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ORIGINAL ARTICLE

Neutrophil-to-lymphocyte ratio as a feasible prognostic marker for pyogenic liver abscess in the emergency department

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Abstract

Purpose The neutrophil-to-lymphocyte ratio (NLR) is an effective predictor of mortality in patients with for various conditions. To date, there are no previous studies on NLR as a prognostic marker for pyogenic liver abscess (PLA), especially on admission to the emergency department (ED).

Methods From January 2013 to December 2015, 102 patients diagnosed with PLA in the ED were included. Clinicoradiological and laboratory results, including NLR, were evaluated as variables. NLR was calculated as absolute neutrophil count/absolute lymphocyte count. To evaluate the prognosis of PLA, data on hospital mortality, intensive care unit (ICU) admission, and development of septic shock were obtained. Multivariate logistic regression analyses and receiver-operating characteristic (ROC) curve analysis were performed.

Results Among 102 patients, 10 (9.8%) died, 14 (13.7%) were admitted to the ICU, and 15 (14.7%) developed septic shock during hospitalization. Multivariate logistic regression analysis revealed NLR as an independent factor in predicting death [odds ratio (OR), 1.4; $p=0.020$], ICU admission (OR, 1.4; $p=0.021$), and development of septic shock (OR, 1.6; $p=0.041$). NLR showed an excellent predictive performance for death (areas under the ROC curves [AUC], 0.941; cut-off value, 19.7; $p<0.001$), ICU admission (AUC, 0.946; cut-off value, 16.9; $p<0.001$), and development of septic shock (AUC, 0.927; cut-off value, 16.9; $p<0.001$).

Conclusion NLR was positively associated with poor prognosis of PLA; elevated NLR could predictor of high risk of death, ICU admission, and development of septic shock. Emergency physicians should consider NLR for the prognosis of PLA and early aggressive treatment, especially in patients with NLR > 16.9.

Keywords Neutrophil-to-lymphocyte ratio · Pyogenic liver abscess · Mortality · Outcome · Prognostic marker

Introduction

Pyogenic liver abscess (PLA), although uncommon, is a life-threatening disease, with incidence rates ranging from 2.3 cases per 100,000 hospital admissions in North America to 275.4 cases per 100,000 in Taiwan [1, 2]. Because of improved diagnostic modalities and proper treatment, the mortality of PLA has markedly decreased, ranging from 10 to 40% [3–5]. However, diagnostic and therapeutic concerns remain [6, 7].

In the emergency department (ED), the identification of prognostic markers is essential in providing more aggressive, timely resuscitation of patients, and in planning future treatment of PLA patients for good prognosis [6–9]. Although several factors that predict poor prognosis of PLA have been reported [6–12], there are no previous studies on the use of NLR, which has been used as a prognostic marker for

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various conditions [13–15], for predicting prognosis of PLA patients. We hypothesized that NLR is associated with prognosis of the PLA and could be helpful for predicting death, ICU admission, and development of septic shock. Therefore, we aimed to evaluate the association between NLR and prognosis of PLA and independent factor for predicting death, ICU admission, and development of septic shock diagnosed in the ED.

Materials and methods

Study design

The institutional review board (IRB) of the First Affiliated Hospital (Sanggye Paik Hospital, Inje University College of Medicine) approved this study (IRB number: SGPAIK 2017-04-003). As this was a retrospective, non-interventional study based on electronic medical records (EMR) of patients diagnosed with PLA in the ED, informed consent was exempted by the Sanggye Paik hospital ethics committee.

Study population

From January 2013 to December 2015, the number of annual emergency visits in our hospital, a tertiary university teaching hospital, reached 65,000. The inclusion criteria for patients in our study were as follows: (1) patients aged $\geq$ 18 years, (2) patients who visited the ED and were diagnosed with PLA by blood/abscess culture and contrast-enhanced abdomen computed tomography, and (3) patients whose hospitalization was terminated because of discharge, or died before discharge. The exclusion criteria were as follows: (1) presence of a solid tumor, which influenced the absolute neutrophil and absolute lymphocyte counts [15]; (2) death due to an underlying disease, such as myocardial infarction; (3) anti-inflammatory drug medication, which also influenced the neutrophil and lymphocyte counts; and (4) insufficient EMR. We initially enrolled 150 patients, of which 48 were excluded based on the above exclusion criteria (hepatocellular cancer, $n = 15$; pancreatic cancer, $n = 11$; cholangiocarcinoma, $n = 10$; anti-inflammatory drug medication, $n = 9$; insufficient EMR, $n = 2$; death due to myocardial infarction, $n = 1$). Thus, 102 patients were included in the final analysis.

Data collection and outcome measurements

One board-certified emergency physician collected data from the EMR of eligible patients. The data included patient demographics, such as sex and age; clinical manifestations, such as systolic and diastolic blood pressures (BP), pulse rate, and body temperature on ED admission; underlying or concomitant conditions and laboratory results, including white blood cell count, neutrophil count, lymphocyte count, calculated NLR, hemoglobin, platelet, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), C-reactive protein (CRP), serum glucose, serum BUN, serum creatinine, and microorganisms; and the clinical progress of patients, including hospital days, in-hospital mortality, intensive care unit (ICU) admission, and development of septic shock. We observed at 3 months for mortality.

