Am J Transl Res 2025;17(3):1901-1909
www.ajtr.org /ISSN:1943-8141/AJTR0158590

Original Article

Construction and validation of a nomogram model to predict mortality risk in patients with acute diquat poisoning

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Received June 20, 2024; Accepted December 28, 2024; Epub March 15, 2025; Published March 30, 2025

Abstract: Objective: To analyze the risk factors for mortality in patients with acute diquat (DQ) poisoning and construct a nomogram prediction model for clinical assessment and treatment. Methods: A retrospective analysis was performed on the clinical data of 110 patients with acute DQ poisoning who were admitted from March 2022 to April 2024. The enrolled patients were divided into a training set of 80 cases and a validation set of 30 cases. A survival group and a death group were established, with death within 30 days as the endpoint. Among these, in the training group, there were 67 cases in the survival group and 13 cases in the death group. This study further analyzed and compared the baseline and clinical data of the two groups of patients, screened potential risk factors using Least absolute shrinkage and selection operator (LASSO) regression, and determined independent risk factors through multivariate logistic regression analysis. A nomogram predictive model was constructed and validated based on the validation set. Results: Using LASSO regression, this study screened 13 possible risk factors. The dosage of DQ, gastric lavage rate, medication to hospital admission time, alanine aminotransferase, aspartate aminotransferase, blood potassium, creatinine, urea, partial pressure of oxygen, urinary DQ concentration, Systemic Inflammatory Response Syndrome (SIRS) score, Sequential Organ Failure Assessment (SOFA) score, and Acute Physiology and Chronic Health Evaluation (APACHE) II score were found to predict death significantly after acute DQ poisoning. This study further constructed the nomogram predictive model and validated the predictive performance of this model by using a validation set. The Area Under the Curve (AUC) of the training set was 0.961, and that of the validation set was 0.947. The calibration curve of the training and validation sets showed good prediction results of the model, and the calibration curve tended to approach the ideal curve. Conclusion: This study constructed a nomogram model to predict mortality risk in patients with acute DQ poisoning. Clinicians will have a clearer and intuitive understanding of the prognosis of patients, so as to enhance the treatment of patients and optimize the allocation of medical resources.

Keywords: Diquat, poisoning, mortality, nomogram, risk prediction model

Introduction

Diquat (DQ) is a common herbicide that is widely used in agricultural production [1]. Acute DQ poisoning, however, has been recognized as an important issue in clinical emergency treatment due to the high toxicity of DQ to the human body. Patients with acute DQ poisoning may experience rapid development of illness and have relatively high mortality, highlighting the significance of early and accurate assessment of patients' mortality risk for guiding clinical treatment decision-making and improving patient survival [2, 3]. At present, the assessment of the mortality risk in patients with acute DQ poisoning relies mainly on the experience of doctors and the clinical manifestations of patients in clinical practice [4]. Nevertheless, it

https://doi.org/10.62347/XXIL7895

has drawbacks such as strong subjectivity and low accuracy. It is of great clinical significance to develop a more objective and accurate method to evaluate the mortality risk of patients with acute DQ poisoning. With recent development of medical statistics and machine learning, a nomogram predictive models have been widely applied in the medical field [5]. This model can visually indicate patients' risk graphically by integrating multiple clinical indicators, providing clinicians with a more objective and accurate reference for decision-making [6]. Accordingly, the present study was performed to construct a mortality risk prediction model for patients with acute DQ poisoning based on the nomogram, and to evaluate its performance through validation. This research is expected to provide more scientific and effective guidance for the clinical treatment of patients with acute DQ poisoning, reduce patients' mortality, and improve clinical therapeutic efficacy.

Materials and methods

Subjects

A retrospective analysis was performed on the clinical data of 110 patients with acute DQ poisoning who were admitted to multiple hospitals (West China Hospital, Anyue County People's Hospital, Chengdu Shangjinnanfu Hospital, The People's Hospital of Chuxiong Yi Autonomous Prefecture, and The First People's Hospital of Liangshan Yi Autonomous Prefecture) from March 2022 to April 2024. Inclusion criteria [7]: Patients with acute DQ poisoning, with a medication to hospital admission time of within 24 h. Exclusion criteria: Patients with medical history of heart, liver, kidney, or respiratory diseases; and patients with incomplete general data and clinical data. The included patients were randomly divided into a training set of 80 cases and a validation set of 30 cases. With death within 30 days as the endpoint, patients were divided into a survival group and a death group. Among them, in the training group, there were 67 cases in the survival group and 13 cases in the death group. There were 33 males (41.25%) and 47 females (58.75%) in the training set, with an average age of (38.9±16.5) years, and a dosage of DQ of between 10-500 mL; while there were 12 males (40%) and 18 females (60%) in the validation set, with an average age of (39.3±15.8) years, and the dosage of 10-500 mL. The Ethics Committee of West China Hospital of Sichuan University granted approval for this study (HX-IRB-AF-03-V3.0).

