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*Original Article*

# Puncture frequency, coagulopathy, and liver injury as independent risk factors for bleeding in acute diquat poisoning after enhanced blood purification therapy

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**Abstract:** Objective: To identify independent risk factors for bleeding and propose preventive strategies in acute diquat poisoning (ADP) patients undergoing enhanced blood purification therapy (EBPT). Methods: In this retrospective study, a total of 297 ADP patients (May 2022-April 2024) were categorized into a conventional treatment (n=124) and EBPT (n=173) groups according to their treatment regimens. Clinical data, coagulation/liver function, and bleeding events were compared between the two groups. Logistics regression analysis was applied to identify independent risk factors for bleeding. COX regression model was used to explore the risk factors affecting survival prognosis. Kaplan-Meier method was used to draw survival analysis curve. Results: The EBPT group had a significantly higher bleeding incidence (45.05% vs. 4.23%, P<0.05), predominantly at puncture sites. Independent bleeding risk factors included puncture frequency, degree of poisoning, prolonged prothrombin time (PT), activated partial thromboplastin time (APTT), white blood cell count (WBC), elevated alanine aminotransferase (ALT), and aspartate aminotransferase (AST) (P<0.05). Bleeding patients had a higher 28-day mortality rate (50.00% vs. 18.95%, P<0.05) and longer ICU stays. Cox analysis confirmed that ALT, puncture frequency, poisoning severity, and bleeding were significant survival predictors (P<0.05). Conclusion: EBPT increases bleeding risk in ADP patients, mainly due to procedural factors and organ dysfunction. Optimizing puncture techniques and closely monitoring coagulation and liver function may improve patient outcomes.

**Keywords:** Acute diquat poisoning, intensive blood purification therapy, bleeding complications

## Introduction

Diquat is a widely used bipyridinium herbicide, favored in agriculture due to its high efficiency and low cost. However, similar to paraquat, acute diquat poisoning (ADP) has a very high mortality rate, particularly in developing countries. Studies indicate that the mortality rate from ADP can range from 20% to 60%, with primary clinical manifestations including acute liver injury, renal failure, and multiple organ dysfunction. The toxicity mechanism of diquat is complex, primarily causing cellular damage through oxidative stress and inflammatory responses. Free radicals generated during diquat metabolism can severely damage organs such as the lungs, kidneys, and liver [1, 2]. In the lungs, it can cause acute lung injury (ARDS), characterized by damage to alveolar epithelial cells and pulmonary fibrosis. In the kidneys, diquat can induce tubular necrosis, leading to acute kidney injury [3]. In the liver, diquat can cause hepatocyte necrosis and reduce the synthesis of coagulation factors, thereby increasing the risk of bleeding [4].

Enhanced blood purification therapy (EBPT) is considered a key method to improve survival rates in patients with diquat poisoning. The therapeutic principle involves rapidly removing toxins from the blood through physical or chemical methods, thereby alleviating multiple organ damage. Research has shown that EBPT can effectively improve biochemical indicators and clinical symptoms, reducing mortality, particularly in patients with moderate to severe poi-

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soning, significant lung injury, or multiple organ dysfunction [5, 6]. Despite its widespread clinical application and significant effects on improving patient survival rates, EBPT also carries a higher risk of bleeding. Currently, research on the mechanisms underlying bleeding risk following EBPT is limited. Several factors may contribute to bleeding after EBPT, including coagulopathy (resulting from reduced coagulation factors due to liver damage), the use of anticoagulants, and the presence of underlying conditions in patients (such as liver disease, diabetes) [7]. Additionally, individual differences and the severity of poisoning may also influence the incidence of bleeding. Therefore, clinicians must assess the bleeding risk when applying EBPT and implement effective preventive strategies.

This study aims to investigate the independent risk factors for bleeding following EBPT in ADP patients, analyze relevant clinical data, and propose preventive measures. Through this research, we hope to provide clinicians with more comprehensive management recommendations to reduce bleeding risks and improve patient outcomes and survival prognosis.

## Materials and methods

### *Case selection*

This study selected 297 patients with ADP admitted to the Emergency Department of Gansu Provincial Hospital of TCM from May 2022 to April 2024. The study was approved by the Ethics Committee of Gansu Provincial Hospital of TCM (Ethics Approval Number: 1245271). Patients were divided into two groups based on treatment modality: the conventional treatment group (n=124) and the enhanced blood purification therapy (EBPT) group (n=173).

