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Platelet–lymphocyte ratio is not a prognostic predictor for acute paraquat-intoxicated patients

A retrospective analysis

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Abstract

This study aimed to investigate the prognostic predictive value of the platelet–lymphocyte ratio (PLR) in patients with acute paraquat (PQ) intoxication.

A total of 107 patients with acute PQ intoxication via oral ingestion were admitted in Cangzhou Central Hospital from May 2012 to September 2018. Valuable detection indices were screened out by using Cox proportional hazard regression and receiver operating characteristic (ROC) curve analyses, and their diagnostic efficiency was evaluated by using Kaplan–Meier curve.

The 90-day mortality was 58.9% (63/107). The Kaplan–Meier curve showed that PLR was not associated with 90-day survival (log-rank test; $P = .661$). In Cox proportional hazard regression analyses, PLR was not an independent risk factor. Meanwhile, the ROC curves showed that PLR had an AUC value of 0.569 (95% confidence interval: 0.459–0.679, $P = .227$) in predicting 90-day survival.

PLR is not a prognostic predictor for patients with acute PQ intoxication.

Abbreviations: PLR = platelet–lymphocyte ratio, PQ = paraquat.

Keywords: paraquat, platelet–lymphocyte ratio, prognosis

1. Introduction

Paraquat (PQ; 1,1′-dimethyl-4,4′-bipyridinium dichloride) is a widely applied contact herbicide that is highly poisonous. The lethal dose of orally administered PQ is approximately 20 mL of a 20% preparation, and the mortality rate is positively related to PQ intake.[1,2] The current treatment regimens for PQ are mainly early gastric lavage, oral administration of cathartic agents, oral administration of activated carbon and increased infusion quantity, excretion of PQ accelerated by diuretics, early hemoperfusion, and the application of immunosuppressive agents and conventional antioxidants. Nevertheless, the usefulness of these approaches remains indeterminate, and the mortality rate of PQ poisoning is as high as 60% to 80%.[3–6]

A reliable predictor of prognosis may guide the treatment and future clinical research on antidotes and other therapies. Many studies[7–12] have evaluated the outcome indicators of PQ intoxication, but no consensus exists on a practical indicator. Plasma PQ concentration is the most reliable marker for predicting death as a result of PQ poisoning. However, many hospitals do not have the necessary facilities to measure serum PQ levels. The platelet–lymphocyte ratio (PLR) can be calculated using only blood-routine tests, which have the advantages of low cost, stability, and repeatability. Thus, PLR is suitable for use in primary hospitals where most patients with PQ intoxication are admitted. Recently, the PLR has been used as a prognostic marker in patients with cancer,[13,14] chronic obstructive pulmonary disease,[15] acute coronary syndrome,[16] and diabetic peripheral neuropathy.[17] Furthermore, higher values of PLR are associated with unfavorable clinical features in patients with pesticide,[18] carbon monoxide,[19,20] and snakebite.[21] However, the prognostic significance of the PLR has not been previously studied in patients with acute PQ intoxication. Thus, we performed this retrospective study to investigate the prognostic predictive value of the PLR for patients with such condition.

2. Methods

2.1. Ethics and consent

This study was approved by the Medical Ethics Committee of Cangzhou Central Hospital (No. 2017-090-01) and conducted in accordance with the Declaration of Helsinki. Because this study was a retrospective investigation of existing data, a written informed consent from each patient was not required. All individual information of patients with PQ intoxication were securely protected and only available to the investigators.

2.2. Patients

This retrospective cohort study included 107 patients with PQ poisoning and was conducted in the emergency department of

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Cangzhou Central Hospital from May 2012 to September 2018. A presumptive diagnosis of PQ poisoning was based on exposure history, clinical effects, and physical and laboratory examinations, and it was confirmed via plasma PQ test. Blood samples for the measurement of plasma PQ concentration were collected as soon as patients arrived at the emergency department. PQ levels were measured by using high-performance liquid chromatography. In brief, the treatment principle included the following:

(1) extracorporeal elimination,
(2) intravenous antioxidant administration,
(3) diuresis with a fluid, and
(4) immunosuppressive therapy.

The subject selection criteria included the following:

(1) aged >14,
(2) experienced oral PQ poisoning, and
(3) admitted to hospital within 12 hours after PQ ingestion.

Meanwhile, exclusion criteria were as follows:

(1) no follow-up checkup,
(2) unknown time of PQ exposure,
(3) pregnancy,
(4) infection,
(5) immunosuppressive therapy,
(6) blood systemic diseases,
(7) cancer,
(8) chronic obstructive pulmonary disease,
(9) acute coronary syndrome, or
(10) diabetic peripheral neuropathy.