Content

After the completion of routine laboratory and biochemical tests immediately after admission, all patients underwent gastric lavage, catharsis, and other treatments. Patients were also given routine fluid replacement, diuresis, protection of gastrointestinal mucosa, antioxidant and high-dose glucocorticoid therapy, protection of major organs and nutritional support. Patients should undergo hemoperfusion as early as possible (330-II, JaFron, Zhuhai), with 8 h of hemoperfusion on the same day and 6 h on the next day for 2 days continuously, combined with urinary DQ concentration monitoring (semi-quantitative detection) simultaneously. Immediately after admission, patients were subjected to urine sampling and urinary DQ concentration testing. Specifically, urinary DQ concentration was measured using the sodium hydrosulfite colorimetric method. The urine sample of patients (10 mL each) was taken. 2 mL of sodium hydroxide was added and shaken well, followed by 50 mg of sodium hydrosulfite. The color change of the urine was observed and compared with a standard color chart. Urinary DQ concentration was be determined t, and a darker color indicated a higher concentration.

This study further calculated and analyzed patients' systemic inflammatory response syndrome (SIRS) scores, which are a set of indicators for evaluating the presence of systemic inflammatory response in the human body. Patients can be diagnosed with SIRS when meeting at least two of the following criteria: 1. Temperature: > 38°C (fever), or < 36°C (hypothermia); 2. heart rate: > 90 bpm; 3. respiratory rate: > 20 times/min, or the presence of ($PaCO_2$ < 32 mmHg); and 4. white blood cell count: > 12,000/μL (leukocytosis), < 4,000/μL (leukopenia), or the percentage of immature neutrophils (neutrophilic granulocyte band form) > 10%.

SOFA is a scoring system used to evaluate the functional status of multiple organ systems in patients in the intensive care unit (ICU). It primarily assesses functions of the following six organs and systems, including the respiratory

system, blood system, livers, cardiovascular system, central nervous system, and kidneys.

Furthermore, APACHE II is a scoring system widely used to evaluate the severity of the condition of critically ill patients and predict prognosis. It consists of three parts: Acute Physiology Score (APS), Age Score, and Chronic Health Score. Patients with higher scores may have more severe conditions [8, 9]. In this study, the surviving patients after discharge were followed up by telephone 28 d later to get their survival status.

Statistical analysis

Statistical Product Service Solutions (SPSS) 22.0 statistical software was applied for statistical analysis. The measured data were expressed as mean ± standard deviation, and compared using t-test between groups; while the inter-group comparison of counted data used a χ^2 test. LASSO regression was employed to screen potential risk factors, and multivariate logistic regression analysis to determine independent risk factors, with the construction of a nomogram predictive model at the same time [10]. Independent risk factors with $P<0.05$ were included for plotting the receiver operating characteristic (ROC) curve [11]. This study also evaluated the predictive performance of the constructed model on patients' mortality [12]. $P<0.05$ indicated a significant difference.

Results

Comparison of patient data between the survival and death groups

As shown in **Table 1**, among the 80 patients in the training set, there were 67 survivors (83.75%) in the survival group. There were no significant differences in age, gender ratio, hemoperfusion rate, white blood cells, serum albumin, lactate, or pH between the survival group and the death group ($P>0.05$). Compared to the death group, the survival group had a significantly shorter medication to hospital admission time ($P<0.05$); lower levels of alanine aminotransferase, aspartate aminotransferase, creatinine and urea ($P<0.05$); higher partial pressure of oxygen ($P<0.05$); and lower gastric lavage rate, blood potassium, urinary DQ concentration, and dosage of DQ ($P<0.05$); as well as lower SIRS, SOFA, and APACHE II scores ($P<0.05$).

