Observational Study

Medicine

OPEN

The association between the neutrophil to lymphocyte ratio and in-hospital mortality among sepsis patients

A prospective study

Ralph Bou Chebl, MD[a], Mohamad Assaf, MD[a], Nadim Kattouf, MD[a], Saadeddine Haidar, MD[a], Mohamed Khamis, MD[a], Karim Abdeldaem, MD[a], Maha Makki, MSc[b], Hani Tamim, PhD[b], Gilbert Abou Dagher, MD[a,*]

Abstract

The Neutrophil to lymphocyte ratio (NLR) was shown to be associated with disease severity, poor prognosis and increased mortality in sepsis. However, the association between NLR and sepsis prognosis remains controversial.

Our study aims to prospectively examine the prognostic ability of NLR in predicting in-hospital mortality among sepsis patients and determine the optimal cutoff of NLR that can most accurately predict in-hospital mortality in sepsis patients. This study was a prospective cohort study that included adult sepsis patients that presented to the emergency department of a tertiary care center between September 2018 and February 2021.

Receiver operating characteristic curve was used to determine the optimal cutoff of the neutrophil to lymphocyte ratio that predicts in-hospital mortality. Patients were divided into 2 groups: above and below the optimal cutoff. Stepwise logistic regression was performed to assess the magnitude of the association between NLR and in-hospital mortality.

A total of 865 patients were included in the study. The optimal cutoff for the neutrophil to lymphocyte ratio that predicts in-hospital mortality was found to be 14.20 with a sensitivity of 44.8% and a specificity of 65.3% (with PPV = 0.27 and NPV = 0.80). The area under the curve for the ratio was 0.552 with a 95% confidence intervals = [0.504–0.599] with a *P* value = .03. Patients that have a NLR above the cutoff were less likely to survive with time compared to patients below the cutoff based on the Kaplan–Meier curves. In the stepwise logistic regression, the optimal neutrophil to lymphocyte ratio cutoff was not associated with in-hospital mortality (odds ratios = 1.451, 95% confidence intervals = [0.927–2.270], *P* = .103).

In conclusion the optimal cutoff of the NLR that predicts in-hospital mortality among sepsis patients was 14.20. There was no association between the NLR and in-hospital mortality in sepsis patients after adjusting for confounders. Further studies with a larger sample size should be done to determine the optimal NLR cutoff and its prognostic role in septic patients (in-hospital mortality and other clinically significant outcomes).

Abbreviations: APACHE II = acute physiology and chronic health evaluation score, AUC = area under the curve, CI = confidence intervals, NLR = neutrophil to lymphocyte ratio, OR = odds ratios, SOFA = sequential organ failure assessment.

Keywords: cutoff, lymphocyte, mortality, neutrophil to lymphocyte ratio, neutrophil, prognosis, sepsis

1. Introduction

Sepsis and septic shock are a major cause of hospital admissions and in-hospital mortality in developed countries. They contribute to 1.5 million hospital admissions and 250,000 deaths yearly in the United States.[1] Sepsis patients who survive their hospital stay develop long-term complications such as increased long-term mortality, re-infection and have higher hospital readmission rates.[1] A biomarker is a readily measurable test which can help facilitate early recognition of diseases, guide patient management and ameliorate patient outcomes.[2,3] One proposed biomarker is the neutrophil to lymphocyte ratio (NLR) which can be easily obtained through a complete blood count. The ratio has been previously studied in several diseases, in particular malignancies. It was found to be useful in predicting adverse events in breast, lung and ovarian cancer.[4] Studies have shown superiority of the neutrophil to lymphocyte ratio over either lymphocyte or neutrophil

The authors have no funding and conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

[a]Department of Emergency Medicine, American University of Beirut, Beirut, Lebanon, [b]Department of Internal Medicine, American University of Beirut, Beirut, Lebanon.

*Correspondence: Gilbert Abou Dagher, Department of Emergency Medicine, American University of Beirut Medical Center, P.O. Box - 11-0236 Riad El Solh, Beirut 1107 2020, Lebanon (e-mail: ga66@aub.edu.lb).

