Severity Indices of Diquat Poisoning for Triage and Prognosis in Acute Diquat Poisoning: A Multicenter Prospective Cohort Study

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Study objective: To enable emergency physicians to make well-informed triage and treatment decisions, accurate tools to evaluate the severity of diquat poisoning are needed. This study establishes severity indices for diquat poisoning (SIDPs) in assessing the risk of death for patients with acute diquat poisoning for triage purposes and 28-day mortality.

Methods: This multicenter cohort study involved 204 patients. Predictors identified by the Burota algorithm and stepwise Cox regression were incorporated into Cox proportional hazards models to develop SIDPs, one for triage and one for prognosis (SIDP-T and SIDP-P, respectively). SIDP-T predictors were based on self-reported information at emergency department (ED) presentation, and SIDP-P predictors included additional biomarkers obtained in the ED. Models were developed using data from one hospital (n=106), followed by internal validation using bootstrapping and external validation using a data set (n=98) from 35 different hospitals.

Results: SIDP-T found age, estimated diquat amount, heart rate, and Glasgow Coma Scale score to be the key predictors, achieving a C-index of 0.79 (0.70, 0.88), positive predictive value of 0.86 (0.49, 0.99) and negative predictive value of 0.76 (0.66, 0.83) in external validation. SIDP-P included age, initial plasma diquat concentration, white blood cell count, and aspartate aminotransferase, with C-index of 0.82 (0.74, 0.90), positive predictive value of 1 (0.51, 1) and negative predictive value of 0.74 (0.65, 0.82) on the external validation set.

Conclusion: Our derived severity indices can provide rapid mortality prediction. SIDP-T uses self-reported information and basic vital signs at ED admission, and SIDP-P adds biomarkers and accurately predicts 28-day outcome. [Ann Emerg Med. 2025;85:512-520.]

Please see page 513 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Self-poisoning with pesticides is a global public health concern, and its effective control is of importance in reducing both morbidity and mortality.[1] In China, poisoning consistently ranked as the fifth leading cause of death from 2009 to 2013,[2] and the overall incidence rate was 39.43/100,000 population in 2019,[3] with intentional poisoning, mostly related to self-harm.[4]

Paraquat (1,1'-dimethyl-4,4'-bipyridinium) and, after its ban in China, diquat (1,1'-ethylene-2, 2'-bipyridinium) are the agents with the highest rate of mortality due to their inherent toxicity affecting various organs paired with a lack of effective treatments.[5,6] As reported from different hospitals, the inhospital case fatality rate of diquat poisoning was 18.6%, whereas the proportion of case fatalities increased to 60% after follow-up in China.[7] Although uncommon, diquat poisoning occurs in many countries, including the United States, where 2,128 cases were identified between 1998 and 2011,[8] and 466 cases were documented in 2023,[9] according to the Annual Report of the National Poison Data System. The lethality of diquat underscores the necessity for precise prognosis. Estimating survival probability empowers physicians to tailor treatment decisions for patients and enhance communication, especially given the variability in capability of emergency departments (EDs) around the world.

Due to the absence of effective antidotes, the treatment of patients with diquat poisoning in the ED focuses on

Editor's Capsule Summary

What is already known on this topic

Diquat is a lethal insecticide.

What question this study addressed

Can diquat poisoning severity and outcomes be assessed early after care?

What this study adds to our knowledge

Using data from 204 exposed people, the authors created a triage index based on clinical presentation and a prognosis index to predict ultimate outcome after laboratory testing including diquat concentration.

How this is relevant to clinical practice

This could allow rapid and accurate prognostic information to guide care.

measures such as hemoperfusion.[10] However, implementation of these interventions poses challenges in less developed areas. Even when available treatment options are available, prognostic tools are needed to understand which poisoned patients are likely to need more intensive management. The World Health Organization's International Program on Chemical Safety defines the lethal dose of diquat as 6-12 g, without considering other factors such as exposure time, decontamination, comorbid disease, or even age.[11]

Prediction models for survival have mostly been developed for paraquat poisoning, using logistic[12-17] or Cox regression models.[18] Major predictors included age,[15] serum creatinine concentration,[14,15] neutrophil count,[14] plasma paraquat concentration,[12,13,15,19-21] paraquat ingestion amount,[22] white blood cell count,[14] and time since ingestion.[12,13,15,16] One study conducted on diquat poisoning compared survivors and fatalities with regard to diquat concentration and other standard parameters from blood and urine samples.[5] The authors reported significantly increased initial plasma diquat concentration, aspartate aminotransferase, alanine aminotransferase, serum creatinine, and creatine kinase-MB in those who died. No formal survival prediction model was established.

