

Machine Learning Predicts Acute Kidney Injury in Paraquat Poisoning

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Abstract

Background: Acute kidney injury (AKI) is a common and fatal complication of paraquat (PQ) poisoning, with incidence of 40-70% and high mortality. This study aimed to develop and validate a machine learning model to predict AKI after PQ poisoning using readily available clinical parameters.

Methods: We retrospectively analyzed 832 patients with PQ poisoning admitted to West China Hospital between September 10, 2010 and September 30, 2023. Patients were randomly divided into derivation (70%) and validation (30%) cohorts. Predictors were selected using LASSO regression. Logistic regression (LR), Bayesian methods, and support vector machine (SVM) were trained and evaluated using AUC-ROC, calibration, and decision curve analysis (DCA). Performance was compared with the Severity Index of Paraquat Poisoning (SIPP).

Results: The overall incidence of AKI was 65.5% (539/832), and in-hospital mortality was significantly higher in the AKI group (67.9% vs. 26.6%, $P < 0.001$). The LR model achieved the best performance, with an AUC of 0.862 in the derivation cohort and 0.857 in the validation cohort. Five independent predictors were identified: neutrophil-to-lymphocyte ratio (NLR), aspartate aminotransferase (AST), blood urea nitrogen (BUN), cystatin C (CysC), and plasma PQ concentration. The LR model showed superior discrimination compared with SIPP and favorable clinical utility in DCA.

Conclusions: A machine learning model based on NLR, AST, BUN, CysC, and plasma PQ concentration accurately predicts AKI in patients with PQ poisoning and outperforms the traditional SIPP score. This model can support early risk stratification and clinical decision-making.

Introduction

Acute kidney injury (AKI) is a prevalent, heterogeneous, and life-threatening condition associated with increased mortality, prolonged hospital stay, and long-term morbidity[1–5]. Although AKI has a multifactorial etiology, toxin-induced AKI represents a distinct clinical entity characterized by direct cellular damage and systemic toxicity[6–9]. Paraquat (PQ), a widely used herbicide, is highly toxic to humans and frequently causes severe AKI after acute intoxication. The reported incidence of AKI in PQ poisoning ranges from 40% to 70%, and AKI is an independent risk factor for mortality [10–16].

PQ is selectively taken up by renal tubular epithelial cells via organic cation transporter 2 (OCT2), triggering oxidative stress, mitochondrial dysfunction, and inflammatory cascades that lead to renal tubular damage[13, 17–19]. High concentrations of PQ accumulates in the kidney and induces severe nephrotoxicity following poisoning[18, 19]. The resulting renal impairment may further reduce PQ elimination and disrupt homeostasis, ultimately leading to multiple organ failure[20]. Despite advances in supportive care, effective early predictive tools for PQ-induced AKI remain limited[11, 21–23].

Machine learning (ML) models using electronic medical records have shown promise in predicting clinical outcomes in acute poisoning[24]. In this study, we developed and internally validated an ML-based prediction model for AKI in patients with acute PQ poisoning using routinely available admission parameters. We also compared model performance with the conventional SIPP scoring system.

Materials and methods

Clinical data collection

We retrospectively analyzed 832 patients with PQ poisoning admitted to the emergency department of West China Hospital between September 10, 2010 and September 30, 2023. Inclusion criteria were: (1) age ≥ 18 years; (2) detectable plasma PQ concentration (≥ 0.01 ng/mL) confirmed by mass spectrometry (MS). Exclusion criteria included: (1) time from poisoning exposure to presentation > 7 days; (2) co-exposure to other toxins; (3) AKI caused by other known etiologies (shock, sepsis, etc.); (4) history of chronic kidney disease; and (5) missing clinical data. The detailed enrollment process is summarized in Fig. 1.

The study collected the following data categories: (1) demographics information: age, sex, time from PQ exposure to hospital presentation, glasgow coma scale (GCS) score ; (2) initial vital signs: heart rate (HR), respiratory rate (RR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP); (3) admission laboratory parameters: white blood cell count (WBC), neutrophil count (NEUT), lymphocyte count (LYM), monocyte count (MONO); platelet count (PLT), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR), systemic inflammation response index (SIRI), total bilirubin (TBIL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), blood urea nitrogen (BUN), cystatin C (CysC), carbon dioxide combining power (CO_2CP), serum potassium, plasma PQ concentration, severity index of paraquat poisoning (SIPP), peak serum creatinine (Scr) value; (4) Therapeutic interventions: mechanical ventilation and vasopressor administration.

Patients were divided into AKI group and non-AKI group based on the peak Scr levels during hospitalization. AKI was diagnosed as serum creatinine (Scr) $\geq 26.4\mu\text{mol/L}$ within 48h or Scr $\geq 50\%$ within 7days.

This study protocol was approved by the ethics committee of West China Hospital, Sichuan University (Approval No. of the ethics committee: 2022 – 1591), with waiver of informed consent granted for this retrospective analysis.

Derivation and validation data

All eligible patients were randomly allocated to derivation cohort (70%) and validation cohort (30%). The derivation cohort was used to develop the prediction model for AKI following PQ poisoning, while the validation cohort served to evaluate the model's performance.

Outcomes

The primary outcome was the occurrence of AKI, and the secondary outcome was in-hospital mortality.

Statistical Analysis

Descriptive statistics were presented as median (interquartile range, IQR), and categorical variables as frequency (percentage). Between group comparisons were performed using the Wilcoxon rank-sum test (non-normal distributions) and χ^2 test (categorical variables).

To ensure model parsimony, predictors were selected via least absolute shrinkage and selection operator (LASSO) regression with 10-fold cross-validation. Subsequently, three machine learning algorithms were employed: Logistic regression (LR), Bayesian methods, and support vector machine (SVM). Model training utilized 10-fold cross-validation within the derivation cohort (70%) to mitigate overfitting. The optimal model for each algorithm was selected based on the highest area under the receiver operating characteristic curve (AUC-ROC). Final model performance was independently validated in the hold-out validation cohort (30%).