How to cite this article: Chebl RB, Assaf M, Kattouf N, Haidar S, Khamis M, Abdeldaem K, Makki M, Tamim H, Dagher GA. The association between the neutrophil to lymphocyte ratio and in-hospital mortality among sepsis patients: a prospective study. Medicine. 2022;101:30(e29343).

Received: 4 October 2021 / Received in final form: 4 April 2022 / Accepted: 4 April 2022

Cassiano Felippe Gonçalves de Albuquerque.

http://dx.doi.org/10.1097/MD.0000000000029343

count alone in predicting mortality.[5] The NLR was shown to be associated with disease severity, poor prognosis and increased mortality in sepsis.[4,6] The previous studies were limited by either their retrospective nature[4] or low sample size.[6] The association between NLR and sepsis prognosis remains controversial.

Our study aims to prospectively examine the prognostic ability of NLR in predicting in-hospital mortality among sepsis patients and determine the optimal cutoff of NLR that can most accurately predict in-hospital mortality in sepsis patients.

2. Methods

2.1. Setting and sample selection

This study was a prospective cohort study that included adult sepsis patients that presented to the Emergency Department of a tertiary care center between September 2018 and February 2021. The inclusion criteria were: adult patients (≥18 years old) with the diagnosis of sepsis or septic shock. A patient was considered septic based on the sepsis-3 definition which was defined as dysregulated host response due to an infection leading to life-threatening organ dysfunction.[7] An acute change in total (sequential organ failure assessment [SOFA] – which includes 6 variables: coagulation status, respiratory status, cardiovascular status, liver function, renal status and central nervous system status) score ≥2 points as a result to the infection was defined as organ dysfunction.[7] Patients were identified with septic shock if they had sepsis with at least one of the following: a lactate level greater than 2 mmol/L after adequate fluid resuscitation or the requirement of vasopressors to maintain a mean arterial pressure greater than or equal to 65 mm Hg.[7] Those aged below 18 years, Cardiac arrest, pregnant and trauma patients were excluded. In addition, patients with an absolute neutrophil count below 1500 were excluded (neutropenia). Neutropenic patients were excluded because they would distort the association between NLR and in-hospital mortality in sepsis patients. Other immunocompromised patients were not excluded.

2.2. Variables and outcomes

The following were collected from the patients enrolled in our study: history of co-morbidities, vital signs, blood work (CBC, BUN, Creatinine, Electrolytes, Bilirubin, Lactate, Liver Enzymes, 2 blood cultures, urine analysis and urine cultures), neutrophil to lymphocyte ratio, infection site, treatment measures (vasopressors, antibiotics, steroids, inotropes and intubation) and patient disposition. Patients enrolled in the study were followed during their hospital stay to obtain hospital length of stay and in-hospital mortality. The Electronic Health Record system was used to extract the information from patient charts.

The variable of interest was the NLR. The primary outcome of this study was in-hospital mortality. The secondary outcome was to determine the optimal cutoff of the neutrophil to lymphocyte ratio that can predict in-hospital mortality in sepsis patients.

2.3. Patient recruitment process

This study was approved by the hospital's Institutional Ethics Review Board (BIO-2018-0133). Research assistants were involved in the recruitment process. They were responsible for reviewing the ED dashboard 24 hours a day 7 days a week. Informed consent was obtained by the research assistants from the family of patients that met the inclusion criteria.

2.4. Statistical analysis

Receiver operating characteristic curve was used to determine the optimal cutoff of the neutrophil to lymphocyte ratio that separates survivors from nonsurvivors in sepsis patients (in addition to its sensitivity, specificity, positive predictive value and negative predictive value). Patients were divided into 2 groups: those who had a neutrophil to lymphocyte ratio below the optimal cutoff and those who had a ratio above the optimal cutoff. Kaplan–Meier curves were obtained to compare survival rate over time between both groups. Student *t* test and Pearson's Chi-Squared test were used to compare the independent variables (continuous and categorical respectively between both groups. Stepwise logistic regression was performed to identify predictors of mortality (including the optimal neutrophil to lymphocyte ratio cutoff) in sepsis patients. The magnitude of association between the predictor variables and mortality were determined by calculating the odds ratios (OR) and their corresponding 95% confidence intervals (CI). All statistically and clinically significant variables were included in the stepwise logistic regression (The following variables were included in the model: Neutrophil to lymphocyte ratio cutoff; Age; gender (reference: male); Chronic kidney disease; hypertension; dyslipidemia; coronary artery disease; atrial fibrillation; malignancy history of stroke; history of TIA; diabetes mellitus; chronic obstructive pulmonary disease; SBP upon presentation; HR upon presentation; O_2 saturation upon presentation; WBC; hemoglobin; platelets; lactate at presentation; albumin; bun; creatinine; bicarbonate; Bilirubin total; Vasopressor use in the first 24 hours; dobutamine use in the first 24 hours; patient received steroids; intubation within the first 24 hours; intubation within the first 48 hours; IV fluid in first 6 hours; IV fluid in first 24 hours). A predetermined significance level of 0.05 was used.

