridae). J Agric Food Chem 2017; 65: 5908-5915.
[19] Yunta C, Ooi JMF, Oladepo F, Grafanaki S, Pergantis SA, Tsakireli D, Ismail HM and Paine MJI. Chlorfenapyr metabolism by mosquito P450s associated with pyrethroid resistance identifies potential activation markers. Sci Rep 2023; 13: 14124.
[20] Tharaknath VR, Prabhakar YV, Kumar KS and Babu NK. Clinical and radiological findings in chlorfenapyr poisoning. Ann Indian Acad Neurol 2013; 16: 252-254.
[21] Skolnik A and Monas J. The crashing toxicology patient. Emerg Med Clin North Am 2020; 38: 841-856.
[22] Chen X, Zheng J, Teng M, Zhang J, Qian L, Duan M, Zhao F, Zhao W, Wang Z and Wang C. Bioaccumulation, metabolism and the toxic effects of chlorfenapyr in zebrafish (Danio rerio). J Agric Food Chem 2021; 69: 8110-8119.
[23] Kintrup S, Brabenec L, Zurek-Leffers FM, Hellenthal KEM, Cyran L, Meybohm P, Gerke V and Wagner NM. Detection and evaluation of procalcitonin variants as diagnostic tools in systemic inflammation. Anesth Analg 2025; 140: 1073-1082.
[24] Kobayashi H, Amrein K, Lasky-Su JA and Christopher KB. Procalcitonin metabolomics in the critically ill reveal relationships between inflammation intensity and energy utilization pathways. Sci Rep 2021; 11: 23194.
[25] Rimachi R, Bruzzi de Carvahlo F, Orellano-Jimenez C, Cotton F, Vincent JL and De Backer D. Lactate/pyruvate ratio as a marker of tissue hypoxia in circulatory and septic shock. Anaesth Intensive Care 2012; 40: 427-432.
[26] Kobayashi A, Suzuki Y and Sugai S. Specificity of transaminase activities in the prediction of drug-induced hepatotoxicity. J Toxicol Sci 2020; 45: 515-537.
[27] Sottas PE, Kapke GF and Leroux JM. Adaptive Bayesian approach to clinical trial renal impairment biomarker signal from urea and creatinine. Int J Biol Sci 2013; 9: 156-163.
[28] Lim AKH. Predicting acute kidney injury in acute rhabdomyolysis. J Clin Med 2025; 14: 6892.
[29] Talaie H, Pajouhmand A, Abdollahi M, Panahandeh R, Emami H, Hajinasrolah S and Tghaddosinezhad M. Rhabdomyolysis among acute human poisoning cases. Hum Exp Toxicol 2007; 26: 557-561.
[30] Karami-Mohajeri S, Hadian MR, Fouladdel S, Azizi E, Ghahramani MH, Hosseini R and Abdollahi M. Mechanisms of muscular electrophysiological and mitochondrial dysfunction following exposure to malathion, an organophosphorus pesticide. Hum Exp Toxicol 2014; 33: 251-263.
[31] Onishi H, Tsubuda S and Ogawa N. Effect of cytochrome c on carbon tetrachloride damage to the liver. Jpn J Pharmacol 1973; 23: 881-888.
[32] Raghavendra K, Barik TK, Sharma P, Bhatt RM, Srivastava HC, Sreehari U and Dash AP. Chlorfenapyr: a new insecticide with novel mode of action can control pyrethroid resistant malaria vectors. Malar J 2011; 10: 16.
[33] Harijith A, Ebenezer DL and Natarajan V. Reactive oxygen species at the crossroads of inflammasome and inflammation. Front Physiol 2014; 5: 352.
[34] Mandell BF. Infection or not infection, that is the question--is procalcitonin the answer? Cleve Clin J Med 2019; 86: 297-298.
[35] Becker KL, Snider R and Nylen ES. Procalcitonin in sepsis and systemic inflammation: a harmful biomarker and a therapeutic target. Br J Pharmacol 2010; 159: 253-264.