Performance was assessed across three domains: (1) Discrimination: AUC-ROC, accuracy (ACC), sensitivity, and specificity. (2) Calibration: Bias-corrected calibration plots (deviation from the 45° line indicated miscalibration). (3) Clinical Utility: Decision curve analysis (DCA) quantified net benefit across probability thresholds.

Statistical significance was defined as two-sided $P < 0.05$ or 95% confidence intervals (CIs) excluding unity. All analyses were performed in R version 4.3.0.

Results

Patient characteristics

Among 1760 screened patients, 832 were included (Figure 1). Median age was 29.5 years; 55.4% were female. Median time from exposure to emergency department presentation was 7.0 hours (IQR 3.0-20.5); median plasma PQ concentration on admission was 2,300 ng/mL (IQR 380-16,120). During hospitalization, 8.7% (72/832) required mechanical ventilation and 6.7% (56/932) received vasopressor support. The overall incidence of AKI was 65.5% (539/832), and in-hospital mortality was 53.3% (444/832).

The cohort was randomly divided into derivation (n=582, 70%) and validation (n=250, 30%) cohorts. Baseline characteristics are presented in Table 1. No significant differences in baseline characteristics were observed between the derivation and validation cohorts (all $P > 0.05$).

Comparison between AKI and non-AKI groups

In the derivation cohort, the AKI group had significantly higher levels of WBC, NEUT, MONO, NLR, SII, SIRI, TBIL, ALT, AST, BUN, CysC, and plasma PQ concentration, and lower LYM, CO₂CP, and serum potassium (all $P < 0.05$). The AKI group more frequently required mechanical ventilation and vasopressors and had higher mortality ($P < 0.001$, Table 2).

Feature selection

Variable selection was performed using LASSO, with AKI as the dependent variable. The LASSO method addresses multicollinearity and prevents overfitting by shrinking variable coefficients. At the optimal penalty parameter ($\lambda = 0.01898387$, determined by minimum mean squared error), the algorithm selected 12 predictive features from the initial 28 candidate variables (Fig. 2). The retained predictors included: age, MAP, WBC, MONO, NLR, TBIL, AST, BUN, CysC, CO₂CP, serum potassium and plasma PQ concentration.

Model performance comparison

To account for potential confounding effects, we employed three ML approaches LR, Bayesian methods, and SVM to analyze the 12 selected predictors and develop predictive models. The LR model achieved the highest AUC (0.862, 95% CI: 0.832-0.891), followed by Bayesian (0.803, 95% CI: 0.747-0.859) and SVM (0.702, 95% CI: 0.644-0.760) (Figure 3, Table 3). Complete model performance metrics are presented in Table 3. Notably, the LR model achieved the highest specificity (87.7%). Based on these results, we selected the LR model as our final predictive tool. Multivariable LR analysis identified five independent risk factors for AKI: NLR, AST, BUN, CysC and plasma PQ concentration at admission (Table 4). We developed a clinically practical nomogram incorporating these predictors (Figure 4). The model demonstrated excellent calibration, with predicted probabilities closely aligning with observed outcomes. DCA confirmed the clinical utility of the model across a reasonable probability threshold range (Figure 5).

Internal validation

In the validation cohort, the LR model maintained good performance: AUC 0.857 (95% CI: 0.812-0.903), accuracy 0.776, sensitivity 0.770, specificity 0.787. Similarly, the calibration curves demonstrated favorable consistency between predicted probabilities and observed outcomes. In terms of clinical applicability, LR showed robust net benefit across a wide range of threshold probabilities (Figure 5).

Comparison of SIPP

We conducted a comparative analysis between our prediction model and SIPP (Table 5). The LR model had significantly higher AUC than SIPP in both derivation (0.862 vs. 0.751) and validation (0.857 vs. 0.688) cohorts (Figure 6, Table 5).

Discussion

In the present study, we developed and internally validated a ML–derived predictive model for AKI in patients with acute PQ poisoning. The model was constructed using five routinely available admission parameters: NLR, AST, BUN, cystatin C, and plasma PQ concentration. It achieved excellent discriminative performance (AUC = 0.862 in derivation, 0.857 in validation) and outperformed the traditional Severity Index of Paraquat Poisoning (SIPP). These findings support the use of this model for early risk stratification and clinical decision-making in PQ-induced nephrotoxicity, which aligns with the core scope of Toxicology focusing on mechanism-based human risk assessment and predictive toxicology.

PQ is a classic redox-cycling toxicant that selectively accumulates in renal proximal tubular epithelial cells via organic cation transporter 2 (OCT2)[17, 25]. Once inside cells, PQ triggers persistent reactive oxygen species (ROS) production, mitochondrial dysfunction, lipid peroxidation, and inflammatory cascade amplification, all of which directly damage renal tubular structure and function[19, 26]. AKI is therefore not only a common complication but also a key driver of mortality in PQ poisoning. In our cohort, the incidence of AKI reached 65.5%, and in-hospital mortality in the AKI group was 67.9%, significantly higher than that in the non-AKI group (26.6%). A South Korea cohort study (n = 278) reported an incidence of 51.4% AKI [22], and another study (n = 222) observed an incidence of 46.4%[11]. These data highlight the critical role of renal toxicity in determining the outcome of PQ poisoning and underscore the urgency of early identification.