NLR was calculated as absolute neutrophil count/absolute lymphocyte count, while hospital days were defined as the number of days from ED admission to discharge or from ED admission to patient death. In-hospital mortality was defined as death from liver abscess during the patient's hospitalization. Death from liver abscess was clinically and radiologically verified. If PLA aggravated clinically (e.g., elevated liver function test) and radiologically (e.g., increased number or size of the abscesses) without newly developed cardiopulmonary disease, we determined liver abscess to be the cause of death. ICU admission was defined as admission to the ICU from the ED and was determined according to the guidelines of the Society of Critical Care Medicine [16]. The patients with priority 1 (critically ill patients requiring life support for organ failure, intensive monitoring, and therapies only provided in the ICU environment) were admitted to the ICU from the ED. On the other hand, development of septic shock was defined as sepsis (suspected infection + sepsis-related organ failure assessment (SOFA) score $\geq$ 2 or rise in SOFA score $\geq$ 2), vasopressors for mean arterial pressure > 65, and serum lactate > 2 mmol/L after adequate fluid resuscitation according to the recent definition of septic shock (Sepsis-3) [17]. In addition, we evaluated radiological findings (maximal diameter of the largest abscess and multiplicity) on the initial contrast-enhanced abdomen computed tomography.

Statistical analysis

To assess the difference between good and poor outcomes (survival vs. death, general ward admission from the ED vs. ICU admission from the ED, absence of septic shock during hospitalization vs. septic shock during hospitalization) in PLA patients, the independent *t* test or Mann–Whitney *U* test was performed for the continuous variables and Pearson's Chi-square test or Fisher's exact test was performed for the nominal variables. To determine the independent prognostic factors for PLA, multivariate logistic regression analysis was applied. The multivariate logistic regression analysis was conducted on variables with a *P* value of < 0.1 on univariate analysis. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were obtained from the multivariate analyses. Furthermore, to determine the predictive performance of significant variables for differentiation between good and poor prognoses, a receiver-operating characteristic (ROC) curve analysis was performed. Areas under the ROC curves (AUCs) and 95% CIs were calculated. Optimal cut-off values were defined as the point at which the value of "sensitivity + specificity − 1" was maximum (Youden's index) [18]. The AUCs were compared using DeLong's method [19]. Meanwhile, $P < 0.05$ was considered statistically significant. The statistical analyses were conducted using MedCalc Version 12.3.0 (MedCalc Software, Mariakerke, Belgium).

Results

Baseline characteristics

The baseline characteristics are presented in Table 1. The time interval between recordings of elevated NLR and death was 30.4 days.

All patients were empirically commenced on broad-spectrum intravenous antibiotics after confirming PLA on contrast-enhanced abdomen computed tomography. The 41 patients with large liquefied abscesses (> 5 cm) underwent radiologically guided percutaneous drainage of the liver abscess at the time of diagnosis or within 24 h. None of patients underwent surgical interventions.

Factors associated with the prognosis of PLA

Associations between death and clinico-radiological and laboratory variables are shown in Table 2. In the univariate analysis, leukocyte, neutrophil, NLR, and CRP levels were significantly higher in patients who died than in surviving patients, whereas systolic BP, diastolic BP, and lymphocyte levels were significantly lower in patients who died than those in surviving patients (all, $p \leq 0.040$). In the multivariate logistic regression analysis, NLR ($p = 0.020$; OR, 1.4; 95% CI, 1.1–1.8) was the only significant independent variable for prediction of death.

A comparison analysis between ICU admission and clinico-radiological and laboratory variables is presented in Table 3. Univariate analysis revealed that leukocyte, neutrophil, NLR, and CRP levels were significantly higher in patients admitted to the ICU than in those admitted to the general ward, whereas systolic BP, diastolic BP, and lymphocyte levels were significantly lower in patients admitted to the ICU than in those admitted to the general ward (all, $p \leq 0.046$). Multivariate logistic regression analysis revealed systolic BP ($p = 0.028$; OR, 1.2; 95% CI, 1.1–1.5) and NLR ($p = 0.021$; OR, 1.4; 95% CI, 1.1–1.8) as significant independent variables for prediction of ICU admission.

Associations between development of septic shock during hospitalization and clinico-radiological and laboratory