Inclusion criteria: (1) Patients who met the clinical diagnostic criteria for ADP [8]: Patients with a clear history of diquat exposure or poisoning. The severity of poisoning was confirmed based on clinical symptoms (e.g., difficulty breathing, cough, chest pain, pulmonary infiltrates on imaging) and laboratory tests (e.g., arterial blood gas analysis, liver and kidney function, inflammatory markers); (2) Age >14 years; (3) Patients who received blood purification treatment (conventional treatment or EBPT) after admission, with EBPT adhering to clinical guideline standards; (4) Records of systematic monitoring for bleeding complications during treatment, including detailed data on the time, type, and management of bleeding events; (5) Complete medical records.

Exclusion criteria: (1) Patients with severe cardiopulmonary dysfunction, liver or kidney failure, or other life-threatening conditions (e.g., severe infections, acute cerebrovascular events); (2) Patients with a history of bleeding tendencies, coagulation disorders, or hematological diseases (e.g., hemophilia, leukemia); (3) Patients who received other forms of blood purification treatment prior to admission, or those who received medications during treatment that could affect bleeding risk (e.g., anticoagulants, high-dose corticosteroids); (4) Patients who were transferred to another hospital or withdrew from treatment for other reasons during the treatment period, making follow-up or data collection impossible.

### *Intervention methods*

*Conventional treatment group:* (1) Basic supportive care: Oxygen therapy or mechanical ventilation support was provided based on the patient's respiratory condition, and intravenous fluids are administered to maintain electrolyte balance. (2) Medication: Gastric lavage was performed as soon as possible after admission, using 2% sodium bicarbonate, along with oral montmorillonite powder for adsorption and 20% mannitol for bowel cleansing. (3) Symptomatic treatment: Supportive treatment was provided. For pulmonary complications, antibiotics were given to prevent or treat infections; In patients with liver dysfunction, hepatoprotective agents (e.g., silymarin) were used to mitigate liver injury. Electrolyte abnormalities (e.g., hyperkalemia) were monitored and corrected.

*EBPT group:* Basic supportive care was the same as in the conventional treatment group. For patients admitted within 24 hours of poisoning, an EBPT regimen using sustained hemoperfusion (SHP) combined with continuous venovenous hemofiltration (CVVH) was employed. (1) SHP treatment: A hemoperfusion machine and disposable hemoperfusion cartridges are used for 1-2 sessions (2 hours/session). Before starting, heparin sodium (1.25 wIU) was injected to fully prime and flush the hemoperfusion circuit. Low molecular

weight heparin (4100 IU) was administered for systemic anticoagulation 15 minutes before treatment. During the hemoperfusion, the blood pump speed was set at 150-180 mL/min and maintained for 10 hours. Vital signs and laboratory parameters were monitored, with particular attention to bleeding, infection, and other complications. (2) CVVH treatment: After SHP, the Prismaflex CRRT machine with STI-00SSET filters was used for treatment, with each session lasting at least 12 hours for a total of 3 days. Replacement fluid for hemofiltration was used, and heparin sodium (12,500 IU) was administered to prime the circuit and ensure patency. During treatment, sodium citrate solution was used for local anticoagulation at a flow rate of 1.2-1.5 times the blood flow rate. The blood pump speed was set at 180-200 mL/min, and the replacement fluid flow rate was set at 2300 mL/h. Vital signs and laboratory parameters were regularly monitored throughout the treatment.

*Data collection and outcome measurement*

Primary outcomes: (1) Incidence and severity of bleeding complications (classified as general or severe). (2) The 28-day mortality rate.

Secondary outcomes: (1) ICU length of stay. (2) Treatment success rate (defined as survival with organ recovery).

Collected data: (1) Baseline characteristics: Age, sex, body mass index (BMI), poisoning dose, and severity (mild/moderate/severe). (2) Laboratory examination indicators: prothrombin time (PT), activated partial thromboplastin time (APTT), and white blood cell count (WBC) related to the coagulation function; alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBiL) related to the liver and kidney functions. (3) Number of punctures and catheter insertion sites.

Bleeding group classification: Patients in the EBPT group were categorized into bleeding (n=78) or non-bleeding (n=95) subgroups based on documented bleeding events during treatment.

