

*Short Communication*

## The Neutrophil to Lymphocyte Ratio Is Superior to Other Inflammation-Based Prognostic Scores in Predicting the Mortality of Patients with Pneumonia

Yuichiro Shimoyama<sup>a\*</sup>, Osamu Umegaki<sup>a</sup>, Satsuki Inoue<sup>b</sup>, Tomoyuki Agui<sup>c</sup>,  
Noriko Kadono<sup>a</sup>, and Toshiaki Minami<sup>b</sup>

*Departments of<sup>a</sup>Anesthesiology, and<sup>c</sup>Surgery, Osaka Medical College, Intensive Care Unit,  
<sup>b</sup>Anesthesiology, Osaka Medical College, Osaka Medical College Hospital, Takatsuki, Osaka 569-8686, Japan*

A neutrophil-to-lymphocyte ratio (NLR) >7 is reportedly an independent marker of mortality in patients with bacteremia. However, no studies have shown an association between inflammation-based prognostic scores (including the Glasgow Prognostic Score, the NLR, the platelet-to-lymphocyte ratio, the Prognostic Nutritional Index, and the Prognostic Index) and mortality in patients with pneumonia. We retrospectively examined the cases of 33 patients diagnosed with pneumonia who were treated in the ICU of Osaka Medical College Hospital between January 2014 and June 2016. A multivariate analysis revealed that the NLR was a significant predictor of mortality in these pneumonia patients.

**Key words:** inflammation-based prognostic score, pneumonia, in-hospital mortality

The neutrophil-to-lymphocyte ratio (NLR) has been shown to predict outcomes in oncology patients, including lung, ovary, and breast cancer patients [1]. The preoperative NLR is reportedly a prognostic factor in patients undergoing colorectal cancer resection [2], and the NLR measured upon admission to an intensive care unit (ICU) was found to be associated with both short- and long-term mortality in critically ill adult patients [1]. Compared to other inflammation-based prognostic scores, the NLR and the platelet-to-lymphocyte ratio (PLR) have been reported to have superior predictive power for mortality in patients with a gastrointestinal perforation [3]. The NLR can also predict bacteremia better than other infection markers [4], with an NLR >7 reported to be an independent marker of mortality in patients with bacteremia [5].

No study has reported an association between the mortality in patients with pneumonia and inflammation-based prognostic scores, including the Glasgow Prognostic Score (GPS; based on the serum levels of C-reactive protein [CRP] and albumin), the NLR, the PLR, the Prognostic Nutritional Index (PNI; based on albumin and lymphocyte counts), and the Prognostic Index (PI; based on serum CRP and white blood cell counts), which are also significant prognostic markers in several types of cancer [6]. Here, we hypothesized that the NLR measured at the time of admission to an ICU may better predict in-hospital mortality in patients with pneumonia compared to other inflammation-based prognostic scores.

The study protocol was approved by the Ethics Committee of Osaka Medical College (Osaka, Japan, #2207). We retrospectively analyzed the cases of 33 patients diagnosed with pneumonia based on symptoms

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\*Corresponding author. Phone: +81-72-683-1221; Fax: +81-72-684-6547  
E-mail: shimocchiliebesfreud512@yahoo.co.jp (Y. Shimoyama)

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and examination (e.g., cough, sputum, fever, infiltrates on chest radiographs, positive sputum culture) who were treated and intubated in the ICU of Osaka Medical College Hospital between January 2014 and June 2016. The main outcome measure was in-hospital mortality. The indication criteria for tracheal intubation were (1) respiratory distress with  $\text{FiO}_2 \geq 0.5$  and  $\text{SaO}_2 < 90\%$ , and/or (2)  $\text{pCO}_2 \geq 50$  with a decreased respiratory rate or respiratory distress. We excluded the patients aged  $\leq 18$  years, those who had any immunosuppressive disease (e.g., HIV), and those undergoing immunosuppressive therapy (e.g., chemotherapy, chronic steroid use, autoimmune disease treatment) within 1 month of

the study.

We collected the patients' demographic and clinical data from their medical records (Table 1). Continuous variables are expressed as the median (interquartile range), and categorical variables are expressed as counts (percentage). Patient characteristics were compared between the survivors ( $n=22$ ) and non-survivors ( $n=11$ ) using the Mann-Whitney  $U$ -test. Significant variables identified in a univariate analysis were subsequently assessed with a multivariate logistic regression analysis. Receiver operating characteristics (ROC) curves were generated for variables which were significant in the multivariate analysis.