Table 1 Demographic characteristics and clinical information of 102 patients

Characteristic	
Age (years)	64.8 (14.8)
Sex	
Men	56 (54.9)
Women	46 (45.1)
Systolic blood pressure (mmHg)	128.4 (25.2)
Diastolic blood pressure (mmHg)	74.3 (12.9)
Pulse rate (/min)	94.1 (17.6)
Body temperature (℃)	38.0 (1.3)
Underlying or concomitant conditions	
Biliary disease	43 (42.2)
Hypertension	18 (17.6)
Intra-abdominal infection	16 (15.7)
Diabetes mellitus	14 (13.7)
Others	11 (10.8)
Leukocyte (10^9/L)	12.2 (6.5)
Lymphocyte (10^9/L)	1.4 (1.3)
Neutrophil (10^9/L)	10.2 (6.0)
Neutrophi-to-lymphocyte ratio (NLR)	11.5 (9.0)
Hemoglobin (g/dL)	12.2 (2.0)
Platelet (10^9/L)	310.8 (104.0)
Albumin (g/dL)	3.2 (0.6)
Aspartate aminotransferase (IU/L)	87.0 (103.4)
Alanine aminotransferase (IU/L)	78.7 (84.9)
Alkaline phosphatase (IU/L)	198.1 (143.5)
C-reactive protein (mg/dL)	18.4 (8.9)
Glucose (mg/dL)	156.9 (82.1)
Blood urea nitrogen (mg/dL)	19.7 (20.4)
Creatinine (mg/dL)	1.0 (0.5)
Microorganism	
Escherichia coli	34 (33.3)
Klebsiella pneumoniae	26 (25.5)
Bacteroides species	13 (12.7)
Others[a]	29 (28.4)
Mean size (cm)	4.7 (2.5)
Multiplicity of the abscess	
Single	68 (66.7)
Multiple (≥ 2 abscesses)	34 (33.3)
Treatment	
Antibiotics only	61 (59.8)
Percutaneous drainage + antibiotics	41 (40.2)
Hospital day (days)	19.3 (13.3)
Survival	
Alive	92 (90.2)
Death	10 (9.8)
Admission	
General ward	88 (86.3)
Intensive care unit	14 (13.7)
Development of the septic shock during hospitalization	
No	87 (85.3)
Yes	15 (14.7)

Data are mean (standard deviation) or number (%)

[a]Others: Pseudomonas aeruginosa, Proteus mirabilis, Serratia marc-

Table 1 (continued)

escens, Flavobacterium spp., Acinetobacter spp., Citrobacter spp., Stenotrophomonas maltophilia, unidentified bacilli., Enterococcus spp., Streptococcus spp., Bifidobacterium spp., Fusobacterium spp., Clostridium spp., Staphylococcus spp., and Corynebacterium spp

variables are presented in Table 4. Univariate analysis revealed that leukocyte, neutrophil, NLR, and hemoglobin levels were significantly higher in septic shock patients than in those without septic shock, whereas systolic BP, diastolic BP, and lymphocyte levels were significantly lower in septic shock patients than in those without septic shock (all, $p \leq 0.038$). The multivariate logistic regression analysis showed that systolic BP ($p = 0.039$; OR, 1.5; 95% CI, 1.2–1.8) and NLR ($p = 0.041$; OR, 1.6; 95% CI, 1.2–2.1) were significant independent variables for prediction of the presence of the septic shock.

Predictive performance of significant factors for poor outcomes

The ROC curves of significant factors for the prediction of death, ICU admission, and development of septic shock during hospitalization are shown in Fig. 1. The AUC of NLR for the prediction of death was 0.941 (95% CI, 0.876–0.978) and the cut-off value was 19.7 (Fig. 1a). The AUCs of NLR and systolic BP for the prediction of ICU admission were 0.946 (95% CI, 0.883–0.981) and

Table 2 Associations between death and clinical variables

	Univariate analysis[a]		*p*	Multivariable logistic regression OR[†]	B	*p*
	Alive ($n = 92$)	Death ($n = 10$)				
Age (years)	65.0 (15.6)	63.8 (10.7)	0.76			
Sex			0.82			
Men	53 (54.6)	3 (60)				
Women	44 (45.4)	2 (40)				
Systolic BP (mmHg)	130.7 (25.3)	117.3 (22.2)	**0.040**	1.0 (0.95, 1.1)	0.005	0.87
Diastolic BP (mmHg)	75.7 (13.2)	67.6 (8.8)	**0.014**	0.95 (0.82, 1.1)	− 0.052	0.48
Pulse rate (/min)	92.9 (16.7)	99.5 (16.5)	0.15			
Body temperature (℃)	37.9 (1.3)	38.2 (1.3)	0.35			
Underlying or concomitant conditions			0.32			
Biliary disease	37 (40.2)	6 (60)				
Non-biliary disease	55 (59.8)	4 (40)				
Leukocyte (10^9/L)	11.5 (5.5)	15.9 (9.1)	**0.008**	1.0 (1.0, 1.0)	− 0.001	0.67
Lymphocyte (10^9/L)	1.6 (1.3)	0.7 (0.4)	**0.037**	1.0 (1.0, 1.0)	− 0.001	0.54
Neutrophil (10^9/L)	9.3 (4.9)	14.6 (8.7)	**0.001**	1.0 (1.0, 1.0)	0.001	0.68
Neutrophil-to-lymphocyte ratio	8.5 (4.8)	25.5 (10.7)	**0.001**	1.4 (1.1, 1.8)	0.33	**0.020**
Hemoglobin (g/dL)	12.0 (2.0)	12.9 (1.9)	0.092	0.90 (0.50, 1.6)	− 0.028	0.83
Platelet (10^9/L)	340.0 (114.4)	176.3 (92.1)	0.55			
Albumin (g/dL)	3.1 (0.7)	3.2 (0.5)	0.70			
AST (IU/L)	87.3 (110.7)	85.9 (60.9)	0.95			
ALT (IU/L)	79.6 (90.7)	74.5 (51.4)	0.82			
ALP (IU/L)	205.6 (152.2)	163.4 (87.9)	0.26			
C-reactive protein (mg/dL)	17.5 (9.0)	22.4 (7.8)	**0.039**	0.99 (0.89, 1.1)	− 0.003	0.98
Glucose (mg/dL)	157.5 (82.2)	154.3 (84.3)	0.88			
BUN (mg/dL)	19.0 (19.4)	23.2 (24.9)	0.44			
Creatinine (mg/dL)	1.0 (0.3)	1.2 (1.0)	0.54			
Mean size (cm)	4.1 (2.2)	5.5 (3.0)	0.069	0.95 (0.82, 1.2)	0.006	0.52
Multiplicity of the abscess	29 (31.5)	5 (50)	0.41			
Percutaneous drainage	35 (38.0)	6 (60)	0.31			

