

Sequential Organ Failure Assessment Score Can Predict Mortality in Patients with Paraquat Intoxication

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Abstract

Introduction: Paraquat poisoning is characterized by multi-organ failure and pulmonary fibrosis with respiratory failure, resulting in high mortality and morbidity. The objective of this study was to identify predictors of mortality in cases of paraquat poisoning. Furthermore, we sought to determine the association between these parameters.

Methods: A total of 187 patients were referred for management of intentional paraquat ingestion between January 2000 and December 2010. Demographic, clinical, and laboratory data were recorded. Sequential organ failure assessment (SOFA) and acute kidney injury network (AKIN) scores were collected, and predictors of mortality were analyzed.

Results: Overall hospital mortality for the entire population was 54% (101/187). Using a multivariate logistic regression model, it was found that age, time to hospitalization, blood paraquat level, estimated glomerular filtration rate at admission (eGFR_{first day}), and the SOFA_{48-h} score, but not the AKIN_{48-h} score, were significant predictors of mortality. For predicting the in-hospital mortality, SOFA_{48-h} scores displayed a good area under the receiver operating characteristic curve (AUROC) (0.795±0.033, $P<0.001$). The cumulative survival rate differed significantly between patients with SOFA_{48-h} scores <3 and those ≥ 3 ($P<0.001$). A modified SOFA (mSOFA) score was further developed by using the blood paraquat level, and this new score also demonstrated a better AUROC (0.848±0.029, $P<0.001$) than the original SOFA score. Finally, the cumulative survival rate also differed significantly between patients with mSOFA scores <4 and ≥ 4 ($P<0.001$).

Conclusion: The analytical data demonstrate that SOFA and mSOFA scores, which are based on the extent of organ function or rate of organ failure, help to predict mortality after intentional paraquat poisoning.

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Introduction

Due to ease of access, pesticides [1] and herbicides [2] are commonly ingested in Taiwan, both intentionally and by accident. Paraquat is a popular bipyridal herbicide with a good safety record when used properly. However, the lethal toxicity of this compound leads to a high mortality rate (60–80%). After ingestion of approximately 40 mL of a 24% solution of paraquat, patients normally die within several hours to days from multiple organ failure. After ingesting approximately 16 mL, patients experience moderate to severe poisoning and die within 1–2 weeks from pulmonary fibrosis and severe hypoxemia [3,4]. Many treatment modalities have been developed for paraquat poisoning, including adsorbents, hypo-oxygenation, lung radiotherapy [5], prolonged extracorporeal detoxification [6], and lung transplantation. However, the efficacies of these therapeutic methods remain uncertain.

At our hospital, all paraquat patients are usually treated using a standard detoxification protocol [2–4,7–10]. This protocol consists of repeated pulses of methylprednisolone and cyclophosphamide,

followed by prolonged dexamethasone therapy. With this approach, it was demonstrated that both respiratory function and blood oxygen concentrations in most patients returned to near-normal levels in 3–6 months [11]. Methylprednisolone, cyclophosphamide, and dexamethasone are potent anti-inflammatory medical therapies. Therefore, it is the severe inflammation (not lung fibrosis) that plays a critical role in producing lethal hypoxemia after paraquat poisoning.

Regarding patient prognosis, Sawada *et al.* showed that a severity index of paraquat poisoning (SIPP) may be a good clinical predictor of mortality [12]. However, many hospitals do not have the necessary facilities for measuring serum paraquat levels. Huang *et al.* [13] demonstrated that an Acute Physiology And Chronic Health Evaluation II (APACHE II) score of >13 , calculated 24 h after admission, could predict in-hospital mortality with 67% sensitivity and 94% specificity. Furthermore, the APACHE II system yielded better discriminative power than SIPP score, plasma paraquat concentration, or estimated paraquat ingestion dosage [13]. Nevertheless, the APACHE II score does

Table 1. SOFA scoring system.