Supplementary Table 1. Univariable analysis of all variables in the entire cohort (N=130)

Variable	Survivors (N=79)	Non-survivors (N=51)	P
Age, years	44.80 ± 10.87	45.12 ± 8.99	0.861
Male Sex, n (%)	47 (59.5)	29 (56.9)	0.856
medication to hospital admission time, h	9.00 (6.00-11.00)	9.00 (6.00-11.50)	0.859
therapy duration, h	7.00 (5.00-10.00)	9.00 (5.00-11.00)	0.327
Ingestion Dose, mg	40.00 (30.00-57.50)	120.00 (95.00-120.00)	<0.001
Presence of Fever, n (%)	24 (30.4)	19 (37.3)	0.449
Presence of Sweating, n (%)	37 (46.8)	20 (39.2)	0.151
ATP Cytochrome C Use, n (%)	24 (30.4)	34 (66.7)	<0.001
Blood Purification, n (%)	37 (46.8)	36 (70.6)	0.011
Methylprednisolone Use, n (%)	35 (44.3)	15 (29.4)	0.100
Procalcitonin, ng/mL	1.22 (1.04-1.56)	1.67 (1.44-2.09)	<0.001
Lactate, mmol/L	1.40 ± 0.76	2.33 ± 1.03	<0.001
lactic dehydrogenase, U/L	205.44 (167.16-248.34)	227.42 (189.79-257.27)	<0.001
C-reactive Protein, mg/L	17.08 (10.18-20.99)	17.08 (11.64-19.02)	0.701
White Blood Cell Count, $\times 10^9$/L	20.82 ± 5.81	21.51 ± 8.07	0.572
Neutrophil Percentage, %	60.83 (50.37-69.56)	65.60 (54.86-75.84)	0.049
Lymphocyte Absolute Value, $\times 10^9$/L	1.50 ± 0.57	1.56 ± 0.63	0.580
Lymphocyte Percentage, %	18.23 ± 5.86	18.50 ± 5.55	0.794
Monocyte Absolute Value, $\times 10^9$/L	0.78 ± 0.33	0.71 ± 0.35	0.281
Monocyte Percentage, %	7.35 ± 2.62	7.58 ± 2.28	0.605
Eosinophil Ratio, %	0.83 (0.43-1.05)	0.83 (0.73-1.10)	0.167
Eosinophil Absolute Value, $\times 10^9$/L	0.06 (0.04-0.07)	0.06 (0.05-0.07)	0.352
Basophil Ratio, %	0.22 (0.15-0.28)	0.23 (0.17-0.29)	0.277
Alanine Aminotransferase, U/L	54.19 (34.49-69.24)	88.13 (60.60-127.96)	<0.001
Aspartate Aminotransferase, U/L	75.46 (50.14-107.19)	113.77 (83.83-192.21)	<0.001
Gamma-glutamyl Transferase, U/L	44.91 (31.78-65.27)	55.12 (36.20-75.37)	0.045
Total Bilirubin, μmol/L	15.93 (9.49-22.14)	16.58 (11.56-23.04)	0.546
Direct Bilirubin, μmol/L	5.91 ± 2.30	6.70 ± 2.62	0.071
Indirect Bilirubin, μmol/L	10.77 (6.43-14.88)	10.77 (4.42-14.92)	0.621
Total Protein, g/L	60.45 ± 6.45	59.64 ± 6.86	0.500
Albumin, g/L	35.64 ± 4.31	35.84 ± 4.80	0.805
Globulin, g/L	23.38 ± 2.96	23.80 ± 2.95	0.437
Creatinine, μmol/L	67.64 (58.35-75.75)	76.50 (72.00-85.13)	<0.001
Urea, mmol/L	6.88 (5.00-9.19)	7.75 (6.00-9.72)	0.047
Creatine Kinase, U/L	188.90 (133.37-257.32)	227.06 (145.61-332.50)	0.048
Creatine Kinase-MB, U/L	26.35 (17.41-36.74)	30.00 (17.92-46.88)	0.048
Myoglobin, ng/mL	162.34 (158.36-168.45)	168.54 (163.48-168.78)	0.017
Amylase, U/L	66.51 ± 18.61	64.73 ± 18.06	0.590
Activated Partial Thromboplastin Time, s	32.37 (27.77-35.77)	33.84 (29.80-36.71)	0.046
Prothrombin Time, s	14.35 (9.20-20.50)	14.84 (7.77-19.99)	0.664
Thrombin Time, s	47.43 (29.71-69.78)	44.74 (22.66-64.81)	0.409
Fibrinogen Degradation Products, μg/mL	3.06 (1.60-4.67)	3.66 (1.83-5.79)	0.049
D-dimer, μg/mL	4.22 (3.15-4.22)	4.22 (2.95-5.53)	0.647
Partial Pressure of Oxygen, mmHg	84.50 ± 10.32	77.16 ± 12.44	<0.001
Partial Pressure of Carbon Dioxide, mmHg	33.11 ± 3.57	32.94 ± 2.91	0.786
pH	7.44 ± 0.04	7.44 ± 0.03	0.648
Base Excess, mmol/L	0.02 (-1.12-1.21)	0.45 (-0.78-1.75)	0.052