Multivariate logistic regression analysis of mortality risk in patients with acute DQ poisoning

This study screened 13 potential risk factors using LASSO regression. It was observed that the dosage of DQ, gastric lavage rate, medication to hospital admission time, alanine aminotransferase, aspartate aminotransferase, blood potassium, creatinine, urea, partial pressure of oxygen, urinary DQ concentration, SIRS score, SOFA score, and APACHE II score were influential factors related to the mortality of patients with acute DQ poisoning (**Figure 1A**). Based on a 10-fold cross-validation, we plotted the natural logarithmic transformation trend of mean square error (MSE) with the parameter of lambda (λ). At the minimum value of λ of 0.835, i.e., when its logarithmic value was -4.865, MSE reached the valley (dashed line on the left); and the dashed line on the right represented the λ value within one standard error (**Figure 1B**).

Further multivariate analysis revealed that the dosage of DQ, medication to hospital admission time, aspartate aminotransferase, urinary DQ concentration, SIRS score, and APACHE II score were risk factors for mortality in patients with acute DQ poisoning (**Table 2**).

A nomogram model for predicting mortality risk in patients with acute DQ poisoning

Using a Logistic "step by step method", the predictive model was established: $P=1/[1+e^{(2.782-1.256\times\text{the dosage of DQ}-0.880\times\text{Medication to hospital admission time}-1.143\times\text{aspartate aminotransferase}-1.029\times\text{urinary DQ concentration}-0.958\times\text{SIRS score}-1.358\times\text{APACHE II score})}]$ (**Figure 2**). In the nomogram, the total score was obtained by adding the scores corresponding to each variable predicted together. A higher total score indicated a higher risk of mortality in patients.

Validation of the nomogram model of mortality risk in patients with acute DQ poisoning

This study validated the prediction performance of the constructed model by using a validation set. The area under the curve (AUC) of the training set was 0.961, and that of the validation set was 0.947 (**Figure 3**). The calibration curve of the training and validation sets showed good predictive results of the model, and the calibration curve approached the ideal curve (**Figure 4**).

Table 1. Comparison of data between the survival group and the death group

Factor	Survival group (n=67)	Non-survival group (n=13)	Statistical value	*P*
Age (year)	38.2±16.6	39.3±17.2	0.217	0.828
Gender (n/%)			0.154	0.695
male	27/40.3	6/46.2		
female	40/59.7	7/53.8		
Diquat dose (n/%)			21.113	<0.001
<6 mL	41/61.2	2/15.4		
6~60 mL	23/34.3	5/38.5		
>60 mL	3/4.5	6/46.2		
Medication to hospital admission time (h)	7.4±3.2	11.9±4.8	58.642	<0.001
Gastric lavage rate (n/%)	28/41.8	4/30.8	0.551	0.458
Blood perfusion rate (n/%)	21/31.3	3/23.1	0.070	0.791
White blood cells ($\times10^9$/L)	15.8±8.6	16.4±7.9	0.233	9.816
Alanine aminotransferase (U/L)	19.9±12.3	116.3±25.9	20.919	<0.001
Aspartate aminotransferase (U/L)	26.4±5.9	105.1±28.4	20.957	<0.001
Creatinine (umol/L)	6.2±3.1	9.4±4.1	3.225	0.002
Urea (mmol/L)	86.1±16.7	181.4±55.2	11.845	<0.001
Blood potassium (mmol/L)	3.2±0.7	5.0±1.0	7.878	<0.001
Serum albumin (g/L)	49.2±5.6	48.3±5.9	0.526	0.601
Lactic acid (mmol/L)	2.1±1.2	2.2±1.3	0.271	0787
Blood oxygen partial pressure (mmHg)	106.2±19.2	91.7±16.1	2.551	0.013
pH	7.5±0.9	7.4±0.7	0.378	0.706
Urinary Diquat Concentration (n/%)			31.530	<0.001
<3 ug/L	10/14.9	0		
3~<10 ug/L	17/25.4	1/7.7		
10~<30 ug/L	29/43.3	3/23.1		
30~<100 ug/L	11/16.4	4/30.8		
>100 ug/L	0	5/38.5		
SIRS score	2.0±0.61	3.0±0.54	5.502	<0.001
SOFA score	2.0±0.47	3.1±0.42	7.845	<0.001
APACHE II score	12.5±3.5	37.2±8.3	17.800	<0.001

pH, Potential of Hydrogen; SIRS, Systemic Inflammatory Response Syndrome; SOFA, Sequential Organ Failure Assessment; APACHE, Acute Physiology and Chronic Health Evaluation.