	0	1	2	3	4
PaO ₂ /FiO ₂	>400	301–400	201–300	101–200 with respiratory support	≤100 with respiratory support
Platelets (1000/ μ L)	>150	101–150	51–100	21–50	≤20
Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Hypotension	MAP \geq 70 mmHg	MAP<70 mmHg	Dopamine 5 or dobutamine (any dose)*	Dopamine >5 or epi \leq 0.1 or norepi \leq 0.1*	Dopamine >15 or epi >0.1 or norepi >0.1*
GCS	15	13–14	10–12	6–9	<6
Cr (mg/dL) or UO	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500 mL/d	>5.0 or <200 mL/d

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not include parameters reflecting liver damage, which are a major complication of paraquat poisoning [10]. Furthermore, calculation of the APACHE II score is complex and not suitable for typical hospital inpatients, such as the paraquat patients assessed in our study. Both the Simplified Acute Physiology Score II (SAPS II) [14] and Expanded Simplified Acute Physiology Score II (SAPS IIe) are also commonly used in intensive care units (ICUs) for predicting mortality. Min *et al.* [15] showed that SAPS II or SAPS IIe, calculated immediately after arrival at the emergency department, may be helpful in predicting outcome after acute paraquat poisoning. However, the SAPS II or SAPS IIe systems are limited by how they are calculated, since the measurement of the ratio of partial pressure of oxygen in arterial blood to the fraction of inspired oxygen (PaO₂/FiO₂) is only applicable to patients undergoing mechanical ventilation. Thus, it is absolutely unsuitable for spontaneously breathing patients. On the other hand, the SOFA score has been extensively used to predict the outcome of ICU patients [16] because the measurement of PaO₂/FiO₂ is not limited to mechanically ventilated patients, as in the SAPS II or SAPS IIe system. The calculation is simple and involves only PaO₂/FiO₂, platelet count, serum bilirubin level, hypotension, Glasgow Coma Score, and serum creatinine or urine output.

Paraquat poisoning is characterized by multi-organ failure and pulmonary fibrosis leading to respiratory failure, with acute kidney injury being the major cause of mortality [10]. Despite this, the prognostic significance of the AKIN scoring system [17] has not been previously studied. Consequently, the objective of this study was to identify predictors of mortality (clinical features, physiological markers, and SOFA and AKIN scores) in cases of paraquat

poisoning. Furthermore, we sought to identify potential associations between these parameters.

Materials and Methods

This retrospective observational study complied with the guidelines of the Declaration of Helsinki and was approved by the Medical Ethics Committee of Chang Gung Memorial Hospital, a tertiary referral center located in the northern part of Taiwan. Since this study involved retrospective review of existing data, approval from the Institutional Review Board was obtained, but without specific informed consent from patients [1]. However, informed consent regarding risks associated with acute paraquat poisoning and all treatment modalities (particularly charcoal hemoperfusion) was obtained from all patients upon their initial admission. Furthermore, not only were all data securely protected (by delinking identifying information from the main data sets) and made available only to investigators, but they were also analyzed anonymously. The Institutional Review Board of Chang Gung Memorial Hospital specifically waived the need for consent for these studies. Finally, all primary data were collected according to procedures outlined in epidemiology guidelines that strengthen the reporting of observational studies.

Patients

A total of 187 patients were referred for management of intentional paraquat ingestion between January 2000 and December 2010. Diagnoses of paraquat poisoning were based on clinical history, physical and laboratory examinations (especially urine sodium dithionite reaction), and confirmed via blood test (spectrophotometry; Hitachi, Tokyo, Japan) [18]. The urine

Table 2. AKIN scoring system.

Category	Serum Cr criteria	Urine output criteria
Stage 1	Increase in serum Cr of \geq 0.3 mg/dL or increase to \geq 150% to 200% (1.5 to 2-fold) from baseline	<0.5 mL/kg/h for more than 6 h
Stage 2	Increase in serum Cr to >200% to 300% (>2 to 3-fold) from baseline	<0.5 mL/kg/h for more than 12 h
Stage 3	Increase in serum Cr to >300% (3-fold) from baseline (or serum Cr of \geq 4.0 mg/dL with an acute increase of at least 0.5 mg/dL)	<0.3 mL/kg/h for 24 h or anuria more for 12 h

*Adrenergic agents administered for at least 1 h (doses are given in μ g/kg per minute). Abbreviations. PaO₂: partial pressure of oxygen in arterial blood, FiO₂: fractional inspired oxygen, MAP: mean arterial pressure, epi: epinephrine, norepi: norepinephrine, GCS: Glasgow Coma Scale score, Cr: creatinine, UO: urine output.