Hemoglobin, g/L	136.50 ± 15.95	137.86 ± 19.89	0.669
packed cell volume, %	0.42 ± 0.09	0.43 ± 0.10	0.466
Red Blood Cell Count, $\times 10^{12}$/L	4.41 ± 0.47	4.33 ± 0.60	0.365
Platelet Count, $\times 10^{9}$/L	185.43 ± 65.58	176.76 ± 68.65	0.471
thrombocytocrit, %	0.17 ± 0.05	0.18 ± 0.06	0.708
Neutrophil Absolute Value, $\times 10^{9}$/L	7.94 ± 4.27	8.36 ± 3.66	0.567
Cardiac Troponin I, ng/mL	0.08 (0.04-0.08)	0.08 (0.07-0.08)	0.344
Antithrombin III, %	99.03 ± 9.32	98.95 ± 11.84	0.964

This table presents the comparison of all collected baseline variables between survivors (n=79) and non-survivors (n=51) in the entire study population. Data are presented as mean ± standard deviation, median (interquartile range), or n (%) as appropriate. *P*-values are derived from Student's t-test, Mann-Whitney U test, or Fisher's exact test.

Supplementary Table 2. Univariable analysis of all variables in the training set (N=91)

Variable	Survivors (N=53)	Non-survivors (N=38)	P
Age, years	44.49 ± 11.35	44.87 ± 8.55	0.863
Male Sex, n (%)	31 (58.5)	18 (47.4)	0.394
medication to hospital admission time, h	9.00 (6.00-11.00)	9.00 (6.00-12.75)	0.512
therapy duration, h	7.60 ± 3.80	8.03 ± 3.89	0.606
Ingestion Dose, mg	45.00 (30.00-60.00)	120.00 (100.00-120.00)	<0.001
Presence of Fever, n (%)	16 (30.2)	13 (34.2)	0.820
Presence of Sweating, n (%)	26 (49.1)	14 (36.8)	0.206
ATP Cytochrome C Use, n (%)	20 (37.7)	23 (60.5)	0.036
Blood Purification, n (%)	26 (49.1)	25 (65.8)	0.137
Methylprednisolone Use, n (%)	26 (49.1)	12 (31.6)	0.132
Procalcitonin, ng/mL	1.24 (1.09-1.57)	1.65 (1.38-2.10)	<0.001
Lactate, mmol/L	1.43 ± 0.77	2.32 ± 0.94	<0.001
lactic dehydrogenase, U/L	209.53 ± 42.02	221.41 ± 45.84	0.204
C-reactive Protein, mg/L	17.08 (10.75-22.43)	17.05 (11.51-17.08)	0.185
White Blood Cell Count, $\times 10^{9}$/L	20.79 ± 6.00	22.13 ± 7.61	0.350
Neutrophil Percentage, %	62.56 (50.75-69.07)	65.73 (57.12-76.05)	0.107
Lymphocyte Absolute Value, $\times 10^{9}$/L	1.56 ± 0.60	1.62 ± 0.56	0.636
Lymphocyte Percentage, %	18.42 ± 6.56	18.49 ± 5.39	0.955
Monocyte Absolute Value, $\times 10^{9}$/L	0.79 ± 0.35	0.74 ± 0.32	0.528
Monocyte Percentage, %	7.38 ± 2.79	7.44 ± 2.35	0.917
Eosinophil Ratio, %	0.83 (0.48-1.02)	0.83 (0.73-1.00)	0.236
Eosinophil Absolute Value, $\times 10^{9}$/L	0.06 (0.04-0.07)	0.06 (0.05-0.06)	0.974
Basophil Ratio, %	0.23 ± 0.11	0.27 ± 0.13	0.120
Alanine Aminotransferase, U/L	50.88 (30.54-69.24)	89.44 (61.98-116.22)	<0.001
Aspartate Aminotransferase, U/L	74.03 (45.43-107.19)	109.47 (81.53-188.35)	<0.001
Gamma-glutamyl Transferase, U/L	41.02 (31.42-65.88)	56.63 (37.06-73.68)	0.085
Total Bilirubin, μmol/L	16.11 ± 7.92	16.71 ± 8.93	0.736
Direct Bilirubin, μmol/L	5.80 ± 2.34	6.96 ± 2.90	0.038
Indirect Bilirubin, μmol/L	10.77 (5.19-14.93)	10.84 (4.85-15.57)	0.690
Total Protein, g/L	60.40 ± 6.98	59.95 ± 7.30	0.768
Albumin, g/L	35.54 ± 4.57	35.88 ± 4.80	0.735
Globulin, g/L	23.89 (20.73-25.53)	23.84 (21.56-26.32)	0.476
Creatinine, μmol/L	67.95 ± 13.62	79.21 ± 12.68	<0.001
Urea, mmol/L	7.14 (5.38-9.15)	8.36 (5.99-10.27)	0.115
Creatine Kinase, U/L	172.25 (128.47-233.43)	220.32 (146.01-342.56)	0.019

