Relationship between platelet/lymphocyte ratio and prognosis of patients with septic acute kidney injury: A pilot study

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Abstract

Background: To explore the potential role of the platelet/lymphocyte ratio (PLR) as a prognostic marker in septic patients with acute kidney injury (AKI) and to provide theoretical evidence for the epidemiological study of the prognosis of patients with septic AKI in its early stage.

Methods: A pilot study was conducted. A logistic regression analysis was conducted to screen the risk factors, and the selected factors were performed using multiple logistic regression analysis; a Receiver Operating Characteristic curve was used to determine the optimal cutoff value of the PLR and then to calculate the sensitivity and specificity of the PLR ratio.

Results: Mechanical ventilation, platelet count, PLR, and arterial blood lactate concentration have a correlation with sepsis ($p < 0.05$). An elevated PLR is significantly associated with a worse prognosis of sepsis-induced AKI (higher mortality).

Conclusion: The PLR might be an effective factor in predicting a worse prognosis of septic AKI patients.

Keywords: Acute kidney injury; Platelet/Lymphocyte Ratio; Sepsis

1. INTRODUCTION

Patients in the intensive care unit (ICU) generally have high morbidity and mortality rates stemming from acute kidney injury (AKI); here, of all critically ill patients, about 50% with sepsis developed AKI.[1] Meanwhile, the patients with septic AKI had a worse prognosis compared with those without.[2–4] According to the literature, the 1-year mortality rate in patients with septic AKI is as high as 60%–70%.[5–7] With more attention being given to the high incidence of septic AKI and its adverse prognosis, more and more efforts have been carried out to seek meaningful clinical biomarkers that are highly associated with the prognosis of septic AKI. Several biomarkers have been assessed with a view to assisting the diagnosis and the prognosis but, so far, none have been of sufficient accuracy to be used in routine practice. The platelet/lymphocyte ratio (PLR) is a new nonspecific inflammatory marker that has been widely studied recently because of its easy detection.[8] Research on the respiratory system, the digestive system, and the reproductive system has shown that the PLR is closely related to the diagnosis, disease monitoring, and prognosis of the tumor.[9,10] PLR elevation is usually associated with a poor prognosis in patients affected by tumors. In addition, an abnormally high level of PLR in acute appendicitis,[11] allergic rhinitis,[12] chronic obstructive pulmonary disease,[13] systemic lupus erythematosus,[14] and chronic hepatitis C virus[15] shows the practical application value of the PLR in the evaluation of various diseases. However, there is little research on the contribution of the PLR to the prognosis of patients with AKI, and the correlation between the PLR and prognosis of patients with septic AKI has not been examined to date.[16] Therefore, new evidence of the PLR is needed to determine if there is a probable association with the prognosis of patients with septic AKI. Our research aims to investigate the clinical value of the PLR in the prognosis of septic AKI, hence providing some theoretical reference for the epidemiological prediction study of septic AKI.

2. METHODS

A pilot study was applied in the current study.

2.1. Compliance with ethical standards

The entire procedure was approved by the medical ethics committee of Lanzhou University Second Hospital, Number: 2018A-042.

The authors declare that they have no competing interests.

This is a pilot study, the data were extracted from our ongoing study, which named "The Epidemiology of Acute kidney injury in critically ill patients in Gansu Province" (EACG study), and this study was already registered in Chinese Clinical Trail Register, the number is CHiCTR1800016945. Our submission is a reanalysis of the EACG study. Patients and public were not involved. No additional burden for patients. And the data are taken care by specially assigned person, so that to keep the data safely.

2.2. Enrollment

We successively included patients with sepsis who were in the ICU of Lanzhou University Second Hospital from January 1, 2015 to January 1, 2017. The data were collected when the

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patients were at the ICU admission. The exclusion criteria were the following: (1) the patient being less than 18 years old, (2) patients with chronic renal dysfunction (any stage), (3) patients who have received renal transplantation before admission, and (4) patients with a hematological disease.