Discussion

The main toxicologic mechanism of acute DQ poisoning involves release of reactive oxygen species (ROS) and reactive nitrogen species (RNS) intracellularly during the reduction-oxidation process, leading to oxidative stress and cellular dysfunction subsequently [13, 14]. DQ has a relatively high reduction-oxidation (redox) potential, stronger than for other herbicides, resulting in significant damage to cells after poisoning [15]. Acute DQ-poisoned patients may usually experience digestive symptoms, such as oral burning pain, ulcers, mucosal edema, nausea, vomiting, abdominal pain, and diarrhea. Acute DQ poisoning may also damage the kidney and liver, causing renal tubular epithelial cell injury and liver dysfunction, inducing proteinuria and even acute renal failure [16, 17]. If there is damage to the nervous system, patients exhibit symptoms such as consciousness disorder and convulsion, with high mortality [18]. Moreover, acute DQ poisoning shows rapid progression, and patients may have rapid deterioration of their physical condition [19]. Therefore, to alleviate the symptoms and prevent further deterioration of the condition, patients should be given

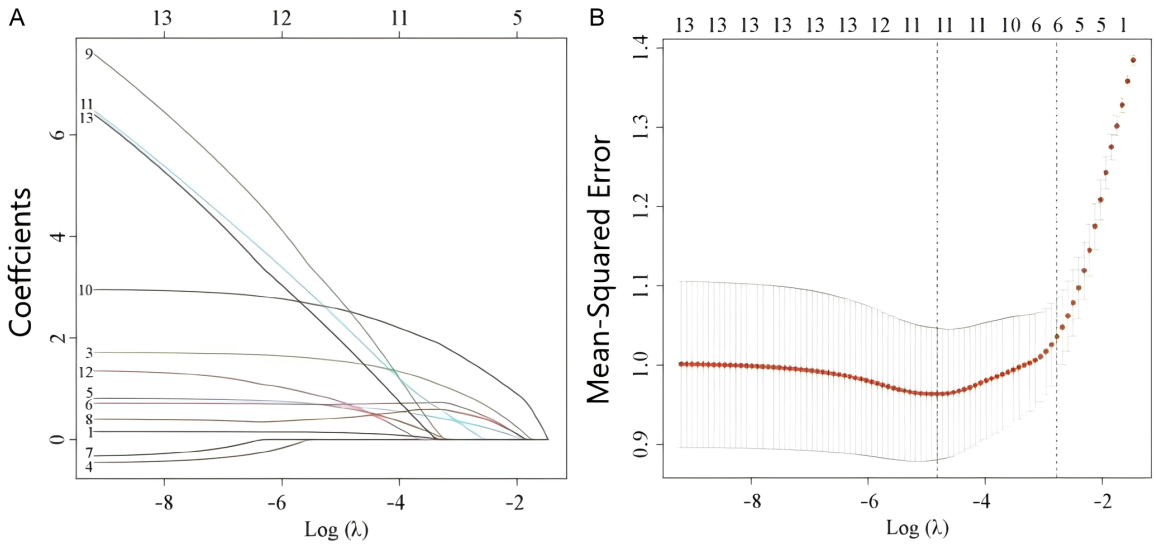

Figure 1. Results of LASSO regression analysis. A. LASSO regression coefficient path; B. Results of LASSO regression cross-validation

Table 2. Multivariate logistic analysis of mortality risk factors in patients with acute diquat poisoning

Factor	β	*SE*	Wald X^2	OR	95% CI	P
Diquat dose	0.254	0.081	9.833	1.289	1.078, 5.997	<0.001
Medication to hospital admission time	1.273	0.552	5.318	3.572	1.475, 8.153	0.002
Aspartate aminotransferase	2.112	0.445	22.525	8.265	1.417, 16.857	<0.001
Urinary Diquat Concentration	2.984	0.669	19.895	19.766	5.674, 26.596	<0.001
SIRS score	2.131	0.267	63.700	8.423	2.167, 12.277	<0.001
APACHE II score	1.863	0.315	34.978	6.443	3.423, 11.892	<0.001

SE, Standard Error; CI, Confidence Interval; SIRS, Systemic Inflammatory Response Syndrome; APACHE, Acute Physiology and Chronic Health Evaluation.