Creatine Kinase-MB, U/L	27.11 (18.58-36.45)	30.45 (15.79-45.73)	0.127
Myoglobin, ng/mL	162.34 (158.36-168.45)	168.54 (163.48-168.78)	0.004
Amylase, U/L	65.75 ± 16.06	65.50 ± 18.77	0.946
Activated Partial Thromboplastin Time, s	33.15 (29.32-36.34)	34.00 (28.93-37.19)	0.281
Prothrombin Time, s	14.82 (9.61-21.86)	14.84 (7.75-19.73)	0.847
Thrombin Time, s	47.43 (29.21-61.49)	40.83 (23.04-66.68)	0.763
Fibrinogen Degradation Products, μg/mL	3.31 (1.75-4.80)	3.90 (1.98-5.99)	0.065
D-dimer, μg/mL	4.22 (2.76-4.22)	4.22 (2.94-5.50)	0.317
Partial Pressure of Oxygen, mmHg	83.34 (77.59-91.67)	78.78 (68.35-85.32)	0.008
Partial Pressure of Carbon Dioxide, mmHg	33.52 ± 3.15	33.23 ± 2.88	0.646
pH	7.44 ± 0.03	7.44 ± 0.04	0.450
Base Excess, mmol/L	0.01 (-1.11-1.23)	0.40 (-0.66-1.76)	0.101
Hemoglobin, g/L	136.21 ± 16.19	136.89 ± 19.99	0.857
packed cell volume, %	0.43 ± 0.10	0.44 ± 0.11	0.586
Red Blood Cell Count, $\times 10^{12}$/L	4.41 ± 0.48	4.35 ± 0.60	0.598
Platelet Count, $\times 10^{9}$/L	185.74 ± 65.20	172.00 ± 74.53	0.353
thrombocytocrit, %	0.18 ± 0.06	0.17 ± 0.06	0.906
Neutrophil Absolute Value, $\times 10^{9}$/L	8.41 ± 4.18	8.34 ± 3.83	0.938
Cardiac Troponin I, ng/mL	0.08 (0.04-0.08)	0.08 (0.07-0.08)	0.137
Antithrombin III, %	98.30 ± 9.31	97.60 ± 12.66	0.761

This table presents the comparison of all collected baseline variables between survivors (n=53) and non-survivors (n=38) in the training set, which was used for model development. Data presentation and statistical tests are as described in Supplementary Table 1.