Boldface type indicates statistical significance ($p < 0.05$)

OR odds ratio, *B* regression coefficient, *BP* blood pressure, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase, *BUN* blood urea nitrogen

[a]Data are mean (standard deviation) or number (%)

[†]Data in parentheses are 95% confidence intervals, conducted on variables with a *p* value of < 0.1 on univariate analysis

Table 3 Associations between intensive care unit (ICU) admission and clinical variables

	Univariate analysis[a]		*p*	Multivariable logistic regression OR[†]	B	*p*
	General ward admission ($n=88$)	ICU admission ($n=14$)				
Age (years)	65.2 (15.5)	63.1 (11.1)	0.58			
Sex			0.91			
Men	49 (55.7)	7 (50)				
Women	39 (44.3)	7 (50)				
Systolic BP (mmHg)	131.9 (24.6)	113.0 (22.1)	**0.001**	1.2 (1.1, 1.5)	− 0.067	**0.028**
Diastolic BP (mmHg)	75.8 (12.5)	67.9 (12.7)	**0.016**	0.95 (0.81, 1.1)	0.081	0.52
Pulse rate (/min)	92.5 (17.3)	100.9 (17.5)	0.061	1.0 (0.95, 1.0)	0.033	0.97
Body temperature (℃)	37.9 (1.3)	38.2 (1.4)	0.30			
Underlying or concomitant conditions			0.25			
Biliary disease	35 (39.8)	8 (57.1)				
Non-biliary disease	53 (60.2)	6 (42.9)				
Leukocyte (10^9/L)	11.3 (5.4)	16.4 (8.9)	**0.002**	1.0 (1.0, 1.0)	− 0.001	0.67
Lymphocyte (10^9/L)	1.6 (1.9)	0.7 (0.5)	**0.046**	1.0 (1.0, 1.0)	− 0.001	0.54
Neutrophil (10^9/L)	9.1 (4.8)	15.0 (8.4)	**0.001**	1.0 (1.0, 1.0)	0.001	0.68
Neutrophil-to-lymphocyte ratio	8.4 (4.7)	25.1 (10.5)	**0.001**	1.4 (1.1, 1.8)	0.45	**0.021**
Hemoglobin (g/dL)	12.3 (1.9)	12.6 (1.9)	0.070	0.97 (0.54, 1.8)	− 0.075	0.92
Platelet (10^9/L)	342.3 (115.1)	173.2 (95.9)	0.53			
Albumin (g/dL)	3.1 (0.6)	3.2 (0.6)	0.69			
AST (IU/L)	86.6 (110.4)	88.6 (66.7)	0.94			
ALT (IU/L)	77.8 (90.7)	82.4 (53.7)	0.83			
ALP (IU/L)	208.6 (152.4)	152.6 (83.6)	0.13			
C-reactive protein (mg/dL)	17.3 (9.0)	23.0 (7.3)	**0.015**	0.99 (0.88, 1.1)	0.027	0.98
Glucose (mg/dL)	151.6 (70.1)	180.2 (121.4)	0.17			
BUN (mg/dL)	19.4 (22.2)	21.3 (10.0)	0.71			
Creatinine (mg/dL)	1.0 (0.6)	1.1 (1.3)	0.73			
Mean size (cm)	4.2 (2.2)	5.4 (2.9)	0.073	0.95 (0.82, 1.2)	0.005	0.68
Multiplicity of the abscess	27 (30.7)	7 (50)	0.26			
Percutaneous drainage	34 (38.6)	7 (50)	0.61			

Boldface type indicates statistical significance ($p<0.05$)

OR odds ratio, *B* regression coefficient, *BP* blood pressure, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase, *BUN* blood urea nitrogen

[a]Data are mean (standard deviation) or number (%)

[†]Data *in* parentheses are 95% confidence intervals, conducted on variables with a *p* value of <0.1 on univariate analysis

0.716 (95% CI, 0.618–0.801), respectively. The cut-off values for NLR and systolic BP were 16.9 and 128 mmHg, respectively (Fig. 1b), and the AUC of NLR was significantly higher than that of systolic BP ($p=0.002$). For the development of septic shock, the AUCs of NLR and systolic BP were 0.927 (95% CI, 0.859–0.969) and 0.660 (95% CI, 0.559–0.751), respectively. The cut-off values were identical for the prediction of ICU admission (Fig. 1c) and the AUC of NLR was significantly higher than that of systolic BP ($p<0.001$).