2.3. Data collection

Patient data (including the following: sex and age of patients, heart rate, mean arterial pressure, respiration, hypertension, diabetes, cerebral stroke, coronary heart disease, chronic bronchitis, mental disease, acute physiology and chronic health evaluation II score, sequential organ failure assessment score, time interval from PQ ingestion to gastric lavage, alveolar oxygen partial pressure, platelet, lymphocyte, creatinine, alanine aminotransferase, and plasma PQ concentration upon admission) were collected by 2 clinicians on the basis of a unified form. PLR was defined as the absolute PLT count divided by the absolute lymphocyte count. Receiver operating characteristic (ROC) curve analysis was used to determine prediction points of PLR levels for mortality.[7] Patient with PLR values greater and less than the determined thresholds were classified as high risk and low risk, respectively.[7] The primary outcome measure was the occurrence of death within 90 days after PQ ingestion. Survival time was identified from medical records or telephone follow-up.

2.4. Statistical analysis

All analyses were performed using SPSS (v. 13.0, SPSS Inc, IBM, Chicago, IL). Student *t* test or Wilcoxon rank-sum test was applied on the numerical data among groups, whereas chi-square test was used for the categorical data. Valuable detection indices were screened out by Cox proportional hazard regression and ROC curve analyses, and their diagnostic efficiency was evaluated by Kaplan–Meier curve. $P < .05$ indicated a statistically significant difference.

3. Results

3.1. Patient characteristics

We enrolled 107 patients with a mean age of 39.9 ± 16.4 years. Male patients (43.0%) were higher in number than females. Within the 90-day follow-up period after poisoning, 63 patients succumbed to poisoning, and 44 patients survived; the mortality rate was 58.9%. Demographic characteristics and baseline laboratory results for the survival and mortality groups of patients are summarized in Table 1. No significant difference in NLR was detected between the survival group and mortality group ($P > .05$).

3.2. Kaplan–Meier survival analysis and Cox proportional hazard regression analyses

The Kaplan–Meier survival curves (Fig. 1) showed that PLR was not associated with 90-day survival (log-rank test; $P = .661$). Meanwhile, Cox proportional hazard regression analyses showed that PLR was not an independent risk factor (Table 2).

3.3. ROC curve analysis for 90-day mortality

The ROC curves of PLR showed an AUC value of 0.569 (95% confidence interval: 0.459–0.679, $P = .227$; Fig. 2), suggesting that PLR was not a valuable predictor for PQ poisoning.

4. Discussion

Self-poisoning with pesticides is a major public health problem in developing countries, with an estimated 300,000 deaths occurring in the Asia–Pacific region alone annually.[22,23]

Table 1

General characteristics upon arrival between survival and mortality groups.

	Mortality group (n = 63)	Survival group (n = 44)	*P*
Age, yr	42.00 (32.00)	33.00 (21.00)	.074
Gender (male/female)	26/37	20/24	.667
Hear rate, bpm	80.00 (23.00)	85.00 (19.75)	.664
Mean arterial pressure, mm Hg	93.33 (13.33)	96.67 (11.17)	.358
Respiration rate, bpm	18.00 (3.00)	18.00 (3.75)	.408
Time from ingestion to gastric lavage, h	1.00 (1.00)	1.00 (1.38)	.554
Alanine aminotransferase (ALT), μ/L	32.50 (16.70)	26.80 (9.78)	.013
Creatinine, mg/dL	104.00 (69.00)	62.00 (21.50)	<.001
Alveolar oxygen partial pressure (PaO_2), mm Hg	89.83 ± 10.59	93.57 ± 9.26	.061
Plasma paraquat concentration, ng/mL	4.20 (8.80)	0.30 (0.85)	<.001
PLR	200.67 (147.02)	170.83 (101.91)	.227
APACHE-II score	7.00 (6.00)	3.00 (3.75)	<.001
SOFA score	1.00 (1.00)	0.00 (0.00)	<.001
Hypertension (yes/no)	11/52	3/41	.108
Diabetes (yes/no)	1/62	1/43	.797
Cerebral stroke (yes/no)	7/56	2/42	.229
Coronary heart disease (yes/no)	1/62	1/43	.797
Chronic bronchitis (yes/no)	0/63	1/43	.229
Mental disease (yes/no)	14/49	3/40	.036

APACHE-II = acute physiology and chronic health evaluation II score, PLR = platelet–lymphocyte ratio, SOFA = sequential organ failure assessment score.