Plasma PQ concentration was identified as an independent predictor of AKI, consistent with the fundamental toxicological principle that internal exposure dose determines the severity of target organ injury. Plasma PQ concentration has been consistently validated as the strongest independent prognostic indicator in PQ-poisoned patients, with demonstrated superiority over clinical scoring systems and other biochemical markers[27, 28]. The quantification of plasma PQ levels serves as a clinically valuable indicator, as it correlates with the ingested dose and provides important prognostic information[29, 30]. Higher plasma PQ levels lead to greater accumulation in renal tissue, stronger oxidative stress, and more severe mitochondrial and tubular damage. Compared with SIPP, which integrates both PQ concentration and admission time, our model directly uses plasma PQ concentration as a core predictor, which better reflects the real-time toxic burden and improves predictive accuracy for early-onset AKI.

NLR was another independent risk factor, it has been recognized as a powerful biomarker for systemic inflammatory and immune reactions[24, 31–34]. Our findings reflect the intense systemic inflammatory response triggered by PQ. PQ-mediated oxidative stress promotes excessive neutrophil activation and inhibits neutrophil apoptosis, while simultaneously inducing lymphocyte apoptosis via ROS-dependent pathways[35, 36]. This shift causes a persistent elevation in the NLR, indicating profound imbalance between pro-inflammatory and anti-inflammatory processes. Such immune dysregulation further exacerbates renal microcirculatory disturbance and tubular epithelial injury, making NLR an early, readily available, and robust biomarker of inflammation-mediated renal toxicity in acute PQ poisoning.

Interestingly, our study identifies AST as an independent risk factor for AKI in patients with PQ poisoning. AST is mainly distributed in the myocardium, followed by the liver, skeletal muscle and kidneys. AST is predominantly localized within mitochondria (approximately 70%), and this unique subcellular distribution renders it a critical biomarker for assessing the severity and extent of cellular injury. PQ initiates a characteristic redox cycling process within cells, perpetually generating ROS including superoxide anions and hydrogen peroxide. Mitochondria are the primary source of intracellular ROS and are central to PQ toxicity's pathogenesis[19, 37, 38]. When mitochondrial damage reaches a critical threshold, inner membrane integrity is compromised, triggering massive release of matrix localized AST into the cytoplasm through damaged outer membranes, ultimately entering circulation via permeabilized plasma membranes. Thus, elevated serum AST levels directly mirror the severity of intracellular mitochondrial injury. Notably, renal tubular epithelial cells with their high metabolic activity exhibit exceptional mitochondrial vulnerability to PQ toxicity, which explains the predictive value of AST for nephrotoxic injury[17, 20, 39]. Additionally, in PQ poisoning, the liver as the primary detoxifying organ sustains early and severe injury, resulting in substantial AST release from hepatocytes[29, 40, 41]. Concurrently, the extreme susceptibility of cardiomyocytes to PQ toxicity drives further AST elevation, while skeletal muscle injury (frequently observed in these patients) contributes additively to rising serum AST levels[36, 42, 43]. Critically, this systemic enzyme surge not only reflects direct cellular damage but also exacerbates kidney injury through secondary mechanisms, including systemic hypotension and homeostatic collapse, thereby creating a vicious cycle of multi-organ dysfunction. In brief, AST as an independent risk factor for AKI following PQ poisoning redefines its clinical implications in nephrotoxic syndromes. In this context, elevated AST levels serve not merely as markers of hepatocellular or myocardial injury, but more significantly as harbingers of impending renal damage, suggesting potential organ crosstalk in PQ-induced multiorgan dysfunction.

Notably, CysC and BUN emerged as independent risk factors for AKI in PQ-poisoned patients. Accumulating evidence suggests that an early elevation in CysC levels (within 24 to 48 hours post-exposure) reliably predicts both AKI progression and clinical outcomes in PQ poisoning[21, 44, 45]. This finding gains particular significance in light of a prospective multicenter study demonstrating Scr limitations as a reliable AKI marker in this context, given its susceptibility to confounding by gender, age, muscle mass, and nutritional status[44]. In contrast, CysC has been consistently validated as a superior biomarker for detecting AKI across multiple clinical scenarios, including PQ-induced nephrotoxicity[45, 46]. The pathophysiological basis may be related to the direct effect of PQ on CysC metabolism [23], though our current understanding remains incomplete. In the present study, the AKI group exhibited significantly elevated CysC levels compared to non-AKI group, a finding that aligns with histopathological observations of PQ-induced renal damage. Mechanistically, PQ exposure induces profound glomerular alterations, including collapse of Bowman's space, glomerular vacuolization and atrophy, and podocyte depletion. These structural changes culminate in marked reductions in glomerular filtration rate[47]. In vitro studies further demonstrate differential cellular susceptibility to PQ toxicity, with particular sensitivity observed in podocytes followed by mesangial cells and tubular epithelial compartments[48]. These collective findings establish CysC as both a sensitive early-warning biomarker for PQ-induced renal injury and a robust prognostic indicator that reflects glomerular dysfunction severity, offering substantial clinical utility for early intervention and risk stratification.

BUN has been established as an independent predictor of AKI across multiple clinical settings, including sepsis, diabetes, and post-cardiac surgery[49–51]. In the present study, BUN levels were significantly elevated in AKI patients compared to non-AKI controls, likely attributable to PQ-induced systemic inflammation and immune dysregulation. Notably, all enrolled PQ poisoning cases resulted from intentional oral ingestion, and subsequent therapeutic interventions such as forced emesis, gastric lavage, and extracorporeal purification may have exacerbated renal hypoperfusion, further elevating BUN levels. These observations collectively highlight the dual role of BUN in PQ poisoning. Firstly, as a biomarker reflecting direct nephrotoxic injury, and secondly, as an indicator of iatrogenic hemodynamic compromise, reinforcing its utility in comprehensive renal function assessment.