Discussion

To the best of our knowledge, this is the first study to evaluate the association between NLR and prognosis of PLA. The results demonstrated that NLR independently predicted in-hospital mortality of PLA patients. A positive association was observed between high NLR and poor prognosis of PLA, as evidenced by ICU admission, development of septic shock, and in-hospital death. This

Table 4 Associations between development of septic shock during admission and clinical variables

	Univariate analysis*		p	Multivariable logistic regression OR†	B	p
	No septic shock ($n=87$)	Septic shock ($n=15$)				
Age (years)	64.7 (15.6)	65.2 (11.3)	0.91			
Sex			0.48			
Men	46 (52.9)	10 (66.7)				
Women	41 (47.1)	5 (33.3)				
Systolic BP (mmHg)	131.2 (25.1)	116.9 (22.7)	**0.004**	1.5 (1.2, 1.8)	− 0.019	**0.039**
Diastolic BP (mmHg)	75.7 (12.7)	68.6 (12.3)	**0.027**	1.0 (0.91, 1.1)	0.002	0.91
Pulse rate (/min)	92.7 (17.2)	99.7 (18.5)	0.12			
Body temperature (℃)	37.9 (1.3)	38.1 (1.4)	0.50			
Underlying or concomitant conditions			0.78			
Biliary disease	36 (41.4)	7 (46.7)				
Non-biliary disease	51 (58.6)	8 (53.3)				
Leukocyte (10^9/L)	11.4 (5.4)	15.7 (9.0)	**0.007**	1.0 (1.0, 1.0)	− 0.001	0.97
Lymphocyte (10^9/L)	1.6 (1.9)	0.7 (0.5)	**0.038**	1.0 (1.0, 1.0)	0.001	0.61
Neutrophil (10^9/L)	9.2 (4.8)	14.4 (8.6)	**0.001**	1.0 (1.0, 1.0)	0.001	0.96
Neutrophil-to-lymphocyte ratio	8.5 (4.9)	24.0 (10.9)	**0.001**	1.6 (1.2, 2.1)	0.244	**0.041**
Hemoglobin (g/dL)	12.0 (2.0)	12.8 (2.0)	**0.014**	0.87 (0.52, 1.5)	− 0.032	0.60
Platelet (10^9/L)	343.3 (115.8)	178.0 (93.7)	0.53			
Albumin (g/dL)	3.2 (0.6)	3.2 (0.6)	0.86			
AST (IU/L)	87.4 (110.0)	85.2 (65.7)	0.93			
ALT (IU/L)	80.0 (91.3)	73.8 (52.4)	0.77			
ALP (IU/L)	206.7 (153.7)	163.5 (84.9)	0.23			
C-reactive protein (mg/dL)	17.6 (9.0)	21.8 (8.1)	0.062	0.98 (0.89, 1.1)	0.018	0.74
Glucose (mg/dL)	150.5 (70.0)	183.5 (119.0)	0.11			
BUN (mg/dL)	19.6 (22.2)	20.5 (10.3)	0.85			
Creatinine (mg/dL)	1.0 (0.6)	1.0 (1.3)	0.77			
Mean size (cm)	4.2 (2.2)	5.4 (2.9)	0.073	0.90 (0.65, 1.3)	0.002	0.98
Multiplicity of the abscess	27 (31.5)	7 (50)	0.27			
Percutaneous drainage	33 (38.0)	8 (60)	0.19			

Boldface type indicates statistical significance ($p<0.05$)

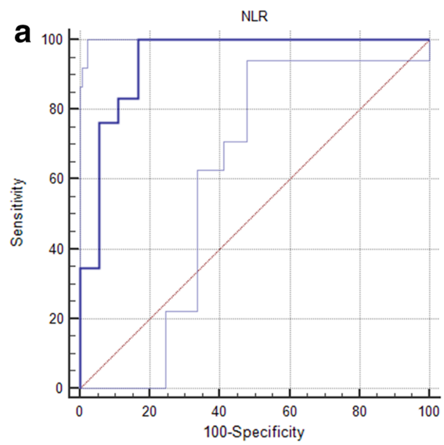
OR odds ratio, *B* regression coefficient, *BP* blood pressure, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase, *BUN* blood urea nitrogen

†Data *in parentheses* are 95% confidence intervals, conducted on variables with a p value of <0.1 on univariate analysis