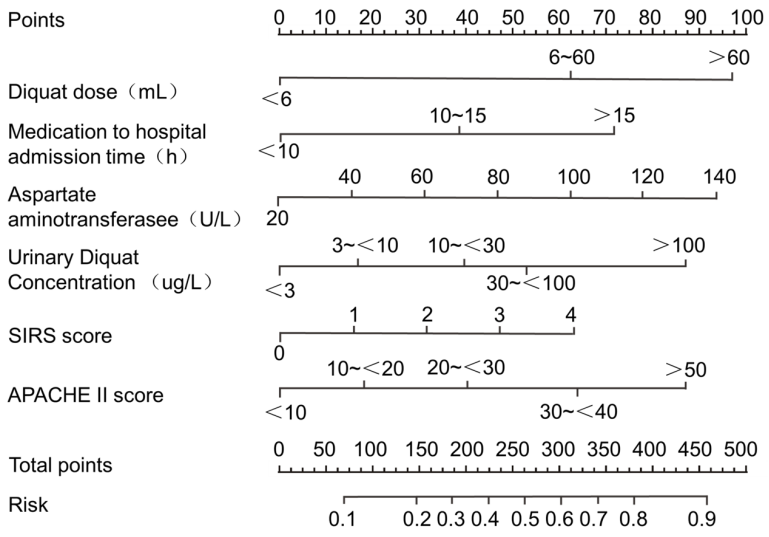

Figure 2. Line chart model for predicting the risk of death in patients with acute diquat poisoning. SIRS, Systemic Inflammatory Response Syndrome; APACHE II, Acute Physiology And Chronic Health Evaluation II.

immediate medical attention as well as professional treatment and management upon the onset of symptoms of acute DQ poisoning.

In the present study, we analyzed and compared the clinical data of 110 patients with acute DQ poisoning who were admitted to multiple centers, with the purposes of exploring risk factors affecting the mortality of these patients, and constructing a nomogram predictive model based on these risk factors. Consequently, it was observed that the dosage of DQ in the death group was significantly higher than that

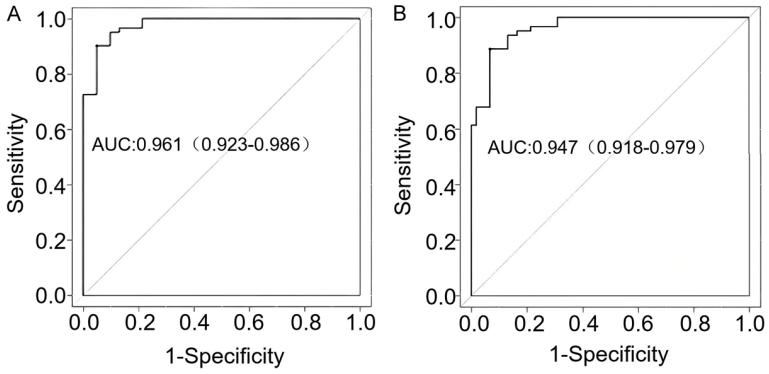

Figure 3. Validation of the line graph model for predicting mortality risk in patients with acute diquat poisoning. A. The Receiver Operating Characteristic curve (ROC) curve of the nomogram model for predicting the risk of death in patients with acute diquat poisoning; B. The ROC curve of the nomogram model for predicting the risk of death in patients with acute diquat poisoning was drawn by leave-one-out cross-validation. AUC, Area Under Curve.

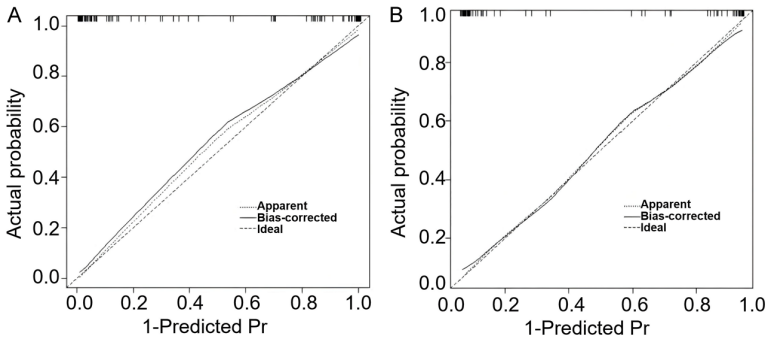

Figure 4. Correction curve of the line graph model for predicting the risk of death in patients with acute diquat poisoning. A. Correction curve of the training set; B. Calibration curve of the validation set. Pr, Positive Rate.