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Table 3. Comparison of baseline demographics and clinical characteristics between survivors and non-survivors (n = 187).

Parameter	All (n = 187)	Survivors (n = 86)	Non-survivors (n = 101)	P
Age (year)	42.1±15.4	36.2±12.4	47.1±16.0	<0.001
Gender (male/female)	145/42	65/21	80/21	0.6
Time to hospitalization (days)	13.5±21.1	19.1±26.9	8.7±12.9	0.001
Estimated ingestion amount (mL)	80.9±104.7	56.3±65.7	101.9±125.5	0.002
Blood paraquat level _{first day} (ppm)	4.8±5.6	1.4±2.0	7.6±6.1	<0.001
Cr level (mg/dL) _{first day}	1.6±1.4	1.3±1.2	1.8±1.6	0.001
AST _{first day} level (U/L)	137.5±156.1	54.4±37.3	190.0±179.6	0.005
ALT _{first day} level	126.8±114.1	116.8±62.8	135.5±144.9	0.436
Bilirubin _{first day} level (U/L)	2.7±2.6	1.3±0.7	3.5±3.0	0.001
PaO ₂ _{first day} (mmHg)	84.9±19.0	86.4±12.2	83.7±23.2	0.343
AaDO ₂ _{48-h} (mmHg)	46.6±28.3	29.8±20.1	61.0±26.4	<0.001
PaCO ₂ _{48-h} (mmHg)	33.7±12.4	38.7±12.7	29.4±10.4	<0.001
PaO ₂ _{48-h} (mmHg)	61.3±24.9	72.1±18.5	52.1±25.9	<0.001
HCO ₃ ⁻ _{48-h} (meq/dL)	19.9±6.8	24.8±3.5	15.7±6.1	<0.001
PaO ₂ /FiO ₂ _{first day}	424.6±94.8	431.8±61.0	418.56±116.0	0.322
PaO ₂ /FiO ₂ _{48-h}	291.8±119.0	343.3±88.0	247.1±124.6	<0.001
PLT _{first day} (1000/ μ L)	241.2±67.4	240.2±66.3	242.1±68.5	0.843

Abbreviations. AST: aspartate transaminase, AST_{first day}: AST at admission, ALT_{first day}: alanine transaminase at admission, Bilirubin_{first day}: bilirubin at admission, PaO₂_{first day}: partial pressure of oxygen in arterial blood at admission, PaCO₂_{48-h}: partial pressure of carbon dioxide in the blood 48 h after admission, PLT_{first day}: platelet count at admission, AaDO₂: alveolar-arterial differences in oxygen tension, Cr: creatinine.
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sodium dithionite test was based on the reduction of paraquat by sodium thionite under alkaline conditions to form stable, blue-colored radical ions. Generation of a strong navy or dark blue color generally indicates significant paraquat ingestion and often forebodes a poor prognosis [2–4,7–10].

Inclusion and Exclusion Criteria

Patients were included in this study if they were older than 18 years of age and had urine paraquat tests that showed dark or navy blue coloring (>5 ppm). Patients were excluded from the study if the paraquat exposure was dermal [19] or intravascular [20]. They were also excluded if they did not have detectable paraquat levels in their urine and blood or if they had major comorbidities, such as cancer or heart, lung, renal, or liver diseases. The diagnoses of major comorbidities were based on detailed clinical, physical, and laboratory examinations. Patients with pre-existing serum creatinine levels >1.4 mg/dL or alanine aminotransferase (ALT) levels >36 mg/dL or total bilirubin levels >3 mg/dL were also excluded.

SOFA and AKIN Scores

The following data were prospectively collected: baseline demographics; SOFA [16] and AKIN score [17] 48 h after admission (SOFA_{48-h} and AKIN_{48-h}), duration of hospitalization, and outcomes. As shown in Table 1 and 2, the SOFA score [16] consists of six variables, each representing an organ system. Each organ system is assigned a point value from 0 (normal) to 4 (high degree of dysfunction/failure). The AKIN criteria [17] classify acute kidney injury into three stages of severity (stages 1, 2 and 3).

Protocol for Paraquat Detoxification

The protocol includes gastric lavage with a large amount of normal saline followed by active charcoal administration, charcoal hemoperfusion, pulse therapies of cyclophosphamide and methylprednisolone followed by dexamethasone therapy, as well as repeated glucocorticoid and cyclophosphamide pulse therapies in case of hypoxemia [2–4,7–10].

Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation. All variables were tested for normal distribution using the Kolmogorov–Smirnov test. The Student's *t* test was used to

Table 4. Comparison of AKIN and SOFA scores between survivors and non-survivors (n = 187).

	All patients (n = 187)	Survivors (n = 86)	Non-survivors (n = 101)	P value
AKIN _{48-h} (stage 0/1/2/3)	99/48/16/24	60/17/4/5	39/31/12/19	<0.001
SOFA _{48-h}	3±2	2±2	4±2	<0.001
mSOFA	4±2	2±2	5±2	<0.001

Abbreviations. AKIN: acute kidney injury network, SOFA: sequential organ failure assessment, mSOFA: modified sequential organ failure assessment.
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Table 5. Comparison of calibration and discrimination power of AKIN and SOFA scoring methods for predicting mortality (n = 187).

	Calibration			Discrimination		
	Hosmer – Lemeshow goodness of fit	df	P	AUROC ± SE	95% CI	P
AKIN _{48-h}	0.0	2	1.0	0.671±0.039	0.594–0.748	<0.001
SOFA _{48-h}	5.582	5	0.349	0.795±0.033	0.31–0.860	<0.001
mSOFA _{48-h}	0.0	6	1.0	0.848±0.029	0.791–0.904	<0.001

Abbreviations. *df*: degree of freedom, SE: standard error, CI: confidence interval, AKIN: acute kidney injury network, SOFA: sequential organ failure assessment, mSOFA: modified sequential organ failure assessment.

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compare the means of continuous variables and normally distributed data. Otherwise, the Mann–Whitney *U* test was used for non-normally distributed data. Categorical data were analyzed using a chi-square test. Finally, risk factors were assessed by univariate Cox regression analysis, and variables that were statistically significant ($P < 0.05$) were included in a multivariate analysis by applying a multiple Cox regression based on forward elimination of data. Calibration was assessed using the Hosmer–Lemeshow goodness of fit test to compare the number of observed and predicted deaths in risk groups for the entire range of death probabilities. Discrimination was assessed by AUROC. The AUROCs were compared using a non-parametric approach. AUROC analyses were also used to calculate cutoff values, sensitivity, specificity, and overall correctness. Finally, the cutoff points were calculated by acquiring the best Youden index (sensitivity+specificity - 1). The cumulative survival curves as a function of time were generated using the Kaplan–Meier approach and compared by log-rank test. All statistical tests were

two-tailed, with *P* values < 0.05 being considered as statistically significant. Data were analyzed using SPSS 12.0 software for Windows (SPSS, Inc, Chicago, III).

Results

Subject Characteristics

Baseline demographics and clinical characteristics of survivors and non-survivors are shown in Table 3 and 4. The mean age of the patients was 42.1 ± 15.4 years, with 145 (77.5%) being men and 42 (22.5%) women. Overall hospital mortality for the entire population was 54% (101/187). Non-survivors were significantly older, hospitalized more quickly, and had a higher mean ingestion amount of paraquat, blood levels of paraquat, creatinine (Cr), alanine transaminase (AST), and bilirubin upon admission. They also had higher alveolar-arterial differences in oxygen tension ($AaDO_2$) 48 h after admission, and had lower partial pressures of carbon dioxide in arterial blood ($PaCO_2$), PaO_2 , HCO_3^- , and