This study has several limitations that should be acknowledged. First, despite having a relatively large sample size, as a single-center retrospective analysis, the findings may be influenced by selection bias and potential confounding factors inherent to the study design. The reliance on pre-existing medical records resulted in incomplete data for certain variables, which may affect the robustness of the conclusions. Moreover, the lack of external validation limits the generalizability of our results, underscoring the need for future multicenter prospective studies to confirm these observations. Additionally, our analysis was restricted to in-hospital outcomes, leaving the long-term renal functional trajectory and clinical prognosis unexplored. Future investigations should incorporate extended follow-up periods to assess delayed renal recovery, chronic kidney disease progression, and other clinically relevant endpoints. Such longitudinal data would provide a more comprehensive understanding of PQ-induced nephrotoxicity and its management.

Conclusion

This study revealed a high incidence (65.5%) of AKI among PQ-poisoned patients, with associated in-hospital mortality reaching 53.3%. The in-hospital mortality rate was significantly higher in the AKI group compared to the non-AKI group. Multivariate logistic regression identified five independent predictors of AKI development at admission: NLR, AST, BUN, CysC and plasma PQ concentration. A prediction model based on these indicators demonstrated high sensitivity and specificity in assessing the risk of AKI following PQ poisoning, with significantly better predictive performance than the SIPP.

Abbreviations

- AKI: Acute kidney injury
- PQ: Paraquat
- OCT2: Organic cation transporter 2
- ML: Machine learning
- EMRs: Electronic medical records
- GCS: Glasgow coma scale
- HR: Heart rate
- RR: Respiratory rate
- SBP: Systolic blood pressure
- DBP: Diastolic blood pressure
- MAP: Mean arterial pressure
- WBC: White blood cell count
- NEUT: Neutrophil count
- LYM: Lymphocyte count
- MONO: Monocyte count
- PLT: Platelet count (PLT)
- NLR: Neutrophil-to-lymphocyte ratio
- SII: Systemic immune-inflammation index
- PLR: Platelet-to-lymphocyte ratio
- SIRI: Systemic inflammation response index
- TBIL: Total bilirubin
- AST: Aspartate aminotransferase

ALT: Alanine aminotransferase

ALP: Alkaline phosphatase

BUN: Blood urea nitrogen

CysC: Cystatin C

CO2CP: Carbon dioxide combining power

SIPP: Severity index of paraquat poisoning

Scr: Serum creatinine ()

KDIGO: Kidney Disease Improving Global Outcomes

IQR: Interquartile range

LASSO: Least absolute shrinkage and selection operator

LR: Logistic regression

SVM: Support vector machine

AUC-ROC: Receiver operating characteristic curve

ACC: Accuracy

DCA: Decision curve analysis

CI: Confidence interval

Declarations

Ethics approval and consent to participate

This study protocol was conducted in accordance with the Declaration of Helsinki. This study was approved by the ethics committee of West China Hospital, Sichuan University (Approval No. of the ethics committee: 2022-1591), with waiver of informed consent granted for this retrospective analysis.

Availability of data and materials

Data are available from the corresponding author upon reasonable request.

Competing interests

No potential conflict of interest was reported by the authors.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Tables

Table 1 Comparison of baseline characteristics between derivation and validation cohorts

	All (n=832)	Derivation cohort (n=582)	Validation cohort (n=250)	P value
Demographics				
Sex female (%)	461 (55.4)	331 (56.9)	130 (52.0)	0.222
Age (years) ^a	29.50[22.00, 42.00]	30.00 [23.00, 43.00]	28.50 [20.25, 41.00]	0.605
Time from poisoning exposure to presentation (h) ^a	7.00 [3.00, 20.50]	7.00 [3.00, 20.00]	7.00 [3.00, 21.00]	0.981
GCS $\geq$ 15, n (%)	64 (7.7)	43 (7.4)	21 (8.4)	0.719
Initial vital signs at emergency department				
Heart rate (beat/min.) ^a	85.00 [75.00, 96.00]	85.00 [75.00, 94.00]	85.00 [75.00, 98.75]	0.189
Respiration rate (breath/min.) ^a	20.00 [20.00, 22.00]	20.00 [20.00, 22.00]	20.00 [20.00, 22.00]	0.505
Systolic blood pressure (mmHg) ^a	120.00 [110.00,132.00]	120.00 [110.00, 130.00]	121.00 [112.00, 132.75]	0.227
Diastolic blood pressure (mmHg) ^a	75.00 [67.00, 82.00]	74.00 [67.00, 82.00]	76.00 [67.00, 84.00]	0.198
Mean arterial pressure(mmHg) ^a	90.00 [82.00, 97.67]	89.33 [81.67, 97.00]	91.33 [82.08, 99.67]	0.158
Laboratory measures				
WBC ($\times 10^9$ /L) ^a	13.64 [9.52, 19.97]	13.53 [9.35, 19.52]	14.25 [9.62, 20.96]	0.188
NEUT ($\times 10^9$ /L) ^a	11.71 [7.61, 17.79]	11.63 [7.50, 17.34]	11.83 [7.97, 18.74]	0.240
LYM ($\times 10^9$ /L) ^a	1.15 [0.78, 1.69]	1.15 [0.77, 1.68]	1.16 [0.83, 1.74]	0.598
MONO ($\times 10^9$ /L) ^a	0.49 [0.28, 0.81]	0.47 [0.28, 0.79]	0.51 [0.29, 0.84]	0.310
PLT ($\times 10^9$ /L) ^a	173.00 [135.00,223.95]	171.00 [131.00, 219.75]	176.74 [140.06, 230.75]	0.151
NLR ^a	10.38 [5.48, 17.63]	10.29 [5.45, 16.81]	10.50 [5.58, 18.73]	0.602
SII ^a	1665.32 [893.94, 3132.74]	1630.87 [890.64,2975.64]	1738.82 [895.12,3452.32]	0.319
PLR ^a	148.25 [95.83,223.94]	146.81 [95.51, 227.32]	152.07 [97.06, 214.72]	0.997
SIRI ^a	4.35 [1.82, 11.03]	4.12 [1.83, 10.91]	4.60 [1.81, 11.48]	0.678
TBIL (μ mol/L) ^a	14.30 [10.10, 22.00]	14.25 [10.10, 21.68]	14.31 [10.22, 22.95]	0.854
ALT (IU/L) ^a	21.00 [15.00, 35.00]	22.00 [15.00, 36.75]	20.00 [15.00, 32.00]	0.343
AST (IU/L) ^a	27.00 [21.00, 41.00]	28.00 [21.00, 42.00]	25.50 [21.00, 39.75]	0.125
ALP (IU/L) ^a	78.00 [60.00,103.00]	78.00 [62.00, 102.00]	77.00 [58.00, 104.75]	0.232
BUN (mmol/L) ^a	5.94 [4.50, 7.89]	5.96 [4.52, 8.05]	5.82 [4.44, 7.75]	0.575
CysC (mg/L) ^a	0.78 [0.65, 0.98]	0.79 [0.65, 0.98]	0.77 [0.65, 0.98]	0.592
CO ₂ CP (mmol/L) ^a	18.70 [14.47, 21.50]	18.70 [14.53, 21.40]	18.80 [14.30, 21.70]	0.938
serum potassium (mmol/L) ^a	3.23 [2.81, 3.61]	3.24 [2.80, 3.60]	3.19 [2.82, 3.62]	0.419
Plasma PQ concentration (ng/mL) ^a	2300.00 [380.00,16120.00]	2050.00 [370.00,13930.00]	2840.00[400.00, 23640.00]	0.187
Treatment				
Mechanical Ventilation (%)	72 (8.7)	47 (8.1)	25 (10.0)	0.441
Vasopressors (%)	56 (6.7)	35 (6.0)	21 (8.4)	0.268
Outcome				
The incidence of AKI, n (%)	539 (65.5)	378 (64.9)	161 (64.4)	0.942
In-hospital mortality, n (%)	444 (53.3)	305 (52.4)	139 (55.6)	0.441