of the survival group, indicating a direct correlation between the dosage of DQ and patient survival rate. The Vanholder et al. [20] study showed that ingesting a rapid dose of 20% concentrated formulation of Diphthera above 15 mL was usually fatal. The medication to hospital admission time was also a key factor, and the average time was calculated to be shorter in the survival group than that of the death group, suggesting that seeking medical advice at an early stage could improve the prognosis of patients. Furthermore, lower levels of liver function indicators (alanine aminotransferase, and aspartate aminotransferase) and renal function indicators (creatinine, and urea) in the survival group than in the death group also supported an intimate association of the damage of acute DQ poisoning to liver and kidney functions with patient survival rate. Acute DQ poisoning may greatly affect liver function, manifested as elevated liver enzymes, and jaundice. It can be speculated that after a series of biochemical reactions *in vivo*, DQ can produce metabolites that are toxic to liver cells, leading to liver cell damage and subsequent liver dysfunction [21]. The kidney is the main excretory organ and the main target organ of damage after absorption of DQ. The kidney may be damaged directly after acute DQ poisoning, presenting necrosis and shedding of renal tubular epithelial cells, leading to acute tubular necrosis and acute renal failure [22]. Clinically, patients may experience oliguria, anuria, hematuria, and proteinuria. In severe cases, hemoperfusion, hemodialysis, and other therapeutic methods may be required to flush toxins out of the body. Therefore, emphasis on the detection of liver and kidney functions in acute DQ-poisoned patients may facilitate the determination and monitoring of patients' poisoning status and prognosis. Simultaneously, the partial pressure of oxygen in the survival group was higher than that of the death group, revealing that blood oxygen may be an important physiologic indicator for predicting prognosis. Notably, urinary DQ concentration is also critical for patient survival, and was detected to be significantly higher in the death group than in the survival group. This further supports the correlation between DQ concentration and patient prognosis. According to previous research, there might be an inconsistency between the recorded intake dose in the medical history and the actual intake dose, which may be related to patients' erroneous recall, vomiting after exposure, or confusion in pesticide production supervision. [23]. Therefore, DQ concentration measurement by urine test can give a more accurate determination of patients' poisoning situation, and this calls for accurate and

quantitative detection methods. Meanwhile, when assessing the severity of the condition, SIRS and APACHE II scores were both lower in the survival group than those of the death group, indicating a significant negative correlation between the severity of the condition and patient survival rate. As evidenced by several case reports, acute high-dose DQ poisoning usually affects the kidney, liver, brain, and heart [24, 25]. Existing toxicologic studies have documented that the DQ dose not bind covalently with large molecules (i.e. lipids, proteins, and nucleic acids) [26], but induces the production of intracellular ROS through redox cycling, leading to increased permeability of the phospholipid membrane. Recent data revealed that fatal DQ poisoning can cause damage to the central nervous system, including cerebral ischemia, cerebral hemorrhage, and brain swelling [27]. Significant necrosis of capillary walls of the pons and perivascular bleeding were detected by pathologic examination in acute DQ-poisoned patients [28]. In addition, some cases were reported to have symptoms of encephalopathy such as mania, epilepsy, drowsiness, or coma after acute DQ poisoning [27, 28]. This suggests that DQ can invade the brain and central nervous system of poisoned individuals. Thus, patients' brain status and neurologic health should be considered in clinical treatment.

As an effective strategy for feature selection and model simplification, LASSO regression exhibits significant advantages in processing high-dimensional data and avoiding over-fitting [23]. In this study, on the basis of clinical data and laboratory test results, LASSO regression was used to screen variables for subsequent multivariate logistic regression analysis and construction of the nomogram prediction model. A nomogram predictive model was established based on the training set, and its predictive effect was verified using the training and validation sets. The AUC values were 0.961 and 0.947, respectively, suggesting a high accuracy of the constructed model. A good predictive effect of this model was evident from the plotted calibration curve, which approached the ideal curve. Based on the predictive power of this model, it can assist doctors in recognizing high-risk patients in a timely manner and develop personalized treatment plans, so as to improve prognosis.