To make well-informed triage and treatment decisions, models for accurate severity evaluation after diquat poisoning are needed. Since the analysis of blood samples in cases of diquat poisoning often requires more than an hour and may not be available in many hospitals, separate severity indices are necessary for initial triage decisions at admission and a more accurate prognosis once laboratory results are available. Therefore, we aimed to develop severity indices of diquat poisoning for triage (SIDP-T) and prognosis (SIDP-P) that accurately assessed the risk of death in diquat poisoning based on 28-day survival outcomes.

METHODS

Study Design and Setting

This is a multicenter prospective cohort study involving data from 36 hospitals. All hospitals were located in Jiangsu Province, China, the fifth most populous and the most densely populated province with the highest gross domestic product per capita. The study center (Teaching Hospital of Nanjing Medical University) was located in Nanjing, China, the capital city of Jiangsu Province, with 8.4 million inhabitants. Data from the study center were used for model development, and data from other hospitals were used for external validation. The flowchart of this study is shown in the Figure. Data were reported according to TRIPOD guidelines.

Data Collection

Our research team developed the Clinical Toxicology Information Platform for Jiangsu Province to streamline the storage, organization, and retrieval of data on poisoning patients. The Clinical Toxicology Information Platform was implemented in the EDs of 36 hospitals across Jiangsu Province starting on February 1, 2022. Diquat cases identified between February 1, 2022, and July 31, 2023, from the Clinical Toxicology Information Platform were analyzed for this study.

The data collection process was coordinated through collaborative meetings with the ED directors from each hospital, taking into account the diagnostic or testing capabilities available at each hospital. The finalized data fields included demographic details, exposure history, treatments administered prior to admission, clinical characteristics (such as initial blood test results), and follow-up outcomes.

Each hospital designated a trained data manager responsible for uploading the information into the Clinical Toxicology Information Platform to facilitate the data entry. Prior to the implementation of the Clinical Toxicology Information Platform, data managers underwent standardized training and certification provided by our research team. Patient information was uploaded in real time during visits when poisoning was suspected upon presentation to the ED. For patients discharged from the hospital, data managers conducted follow-up phone calls for 28 days from the index date to monitor outcomes.