a interquartile range(Q1,Q3); AKI acute kidney injury; GCS glasgow coma scale; WBC white blood cell; NEUT neutrophils; LYM lymphocyte; MONO monocyte; PLT platelet; NLR neutrophil lymphocyte ratio; SII systemic immune-inflammation index; PLR platelet-to-lymphocyte; SIRI systemic inflammation response index; TBIL total bilirubin; AST aspartate aminotransferase; ALT alanine aminotransferase; ALP alkaline phosphatase; BUN blood urea nitrogen; Scr serum creatinine; CysC cystatin C; CO₂CP carbon dioxide combining power; PQ paraquat.

Table 2 Comparison of baseline characteristics between AKI and non-AKI groups in the derivation cohort

	AKI (n=378)	non-AKI (n=204)	P value
Demographics			
Sex female (%)	211 (55.8)	120 (58.8)	0.542
Age (years) ^a	29.00 [23.00, 42.75]	31.00 [21.00, 43.50]	0.978
Time from poisoning exposure to presentation (h) ^a	8.00 [4.00, 24.00]	5.50 [3.00, 13.50]	0.055
GCS ¹⁵ , n (%)	36 (9.5)	7 (3.4)	0.012
Initial vital signs at emergency department			
Heart rate (beat/min.) ^a	84.50 [75.00, 95.75]	85.00 [74.00, 94.00]	0.883
Respiration rate (breath/min.) ^a	20.00 [20.00, 22.00]	20.00 [20.00, 21.00]	<0.001
Systolic blood pressure (mmHg) ^a	120.00 [109.00, 129.00]	120.50 [110.75, 132.00]	0.269
Diastolic blood pressure (mmHg) ^a	72.00 [67.00, 82.00]	75.00 [68.00, 81.25]	0.151
Mean arterial pressure (mmHg) ^a	88.33 [81.00, 97.00]	90.33 [83.33, 97.08]	0.126
Laboratory measures			
WBC (×10 ⁹ /L) ^a	15.27 [11.14, 21.71]	10.12 [7.78, 13.99]	<0.001
NEUT (×10 ⁹ /L) ^a	13.22 [9.08, 19.56]	8.39 [6.05, 12.12]	<0.001
LYM (×10 ⁹ /L) ^a	1.11 [0.72, 1.63]	1.22 [0.89, 1.69]	0.029
MONO (×10 ⁹ /L) ^a	0.55 [0.33, 0.95]	0.40 [0.26, 0.54]	<0.001
PLT (×10 ⁹ /L) ^a	166.50 [129.25, 218.00]	180.46 [137.75, 221.24]	0.211
NLR ^a	12.20 [7.39, 20.77]	7.46 [4.30, 11.91]	<0.001
SII ^a	1934.22 [1074.47, 3522.46]	1274.36 [648.32, 2068.80]	<0.001
PLR ^a	151.62 [93.28, 243.08]	140.18 [97.38, 205.88]	0.233
SIRI ^a	6.25 [2.50, 13.85]	2.43 [1.30, 4.89]	<0.001
TBIL (μmol/L) ^a	14.83 [10.30, 23.50]	13.70 [9.55, 18.92]	0.019
ALT (IU/L) ^a	24.00 [17.00, 41.03]	19.00 [14.00, 28.25]	<0.001
AST (IU/L) ^a	31.00 [24.00, 52.00]	23.00 [19.00, 30.25]	<0.001
ALP (IU/L) ^a	78.00 [61.09, 102.02]	79.88 [63.00, 102.00]	0.367
BUN (mmol/L) ^a	6.61 [5.18, 9.69]	4.76 [3.69, 6.31]	<0.001
CysC (mg/L) ^a	0.82 [0.67, 1.10]	0.74 [0.63, 0.84]	<0.001
CO ₂ CP (mmol/L) ^a	17.34 [12.60, 20.48]	20.50 [18.50, 23.20]	<0.001
serum potassium (mmol/L) ^a	3.08 [2.65, 3.51]	3.49 [3.14, 3.74]	<0.001
Plasma PQ concentration (ng/mL) ^a	410.00 [200.00, 3770.00]	3830.00 [680.00, 26080.00]	<0.001
Treatment			
Mechanical Ventilation (%)	43 (11.4)	4 (2.0)	<0.001
Vasopressors (%)	33 (8.7)	2 (1.0)	<0.001
Outcome			
In-hospital mortality, n (%)	256 (67.7)	49 (24.0)	<0.001