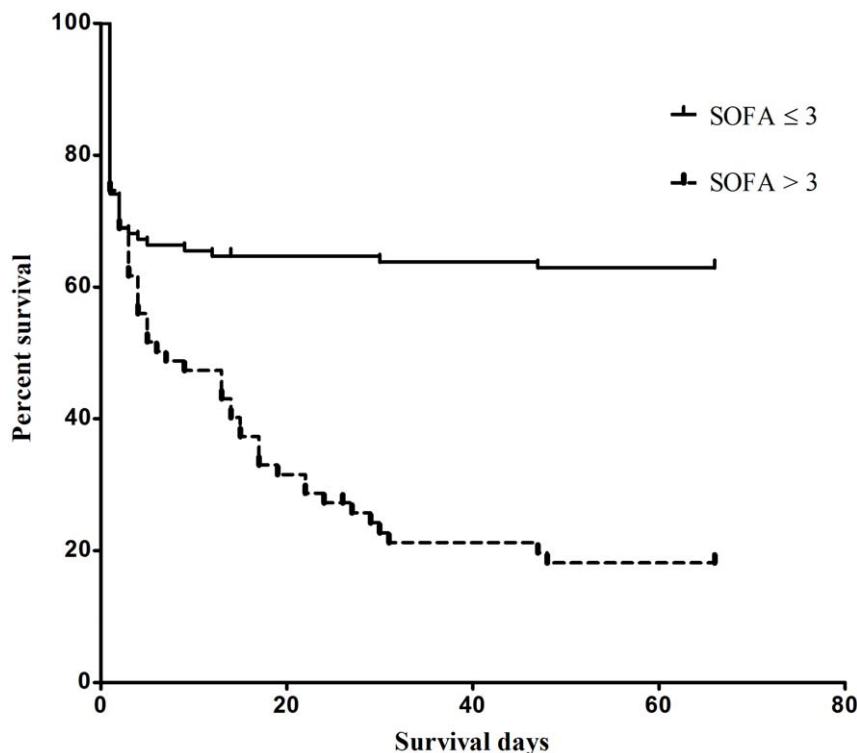


Figure 1. Cumulative survival rates based on SOFA_{48-h} score. Abbreviation. SOFA: sequential organ failure assessment.
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Table 6. Analysis of mortality using univariate and multivariate logistic regression models (n = 187).

Parameter	β Coefficient	SE	Odds ratio (95% CI)	P
<i>Univariate</i>				
Age (year)	0.032	0.006	1.003 (1.020–1.045)	<0.001
Time to hospitalization (days)	−0.020	0.007	0.980 (0.967–0.994)	0.004
Estimated ingestion amount (mL)	0.002	0.001	1.002 (1.001–1.004)	<0.001
Blood paraquat level _{first day} (ppm)	0.133	0.015	1.143 (1.109–1.177)	<0.001
AaDO _{2 first day} (mmHg)	0.019	0.006	1.020 (1.007–1.032)	0.002
PH _{48-h}	−3.400	0.495	0.033 (0.013–0.088)	<0.001
PaO _{2 48-h} (mmHg)	−0.019	0.004	0.981 (0.972–0.989)	<0.001
PaCO _{2 48-h} (mmHg)	−0.067	0.012	0.935 (0.913–0.958)	<0.001
HCO _{3 48-h} (meq/dL)	−0.146	0.015	0.864 (0.839–0.890)	<0.001
AaDO _{2 48-h} (mmHg)	0.022	0.004	1.022 (1.015–1.030)	<0.001
eGFR _{first day} (mL/min)	−0.012	0.003	0.988 (0.983–0.994)	<0.001
AKIN _{48-h}	0.246	0.084	1.279 (1.086–1.507)	0.003
SOFA _{48-h}	0.193	0.036	1.213 (1.130–1.303)	<0.001
<i>Multivariate</i>				
Age (year)	0.013	0.007	1.013 (1.000–1.026)	0.049
Time to hospitalization (days)	−0.035	0.010	0.965 (0.947–0.984)	<0.001
Blood paraquat level _{first day} (ppm)	0.098	0.017	1.103 (1.066–1.140)	<0.001
eGFR _{first day} (mL/min)	−0.018	0.004	0.982 (0.974–0.991)	<0.001
SOFA _{48-h}	0.101	0.042	1.106 (1.019–1.201)	0.016

Abbreviations: AKIN: acute kidney injury network, SOFA: sequential organ failure assessment, SE: standard error, CI: confidence interval, AaDO₂: alveolar–arterial differences in oxygen tension, PaO_{2 48-h}: partial pressure of oxygen in arterial blood 48 h after admission, PaCO_{2 48-h}: partial pressure of carbon dioxide in the blood 48 h after admission, eGFR_{first day}: estimated glomerular filtration rate at admission. doi:10.1371/journal.pone.0051743.t006

PaO₂/FiO₂ in their arterial blood at the same time point. Survivors and non-survivors differed significantly in their SOFA_{48-h} scores (2±2 versus 4±2, $P<0.001$) (Table 4). Using AKIN_{48-h} classification, the in-hospital mortality was found to be 39.4% (39/99) for stage-0, 64.6% (31/48) for stage-1, 75.0% (12/16) for stage-2, and 79.2% (19/24) for stage-3 patients ($P<0.001$).