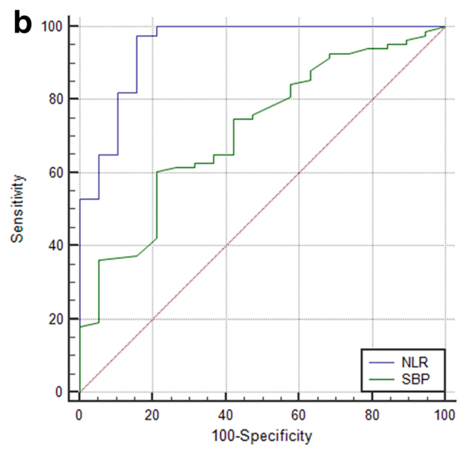
*Data are mean (standard deviation) or number (%)

is consistent with another report demonstrating that high NLR measured in the ED was independently associated with in-hospital mortality, multi-organ failure, and development of sepsis [14]. In addition, we presented the cut-off value of poor prognosis of PLA. For in-hospital mortality during hospitalization, the cut-off value was 19.7 and the AUC was 0.941 (95% CI, 0.876–0.978). The NLR cut-off values for ICU admission and development of septic shock were identical, i.e., 16.9. Although systolic BP was statistically significant for two prognostic factors, the AUC of NLR was superior to that of systolic BP. Therefore, if NLR is > 16.9 during the initial presentation of PLA patients, emergency physicians should anticipate poor prognosis of PLA and should consider more careful resuscitation and proper, timely treatment.

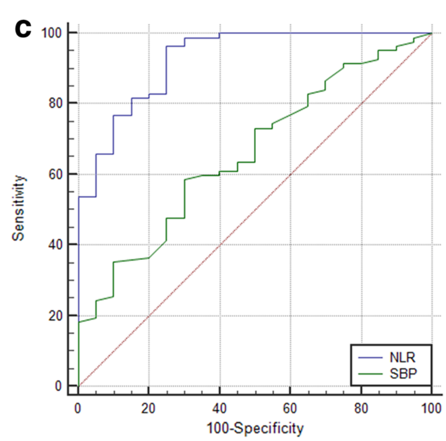
The activation of neutrophils is essential for host defense in systemic inflammatory response syndrome (SIRS). Neutrophils respond by phagocytosis, which directly kills the pathogens, and by release of various inflammatory and proinflammatory cytokines (which activate T cells), granule enzymes, and reactive oxygen species. However, an increased number of cytokines can result in an uncontrolled innate immune system, influence tissue destruction, and lead to septic shock and organ failure due to the activation of aggressive defense mechanisms. This situation may require immunosuppression, where lymphocytes play an important



	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	AUC	*p*-value
NLR	19.7	100 (95.7-100.0)	83.3 (58.6-96.4)	0.941 (0.876-0.978)	<0.001



	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	AUC	*p*-value
NLR	16.9	97.6 (91.6-99.7)	84.2 (60.4-96.6)	0.946 (0.883-0.981)	<0.001
SBP	128	60.2 (48.9-70.8)	79.0 (54.4-93.9)	0.716 (0.618-0.801)	<0.001



	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	AUC	*p*-value
NLR	16.9	96.3 (89.7-99.2)	75.0 (50.9-91.3)	0.927 (0.859-0.969)	<0.001
SBP	128	58.5 (47.1-69.3)	70.0 (45.7-88.1)	0.660 (0.559-0.751)	<0.001

Fig. 1 Receiver-operating characteristic (ROC) curves for predicting death (**a**), intensive care unit admission (**b**), and development of septic shock during hospitalization (**c**). *NLR* neutrophil-to-lymphocyte ratio, *SBP* systolic blood pressure, *AUC* area under the ROC curve, *CI* confidence interval

role by undergoing apoptosis with various anti-inflammatory cytokines [13, 20–23]. NLR indicates a balance between the immune system and the immunosuppression system in an SIRS patient. However, prolonged elevated neutrophil count and decreased lymphocyte count (an elevated NLR) may reflect an imbalance in the immune system, and these findings are reported to be a predictor for mortality in septic patients [20]. In other words, NLR reflects the acute alteration of the immune system during a systemic inflammatory process to infection. With this background, NLR has been investigated to be associated with the poor prognosis of various diseases [24–30]. These studies [24–30] concluded that NLR reflects subclinical inflammation and thrombotic events, such as myocardial infarction, meningitis, stroke, and pulmonary embolism.

Comparing with a few previous studies using neutrophil and lymphocyte for PLA, Foo, et al. [31] demonstrated that neutrophil count > 70% was a significant predictor of fatality. This was consistent with a recent study on the apoptosis of the neutrophil. Lee et al. [32] showed that K1 serotype Klebsiella infection (common pathogen in PLA) regulates neutrophil apoptosis and enhances the survival of the infected neutrophils that serve as a vector for the dissemination of the bacteria; this is the cause of neutrophilia in PLA patients. In addition, they also showed that some species related to PLA are able to inhibit lymphocyte proliferation, which suggests its ability to evade the immune system [33]. These findings, coupled with the organism's ability to cause disease in concert with other bacteria, add to its pathogenic potential. Several previous studies [6–12] reported other prognostic values for PLA, including older age, increased BUN and serum creatinine levels, low serum albumin and hemoglobin levels, polymicrobial infection, liver abscess of biliary origin, multiple abscesses, concomitant malignancy, and pleural effusions. However, in our study, age, BUN, serum creatinine, albumin, and hemoglobin levels were not associated with poor prognosis of PLA. Although systolic BP was associated with ICU admission and development of septic shock, it may be influenced by an initial septic condition, leading to poor prognosis of PLA, which is consistent with a previous report [34]. The most appropriate biomarker for predicting liver abscess has not been established thus far. However, in addition to other factors, NLR has shown great advantage as a biomarker, because it is simple, economically efficient, and readily available, and can be easily calculated in the ED. In addition, NLR does not entail further laboratory evaluation or cost.