2.3. Sepsis and AKI assessment

The diagnosis of sepsis is consistent with the diagnostic criteria of the 2015 International Sepsis Conference (Sepsis 3.0), that is, there is a definite or suspicious infective focus, and the qSOFA score is greater than or equal to 2 (score standard: the systolic pressure ≤ 100 mm Hg, 1 point; Glasgow Coma Scale ≤ 13, 1 point; respiratory rate is ≥ 22 times per minute, 1 point). In the current study, the subjects were divided into either a sepsis non-AKI group or septic AKI group by following the Kidney Disease Improving Global Outcomes (KDIGO) diagnosis standard. Depending on whether the patient survived 28 days after admission, the septic AKI group was categorized into either the septic AKI survival group or septic AKI nonsurvival group.

2.4. Data collection

Data including patients' basal information (age, sex, body temperature, respiratory rate, systolic pressure, diastolic pressure, acute physiology and chronic health evaluation II score, urine output, causes of sepsis, received continuous renal replacement treatment (CRRT) or not, and mechanical ventilation) and biochemical indicators (leukocyte count, lymphocyte count, platelet count, platelet/lymphocyte value, serum creatinine, blood urea nitrogen concentration, arterial blood lactate concentration, and procalcitonin concentration) were collected at day 1 of ICU admission and entered in an Excel form by two investigators.

2.5. Statistics

SPSS version 21.0 was used for data analysis. A logistic regression analysis was conducted to screen the risk factors, and the selected factors were performed using a multiple logistic regression analysis through which we acquired the equation and plotted it on an receiver characteristic operator (ROC) curve. The ROC curve was used to determine the optimal cutoff value of PLR, and after then to calculate the sensitivity and specificity of the PLR. Regarding the prediction of prognosis in patients with septic AKI, the differences were considered statistically significant whenever $p < 0.05$.

3. RESULTS

We collected a total of 158 clinical cases consecutively (see Fig. 1), excluding 38 cases that did not meet the inclusion criteria; among these exclusions, there were 20 cases with chronic renal disorder, 3 cases with hematological disease, 12 cases admitted in the ICU for less than 48 hours, and 3 cases of incomplete basic information. Eventually, 120 sepsis patients were enrolled in the current study. Among them, 67 cases were septic AKI patients. The cases were then divided into survival group (26 cases) or nonsurvival group (41 cases). The incidence of septic AKI was 55.8% throughout the whole study. In the septic AKI patients, only 26 patients survived from septic AKI, with the mortality rate of septic AKI being 61.2%. Of all the 67 patients in AKI group, 9 patients were not received CRRT, and there was no statistical significance between the survival group and the nonsurvival group ($p = 0.78$). Here, multiple indicators which were collected at day 1 of ICU admission were showed in Table 1. To identify which indicators play a crucial role in the kidney impairment stage of sepsis. A univariate analysis was performed using the parameters in Table 1 as the independent variables with survival/death (survival 0, death 1) as

the dependent variables. The results indicated that regarding mechanical ventilation, platelet count, the PLR, and the concentration of arterial blood lactate showed correlation with death, the difference was statistically significant ($p < 0.05$). (Table 2) After this, these four indicators were applied for multivariate logistic regression analysis with survival/death (survival 0, death 1) as the dependent variables. Our data showed that the prognosis of patients with septic AKI was highly related to factors such as mechanical ventilation, platelet count, the PLR, and arterial blood lactate concentration (Table 3). In addition, with a Spearman correlation analysis run on the PLR, mechanical ventilation, platelet count, arterial blood lactate concentration, and the nonsurvival group of AKI with sepsis, the correlation coefficient was −0.225, $p < 0.05$ (the PLR); 0.08, $p = 0.385$ (mechanical ventilation); −0.219, $p = 0.016$ (platelet count); 0.318, $p = 0.000$ (arterial blood lactate concentration) (Table 4). After this analysis, we plotted the ROC curve for the PLR and obtained an Area Under the Receiver Operating Characteristic curve (AUROC) value of 0.726 (Fig. 2). All of the above evidence shows the guidance value of the PLR in the prediction of prognosis (survival or death) for patients with septic AKI, the optimal cutoff value for the PLR to determine the prognosis being 120, the sensitivity of the cutoff value being 70.7%, and the specificity being 65.4%.