Despite unique advantages and value in the clinical management of acute DQ-poisoned patients, the constructed model has limitations. In clinical practice, doctors should use the model reasonably by integrating the specific situation of patients and the characteristics of the model to improve the accuracy of clinical decision-making. In our future research, we intend to develop effective therapeutic regimens based on these factors to improve patient survival.

To sum up, this study suggests that the dosage of DQ, medication to hospital admission time, degree of liver and kidney dysfunction, partial pressure of oxygen, urinary DQ concentration, and severity of the condition are all important factors affecting the survival of acute DQ-poisoned patients. By constructing a predictive model, the death risk of patients with acute dioxalosis can be accurately quantified and evaluated. Knowing the prognosis of patients can help enhance treatment and optimize the allocation of medical resources. However, this study has limitations. As a retrospective study, the sample size of this study is small, and the multi-center area is relatively concentrated, which may cause certain bias. In addition, individual predictors are subject to subjective influence, for example, oral dose is a patient subjective statement, and may not be very accurate. In the future, we hope to continue to expand the sample size, at the same time summarize and summarize the previous research experience, strengthen the cooperation between basic and clinical factors, and carry out high-quality, multi-center clinical research.

Disclosure of conflict of interest

None.

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References

[1] Fu G, Duan Y, Yi W, Zhang S, Liang W, Li H, Yan H, Wu B, Fu S, Zhang J, Zhang G, Wang G, Liu Y and Xu S. A rapid and reliable immunochromatographic strip for detecting paraquat poin-