With this knowledge, NLR may lead physicians to easily identify high risk patients who require priority care because of increased risks of death. However, when applying NLR for PLA patients, there are certain considerations. NLR shows high sensitivity but appears to be of lower specificity if applied to critically ill patients [35]. We also see that

NLR for PLA patients have high sensitivity but relatively low specificity, which hints that high NLR level, is just a preliminary tool and it may be necessary to combine it with other indicators to provide more accurate evaluation information. Together with other indicators such as Acute Physiology and Chronic Health Evaluation (APACHE) II and the simplified acute physiology score (SAPS) II, the specificity may improve [9].

The possible criticism is that in general, the criteria for ICU admission often include several physiological parameters, such as vital signs, laboratory values, and physical findings [16]. Similarly, septic shock is often defined as the presence of infection together with SIRS and sepsis-induced low blood pressure. The assessment of SIRS is based on vital signs and WBC [17]. Thus, overall physiological parameters may be important for ICU admission and development of septic shock at the time of ED admission. However, we considered that evaluation of systolic BP and NLR for predicting ICU admission and development of septic shock was also important. According to our results, patients with high systolic BP and NLR were at a risk of ICU admission and development of septic shock, although their vital signs were stable at the time of ED admission. Moreover, these patients may require careful follow-up of systolic BP and NLR for good outcomes.

Our study had several limitations. First, the in-hospital mortality rate of PLA patients was considerably small (10 non-survivors). Second, because ours was a single-center retrospective study, a selection bias and a problem in generalizing the results may have occurred. Second, neutrophils and lymphocytes are influenced by various factors such as general patient condition and time interval between symptom onset to ED visit, which were not considered in the study. Third, we did not include pathological variables, such as microorganisms and its sources as potential independent predictive factors, because our study was focused on predictive performance of the clinico-radiological and laboratory variables, which could be obtained immediately in the ED before the initial management. Fourth, although we attempted to confirm the patients' medication history from the EMR, which is based on patients' previous prescriptions, we could not confirm the exact emergency medication taken by the patient. Fifth, all PLA patients included in our study showed mono-microbial infection. This may be because of the selection bias. However, polymicrobial infection did not significantly increase the mortality of PLA patients in the previous studies [6–12]. In addition, approximately 60% of PLA patients received antibiotic therapy in the present study. This was related to our institutional protocols for PLA. Percutaneous drainage was performed in abscess > 5 cm at our institution. In present study, the mean size of the abscess was smaller and multiplicity was higher than the previous studies [6–12]. However, mean size, multiplicity, and treatment method were not significantly different in univariate analysis. Thus, these factors did not affect patients' outcome. These limitations demonstrate the need for a careful interpretation of NLR and a large prospective multi-center research in the future.

Conclusion

In conclusion, we demonstrated that NLR was positively associated with poor prognosis of PLA; elevated NLR could predict the high risk of death, ICU admission, and development of septic shock. Therefore, as emergency physicians, we should consider NLR while predicting poor prognosis and achieving early aggressive treatment, especially in patients with NLR > 16.9.

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Compliance with ethical standards

Ethical approval This study has been approved by the ethics committee and has been performed in accordance with the ethical standards laid down in the Declaration of Helsinki.

Informed consent Due to the retrospective nature of the study, no informed consent was obtained from the included cohort as judged by the ethics committee..

Conflict of interest The authors declare that there is no conflict of interest.

References

1. Lin YT, Liu CJ, Chen TJ, Chen TL, et al. Pyogenic liver abscess as the initial manifestation of underlying hepatocellular carcinoma. Am J Med. 2011;124:1158–64.
2. Chen CH, Wu SS, Chang HC, Chang YJ. Initial presentations and final outcomes of primary pyogenic liver abscess: a cross-sectional study. BMC Gastroenterol. 2014;14:133.
3. Huang CJ, Pitt HA, Lipsett PA, Osterman FA Jr, et al. Pyogenic hepatic abscess. Changing trends over 42 years. Ann Surg. 1996;223:600–7.
4. Law ST, Li KK. Is hepatic neoplasm-related pyogenic liver abscess a distinct clinical entity? World J Gastroenterol. 2012;18:1110–6.
5. Keller JJ, Tsai MC, Lin CC, Lin YC, et al. Risk of infections subsequent to pyogenic liver abscess: a nationwide population-based study. Clin Microbiol Infect. 2013;19:717–22.
6. Mischinger HJ, Hauser H, Rabl H, Quehenberger F, et al. Pyogenic liver abscess: studies of therapy and analysis of risk factors. World J Surg. 1994;18:852–7.
7. Alvarez Pérez JA, González JJ, Baldonedo RF, Sanz L, et al. Clinical course, treatment, and multivariate analysis of risk factors for pyogenic liver abscess. Am J Surg. 2001;181:177–86.
8. Hsieh CB, Tzao C, Yu CY, Chen CJ, et al. APACHE II score and primary liver cancer history had risk of hospital