**Table 1** Demographics of the study population

Variable	All patients		Univariate analysis
	Non-survivors ( $n=11$ )	Survivors ( $n=22$ )	$P$ -value
Age, years	74 (65.5–79.5)	77 (73.3–79)	0.57
Male	10 (91)	13 (59)	0.108
Female	1 (9)	9 (41)	
CAD	1 (9)	8 (36.4)	0.68
Diabetes	1 (9)	6 (27.3)	1.000
Hypertension	3 (27.3)	10 (45.5)	0.702
Renal disease	5 (45.5)	4 (18.2)	0.121
In-ICU LOS	12 (4–15.5)	9 (4–15)	0.924
A-DROP score	3 (2–4.5)	3 (2–4)	0.660
Albumin (g/l)	22 (17.5–25)	24 (21–27.8)	0.235
CRP (mg/l)	13 (5.6–17.6)	10.8 (3.4–19.8)	0.818
WBC ( $\times 10^9/l$ )	8.8 (5.9–13.1)	9.7 (7.1–11.8)	0.878
Neutrophil count ( $\times 10^9/l$ )	7.8 (5–11.7)	8.5 (5.3–10.1)	0.64
Lymphocyte count ( $\times 10^9/l$ )	0.36 (0.21–0.49)	0.78 (0.31–0.97)	0.027
Plt count ( $\times 10^4/mm^3$ )	6 (3–21)	17.6 (11.5–26.5)	0.067

CAD, coronary artery disease; ICU, intensive care unit; LOS, length of stay; CRP, C-reactive protein; WBC, white blood cell; Plt, platelets.

**Table 2** Inflammation-based prognostic scores

Variables	All patients		Univariate analysis
	Non-survivors ( $n=11$ )	Survivors ( $n=22$ )	$P$ -value
SOFA score at ICU admission	8 (6.5–10)	5.5 (4–7)	0.03
MPM II	65.5 (46.9–72.9)	55.4 (27.9–64.5)	0.35
GPS (0/1/2)	(0/11/0)	(1/21/0)	0.479
NLR	21.8 (17.5–44.9)	9.4 (7.2–19)	0.022
PLR	401.5 (95.9–534.7)	302.1 (163.5–517.5)	0.73
PI (0/1/2)	(0/6/5)	(0/14/8)	0.69
PNI	24.5 (18.7–26.8)	27.3 (22.1–32)	0.056

SOFA, sequential organ failure assessment; ICU, intensive care unit; MPM II, Mortality Probability Model II; GPS, Glasgow prognostic score; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; PI, prognostic index; PNI, prognostic nutritional index.

**Table 3** Predictors of mortality by multivariate logistic regression analysis

Predictor	Odds ratio	95%CI	P-value
SOFA score	1.418	0.956–2.104	0.083
NLR	1.074	1.001–1.152	0.047
Lymphocyte count	0.998	0.994–1.001	0.213

SOFA, sequential organ failure assessment; NLR, neutrophil to lymphocyte ratio.

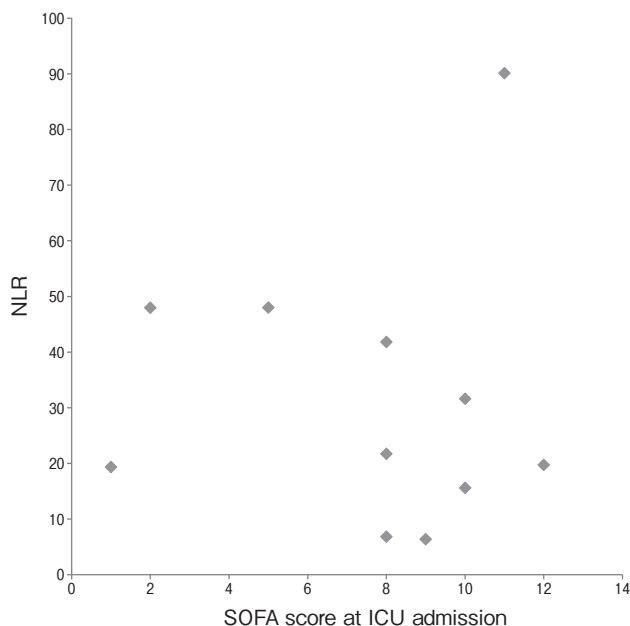
The baseline characteristics of the patients are summarized in Table 1. The univariate analysis revealed that the SOFA score (sequential organ failure assessment) at ICU admission, the lymphocyte count, and the NLR were significant predictors of mortality (Tables 1 and 2). The multivariate analysis of these significant variables revealed the NLR (odds ratio: 1.074, 95% confidence interval [CI]: 1.001-1.152,  $p=0.047$ ) as an independent significant predictor of mortality (Table 3).

An ROC curve was generated for the NLR, and the cut-off value for mortality was 15.6 (sensitivity, 81.8%; specificity, 68.2%; positive predictive value, 56.3%; negative predictive value, 88.2%; positive likelihood ratio, 2.57; negative likelihood ratio, 0.27; area under the curve, 0.75; 95%CI, 0.56-0.94;  $p=0.011$ ). The scatter diagram showed no correlation between the NLR and SOFA score at ICU admission in the non-survivors (Fig. 1).

Our results demonstrated that the NLR was superior to other inflammation-based prognostic scores in predicting the mortality of patients with pneumonia. Another study reported that lymphopenia was observed in 89 of 90 oncological ICU patients following major surgery, sepsis, and septic shock, and moreover, there was a correlation between the severity of the clinical course and the extent of lymphopenia [7]. In the present study, lymphopenia was observed significantly more often among the non-survivors compared to the survivors. Previous studies did not assess the associations between inflammation-based prognostic scores (including the GPS, NLR, PLR, PNI, and PI) and mortality. Our results are informative in this respect.

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**Fig. 1** No correlation was observed between the NLR and SOFA score at ICU admission in the non-survivors.

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