3. Results

A total of 865 patients were included in the study (Fig. 1). The optimal cutoff for the neutrophil to lymphocyte ratio that separates survivors from nonsurvivors was found to be 14.20 with a sensitivity of 44.8% and a specificity of 65.3% (Table 1). The positive predictive value (PPV) of the cut-off was 0.27. The negative predictive value (NPV) was 0.80. The area under the curve (AUC) for the ratio was 0.552 with a 95% CI = [0.504–0.599] with a *P* value = .03 (Table 1 and Fig. 2). Based on the Kaplan–Meier curves, patients that have a NLR above the cutoff were less likely to survive with time compared to patients below the cutoff with a *P* value by log rank:<.001 (Fig. 3). There was no significant difference in age between patients that were below or above the cutoff (72.91 ± 15.41 years vs 74.22 ± 14.44 years, *P* = .22). The percentage of males in the group above the cutoff was significantly higher (63.4% vs 56.1%, *P* = .04). Malignancy and atrial fibrillation were significantly higher in the group above the cutoff (40.3% vs 33.2%, *P* = .04 and 24.4% vs 18%, *P* = .02 respectively) (Table 2). There were no significant differences in other comorbidities between both groups (Table 2). There was no significant difference in vital signs at presentation between both groups (Table 3). Total white blood cell count and absolute neutrophil count were significantly higher in the group above the cutoff (14,877 ± 8492 cu.mm vs 10,801 ± 7,651 cu.mm, *P* < .0001 and 13,514 ± 7530 cu.mm vs 8026 ± 4479 cu.mm, *P* < .0001) (Table 3). Absolute lymphocyte count was significantly higher in the group below the cutoff (1661 ± 3417 cu.mm vs 520 ± 323 cu.mm, *P* < .0001). Lactate was found to be significantly higher in the group above the cutoff (3.21 ± 2.69 mmol/L vs 2.80 ± 2.00 mmol/L, *P* = .01) (Table 3).

3.1. Treatment and mortality outcomes

The percentage of patients requiring vasopressors at 24 hours was significantly higher in the group above the cutoff (22.2% vs 16%, *P* = .02). Intravenous fluid requirements at 6 and 24 hours were significantly higher in the group above the cutoff (1.43 ± 1.10 L vs 1.22 ± 0.97 L, *P* = .004 and 2.32 ± 1.48 L