4. DISCUSSION

AKI is a serious complication that commonly occurs in the ICU and tends to produce a longer hospital stay and the use of excess medical resources; even more concerning, there is a higher rate of mortality when AKI is present.[17] However, the related literature has reported that more than 50% of AKI was associated with sepsis in critically ill patients[18] and that the incidence of AKI combined with sepsis is increasing year by year. Therefore, early identification of septic AKI and a proper intervention may reduce the suffering of patients and improve survival rate. In the current study, sepsis patients were divided into septic AKI and sepsis non-AKI groups. After a statistical analysis of the basic indexes between the two groups, we found that respiratory rate, platelet count, the PLR, blood urea nitrogen, and serum creatinine concentration for the two groups were statistically significant.

Several recent studies[15,19] have shown that the PLR is associated with the prognosis of inflammatory diseases such as tumors and coronary thrombosis, suggesting that the PLR could reflect the state of inflammation in the body. Accordingly, we hypothesized that the PLR may be elevated in AKI nonsurvival patients. As expected, in the current study, the mean PLR of the nonsurvival group of septic AKI was significantly higher than that of the survival group, and after conducting a Spearman analysis, the PLR was negatively correlated with 28-day mortality in patients with septic AKI. This means that in patients with sepsis complicated with AKI, high PLR values may predict a poor prognosis. In the acute inflammatory phase, inflammatory mediators such as platelets are overactivated, and lymphocytes appear to be apoptotic; the change in the PLR actually reflects the imbalance between the two cells. In this situation, a rise in the PLR indicates an imbalance between proinflammatory and anti-inflammatory responses in the patient's body. This imbalance of immune responses leads to multiple organ failure and causes metabolism disorder, immunodeficiency, and a mismatch between oxygen supply and demand, which ultimately leads to death.

Also, mechanical ventilation was shown to have adverse effects on the prognosis of patients with septic AKI. Here, patients who required mechanical ventilation always had a worse condition, and in addition, mechanical ventilation might change the hemodynamic state of the kidneys. Additionally, mechanical ventilation
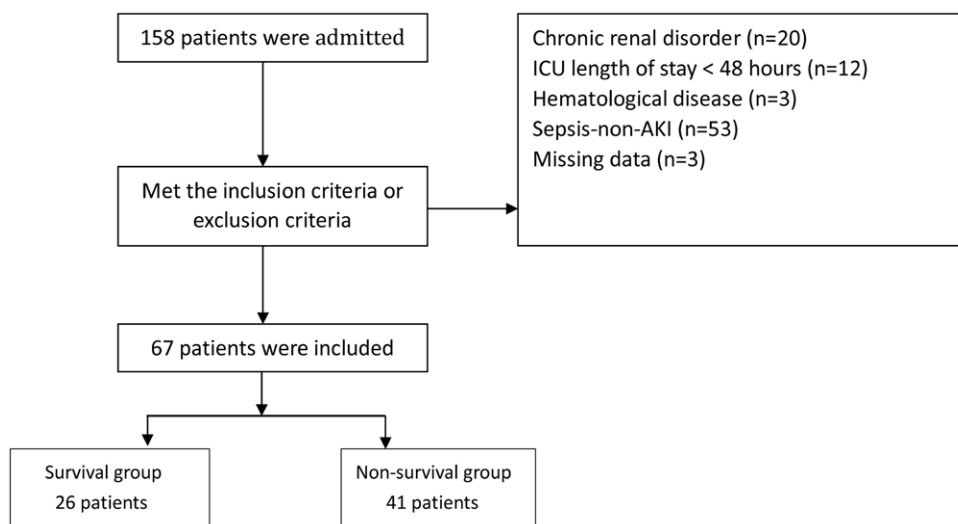
Fig. 1 Flow chart of enrollment.