a interquartile range(Q1,Q3); AKI acute kidney injury; GCS glasgow coma scale; WBC white blood cell; NEUT neutrophils; LYM lymphocyte; MONO monocyte; PLT platelet; NLR neutrophil lymphocyte ratio; SII systemic immune-inflammation index; PLR platelet-to-lymphocyte; SIRI systemic inflammation response index; TBIL total bilirubin; AST aspartate aminotransferase; ALT alanine aminotransferase; ALP alkaline phosphatase; BUN blood urea nitrogen; Scr serum creatinine; CysC cystatin C; CO₂CP carbon dioxide combining power; PQ paraquat.

Table 3 Comparison of the models performance in the derivation cohort

Model	AUC 95% CI	Accuracy	Sensitivity	Specificity
LR	0.862(0.832 0.891)	0.742	0.669	0.877
Bayesian	0.803(0.747 0.859)	0.668	0.843	0.571
SVM	0.702(0.644 0.760)	0.752	0.701	0.770

LR logistic regression; SVM support vector machine; AUC AUC area under the receiver operating characteristic curve; ACC accuracy.

Table 4 Independent risk factors for AKI identified by logistic regression

Variables	B value	Waldχ ²	OR	OR 95% CI	p value
NLR	0.062	4.383	1.064	1.036-1.095	0.001
AST	0.012	2.801	1.012	1.005-1.021	0.001
BUN	0.221	4.649	1.247	1.141-1.374	0.001
CysC	2.02	3.7	7.539	2.659-22.612	0.001
PQ concentration	0.009	2.495	1.007	1.003-1.018	0.012

AKI, acute kidney injury; NLR, neutrophil lymphocyte ratio; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CysC, cystatin C; PQ, paraquat; OR, odds ratio.

Table 5 Performance comparison between the LR model and SIPP

	AUC (95% CI)	ACC	Sensitivity	Specificity
LR model				
derivation cohort	0.862(0.832-0.891)	0.742	0.669	0.877
validation cohort	0.857(0.812-0.903)	0.776	0.770	0.787
SIPP				
derivation cohort	0.751(0.706-0.796)	0.756	0.860	0.564
validation cohort	0.688(0.607-0.759)	0.624	0.540	0.775

LR, logistic regression; SIPP, severity index of paraquat poisoning; AUC, area under the receiver operating characteristic curve; ACC, accuracy.