*Statistical analysis*

Data processing and analysis were performed using SPSS 26.0 statistical software. Continuous variables were expressed as mean ± standard deviation ($\bar{x} \pm s$), with group comparisons made using independent samples t-tests. Categorical variables were expressed as rates or percentages, with group comparisons made using $\chi^2$ tests. Kaplan-Meier survival curves were plotted to estimate survival rates and differences between groups. The log-rank test was used to compare survival curves between different groups. A logistic regression analysis was conducted to identify independent risk factors for bleeding in ADP patients undergoing EBPT treatment. Cox regression analysis was used to explore the impact of clinical factors and bleeding on patient prognosis. Kaplan-Meier curves were plotted for survival analysis. A two-tailed *p*-value of <0.05 was considered statistically significant.

## Results

*Comparison of basic characteristics between the conventional treatment group and EBPT group*

The conventional treatment group (n=124) comprised 78 males and 46 females, with an average age of (37.36±8.99) years. The EBPT group (n=173) comprised 112 males and 61 females, with an average age of (39.24±10.75) years. There were no significant differences between the two groups in terms of gender, age, BMI, poisoning dose, number of punctures, severity of poisoning, coagulation function indicators, or liver and kidney function indicators (P>0.05), as shown in **Table 1**.

*Comparison of incidence and severity of bleeding complications between the conventional treatment group and EBPT group*

Both groups experienced bleeding complications, but the incidence of bleeding in the EBPT group was significantly higher at 45.05%, compared to 3.23% in the conventional treatment group. The primary bleeding site was at the puncture site. While both groups primarily exhibited general bleeding, severe bleeding occurred in 17.34% of the EBPT group. See **Table 2** for details.

*Comparison of clinical characteristics between the bleeding group and non-bleeding group*

Patients were divided into two groups based on the occurrence of bleeding during EBPT treatment: the bleeding group (n=78) and the

**Table 1.** Comparison of baseline characteristics between the conventional treatment group and EBPT group

| Characteristic | Conventional treatment group (n=124) | EBPT group (n=173) | $\chi^2/t$ | P |
|---|---|---|---|---|
| Age (years) | 37.36±8.99 | 39.24±10.75 | 1.589 | 0.113 |
| Male [n (%)] | 78 (62.90%) | 112 (64.74%) | 0.106 | 0.745 |
| BMI (kg/m$^2$) | 23.55±2.83 | 24.01±2.85 | 1.380 | 0.169 |
| Poisoning Dose (ml) | 9.66±3.32 | 10.52±4.52 | 1.799 | 0.073 |
| Number of Punctures [n (%)] | | | 0.027 | 0.869 |
| ≤3 times | 80 (64.52) | 110 (63.57) | | |
| >3 times | 44 (35.48) | 63 (36.43) | | |
| Severity of Poisoning [n (%)] | | | 3.529 | 0.171 |
| Mild | 40 (32.26) | 50 (28.90) | | |
| Moderate | 60 (48.39) | 73 (28.90) | | |
| Severe | 24 (19.35) | 50 (42.20) | | |
| PT (s) | 13.04±1.29 | 13.23±1.25 | 1.275 | 0.203 |
| APTT (s) | 35.53±3.57 | 34.85±3.76 | 1.570 | 0.117 |
| WBC (10$^9$/L) | 9.82±2.34 | 10.03±2.12 | 0.806 | 0.421 |
| ALT (U/L) | 36.90±10.68 | 37.76±10.31 | 0.698 | 0.486 |
| AST (U/L) | 31.62±8.87 | 32.62±8.88 | 0.957 | 0.339 |
| TBiL (μmol/L) | 16.93±4.81 | 17.88±4.56 | 1.719 | 0.087 |

Note: EBPT: Enhanced Blood Purification Therapy, BMI: Body Mass Index, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, WBC: White Blood Cell, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, TBiL: Total Bilirubin.