Supplementary Table 3. Univariable analysis of all variables in the validation set (N=39)

Variable	Survivors (N=26)	Non-survivors (N=13)	P
Age, years	45.42 ± 9.98	45.85 ± 10.53	0.903
Male Sex, n (%)	16 (61.5)	11 (84.6)	0.269
medication to hospital admission time, h	9.19 ± 5.50	7.46 ± 3.20	0.303
therapy duration, h	7.60 ± 3.80	8.03 ± 3.89	0.606
Ingestion Dose, mg	30.00 (20.00-43.75)	120.00 (70.00-140.00)	<0.001
Presence of Fever, n (%)	8 (30.8)	6 (46.2)	0.482
Presence of Sweating, n (%)	11 (42.3)	6 (46.2)	0.520
ATP Cytochrome C Use, n (%)	4 (15.4)	11 (84.6)	<0.001
Blood Purification, n (%)	11 (42.3)	11 (84.6)	0.017
Methylprednisolone Use, n (%)	9 (34.6)	3 (23.1)	0.714
Procalcitonin, ng/mL	1.27 ± 0.46	1.87 ± 0.38	<0.001
Lactate, mmol/L	1.07 (0.82-1.83)	2.05 (1.45-2.57)	0.004
lactic dehydrogenase, U/L	209.53 ± 42.02	221.41 ± 45.84	0.204
C-reactive Protein, mg/L	17.03 (8.00-17.36)	17.08 (15.37-26.42)	0.220
White Blood Cell Count, $\times 10^{9}$/L	20.88 ± 5.52	19.70 ± 9.38	0.623
Neutrophil Percentage, %	58.94 ± 12.05	63.25 ± 13.54	0.319
Lymphocyte Absolute Value, $\times 10^{9}$/L	1.39 ± 0.48	1.40 ± 0.80	0.963
Lymphocyte Percentage, %	17.85 ± 4.19	18.53 ± 6.21	0.689
Monocyte Absolute Value, $\times 10^{9}$/L	0.75 ± 0.30	0.61 ± 0.43	0.250
Monocyte Percentage, %	7.30 ± 2.28	8.02 ± 2.09	0.347
Eosinophil Ratio, %	0.83 (0.41-1.04)	0.83 (0.74-1.11)	0.445
Eosinophil Absolute Value, $\times 10^{9}$/L	0.06 ± 0.03	0.08 ± 0.04	0.041
Basophil Ratio, %	0.23 (0.14-0.24)	0.17 (0.07-0.24)	0.339