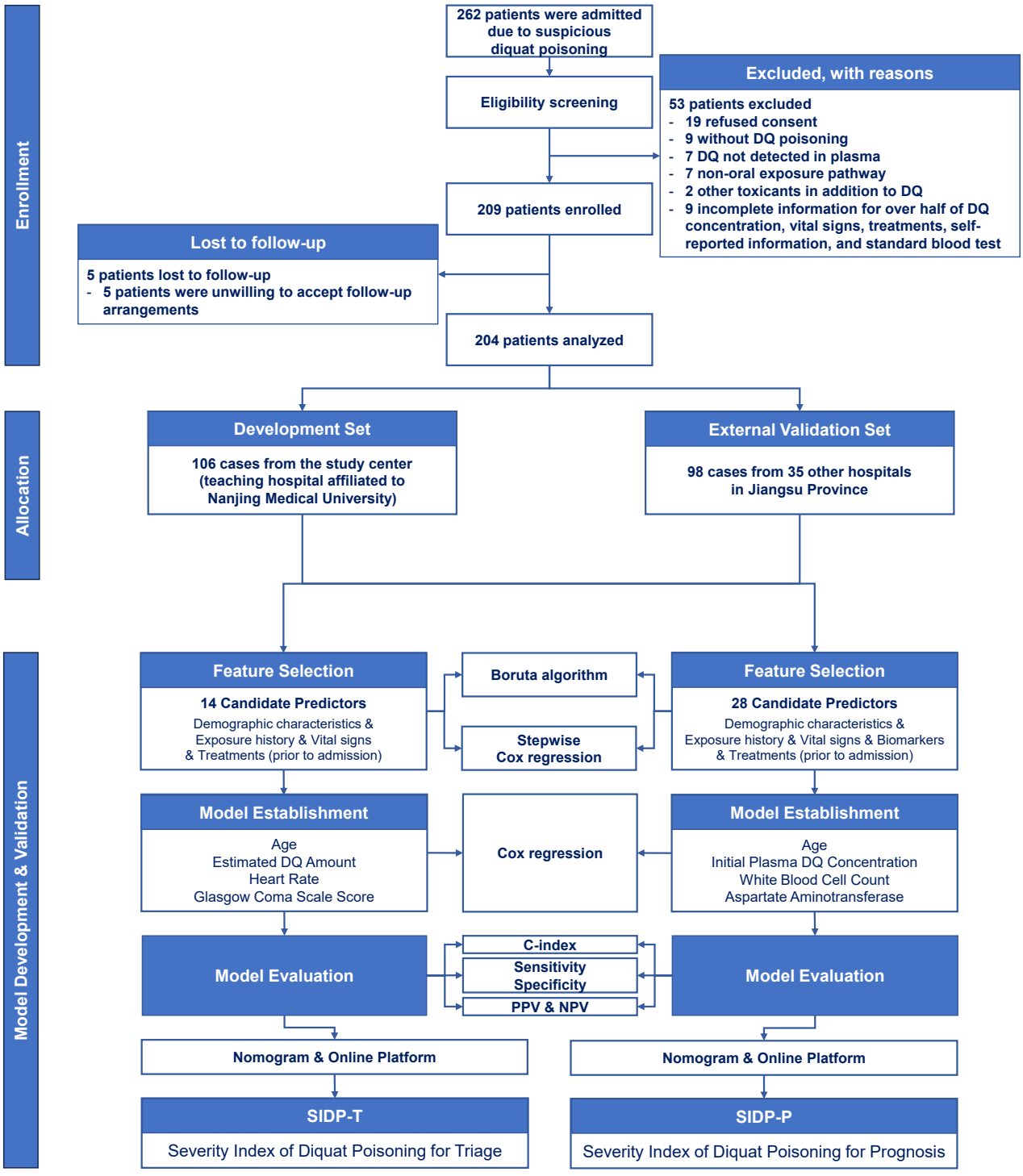

Figure. Flowchart of this study.

Patients were classified as lost to follow-up if they or their proxies missed calls on at least 3 separate days or refused to provide outcome information.

Ethics Statement

This study (Ethics Code: 2021-SR-394) was approved by the Medical Ethics Committee of the study center and

registered in ClinicalTrials.gov (ID: NCT05215457). Written informed consent was obtained from patients receiving blood purification treatment before presentation, while an exemption was granted by the Institutional Review Board for other patients, as the study involved only the analysis of routinely collected data. To protect patient confidentiality, all information was anonymized and deidentified prior to analysis. The study was conducted in compliance with the *Basic & Clinical Pharmacology & Toxicology* policy for experimental and clinical studies.[23]

Eligibility Criteria and Participants

The following criteria were used for patient inclusion: 1) history of oral exposure to diquat solution reported by patient or proxy; 2) a specimen for the diquat plasma concentration collected immediately upon admission; 3) documentation that patients or, in case of unconsciousness of the patient, legal proxies were aware of and agreed to treatment plans. Patients were excluded if: 1) they had ingested other toxicants in addition to diquat; 2) diquat was not detected in biological samples; 3) patients with over half of incomplete information; 4) patients with an exposure time (time from exposure to presentation at ED) longer than 48 hours.

Treatment methods for patients with acute diquat poisoning were based on the Chinese Expert Consensus on the Diagnosis and Treatment of Acute Diquat Poisoning.[7] The recommended treatment strategies include gastrointestinal decontamination through gastric lavage and activated charcoal to remove ingested toxins, and blood purification methods, such as hemoperfusion to clear toxins from the bloodstream. Antioxidant therapy (N-acetylcysteine, vitamin C, etc) is suggested to mitigate oxidative stress and prevent cellular damage. Additionally, organ support measures, including renal replacement therapy (such as continuous venovenous hemodiafiltration), are recommended for managing acute kidney injury or failure.

Measurements

Outcome. The primary outcome measures were 28-day survival and time from exposure to death.

Exposure dose. Estimated diquat amount was estimated either based on the contents of the actual diquat bottle if patients/proxies brought this to the ED (roughly 80%) or patients/proxies should mark the amount consumed on a small water bottle corresponding to the diquat bottle (200 mL).