Figures

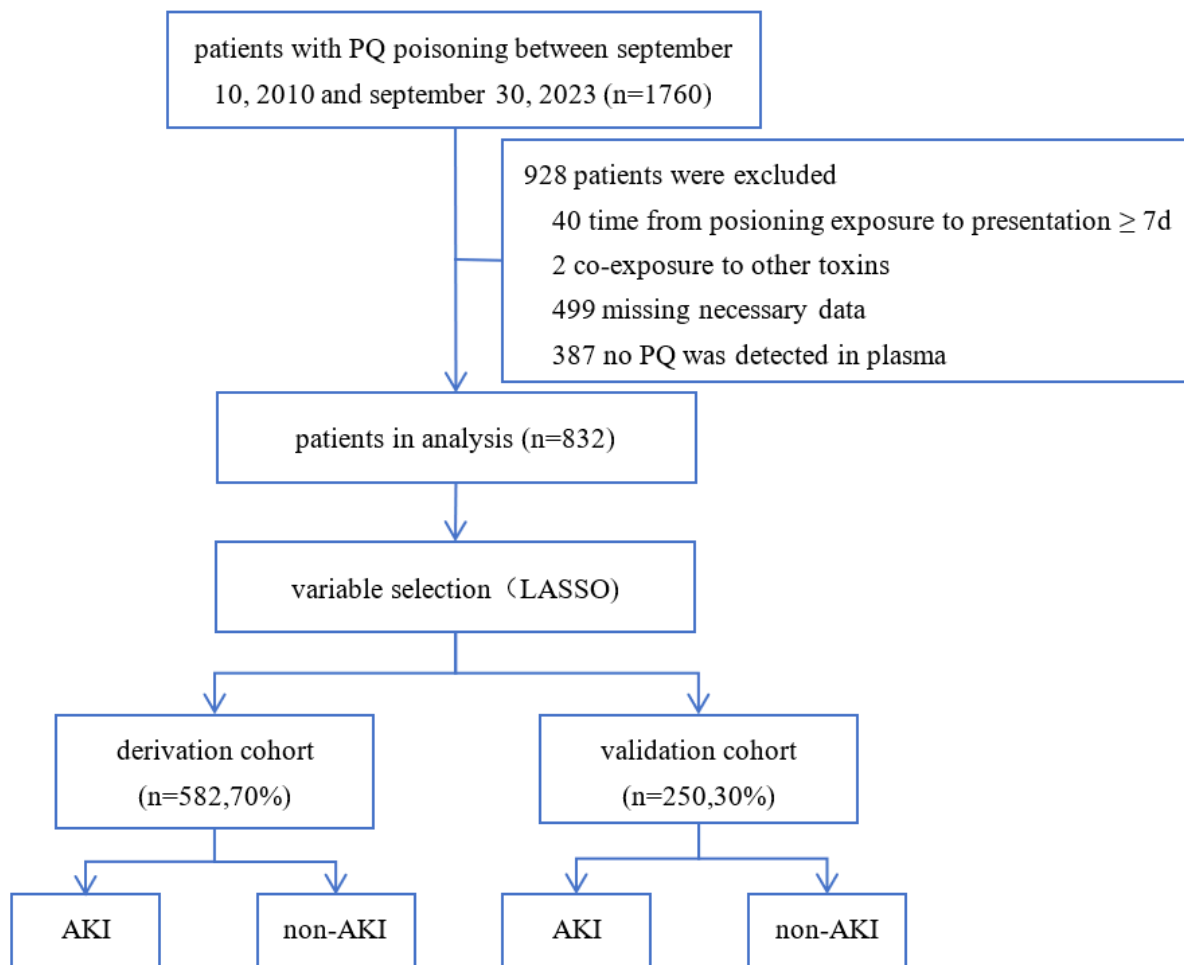


Figure 1

Flow chart of patient enrollment.

PQ paraquat; AKI acute kidney injury; LASSO least absolute shrinkage and selection operator.

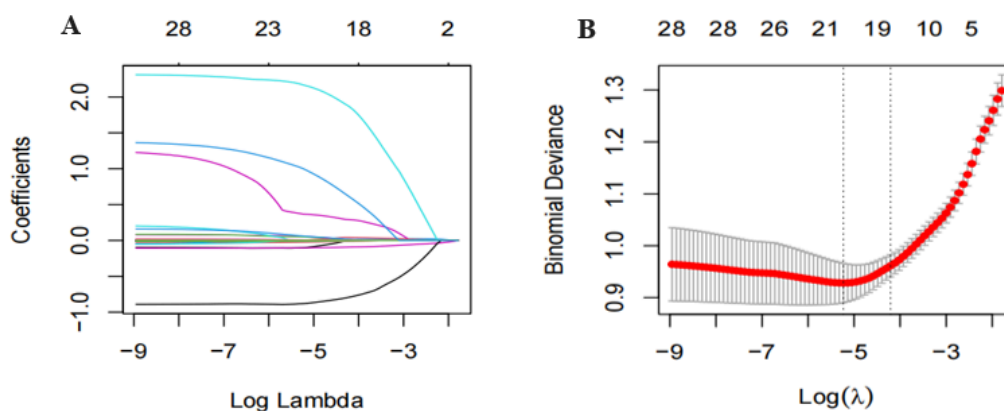


Figure 2

LASSO regression for variable selection.

(A) LASSO coefficient profiles ; (B) Optimal parameter (λ) selection in the LASSO model used 10-fold cross-validation via the minimum criteria ($\lambda=0.01898387$). LASSO least absolute shrinkage and selection operator.

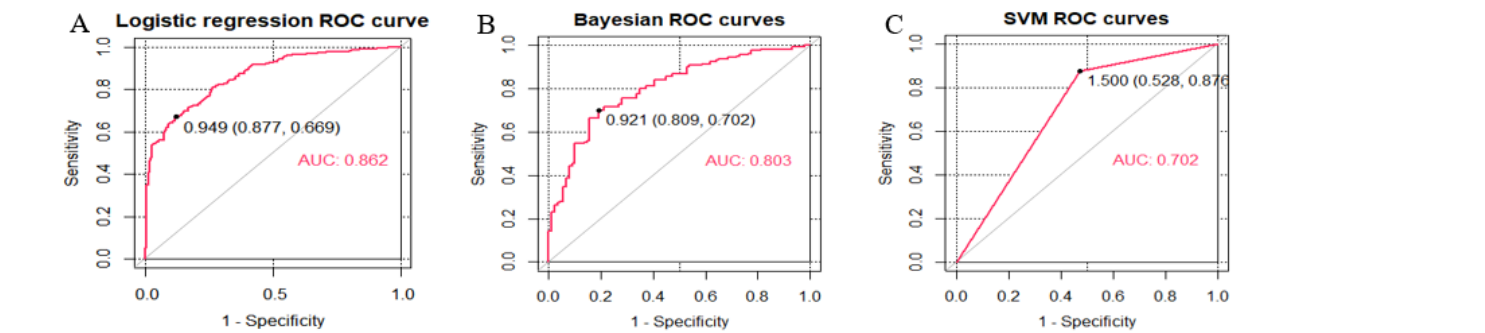


Figure 3
ROC curves of the models in the derivation cohort. (A) Logistic regression; (B) Bayesian methods; (C) support vector machine. ROC receiver operating characteristic; AUC area under the ROC.