Table 1

Basal information of septic patients with AKI at day 1 of ICU admission

Characteristics	Survivors	Nonsurvivors	*p*
Patients	26	41	
Age (years)	61.0 ± 2.9	59.0 ± 2.9	0.934
Gender (male/female)	12/14	24/17	0.899
Temperature (°C)	37.4 ± 0.21	37.2 ± 0.18	0.621
Respiration (bpm)	26 ± 2	29 ± 1	0.063
SBP (mmHg)	97 ± 5	101 ± 5	0.403
DBP (mmHg)	59 ± 3	59 ± 3	0.223
APACHE II score	16.9 ± 3.1	17.2 ± 2.8	0.698
Mechanical	15/11	4/37	0.437
Ventilation (no/yes)			
CRRT (no/yes)	2/24	7/34	0.01
Urine output(average) （mL/h）	26	17	0.027
Causes of sepsis (%)			
Pneumonia	69	72	
BSI	14	17	
Urosepsis	8	4	
GI/biliary	5	6	
Others	4	1	
WBC (10⁹/L)	17.8 ± 2.7	12.8 ± 2.3	0.199
LY (10⁹/L)	0.86 ± 0.15	0.97 ± 0.17	0.605
PLT (10⁹/L)	71 ± 9	113 ± 12	0.009
PLR	115 ± 14	208 ± 20	0.000
BUN (mmol/L)	14.9 (11.2, 17.2)	16.1 (11.4, 21.4)	0.000
SCr (μmol/L)	244 (178.4, 269.6)	242.8 (164.3, 300.5)	0.087
Lac (mmol/L)	4.3 (2.8, 5.1)	6.2 (2.5, 8.9)	0.005
PCT (mmol/L)	65.3 (18.2, 100)	59.2 (10.9, 100)	0.000

AKI = acute kidney injury; APACHE = acute physiology and chronic health evaluation; BSI = blood strem infection; BUN = blood urea nitrogen; CRRT = continuous renal replacement treatment; DBP = diastole blood pressure; GI = gastrointestinal infection; Lac = lactate; LY = lymphocyte; PCT = procalcitonin; PLR = platelet/lymphocyte ratio; PLT = platelet; SBP = systolic blood pressure; SCr = serum creatinine; WBC = white blood cell.

Table 2

Univariate analysis of factors associated mortality in septic patients with AKI

	OR	OR (95% CI)	*p*
Age (years)	1.384	(1.035, 1.851)	0.228
Gender (male//female)	1.011	(1.003, 1.088)	0.304
Temperature (°C)	1.023	(1.011, 1.799)	0.298
Respiration (bpm)	1.017	(1.003, 1.099)	0.781
SBP (mmHg)	1.683	(1.642, 2.481)	0.338
DBP (mmHg)	1.992	(1.389, 2.857)	0.078
APACHE II Score	1.621	(1.228, 2.139)	0.135
Mechanical ventilation (no/yes)	1.079	(1.022, 1.289)	0.000
WBC (10⁹/L)	1.975	(1.362, 2.865)	0.284
LY (10⁹/L)	2.994	(2.250, 3.985)	0.743
PLT (10⁹/L)	1.989	(1.979, 1.998)	0.021
PLR	1.021	(1.003, 1.039)	0.004
BUN (mmol//L)	1.997	(1.986, 2.999)	0.364
SCr (μmol/L)	1.016	(1.001, 1.031)	0.265
Lac (mmol//L)	1.964	(1.944, 1.994)	0.042
PCT (mmol//L)	1.013	(1.003, 1.024)	0.443

AKI = acute kidney injury; APACHE = acute physiology and chronic health evaluation; BUN = blood urea nitrogen; CI = confidence interval; DBP = diastole blood pressure; Lac = lactate; LY = lymphocyte; OR = odds ratio; PCT = procalcitonin; PLR = platelet/lymphocyte ratio; PLT = platelet; SBP = systolic blood pressure; Scr = serum creatinine; WBC = white blood cell.