Diquat concentration in plasma samples of poisoned patients was determined using ultraperformance liquid chromatography (UPLC)-MS/MS detection procedures.[24,25] All analyses were conducted at the Institute of Poisoning, Nanjing Medical University, and were typically completed within 2 hours of sample receipt by the laboratory. Additional details are provided in Appendix E1 (available at http://www.annemergmed.com).

Time from exposure to presentation was self-reported by patient or proxy.

Covariates. Demographics and clinical data were assessed at admission to ED by self-reporting or measurement of vital signs by nurses or physicians. Plasma samples were collected at admission, and laboratory parameters apart from diquat concentration were determined in hospital laboratories according to standard procedures in China. Although these samples were taken immediately upon admission, the analyses were typically completed within 1 hour after sample collection.

Sample Size Calculation

We followed the approach for sample size calculation for binary survival models as suggested by Riley et al.[26] We assumed a 1-month proportion of case fatalities of 50% as previously documented[5] yielding a maximum Cox-Snell R^2 of 0.75 and an adjusted Cox-Snell R^2 of 0.675. To keep the global shrinkage factor ≥ 0.9 and ensure that optimism was small such that there was a difference of $\leq 5\%$ between the apparent and adjusted percentage of variation explained by the model, as well as precision of estimates with margin of error $\leq 5\%$, we estimated a minimum sample size of 84 for a parsimonious model with 4 predictors. This was taken as target sample size for the development set (70%), whereas the external validation set (30%) should include at least 36 patients. Assuming 15% attrition, the enrollment target was 142 participants.

Statistical Analysis. Demographic characteristics, exposure history, treatments, vital signs, and biomarkers that are continuous variables are expressed as mean ± SD or median (interquartile range) when not normally distributed. Categoric variables are expressed as counts (proportions). Differences in medians for continuous variables and proportions for categoric variables, along with their 95% confidence intervals, are reported between survivors and fatalities.

For SIDP-T, predictor candidates included age, sex, estimated diquat amount, temperature, heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), vomiting or not, gastric lavage or not, blood purification or not before presentation, oxygen saturation, Glasgow Coma Scale (GCS) score, and time from exposure to presentation. For SIDP-P, in addition to

the predictors considered in SIDP-T, biomarker candidates included initial plasma diquat concentration, white blood cell count (WBC), monocyte count (MO), eosinophils (EO), basophils (BA), red blood cell count, hemoglobin (HGB), platelet count (PLT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), serum creatinine concentration (Crea), and neutrophil-to-lymphocyte ratio (NLR).

SIDPs were developed on data from study center (development set) with internal validation using bootstrapping and subsequently validated on an external validation set. SIDP-T and SIDP-P were developed separately, and missing values were imputed using multivariate imputation by chained equations. Feature selection was performed in 2 stages. First, the Boruta algorithm was applied to identify and exclude predictors deemed unimportant; details of this algorithm were provided in Appendix E1. The remaining predictors were then evaluated using stepwise Cox regression, and those that minimized the Akaike Information Criterion were selected as the final predictors for the SIDPs. We used Cox proportional hazards regression to develop SIDPs based on 28-day survival probability estimations.

To minimize false positives—incorrectly predicting death in patients who survived—a conservative cutoff of ≥ 0.9 for SIDPs was chosen to predict mortality. Model fit was assessed using the concordance index (C-index), with values of 0.5 indicating random prediction and 1.0 representing perfect accuracy. Further evaluation of model performance was conducted using sensitivity, specificity, positive predictive value (PPV), and negative positive value (NPV), and all of them indicate better performance with higher values. Calibration curves were further provided. Nomograms and user-friendly online platforms were established to support clinical practices. Details for converting from Cox model results into nomograms were provided in Appendix E1, and the online platforms were implemented using Streamlit. All statistical analyses were performed using R software (version 4.1.2) and Python (version 3.6.5). A 2-tailed approach was applied to statistical testing, with a significance level set at alpha=0.05.