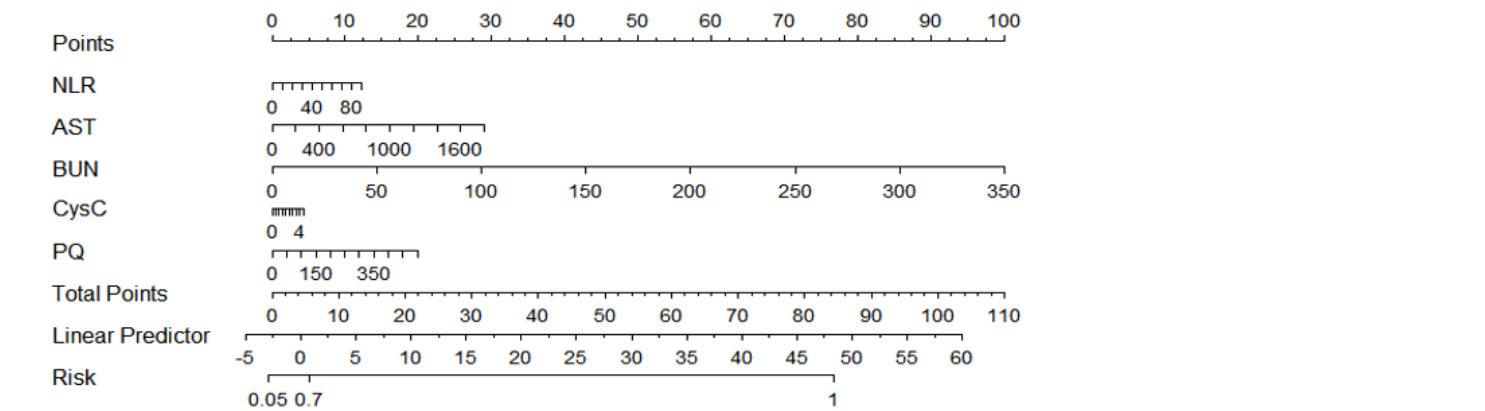


Figure 4
Nomogram of the LR model for predicting PQ poisoning-induced AKI.
NLR neutrophil lymphocyte ratio; AST aspartate aminotransferase; BUN blood urea nitrogen; CysC cystatin C; PQ paraquat; LR logistic regression; AKI acute kidney injury.

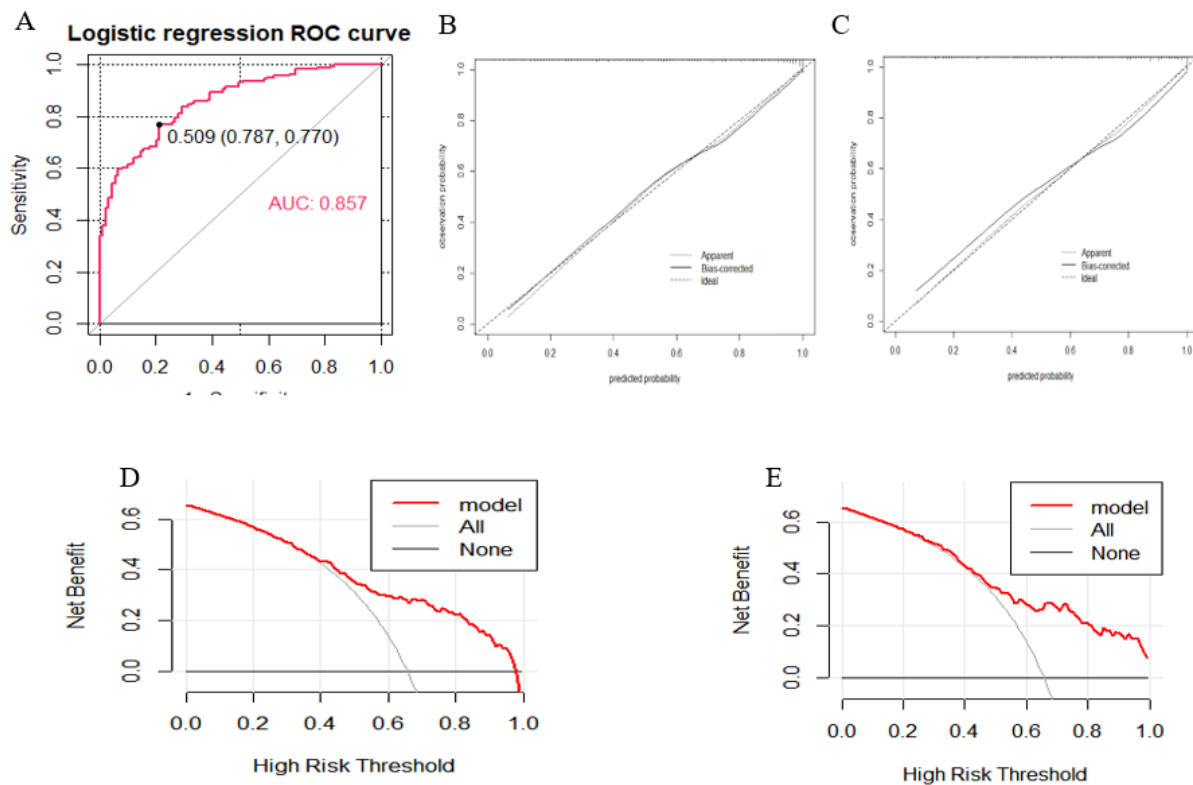


Figure 5

Performance evaluation of the LR model. (A) ROC curve for validation cohort; (B) calibration curve for derivation cohort; (C) calibration curve for validation cohort; (D) decision curve analysis for derivation cohort; (E) decision curve analysis for validation cohort. AUC area under the receiver operating characteristic curve.

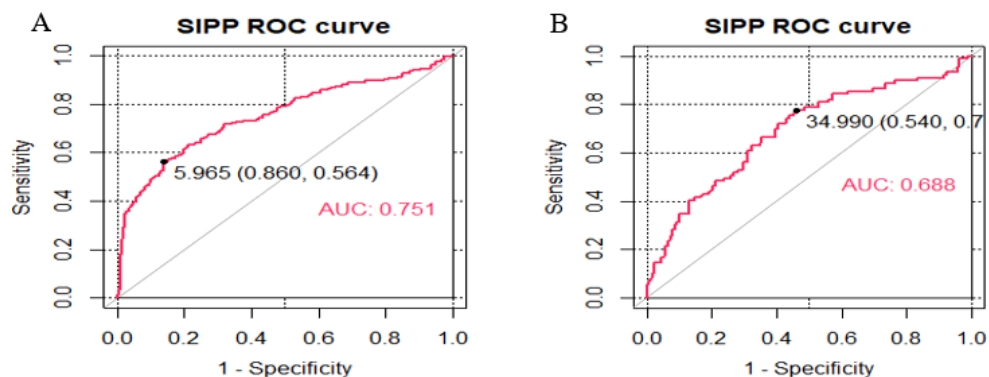


Figure 6

ROC curves of the SIPP in the derivation cohort (A) and validation cohort (B). ROC receiver operating characteristic; AUC area under the ROC curve.