**Table 2.** Comparison of bleeding incidence and severity between the two groups

| | Conventional treatment group (n=124) | EBPT group (n=173) | $\chi^2$ | P |
|---|---|---|---|---|
| Total Hemorrhage Incidence | 4 (3.23) | 78 (45.05) | 63.327 | <0.001 |
| Puncture Site Bleeding | 2 (1.61) | 34 (19.64) | 22.068 | <0.001 |
| Gastrointestinal Bleeding | 0 (0.00) | 18 (11.46) | 13.734 | <0.001 |
| Skin and Mucosal Bleeding | 4 (3.23) | 20 (11.56) | 6.755 | 0.009 |
| Other Bleeding | 0 (0.00) | 6 (3.47) | 4.389 | 0.036 |
| General Bleeding | 6 (4.84) | 48 (28.74) | 26.904 | <0.001 |
| Severe Bleeding | 0 (0.00) | 30 (17.34) | 23.919 | <0.001 |

Note: EBPT: Enhanced Blood Purification Therapy.

non-bleeding group (n=95). Significant differences were observed between the two groups in terms of poisoning dose, number of punctures, severity of poisoning, PT, APTT, WBC, ALT, AST, and TBiL (P<0.05). However, no significant differences were found in age, gender, or BMI. See **Table 3** for details.

*Logistic regression analysis of independent risk factors for bleeding after EBPT treatment in ADP patients*

Logistic regression analysis identified the number of punctures, severity of poisoning, PT, APTT, WBC, ALT, and AST as independent risk factors influencing bleeding after EBPT treatment in ADP patients (P<0.05, **Figure 1**).

*Impact of bleeding on prognosis after EBPT treatment in ADP patients*

The bleeding group exhibited a higher 28-day mortality rate and longer ICU stay compared to the non-bleeding group (P<0.05). Additionally, the treatment success rate was significantly lower in the bleeding group (P<0.05). See **Table 4** for detailed statistics.

*Cox regression analysis of prognostic factors in ADP patients after EBPT treatment*

In the EBPT group, 57 patients died within 28 days, resulting in a survival rate of 67.05%. Univariate Cox regression analysis and survival curve results indicated that poisoning dose,

**Table 3.** Comparison of clinical characteristics between the bleeding group and the non-bleeding group

| Characteristic | Bleeding Group (n=78) | Non-Bleeding Group (n=95) | $\chi^2/t$ | P |
|---|---|---|---|---|
| Age (years) | 40.22±11.34 | 41.11±10.97 | 0.523 | 0.602 |
| Male [n (%)] | 48 (61.54) | 50 (52.63) | 1.384 | 0.240 |
| BMI (kg/m$^2$) | 23.12±4.56 | 22.85±3.89 | 0.420 | 0.675 |
| Poisoning Dose (ml) | 10.60±1.61 | 8.20±1.43 | 10.377 | <0.001 |
| Number of Punctures [n (%)] | | | 27.830 | <0.001 |
| ≤3 times | 34 (43.59) | 78 (82.11) | | |
| >3 times | 44 (56.41) | 17 (17.89) | | |
| Severity of Poisoning [n (%)] | | | 7.416 | 0.025 |
| Mild | 10 (12.82) | 22 (23.16) | | |
| Moderate | 30 (38.46) | 45 (47.37) | | |
| Severe | 38 (48.72%) | 28 (29.47) | | |
| PT (s) | 17.85±3.22 | 15.45±2.68 | 5.351 | <0.001 |
| APTT (s) | 35.56±4.87 | 31.24±3.91 | 6.472 | <0.001 |
| WBC (10$^9$/L) | 13.50±3.45 | 11.80±2.98 | 3.477 | <0.001 |
| ALT (U/L) | 54.12±15.34 | 48.30±12.67 | 2.733 | 0.007 |
| AST (U/L) | 52.45±14.22 | 47.20±10.56 | 2.784 | 0.006 |
| TBiL (μmol/L) | 30.12±7.45 | 27.00±6.78 | 2.880 | 0.004 |

Note: BMI: Body Mass Index, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, WBC: White Blood Cell, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, TBiL: Total Bilirubin.