soning in domestic water and real human samples. Environ Pollut 2022; 315: 120324.
[2] Dai P, Sun J, Yu Z, Zhang T, Wen Z, Jian T, Guo L, Genjiafu A, Kan B, Zhang B and Jian X. Case report: reversible splenial lesion syndrome caused by diquat poisoning. Front Neurol 2023; 14: 1178272.
[3] Chen Y, Chen Y, Zhang H and Wang T. Pterostilbene as a protective antioxidant attenuates diquat-induced liver injury and oxidative stress in 21-day-old broiler chickens. Poult Sci 2020; 99: 3158-3167.
[4] Mao Z, Yu Y, Sun H, Xie W, Zhao H, Jiang Q, Sun Y, Cao Y and Chen F. Development and validation of a sensitive and high throughput UPLC-MS/MS method for determination of paraquat and diquat in human plasma and urine: application to poisoning cases at emergency departments of hospitals. Forensic Toxicol 2022; 40: 102-110.
[5] Watanabe D, Sonoda S and Ohta H. Simultaneous determination of water-soluble herbicides using hydrophilic interaction liquid chromatography-mass spectrometry. Forensic Toxicol 2024; 42: 1-6.
[6] Ness-Cochinwala M, Proaño JS, Bernstein JN, Martinez P, Ladd H and Totapally B. A case of a lethal diquat ingestion in a toddler. J Emerg Med 2022; 62: e16-e19.
[7] Guo H, Li L and Gao L. Paraquat and diquat: recent updates on their pretreatment and analysis methods since 2010 in biological samples. Molecules 2023; 28: 684.
[8] Liu M, Fan F, Zhang J, Fang S, Bai Y, Li Y, Zou Y, An Y and Dai X. Simultaneous determination of diquat, paraquat, glufosinate, and glyphosate in plasma by liquid chromatography/tandem mass spectrometry: from method development to clinical application. Anal Bioanal Chem 2024; 416: 3073-3083.
[9] Pan S, Zhang J, He Q, Chen X and Jin M. Fabrication of benzenesulfonic acid groups modified magnetic microspheres as an MSPE adsorbent for fast determination of paraquat and diquat in human urine combined with UPLC-HRMS. J Chromatogr B Analyt Technol Biomed Life Sci 2020; 1136: 121880.
[10] Nakayama M, Yamamoto S and Hirabayashi H. Novel cell quantification method using a single surrogate calibration curve across various biological samples. AAPS J 2023; 25: 26.
[11] Bahn E and Alber M. On the limitations of the area under the ROC curve for NTCP modelling. Radiother Oncol 2020; 144: 148-151.
[12] Choi S, Kim G, Lee Y, Kim BG, Jang I and Kim JH. Patch augmentation does not provide better clinical outcomes than arthroscopic rotator cuff repair for large to massive rotator cuff tears. Knee Surg Sports Traumatol Arthrosc 2022; 30: 3851-3861.
[13] Magalhães N, Carvalho F and Dinis-Oliveira RJ. Human and experimental toxicology of diquat poisoning: toxicokinetics, mechanisms of toxicity, clinical features, and treatment. Hum Exp Toxicol 2018; 37: 1131-1160.
[14] Basilicata P, Pieri M, Simonelli A, Capasso E, Casella C, Noto T, Policino F and Di Lorenzo P. Diquat poisoning: care management and medico-legal implications. Toxics 2022; 10: 166.
[15] Xing J, Chu Z, Han D, Jiang X, Zang X, Liu Y, Gao S and Sun L. Lethal diquat poisoning manifesting as central pontine myelinolysis and acute kidney injury: a case report and literature review. J Int Med Res 2020; 48: 300060520943824.
[16] Zhang H, Zhang J, Li J, Mao Z, Qian J, Zong C, Sun H and Yuan B. Multi-omics analyses reveal the mechanisms of early stage kidney toxicity by diquat. Toxics 2023; 11: 184.
[17] Yang L, Cheng J, Xu D, Zhang Z, Hua R, Chen H, Duan J, Li X and Li Q. Melatonin ameliorates diquat-induced testicular toxicity via reducing oxidative stress, inhibiting apoptosis, and maintaining the integrity of blood-testis barrier in mice. Toxics 2023; 11: 160.
[18] Huang S, Lin S, Zhou S, Huang Z, Li Y, Liu S, Liu R, Luo X, Li J, Yang J and Yuan Z. Soluble thrombomodulin alleviates Diquat-induced acute kidney injury by inhibiting the HMGB1/IkappaBalpha/NF-kappaB signalling pathway. Food Chem Toxicol 2023; 178: 113871.
[19] Dai X, Liu M, Xu S, Zhao H, Li X, Bai Y, Zou Y, An Y, Fan F, Zhang J and Cai B. Metabolomics profile of plasma in acute diquat-poisoned patients using gas chromatography-mass spectrometry. Food Chem Toxicol 2023; 176: 113765.
[20] Vanholder R, Colardyn F, De Reuck J, Praet M, Lameire N and Ringoir S. Diquat intoxication: report of two cases and review of the literature. Am J Med 1981; 70: 1267-71.
[21] Kumar S, Agrawal S, Raisinghani N and Khan S. Leukocyte count: a reliable marker for the severity of organophosphate intoxication? J Lab Physicians 2018; 10: 185-188.
[22] Zhou JN and Lu YQ. Lethal diquat poisoning manifests as acute central nervous system injury and circulatory failure: a retrospective cohort study of 50 cases. EClinicalMedicine 2022; 52: 101609.
[23] Chen Y, Li HY, Liu JS, Jiang DL, Zheng HN and Dong XS. Analysis of human microRNA expression profiling during diquat-induced renal proximal tubular epithelial cell injury. J Inflamm Res 2023; 16: 4953-4965.
[24] Xu Q, Liu M, Chao X, Zhang C, Yang H, Chen J, Zhao C and Zhou B. Acidifiers attenuate diquat-

induced oxidative stress and inflammatory responses by regulating NF-kappaB/MAPK/COX-2 pathways in IPEC-J2 Cells. Antioxidants (Basel) 2022; 11: 2002.
[25] Park A and Koh HC. NF-kappaB/mTOR-mediated autophagy can regulate diquat-induced apoptosis. Arch Toxicol 2019; 93: 1239-1253.
[26] Zhang X, Wang S, Wu Y, Liu X, Wang J and Han D. Ellagic acid alleviates diquat-induced jejunum oxidative stress in C57BL/6 mice through activating Nrf2 mediated signaling pathway. Nutrients 2022; 14: 1103.
[27] Acar A. In vivo toxicological assessment of diquat dibromide: cytotoxic, genotoxic, and biochemical approach. Environ Sci Pollut Res Int 2021; 28: 47550-47561.
[28] Cui S, Zhang X, Wang C, Sun C, Shi L, Kan B, Li Q and Jian X. Study on the therapeutic effect of glucocorticoids on acute kidney injury in rats exposed to diquat. Biomed Pharmacother 2023; 166: 115310.