RESULTS

Characteristics of Participants

The development set included 106 patients, comprising 67 survivors and 39 fatalities, with a case fatality rate of 36.8%; 56.6% were men. Median ages for survivors and fatalities were 26 (interquartile range [IQR]: 19.5, 33) years and 33 (IQR: 24, 48.5) years, respectively. Survivors had a longer time from exposure to presentation than fatalities (6.5 vs 5 hours), as well as a lower estimated diquat amount (25 vs 100 mL) and plasma diquat concentration (97.8 vs 1,531 ng/mL). Heart rate, respiratory rate, and DBP were significantly lower in survivors. Oxygen saturation and GCS scores were significantly higher in survivors than in fatalities. Additionally, fatalities showed higher WBC, AST, BUN concentrations, and NLR.

The external validation set included 98 patients, comprised of 69 survivors and 29 fatalities, with a case fatality rate of 29.6%; 61.2% were women. Median ages for survivors and fatalities were 20 (IQR: 16.3, 27.5) and 30 (IQR: 23.5, 38.8) years, respectively. Survivors had a longer time from exposure to presentation (11 vs 6.8 hours), as well as a lower estimated diquat amount (40 vs 100 mL) and plasma diquat concentration (64.6 vs 3,219 ng/mL). A comparison between survivors and fatalities in the development and external validation sets is summarized in the Table.

Severity Index of Diquat Poisoning for Triage (SIDP-T)

Age, estimated diquat amount, heart rate, and GCS score were included in the SIDP-T model as key predictors for assessing the mortality risk at 28 days after exposure. These predictors were selected from an initial pool of 14 variables, including demographic characteristics, exposure history, treatments, and vital signs. Appendix E1 provides a comprehensive overview of the feature selection process, model performance on the development set, and a nomogram and an online platform designed to facilitate easy access and real-world application of our model.

The SIDP-T model achieved the C-index of 0.79 (95% confidence interval [CI] 0.70 to 0.88) on the external validation set. For diagnostic accuracy, it achieved a sensitivity of 0.21 (95% CI 0.10 to 0.40) and a specificity of 0.99 (95% CI 0.92 to 1.00), indicating a high rate of accurate identification of true negatives. The model also showed promising predictive values, with a PPV of 0.86 (95% CI 0.49 to 0.99) and an NPV of 0.76 (95% CI 0.66 to 0.83). Age was found to significantly influence risk, with each additional year increasing the hazard by 5% (hazard ratio [HR]: 1.05; 95% CI 1.03 to 1.08). Similarly, the estimated diquat amount showed a relationship with mortality, where higher exposure was associated with greater risk (HR: 1.005; 95% CI 1.002 to 1.008). Heart rate also emerged as a critical predictor, with a higher heart rate contributing to increased risk (HR: 1.01; 95% CI 1.00 to 1.03). Conversely, a higher GCS score was associated with a reduced risk of death (HR: 0.89; 95% CI 0.83 to 0.96).

Table. Comparison of demographic characteristics, exposure history, treatments, vital signs, and biomarkers between survivors and fatalities in patients with acute diquat (DQ) poisoning in the development and external validation sets.