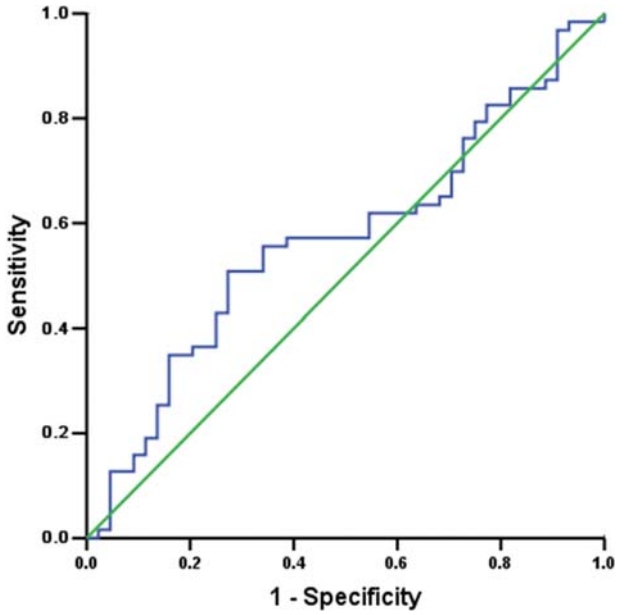

Figure 1. Area under the receiver operating characteristic curve analysis. PLR = platelet–lymphocyte ratio, PQ = paraquat.

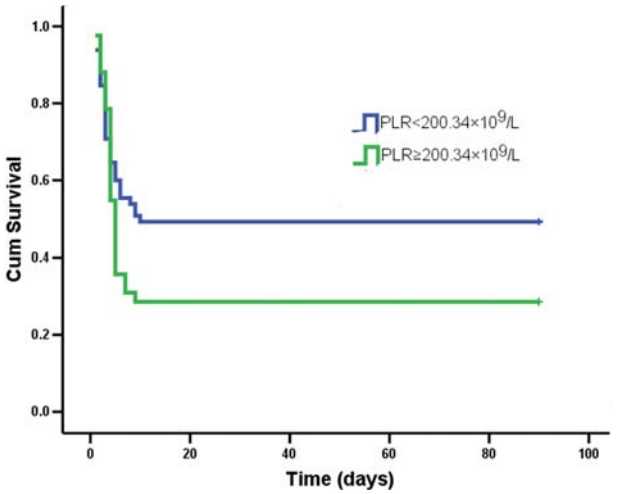

Figure 2. Kaplan–Meier analysis of survival curves for the groups according to the PLR level. PLR = platelet–lymphocyte ratio.

However, the organophosphate poisoning still accounts for the majority of hospital admissions. The fatality of PQ poisoning cases has been an emerging concern. Intentional oral ingestion of even small amounts of PQ can cause severe and irreversible systemic damage that is refractory to any known treatment.

The lung is a major target organ in PQ poisoning, characterized by edema, hemorrhage, interstitial inflammation, and bronchial epithelial cell proliferation.[24] The toxicity of PQ is related to its rapid reduction and subsequent reoxidation, thereby producing reactive oxygen species (ROS). The accumulation of ROS and especially toxic free radicals in various organs can result in PQ poisoning.[25]

In the present study, Cox proportional hazard regression analyses indicated that plasma PQ concentration and creatinine were independent risk factors. Our study agrees well with previous studies that elevated plasma PQ concentration[1,26,27] and creatinine[28,29] are significant predictors of mortality in PQ poisoning. To the best of our knowledge, the present study is the first analysis of the association of PLR with outcomes of PQ poisoning, and our study suggests that PLR is not a prognostic predictor for patients with acute PQ intoxication.

However, this study has some limitations. First, this study is a retrospective study; thus, it has inherent limitations. Second, considering the nature of a single-center study, its external validity is limited. Finally, the authors acknowledged that the study is limited by its retrospective design and potential recall bias, with an inability to recall the accurate death time.

In conclusion, PLR is not a prognostic predictor for patients with acute PQ intoxication. However, well-designed, prospective cohort studies are needed to validate our findings.

Author contributions

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Writing – review & editing: Yong Li.

Table 2

Cox regression model.

	Univariate COX model HR (95% CI)	*P*	Multivariate COX model HR (95% CI)	*P*
Age, yr	1.014 (0.999–1.028)	.061	N/A	
Gender (male/female)	0.869 (0.525–1.436)	.585	N/A	
Time from ingestion to gastric lavage	1.016 (0.856–1.207)	.854	N/A	
Plasma paraquat concentration	1.068 (1.049–1.087)	<.001	1.027 (1.005–1.050)	.017
Alanine aminotransferase (ALT)	1.019 (1.002–1.036)	.025	1.013 (0.994–1.032)	.188
Creatinine	1.019 (1.014–1.024)	<.001	1.016 (1.009–1.022)	<.001
Alveolar oxygen partial pressure (PaO_2)	0.979 (0.954–1.005)	.119	N/A	
Mental disease	2.418 (1.326–4.410)	0.004	2.081 (1.064–4.072)	.032
PLR	1.001 (0.999–1.003)	.454	N/A	

N/A = not applicable, PLR = platelet–lymphocyte ratio.

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