Table 3

Multivariate analysis of factors associated mortality in septic patients with AKI

Factors	*B*	SE	*p*	Exp(*B*)
Mechanical ventilation	2.686	0.789	0.001	14.668
PLT	0.007	0.007	0.263	1.007
PLR	0.010	0.005	0.037	1.010
Lac	0.208	0.109	0.057	1.231

AKI = acute kidney injury; Lac = lactate; PLR = platelet/lymphocyte ratio; PLT = platelet.

also affected the neurobody fluid system of critically ill patients. Bagshaw et al[2] also supported the theory that the use of mechanical ventilation is closely related to a poor prognosis of patients. Damage caused by positive pressure from mechanical ventilation can be attributed to a large number of inflammatory factors first produced in the lungs that then enter the bloodstream, which eventually damage tissues and organs throughout the body. At about the same time, when there is positive pressure in the thoracic cavity, the amount of blood in the diastolic phase drops, the cardiac volume receptor is excited; when this happens, the

Table 4

Spearman correlation analysis of the PLR, mechanical ventilation, arterial blood lactate concentration, platelet count and the nonsurvival group of AKI with sepsis

Nonsurvivors cases with septic AKI	Correlation coefficient	*p*
PLR	−0.225	0.013
Mechanical ventilation	0.08	0.385
PLT	−0.219	0.016
Lac	0.318	0.000

AKI = acute kidney injury; Lac = lactate; PLR = platelet/lymphocyte ratio; PLT = platelet.
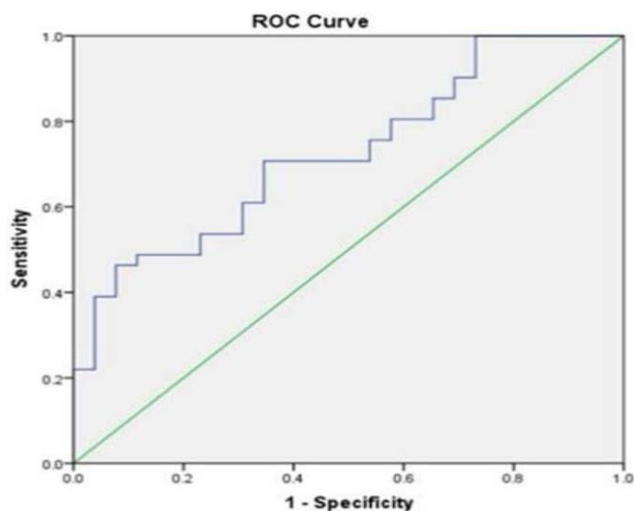
Fig. 2 The ROC curve of PLR. ROC = receiver characteristic operator.

sympathetic–adrenal medulla system and the renin–angiotensin aldosterone system are activated, and the release of arginine vasopressin increases. Therefore, for mechanical ventilation treatment in patients with sepsis complicated by AKI, a lung protective ventilation strategy, that is, using a lower tidal volume, is a common approach to improve the optimal positive end-expiratory pressure for oxygenation; the fundamental purpose of using a protective ventilation strategy is to reduce lung injury, decrease the production of inflammatory factors, and avoid the function impairment in other organs. The main limitation of the current research is that the PLR is just a nonspecific inflammatory marker. Still, we conducted this research only focusing on the relationship between the PLR and the prognosis of septic AKI patients. Thus, future studies should focus on patients with sepsis but without AKI may be helpful in further clarifying the PLR's value of the prognosis in patients with sepsis but without AKI.

In conclusion, the PLR might be an effective factor in predicting a worse prognosis of septic AKI patients.

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