	Development set ($n=106$)			External validation set ($n=98$)		
Parameter	**Survivors ($n=67$)**	**Fatalities ($n=39$)**	**Difference (95% CIs)**	**Survivors ($n=69$)**	**Fatalities ($n=29$)**	**Difference (95% CIs)**
Demographic characteristics						
Sex (male), n (%)	34 (49.3)	26 (66.7)	17.4 (−1.5, 36.3)	24 (34.3)	14 (50)	15.7 (−5.9, 37.3)
Age (y), M (Q1, Q3)	26 (19.5, 33)	33 (24, 48.5)	7 (3, 15.4)	20 (16.3, 27.5)	30 (23.5, 38.8)	10 (6, 14)
Exposure history, M (Q1, Q3)						
Estimated DQ amount (mL)	25 (15, 50)	100 (70, 200)	75 (60, 120.1)	40 (15, 73.8)	100 (92.5, 200)	60 (50, 165)
Time from exposure to presentation (h)	6.5 (5, 13)	5 (4, 7.1)	−1.5 (−3.6, 0.5)	11 (6, 20.8)	6.8 (3.8, 11)	−4.2 (−11.8, −3.7)
Treatments, n (%)						
Vomiting	61 (88.4)	32 (82.1)	−6.4 (−20.6, 7.9)	33 (47.1)	9 (32.1)	−15 (−35.9, 5.9)
Gastric lavage	59 (85.5)	36 (92.3)	6.8 (−5, 18.6)	68 (97.1)	27 (96.4)	−0.7 (−8.6, 7.2)
Blood purification before presentation	9 (13)	2 (5.1)	−7.9 (−18.5, 2.6)	2 (2.9)	4 (14.3)	11.4 (−2.1, 25)
Vital signs, M (Q1, Q3)						
Temperature (°C)	36.5 (36.3, 36.6)	36.5 (36.2, 36.6)	0 (−0.2, 0.2)	36.5 (36.4, 36.8)	36.5 (36.3, 36.8)	0 (−0.1, 0.2)
Pulse rate (beats/min)	90 (79, 97)	100 (80, 123.5)	10 (1.7, 21.9)	89 (83, 102)	95.5 (88.8, 112.3)	6.5 (−3.5, 21.5)
Respiratory rate (breaths/min)	20 (17, 20)	20 (19.5, 22)	0 (0, 1)	18 (16, 20)	21 (17.5, 26)	3 (1, 6.5)
SBP (mmHg)	132 (119, 144)	137 (122.5, 158.5)	5 (−2.3, 20.6)	123 (113.3, 138)	134.5 (121.5, 143.5)	11.5 (−5.4, 11.6)
DBP (mmHg)	80 (74, 93)	90 (78.5, 105.5)	10 (1.3, 15.1)	76 (70, 89.75)	86 (70.8, 92.3)	10 (−2.2, 12.2)
Oxygen saturation	99 (97, 99)	97 (95, 99)	−2 (−3, 0)	98.5 (97, 99)	99 (94.3, 100)	0.5 (−2, 1.5)
GCS score	15 (15, 15)	14 (7, 15)	−1 (−5, 0)	15 (15, 15)	15 (12.8, 15)	0 (−1, 0)
Biomarkers at admission, M (Q1, Q3)						
Concentration (ng/mL)	97.8 (29.9, 316)	1,531 (1,017.2, 3,628)	1,433.2 (973.2, 2,820.7)	64.6 (12, 345.3)	3,219 (719.8, 8,702)	3,154.4 (909.6, 6,385.9)
WBC (×10^9/L)	14.9 (10.4, 18.7)	24.3 (18.9, 31.3)	9.4 (5.9, 14.5)	12.4 (8.4, 15.7)	20.1 (9.7, 27.2)	7.7 (−1.8, 13.6)
MO (×10^9/L)	13 (8.6, 19.4)	24.6 (14.6, 33)	11.6 (4.4, 16.2)	6.5 (3.1, 13)	6.9 (2.9, 17.3)	0.4 (−3.4, 8.5)
EO (×10^9/L)	0.58 (0.34, 0.87)	1.02 (0.63, 1.4)	0.44 (0.1, 0.7)	0.52 (0.32, 0.73)	0.65 (0.51, 1.07)	0.13 (−0.1, 0.4)
BA (×10^9/L)	0.01 (0, 0.03)	0 (0, 0.03)	−0.01 (−0.02, 0.02)	0.03 (0, 0.08)	0.04 (0.01, 0.09)	0.01 (−0.02, 0.05)
RBC (×10^12/L)	0.02 (0.02, 0.04)	0.05 (0.02, 0.1)	0.03 (0, 0.04)	0.02 (0.01, 0.04)	0.03 (0.02, 0.05)	0.01 (−0.01, 0.02)
HGB (g/L)	4.79 (4.23, 5.5)	5.39 (4.9, 5.69)	0.6 (0.1, 1)	4.53 (4.22, 5.04)	4.8 (4.47, 5.47)	0.27 (−0.1, 0.7)
PLT (×10^9/L)	140 (125, 166)	160 (146, 179)	20 (6, 27)	136 (124.3, 149.8)	140 (130.8, 158.8)	4 (−3, 16)
ALT (U/L)	245 (200, 282)	260 (192.5, 330.5)	15 (−35, 67)	250 (201.8, 296.5)	265 (212, 315.5)	15 (−31, 72.5)
AST (U/L)	26.7 (17.5, 40.4)	61.7 (29.8, 133.6)	35 (14.3, 49.1)	20.3 (14.8, 32.8)	38 (23, 120.7)	17.7 (5.5, 80)
BUN (mmol/L)	27.8 (23.2, 37.5)	73.3 (32.55, 189.1)	45.5 (10.3, 74.1)	25.7 (20.9, 36.1)	36.5 (29.8, 191.7)	10.8 (3, 100.7)
Crea (μmol/L)	4.56 (3.51, 6)	6.39 (5.52, 7.92)	1.83 (1.1, 2.9)	4.42 (3.71, 6.08)	5.14 (4.23, 7.42)	0.72 (−0.3, 2)
NLR	66 (46.7, 83.4)	118.4 (92.5, 169.6)	52.4 (31.6, 85)	55.8 (45.3, 79)	94.3 (61.6, 145.1)	38.5 (10, 79.3)