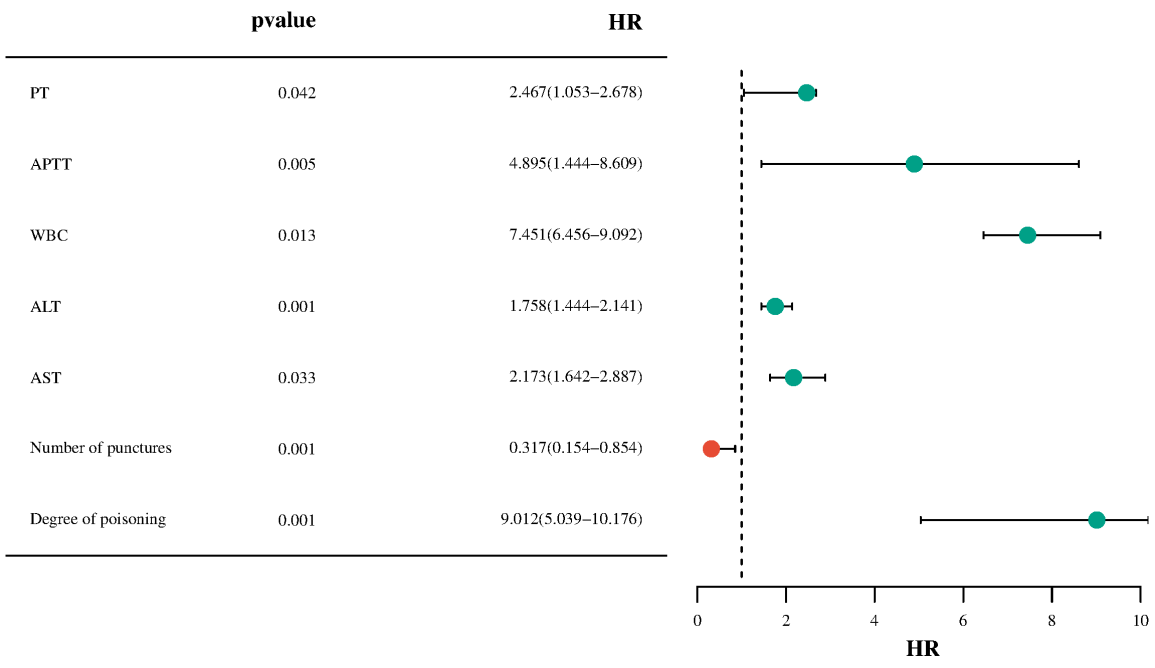



**Figure 1.** Logistic regression analysis of independent risk factors for bleeding in ADP patients following EBPT treatment. Note: ADP: Acute Diquat Poisoning, EBPT: Enhanced Blood Purification Therapy, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, WBC: White Blood Cell, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase.

number of punctures, severity of poisoning, bleeding PT, APTT, WBC, ALT, AST, and TBiL were significantly associated with prognosis in ADP patients after EBPT treatment (P<0.05), as

**Table 4.** Comparison of prognosis in ADP patients after EBPT treatment

| Group | n | Mortality Rate within 28 Days (%) | ICU Length of Stay (Days) | Treatment Success Rate (%) |
|---|---|---|---|---|
| Bleeding Group | 78 | 39 (50.00%) | 18.45±7.12 | 25 (32.20) |
| No Bleeding Group | 95 | 18 (18.95%) | 13.23±6.78 | 53 (56.32) |
| $\chi^2/t$ | | 18.695 | 4.926 | 14.004 |
| *P* | | <0.001 | <0.001 | <0.001 |

Note: ADP: Acute Diquat Poisoning, EBPT: Enhanced Blood Purification Therapy.

**Table 5.** COX univariate regression analysis of factors affecting prognosis in ADP patients after EBPT treatment

| Factor | B | SE | Wald | df | Sig. | Exp(B) | 95.0% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower HR | Higher HR |
| Age | -0.004 | 0.012 | 0.084 | 1 | 0.772 | 0.996 | 0.973 | 1.021 |
| BMI | 0.004 | 0.044 | 0.008 | 1 | 0.929 | 1.004 | 0.921 | 1.094 |
| Poisoning Dose | 0.066 | 0.027 | 5.973 | 1 | 0.015 | 1.068 | 1.013 | 1.126 |
| PT | 0.240 | 0.095 | 6.324 | 1 | 0.012 | 1.271 | 1.054 | 1.533 |
| APTT | 0.079 | 0.032 | 6.335 | 1 | 0.012 | 1.083 | 1.018 | 1.152 |
| WBC | 0.135 | 0.055 | 6.000 | 1 | 0.014 | 1.144 | 1.027 | 1.275 |
| ALT | 0.033 | 0.012 | 7.204 | 1 | 0.007 | 1.033 | 1.009 | 1.059 |
| AST | 0.033 | 0.013 | 6.254 | 1 | 0.012 | 1.033 | 1.007 | 1.060 |
| TBiL | 0.067 | 0.026 | 6.394 | 1 | 0.011 | 1.069 | 1.015 | 1.125 |
| Length of Stay | -0.011 | 0.025 | 0.199 | 1 | 0.656 | 0.989 | 0.942 | 1.039 |
| Male | -0.079 | 0.268 | 0.086 | 1 | 0.769 | 0.924 | 0.546 | 1.564 |
| Puncture Times | -1.883 | 0.432 | 18.969 | 1 | 0.000 | 0.152 | 0.065 | 0.355 |
| Severity of Poisoning | 0.470 | 0.172 | 7.479 | 1 | 0.006 | 1.601 | 1.143 | 2.243 |
| Bleeding Incidence | 0.688 | 0.258 | 7.137 | 1 | 0.008 | 1.990 | 1.201 | 3.298 |