Calibration, Discrimination, and Correlation for SOFA and AKIN Scoring Systems

Calibration of SOFA_{48-h} scores was as carried out as follows: Hosmer–Lemeshow; $X^2_2 = 5.582$, $P = 1.0$ (Table 5). AKIN_{48-h} scores also had good calibration, as estimated by the Hosmer–Lemeshow goodness-of-fit test. Table 3 shows the Goodness of Fit for the predicted mortality risk and the predictive accuracy of SOFA_{48-h} and AKIN_{48-h} scores. Table 4 shows the discrimination power of SOFA_{48-h} and AKIN_{48-h} scores. AUROC analysis found that SOFA_{48-h} scores had better discriminatory power for prediction of mortality.

Clinical Predictors of Mortality

Univariate logistic regression identified several clinical predictors that were significantly associated with mortality (Table 6). Simple linear regression indicated co-linearity between the partial pressure of oxygen in arterial blood 48 h after admission (PaO_{2 48-h}) and SOFA_{48-h} score, and arterial-alveolar differences in oxygen tension at 48 h after admission (AaDO_{2 48-h}) and SOFA_{48-h} score. Therefore, PaO_{2 48-h} and AaDO_{2 48-h} were not introduced into the multivariate logistic regression analyses. Multivariate logistic regression analyses identified age, time to hospitalization, blood paraquat level, eGFR_{first day}, and SOFA_{48-h} score were independent predictors of mortality. Notably, the AKIN_{48-h} score was no longer a significant predictor using multivariate analysis. Mortality, sensitivity, specificity, and overall correctness of SOFA_{48-h} and AKIN_{48-h} scores were calculated to determine their predictive value (Table 7). The cumulative survival rates differed significantly ($P<0.001$) between patients with SOFA_{48-h} scores <3 and SOFA_{48-h} scores ≥ 3 (Fig. 1).

Table 7. Prediction of hospital mortality (n = 187).

Predictive factors	Cutoff point	Youden index	Sensitivity %	Specificity %	Overall correctness %
AKIN _{48-h}	1	0.312	61.4	69.8	54.0
SOFA _{48-h}	3	0.470	77.2	69.8	73.8
mSOFA _{48-h}	4	0.559	73.3	82.6	77.5

Abbreviations: AKIN: acute kidney injury network, SOFA: sequential organ failure assessment, mSOFA: modified sequential organ failure assessment. doi:10.1371/journal.pone.0051743.t007

mSOFA Score

In the multivariate logistic regression model, it was revealed that blood paraquat level was a significant predictor of mortality after intentional paraquat ingestion. Therefore, we recruited this new variable to the original SOFA version, resulting in an mSOFA. Since the mortality prediction of blood paraquat level had a cutoff point of 1.83 ppm ($P < 0.001$), in the mSOFA system we assigned patients with blood paraquat levels ≥ 1.83 ppm one point and those with blood paraquat levels < 1.83 ppm zero points. Notably, we found that the mSOFA_{48-h} displayed better discriminatory power (mSOFA_{48-h} vs. SOFA_{48-h}, 0.848 ± 0.029 vs. 0.795 ± 0.033 , $P < 0.0001$) (Table 5) and better sensitivity, specificity, and overall correctness than the original SOFA_{48-h} scores. The cumulative survival rates also differed significantly ($P < 0.001$) between patients with mSOFA scores < 4 and SOFA_{48-h} scores ≥ 4 . Finally, the survivors and non-survivors differed significantly in their mSOFA scores (2 ± 2 versus 5 ± 2 , $P < 0.001$) (Table 4). Hence, the mSOFA score was a better predictor of death during hospitalization than the original SOFA score.