Abbreviations: *SBP,* systolic blood pressure; *DBP,* diastolic blood pressure; *GCS,* Glasgow Coma Scale; *Concentration*, initial plasma diquat concentration; *WBC,* white blood cell count; *MO,* monocyte count; *EO,* eosinophil; *BA,* basophils; *RBC,* red blood cell count; *HGB,* hemoglobin; *PLT,* platelet count; *ALT,* alanine aminotransferase; *AST,* aspartate aminotransferase; *BUN,* blood urea nitrogen; *Crea,* the serum creatinine concentration; *NLR,* neutrophil-to-lymphocyte ratio.

All biomarkers were tested in the first blood sample collected after admission.

Severity Index of Diquat Poisoning for Prognosis (SIDP-P) with Additional Biomarkers

With 14 predictors considered in SIDP-T, additional 14 biomarkers were included as candidate variables for the SIDP-P model. Age, plasma diquat concentration, WBC, and AST were identified as the final predictors included in the SIDP-P model. Details of the feature selection process, model performance on the development set, and a nomogram and an interactive online platform for streamlined use in clinical settings are provided in Appendix E1.

SIDP-P fitted well with the C-index of 0.82 (95% CI 0.74 to 0.90) on the external validation set. Its diagnostic accuracy metrics showed a sensitivity of 0.14 (95% CI 0.06 to 0.31) and a perfect specificity of 1.00 (95% CI 0.95 to 1.00), indicating its ability to reliably identify true negative cases. The model also exhibited a PPV of 1.00 (95% CI to 0.51, 1) and an NPV of 0.74 (95% CI 0.65 to 0.82), highlighting its utility in ruling out low-risk cases with confidence. Higher age was associated with increased risk (HR: 1.04; 95% CI 1.01 to 1.06), consistent with findings from the SIDP-T model. Similarly, elevated plasma diquat concentration significantly increased risk (HR: 1.05; 95% CI 1.02 to 1.09), reflecting the dose-dependent toxicity of diquat exposure. Among the biochemical markers, higher WBC was a predictor of increased risk (HR: 1.08; 95% CI 1.04 to 1.12). Elevated AST levels also contributed to the risk profile (HR: 1.002; 95% CI 1.000 to 1.003).

LIMITATIONS

Our study has several limitations that warrant discussion. First, several hospitals included in the external validation set provided data for single patients only. This precludes modeling specific hospital-level factors such as ED patient volume or unobserved heterogeneity with random effects. Second, given that our median time to presentation was 7 hours (IQR: 4, 14), our models may not adequately predict outcomes when presentation times are less than 6 hours. Moreover, despite employing a multicenter study design, the small sample size remains a limitation.

The above limitations are balanced by numerous strengths. First, to our knowledge, a prediction model for survival after diquat poisoning had not previously been established. Moreover, we also established models for 2 different situations: at triage using readily available vital sign parameters and exposure history, and for further prognosis, a triage based on laboratory biomarkers that may only become available after treatment has already commenced. Second, emphasis was put on the accuracy and parsimony of models to optimize feasibility for clinical practice while minimizing false predictions of mortality in actual survivors. This aspect makes it especially valuable for countries and regions with restricted medical resources, ensuring both medical resource preservation and patient protection. Third, the machine learning approaches maximized the variable selection, making reproducibility very likely. Furthermore, estimation on an external validation set enhances the generalizability of our findings.

DISCUSSION

This study is the first multicenter study to evaluate individual-level survival outcomes in acute diquat poisoning, and 2 tools were developed to help emergency physicians make informed decisions in acute diquat poisoning cases, the SIDP-T and SIDP-P. SIDP-T (age, estimated diquat amount, heart rate, and GCS score) allows for immediate triage decisions based on readily available information, facilitating timely treatment and transfer decisions. SIDP-P (age, initial plasma diquat concentration, WBC, AST levels) provides more accurate outcome predictions once laboratory results are available, guiding ongoing clinical management and resource allocation.