mortality in patients with pyogenic liver abscess. Dig Liver Dis. 2006;38:498–502.
9. Chen SC, Huang CC, Tsai SJ, Yen CH, et al. Severity of disease as main predictor for mortality in patients with pyogenic liver abscess. Am J Surg. 2009;198:164–72.
10. Chen W, Chen CH, Chiu KL, Lai HC, et al. Clinical outcome and prognostic factors of patients with pyogenic liver abscess requiring intensive care. Crit Care Med. 2008;36:1184–8.
11. Wong WM, Wong BC, Hui CK, Ng M, et al. Pyogenic liver abscess: retrospective analysis of 80 cases over a 10-year period. J Gastroenterol Hepatol. 2002;17:1001–7.
12. Chou FF, Sheen-Chen SM, Chen YS, Chen MC, et al. Prognostic factors for pyogenic abscess of the liver. J Am Coll Surg. 1994;179:727–32.
13. Zahorec R. Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy. 2001;102:5–14.
14. Hwang SY, Shin TG, Jo IJ, Jeon K, et al. Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med. 2017;35:234–9.
15. Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst. 2014;106:dju124.
16. Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Crit Care Med. 1999;27:633–8.
17. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315:801–10.
18. Fluss R, Faraggi D, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biom J. 2005;47:458–72.
19. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988;44:837–45.
20. Taneja R, Parodo J, Jia SH, Kapus A, et al. Delayed neutrophil apoptosis in sepsis is associated with maintenance of mitochondrial transmembrane potential and reduced caspase-9 activity. Crit Care Med. 2004;32:1460–9.
21. Soehnlein O, Lindbom L. Phagocyte partnership during the onset and resolution of inflammation. Nat Rev Immunol. 2010;10:427–39.
22. Nauseef WM, Borregaard N. Neutrophils at work. Nat Immunol. 2014;7:602–11.
23. Maitre B, Magnenat S, Heim V, Ravanat C, et al. The P2 × 1 receptor is required for neutrophil extravasation during lipopolysaccharide-induced lethal endotoxemia in mice. J Immunol. 2015;194:739–49.
24. Zhang Y, Wu W, Dong L, Yang C, et al. Neutrophil to lymphocyte ratio predicts persistent organ failure and in-hospital mortality in an Asian Chinese population of acute pancreatitis. Medicine (Baltimore). 2016;95:e4746.
25. Beliaev AM, Angelo N, Booth M, Bergin C. Evaluation of neutrophil-to-lymphocyte ratio as a potential biomarker for acute cholecystitis. J Surg Res. 2016;209:93–101.
26. Piciucchi M, Stigliano S, Archibugi L, Zerboni G, et al. The neutrophil/lymphocyte ratio at diagnosis is significantly associated with survival in metastatic pancreatic cancer patients. Int J Mol Sci. 2017;18:e730.
27. Gul U, Kayani AM, Munir R, Hussain S. Neutrophil lymphocyte ratio: a prognostic marker in acute ST elevation myocardial infarction. J Coll Physicians Surg Pak. 2017;27:4–7.
28. Xue J, Huang W, Chen X, Li Q, et al. Neutrophil-to-lymphocyte ratio is a prognostic marker in acute ischemic stroke. J Stroke Cerebrovasc Dis. 2017;26:650–7.
29. Kundi H, Balun A, Cicekcioglu H, Cetin M, et al. The relation between platelet-to-lymphocyte ratio and Pulmonary Embolism Severity Index in acute pulmonary embolism. Heart Lung. 2015;44:340–3.
30. Kim JH, Kim HJ, Na JU, Han SK, et al. Hematologic parameters to predict negative cerebrospinal fluid examination results among neurologically intact patients who underwent lumbar puncture on suspicion of central nervous system infection. Clin Exp Emerg Med. 2017;4:25–31.
31. Foo NP, Chen KT, Lin HJ, Guo HR. Characteristics of pyogenic liver abscess patients with and without diabetes mellitus. Am J Gastroenterol. 2010;105:328–35.
32. Lee CH, Chuah SK, Tai WC, Chang CC, et al. Delay in Human Neutrophil Constitutive Apoptosis after Infection with Klebsiella pneumoniae Serotype K1. Front Cell Infect Microbiol. 2017;7:87.
33. Lei WY, Chang WH, Shih SC, Liu CJ, et al. Pyogenic liver abscess with Prevotella species and Fusobacterium necrophorum as causative pathogens in an immunocompetent patient. J Formos Med Assoc. 2009;108:253–7.
34. Cho H, Lee ES, Lee YS, Kim YJ, et al. Predictors of septic shock in initially stable patients with pyogenic liver abscess. Scand J Gastroenterol. 2017;52:589–94.
35. Liu X, Shen Y, Wang H, Ge Q, et al. Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Patients with Sepsis: A Prospective Observational Study. Mediators Inflamm. 2016;2016:8191254.