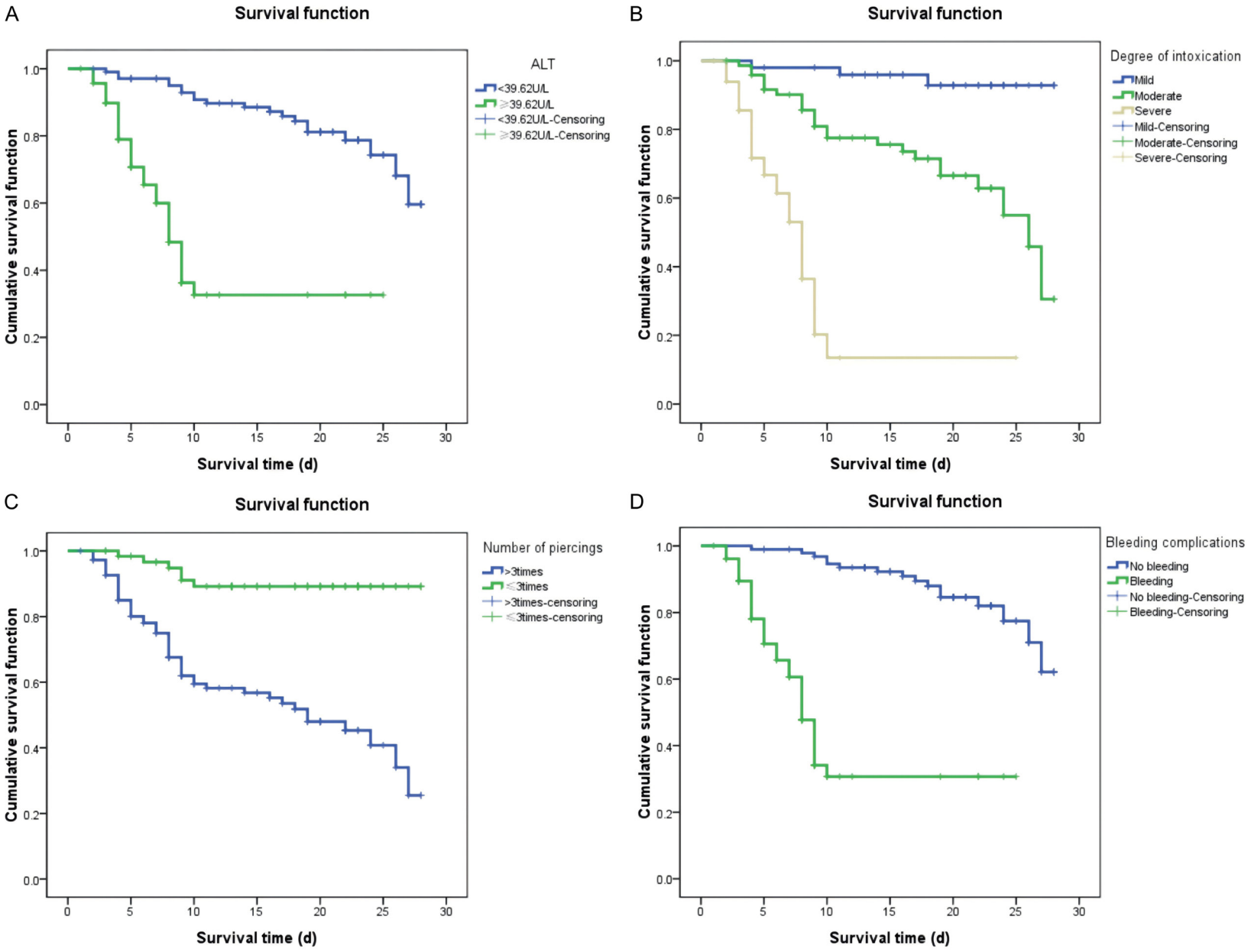
Note: ADP: Acute Diquat Poisoning, EBPT: Enhanced Blood Purification Therapy, SE: Standard Error, df: Degrees of Freedom, HR: Hazard Ratio, BMI: Body Mass Index, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, WBC: White Blood Cell, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, TBiL: Total Bilirubin.