The Chinese government implemented a ban on the sale and use of paraquat in 2016, making diquat the most effective available alternative herbicide. In parallel with the adoption of diquat in agricultural practices, there has been a substantial rise in the number of clinical cases involving acute diquat poisoning, mostly attributed to suicide attempts.[27] Although the equimolar toxicity of diquat is somewhat lower than paraquat,[8] risk is still very high, as confirmed by a case fatality of 33% in the present study and 50% in the study by Zhou and Lu.[5]

Our proposed SIDPs minimize the false positive prediction of death in people who actually survive. Our models were constructed to minimize false positive predictions, which led to a larger number of false negatives (predicted survival but patients die) than would be ideal. Although our approach may occasionally lead to over triage of some patients who may ultimately die, under triage of patients who could be saved is unacceptable. We endorse the provision of comprehensive care with a focus on improving survival for all patients, but patients with an extremely high predicted severity index may not benefit from aggressive interventions or transfer to a higher level of care. In such scenarios, physician-patient/proxy communications about the patient's prognosis are valuable for making well-informed decisions. We did not include previously identified clinical features associated with poor prognosis, such as renal failure and coma, because those factors typically occur later in the course of disease, and our models intend to preempt the worsening of these clinical features.[28]

The best predictors of mortality in the triage model (SIDP-T) were higher age, higher heart rate measured at admission, greater estimated diquat amount, and lower GCS score as reported by patient or proxy. Although age and self-reported exposure dose had been previously reported to be important predictors with paraquat,[15] vital signs, including SBP, pulse rate, respiration rate, body temperature, and mental status, have only recently been discussed in a study by Han et al[29] that predicted mortality in acute poisoning due to various poisoning cases. Pulse rate, in particular, serves as an important indicator of early warning score, whereas lower GCS indicates a reduced level of consciousness, which is often linked to more severe neurologic impairment. As far as clinical utility is concerned, self-reported data on exposure volume and pulse rate may be the only available information that can easily be assessed at admission or in settings with limited diagnostic tools. Biomarker testing is not available at most hospitals, which highlights the need for a tool to determine if sending out testing or patient transfer is warranted. SIDP-T demonstrated good prediction accuracy with a C-index of approximately 0.8 across all datasets. This is comparable with the fit of several models that included laboratory parameters that predict paraquat[20] mortality, demonstrating the practical usefulness of our model for initial triage decisions.

In our SIDP-P model, the best predictors of mortality were higher age, higher plasma diquat concentration, higher WBC, and higher AST. Plasma concentration is an obvious predictor candidate, as demonstrated for paraquat in the past[10,13,17,18,29-31] and reported in a previous study on diquat.[5] The same holds true for WBC, which are known predictors in paraquat[14] and suspected predictors in diquat.[5] WBC count is a generalized indicator of systemic inflammatory response syndrome, and the increased WBC count in poisoning patients typically indicates that a severe infection, toxin exposure,[32] or injury has triggered a deterioration in the patient's condition. Elevated AST levels, a key marker of liver injury and muscle damage, reflect extensive tissue damage in acute diquat poisoning, with oxidative stress and inflammation further complicating recovery. Model fit on our development set was equal[20] or superior[14,16,17] to previous models for paraquat. Moreover, our model performance was comparable with a report on an unspecified model, which was developed with an unspecified procedure estimated on 50 patients[5] that included initial plasma diquat concentration and initial urinary diquat concentration. External validation has not been performed on either paraquat or diquat SIDPs before.

In conclusion, the SIDP-T provides a reliable decisionmaking tool for triage at the time of admission based on self-reported information and basic vital signs, whereas the SIDP-P accurately predicted survival at 28 days. Both SIDP-T and SIDP-P showed comparable performance; SIDP-T can serve as an effective tool to determine if aggressive care is warranted in resource-limited settings when blood tests or biomarker assessments are unavailable, whereas SIDP-P should be used when such resources are accessible.

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access to all the data in the study and accepted responsibility for submitting it for publication. YL, ZM, and WL contributed equally to this work. HS takes responsibility for the paper as a whole.

Data sharing statement: Complete datasets and data dictionary are available upon request from the date of article publication to investigators who provide an IRB letter of approval to Dr. Hao Sun at email haosun@njmu.edu.cn.

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