Alanine Aminotransferase, U/L	60.23 ± 29.86	94.88 ± 61.13	0.022
Aspartate Aminotransferase, U/L	79.46 (55.95-107.19)	140.06 (105.12-192.72)	0.014
Gamma-glutamyl Transferase, U/L	49.60 ± 16.92	56.37 ± 21.92	0.293
Total Bilirubin, μmol/L	13.94 (8.98-23.23)	17.81 (14.87-22.50)	0.541
Direct Bilirubin, μmol/L	6.11 ± 2.25	5.93 ± 1.34	0.791
Indirect Bilirubin, μmol/L	12.19 ± 5.80	8.57 ± 4.94	0.062
Total Protein, g/L	60.56 ± 5.34	58.76 ± 5.53	0.334
Albumin, g/L	35.83 ± 3.78	35.72 ± 4.99	0.936
Globulin, g/L	23.50 ± 2.95	23.69 ± 1.83	0.837
Creatinine, μmol/L	64.61 (60.26-75.62)	74.30 (73.02-77.83)	0.026
Urea, mmol/L	6.38 (4.74-9.11)	7.48 (6.25-8.29)	0.233
Creatine Kinase, U/L	229.75 ± 77.19	236.34 ± 93.43	0.816
Creatine Kinase-MB, U/L	25.31 ± 11.67	31.79 ± 15.08	0.147
Myoglobin, ng/mL	159.68 (158.69-175.85)	165.40 (154.23-168.78)	0.776
Amylase, U/L	68.08 ± 23.24	62.48 ± 16.30	0.443
Activated Partial Thromboplastin Time, s	29.16 (27.19-33.89)	33.84 (30.05-34.56)	0.043
Prothrombin Time, s	12.91 ± 7.45	14.55 ± 8.18	0.535
Thrombin Time, s	54.08 ± 32.66	42.73 ± 27.54	0.289
Fibrinogen Degradation Products, μg/mL	2.84 ± 1.73	3.28 ± 2.07	0.486
D-dimer, μg/mL	4.22 (4.22-5.50)	4.22 (2.98-6.61)	0.703
Partial Pressure of Oxygen, mmHg	82.58 ± 10.55	73.26 ± 13.36	0.022
Partial Pressure of Carbon Dioxide, mmHg	32.48 (29.30-34.75)	33.54 (30.05-34.13)	0.917
pH	7.44 ± 0.04	7.44 ± 0.03	0.781
Base Excess, mmol/L	-0.05 ± 1.44	0.48 ± 1.55	0.297
Hemoglobin, g/L	137.10 ± 15.73	140.67 ± 20.13	0.547
packed cell volume, %	0.41 (0.36-0.47)	0.42 (0.33-0.49)	0.835
Red Blood Cell Count, $\times 10^{12}$/L	4.42 ± 0.46	4.26 ± 0.62	0.369
Platelet Count, $\times 10^{9}$/L	184.79 ± 67.63	190.67 ± 47.21	0.781
thrombocytocrit, %	0.16 ± 0.05	0.18 ± 0.05	0.363
Neutrophil Absolute Value, $\times 10^{9}$/L	6.99 ± 4.39	8.41 ± 3.24	0.311
Cardiac Troponin I, ng/mL	0.08 (0.05-0.11)	0.08 (0.04-0.11)	0.659
Antithrombin III, %	100.51 ± 9.35	102.88 ± 8.21	0.444

This table presents the comparison of all collected baseline variables between survivors (n=26) and non-survivors (n=13) in the independent validation set, which was used to assess the model's generalizability. Data presentation and statistical tests are as described in Supplementary Table 1.

Supplementary Table 4. Training cohort vs. validation cohort baseline feature balance test results (N=130) activated partial thromboplastin time