shown in **Table 5**. After univariate analysis, Kaplan-Meier survival curves were plotted for the significant variables, as shown in **Figure 2**. Multivariate Cox regression analysis further revealed ALT, number of punctures, severity of poisoning, and bleeding complications as independent risk factors for survival rates in ADP patients after EBPT treatment (P<0.05), as shown in **Table 6**.

## Discussion

The core pathological mechanism of ADP is primarily attributed to its strong oxidative stress effects. Diquat generates a large number of oxygen free radicals through metabolism, triggering lipid peroxidation of the cell membrane and leading to damage in multiple organs [8, 9]. This study found that the incidence of bleeding in the EBPT group was as high as 45.05%, significantly higher than 4.84% in the conventional treatment group. This suggests that although EBPT effectively detoxifies the body, it carries a substantial risk of bleeding. This paradox may be related to the following mechanisms: (1) Diquat itself causes coagulation dysfunction by inhibiting the synthesis of coagulation factors and directly damaging the vascular endothelium [10, 11]; (2) Repeated puncture operations during EBPT treatment (e.g., catheter insertion, hemoperfusion) cause local vascular trauma; (3) Liver injury (evidenced by elevated ALT/AST) further weakens the ability to produce coagulation factors [12-14].

Further analysis of bleeding risk factors in ADP patients undergoing EBPT revealed that poisoning dose, number of punctures, severity of poisoning, and coagulation dysfunction (prolonged PT and APTT), as well as liver injury (elevated ALT and AST) were independent risk fac-


A
Survival function
Cumulative survival function
Survival time (d)
ALT
<39.62U/L
≥39.62U/L
<39.62U/L-Censoring
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B
Survival function
Cumulative survival function
Survival time (d)
Degree of intoxication
Mild
Moderate
Severe
Mild-Censoring
Moderate-Censoring
Severe-Censoring
C
Survival function
Cumulative survival function
Survival time (d)
Number of piercings
>3times
≤3times
>3times-censoring
≤3times-censoring
D
Survival function
Cumulative survival function
Survival time (d)
Bleeding complications
No bleeding
Bleeding
No bleeding-Censoring
Bleeding-Censoring

**Figure 2.** Kaplan-Meier curve analysis of survival outcomes based on different factors. A. The Kaplan-Meier (K-M) survival curves depicting 28-day survival for patients with different levels of alanine aminotransferase (ALT). B. The Kaplan-Meier (K-M) survival curves depicting 28-day survival for patients with different degrees of intoxication. C. The Kaplan-Meier (K-M) survival curves depicting 28-day survival for patients with different numbers of punctures. D. The Kaplan-Meier (K-M) survival curves depicting 28-day survival for patients with and without bleeding events.