Discussion

In this study, SOFA_{48-h} scores, age, time to hospitalization, blood paraquat levels and eGFR_{first day} were found to be significant predictors of mortality after paraquat poisoning. Many clinical parameters and scoring systems have previously been proposed as mortality predictors for patients with paraquat intoxication [13,21–24]. Models based on SOFA scores employed at admission performed only slightly worse than APACHE II/III scores and were comparable to SAPS II models in predicting patient mortality in general medical and/or surgical ICUs. Models with sequential SOFA scores appear to have comparable performances to other organ failure scores. Cholongitas *et al.* [25] demonstrated that SOFA scores had the best discriminative ability (AUC = 0.79) when compared to APACHE II scores, Model for End-Stage Liver Disease (MELD) scores and King's College Hospital (KCH) scores. Craig *et al.* [26] also showed that SOFA scores > 7 during the first 96 h post-overdose predicted death/transplantation with a sensitivity of 95.0 (95% CI, 78.5–99.1) and a specificity of 70.5 (95% CI, 66.3–71.6). Apart from these two reports, there have been no other similar studies using SOFA scores to predict mortality for patients with drug overdoses or poisoning, and they have never been used to assess patient outcomes after paraquat intoxication. Therefore, this appears to be the first report demonstrating that SOFA scores > 3 are a poor prognosticator for acute paraquat poisoning. Chang *et al.* [21] noted that APACHE II scores > 9 had a sensitivity of 64% and a specificity of 88% in predicting the 30-day mortality in acute paraquat-poisoned patients [21]. However, the APACHE II scores do not include indicators of liver damage, which is also a major sequela of paraquat poisoning [10]. The SOFA system is a simple, easily performed, inexpensive, and reproducible scoring method. It is suitable for use in typical hospital wards, where most paraquat patients are admitted. Most importantly, SOFA scores also include parameters of major target organs, such as lung, liver, and kidney.

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The scoring system applied in this study showed that SOFA scores > 3 predict a poorer prognosis compared to those ≤ 3 (Table 7 and Fig. 1). SOFA scores can therefore assist in predicting the prognosis for paraquat patients and may also assist in the subsequent decision-making processes [2].

Baseline eGFR was also found to be a predictor of mortality in the present study. The AKIN scores were found to be a predictor of mortality by univariate Cox regression analysis, but not after incorporation into a multivariate Cox regression model. At high doses, paraquat can cause acute tubular necrosis, leading to renal failure. As a result, renal excretion of paraquat is markedly reduced, resulting in higher serum concentrations and increased paraquat accumulation in organs, such as the lung and liver. Although renal damage might be reversible if these patients ingested < 40 mg/kg paraquat [27], mortality may still occur from delayed pulmonary fibrosis and hypoxemia. Serum paraquat levels were found to be negatively correlated with eGFR in this study using a univariate linear regression model ($P = 0.012$). Lower eGFR in the first 24 h after admission may reflect acute paraquat-induced damage to proximal renal epithelial cells, where active tubular transport occurs [28,29]. Alternatively, it could reflect a pre-existing reduced renal reserve, which would lead to decreased paraquat elimination and higher paraquat levels in organs and serum. Nevertheless, minor changes in eGFR may not result in upgrading of AKIN scores [17].

Compatible with previous reports, we found that blood paraquat level was the most consistent predictor of mortality after intoxication [15,30,31]. However, serum paraquat levels decrease rapidly within the first few hours after ingestion and the time interval between ingestion and serum paraquat measurements is variable between patients. Therefore, the relationship between mortality and serum paraquat levels may be unreliable. Nevertheless, adding serum paraquat level at admission to the original SOFA score can significantly improve the mortality prediction power when assessing patients. Therefore, the mSOFA reflects the key role of the serum paraquat level, which is not included in the original SOFA score. In addition, the increased mortality that was observed for patients who present more quickly at the hospital might be attributable to the fact that patients who ingest more paraquat tend to seek medical attention faster.

In summary, our data demonstrate that either SOFA or mSOFA scores, which are based on the extent of organ function or rate of organ failure, can help to predict mortality after intentional paraquat poisoning. Nevertheless, the retrospective nature of the study, the small patient sample, and the short follow-up time limit the certainty of our conclusions.

Author Contributions

Conceived and designed the experiments: C-HW T-HY. Analyzed the data: C-HW. Wrote the paper: C-HW C-CH. Performed the study: C-HW. Supervised the study: J-LL. Contributed to patient care and management: W-HH C-HW J-LL D-TL-T C-WH T-HY. Helped in data analysis and manuscript writing: T-HY.

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