Variable	Training cohort (N=91)	Validation cohort (N=39)	χ^2/U	P
Age, years	44.65 ± 10.22	45.56 ± 10.03	t=-0.47	0.639
Male Sex, n (%)	49 (53.8%)	27 (69.2%)	χ^2=2.07	0.122
medication to hospital admission time, h	9.00 (6.00-11.00)	8.62 ± 4.88	U=1904.00	0.510
therapy duration, h	7.78 ± 3.82	7.97 ± 4.09	t=-0.26	0.795
Ingestion Dose, mg	60.00 (40.00-120.00)	45.00 (30.00-85.00)	U=2153.00	0.054
Presence of Fever, n (%)	29 (31.9%)	14 (35.9%)	χ^2=0.06	0.687
Presence of Sweating, n (%)	50 (54.9%)	18 (46.2%)	χ^2=0.53	0.444
ATP Cytochrome C Use, n (%)	43 (47.3%)	15 (38.5%)	χ^2=0.54	0.442
Blood Purification, n (%)	51 (56.0%)	22 (56.4%)	χ^2=0.00	1.000
Methylprednisolone Use, n (%)	38 (41.8%)	12 (30.8%)	χ^2=0.97	0.325
Lactate, mmol/L	1.80 ± 0.95	1.45 (0.88-2.13)	U=1974.50	0.311
lactic dehydrogenase, U/L	208.75 (184.72-251.13)	208.21 ± 50.59	U=1874.00	0.615
C-reactive Protein, mg/L	17.08 (10.88-20.60)	17.08 (11.05-18.61)	U=1810.00	0.858
White Blood Cell Count, $\times10^9$/L	21.35 ± 6.71	20.49 ± 6.94	t=0.66	0.510
Neutrophil Percentage, %	63.67 (52.30-74.09)	60.38 ± 12.55	U=1986.00	0.284
Lymphocyte Percentage, %	18.45 ± 6.07	18.08 ± 4.88	t=0.34	0.735
Monocyte Absolute Value, $\times10^9$/L	0.77 ± 0.33	0.70 ± 0.35	t=1.04	0.299
Monocyte Percentage, %	7.40 ± 2.60	7.54 ± 2.22	t=-0.29	0.772
Eosinophil Ratio, %	0.83 (0.55-1.02)	0.83 (0.44-1.11)	U=1806.00	0.874
Eosinophil Absolute Value, $\times10^9$/L	0.06 (0.05-0.07)	0.06 (0.04-0.08)	U=1616.50	0.412
Basophil Ratio, %	0.02 (0.01-0.02)	0.02 ± 0.01	U=1473.00	0.126
Gamma-glutamyl Transferase, U/L	45.86 (33.71-67.03)	51.86 ± 18.72	U=1708.00	0.737
Total Bilirubin, μmol/L	16.36 ± 8.31	17.09 ± 9.31	t=-0.44	0.661
Indirect Bilirubin, μmol/L	10.77 (5.10-15.38)	10.98 ± 5.73	U=1737.50	0.853
Total Protein, g/L	60.21 ± 7.08	59.96 ± 5.40	t=0.20	0.844
Globulin, g/L	23.54 ± 3.10	23.56 ± 2.61	t=-0.05	0.963
Creatinine, μmol/L	72.66 ± 14.30	72.92 (62.78-77.76)	U=1933.50	0.421
Urea, mmol/L	7.25 (5.60-9.77)	6.99 ± 2.30	U=1996.50	0.260
Creatine Kinase-MB, U/L	28.93 (17.85-39.64)	27.47 ± 13.08	U=1893.50	0.547
Myoglobin, ng/mL	165.43 (159.68-168.74)	163.48 (158.66-169.16)	U=1807.50	0.869
Amylase, U/L	65.64 ± 17.14	66.21 ± 21.13	t=-0.16	0.872
Activated Partial Thromboplastin Time, s	33.28 (29.23-36.45)	30.13 (27.71-34.52)	U=2219.50	0.024
Prothrombin Time, s	14.84 (9.41-20.74)	13.45 ± 7.63	U=1998.00	0.257
Thrombin Time, s	47.43 (25.79-66.61)	47.43 (28.62-71.44)	U=1657.50	0.553
Fibrinogen Degradation Products, μg/mL	3.74 (1.80-5.38)	2.98 ± 1.83	U=2079.00	0.122
D-dimer, μg/mL	4.22 (2.89-4.23)	4.22 (3.80-5.66)	U=1508.00	0.163
Partial Pressure of Oxygen, mmHg	82.54 ± 11.44	79.47 ± 12.22	t=1.37	0.173
Partial Pressure of Carbon Dioxide, mmHg	33.40 ± 3.03	32.21 ± 3.82	t=1.89	0.061
Base Excess, mmol/L	0.29 (-0.91-1.48)	0.12 ± 1.48	U=1836.50	0.755
packed cell volume, %	0.43 ± 0.10	0.41 ± 0.09	t=1.26	0.211
Red Blood Cell Count, $\times10^{12}$/L	4.39 ± 0.53	4.37 ± 0.51	t=0.23	0.822
Platelet Count, $\times10^9$/L	180.00 ± 69.18	186.75 ± 61.00	t=-0.53	0.599
thrombocytocrit, %	0.18 ± 0.06	0.17 ± 0.05	t=0.58	0.565
Neutrophil Absolute Value, $\times10^9$/L	8.38 ± 4.01	7.46 ± 4.06	t=1.19	0.238
Cardiac Troponin I, ng/mL	0.08 (0.06-0.08)	0.08 (0.05-0.11)	U=1695.50	0.681
Antithrombin III, %	98.01 ± 10.78	101.30 ± 8.95	t=-1.67	0.097

This table presents the comparison of all collected baseline variables between Training cohort (n=91) and Validation cohort (n=39) in the entire study population. Data are presented as mean ± standard deviation, median (interquartile range), or n (%) as appropriate. *P*-values are derived from Student's t-test, Mann-Whitney U test, or Fisher's exact test.