**Table 6.** COX multivariate regression analysis of factors affecting prognosis in ADP patients after EBPT treatment

| Factor | B | SE | Wald | df | Sig. | Exp(B) | 95.0% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower HR | Higher HR |
| Toxic Dose | -0.151 | 0.330 | .208 | 1 | 0.648 | 0.860 | 0.450 | 1.643 |
| PT | 1.522 | 1.871 | .661 | 1 | 0.416 | 4.579 | 0.117 | 179.188 |
| APTT | -0.501 | 0.500 | 1.004 | 1 | 0.316 | 0.606 | 0.227 | 1.614 |
| WBC | -0.862 | 0.814 | 1.122 | 1 | 0.290 | 0.422 | 0.086 | 2.082 |
| ALT | 0.228 | 0.101 | 5.098 | 1 | 0.024 | 1.256 | 1.031 | 1.531 |
| AST | -0.046 | 0.104 | .194 | 1 | 0.659 | 0.955 | 0.779 | 1.172 |
| TBiL | 0.080 | 0.392 | .042 | 1 | 0.838 | 1.083 | 0.502 | 2.337 |
| Puncture Times | -0.990 | 0.463 | 4.570 | 1 | 0.033 | 0.372 | 0.150 | 0.921 |
| Severity of Poisoning | 1.046 | 0.322 | 10.534 | 1 | 0.001 | 2.846 | 1.513 | 5.353 |
| Bleeding Incidence | 1.454 | 0.642 | 5.126 | 1 | 0.024 | 4.278 | 1.216 | 15.058 |

Note: ADP: Acute Diquat Poisoning, EBPT: Enhanced Blood Purification Therapy, SE: Standard Error, df: Degrees of Freedom, HR: Hazard Ratio, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, WBC: White Blood Cell, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, TBiL: Total Bilirubin.

tors for bleeding. This indicates that the severity of poisoning and multiple puncture operations during treatment may increase the risk of bleeding. The metabolic functions of patients, especially the liver and coagulation system, are often severely compromised after poisoning, making them more susceptible to bleeding [15, 16]. This is consistent with previous research findings [17]. The toxic effects of glyphosate on the liver and blood system have been widely reported in clinical settings. A study by Liu KH et al. [18] demonstrated that bleeding in patients with glyphosate poisoning was closely related to coagulation dysfunction. The research indicated that glyphosate damaged endothelial cells through direct toxicity and reduced the synthesis of coagulation factors, aligning with the mechanistic analysis of this study. After glyphosate poisoning, patients exhibit impaired coagulation system function, as evidenced by prolonged coagulation times (PT and APTT) [19, 20]. These indicators reflect damage to both the extrinsic and intrinsic coagulation pathways, suggesting that patients are at a heightened risk of coagulopathy and increased bleeding after poisoning. Additionally, liver injury (evidenced by elevated ALT and AST levels) exacerbates the impairment of coagulation factor synthesis. The liver is the primary organ responsible for synthesizing coagulation factors, and when liver function is compromised, the reduction in coagulation factors increases the likelihood of bleeding [21-23]. These mechanisms become particularly pronounced following enhanced blood purification treatments, as the blood purification process itself is invasive and requires multiple puncture operations, further elevating the risk of bleeding [24].

Previous studies have shown that the in-hospital mortality rate for ADP is high, with various factors influencing patient prognosis [25]. The results of this study indicate that patients in the bleeding group have a poorer prognosis, with a significantly higher 28-day mortality rate compared to the non-bleeding group, along with longer ICU stay and notably lower treatment success rates. This finding underscores the adverse impact of bleeding complications on overall patient prognosis, increasing treatment complexity and mortality rates. COX multivariate regression analysis further confirms that ALT levels, number of punctures, severity of poisoning, and bleeding complications are independent risk factors

affecting patient survival. This suggests that clinicians should not only focus on the severity of poisoning and treatment efficacy but also closely monitor bleeding risks, especially in patients with severe poisoning and frequent puncture procedures.

Preventive strategies targeting these risk factors are crucial. First, during the EBPT process, it is essential to strictly control the number of punctures to minimize bleeding risks associated with catheterization. Second, enhancing coagulation function monitoring, particularly in patients with severe poisoning and impaired coagulation, and preemptively using anticoagulant drugs or related supportive therapies may help reduce bleeding incidence. Additionally, dynamic monitoring of liver function indicators and early interventions could further improve patient outcomes.

This study still has several limitations. First, its single-center retrospective design may have introduced selection bias and restrict generalizability. Additionally, long-term outcomes of bleeding complications were not assessed. Future multicenter prospective studies are warranted to validate risk factors and explore molecular mechanisms.

In conclusion, this study identifies multiple independent risk factors for bleeding in ADP patients undergoing EBPT treatment, including ALT, number of punctures, severity of poisoning, and bleeding complications. It highlights the importance of enhancing bleeding monitoring and optimizing treatment procedures. Future clinical practice should further investigate personalized prevention and treatment plans based on these risk factors to reduce the incidence of bleeding complications, ultimately improving patient survival rates and quality of life.

## Disclosure of conflict of interest

None.

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