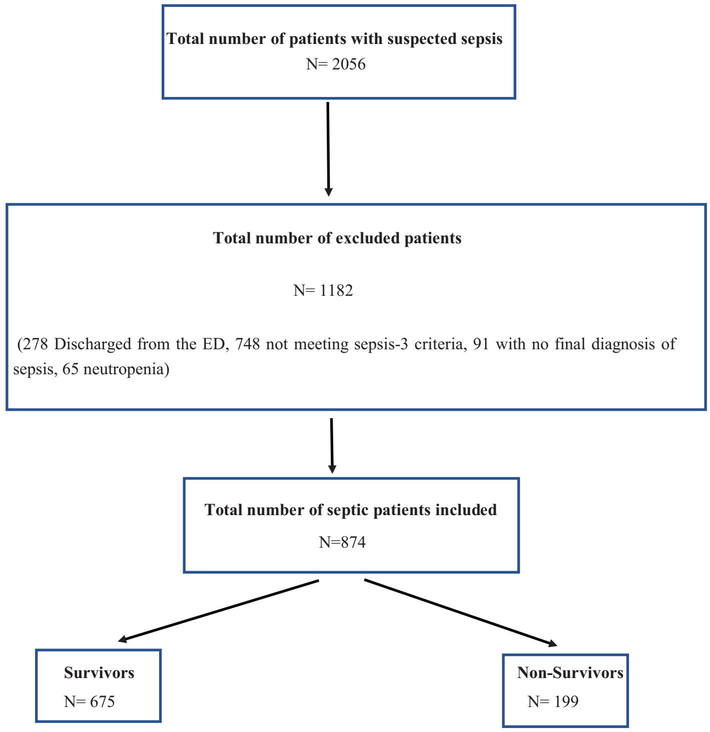

Figure 1. Figure 1 shows the flow chart.

vs 1.98±1.43 L, P = .001 respectively). There was no significant difference between both groups regarding intubation and steroid use during hospital stay (Table 4). The percentages of patients that developed septic shock and that required intensive care unit admission were significantly higher in the group above the cutoff (31.6% vs 20.2, P < .0001 and 47.5% vs 39.4%, P = .02 respectively). Hospital mortality was significantly higher in the group above the cutoff (27.2% vs 19.6%, P = .01). Finally, there was no significant difference in mechanical ventilation and hospital length of stay between both groups (Table 4).

In the stepwise logistic regression, the optimal neutrophil to lymphocyte ratio cutoff was not associated with in-hospital mortality (OR = 1.451, 95% CI = [0.927–2.270], P = .103) (Table 5).

4. Discussion

In our study, the optimal cutoff for the neutrophil to lymphocyte ratio that predicts mortality was found to be 14.20 with a sensitivity of 44.8% and a specificity of 65.3% (with PPV = 0.27 and NPV = 0.80) The area under the curve for the ratio was 0.552 with a 95% CI = [0.504–0.599] with a P value = .03. Patients that have a NLR above the cutoff were less likely to survive with time compared to patients below the cutoff. Hospital mortality was significantly higher in the group above the cutoff (27.2% vs 19.6%, P = .01). However, in the stepwise logistic regression the optimal neutrophil to lymphocyte ratio cutoff was not associated with in-hospital mortality (OR = 1.451, 95% CI = [0.927–2.270], P = .103).

Inflammation and the body's immune response to a pathogen involve neutrophils and lymphocytes. Neutrophilia, tissue damage and potential organ failure in septic patients can result from the activation of the bone marrow, mobilization of neutrophils into the bloodstream and systemic activation.[8] Inflammation and its progression are linked to a decreased lymphocyte count and an increased neutrophil count. However, the decrease in lymphocyte count during inflammation can be delayed limiting its role in evaluating inflammatory disease progression.[9,10] Also, in certain medical conditions, such as cachexia, neutrophil count can fail to increase during inflammation limiting its usefulness in examining inflammatory disease progression.[9] Studies have thus opted to evaluate the prognostic value of the NLR as a marker of infection severity. A meta-analysis involving 14 studies showed variability in the optimal cut-off for NLR in predicting mortality in sepsis patients, ranging from 4.36 to 23.8.[11] Two studies reported a cut-off for NLR of 14.08 (sensitivity and specificity of 78.3% and 50% respectively with an AUC of 0.634) and 9.11 (sensitivity and specificity of 55.1% and 70.7% respectively with an AUC of 0.622) in predicting mortality in septic patients.[4,6] This wide range made it difficult to find the ideal NLR cutoff for prognosis in sepsis. In our study, the optimal cutoff for NLR fell within the reported range and was 14.20 with a sensitivity of 44.8% and a specificity of 65.3% and an AUC of 0.552.

Table 1

AUC for in-hospital mortality among all septic patients and the optimal cut-off value of the neutrophil to lymphocyte ratio that discriminates survivors from nonsurvivors.

		95% CI							
Test result variable(s)	AUC	Lower bound	Upper bound	*P* value	Cutoff	Sensitivity	Specificity	PPV	NPV
Neutrophil to lymphocyte ratio	0.552	0.504	0.599	.030	14.1969	0.4480	0.653	0.27	0.80

*Area under the curve (AUC).

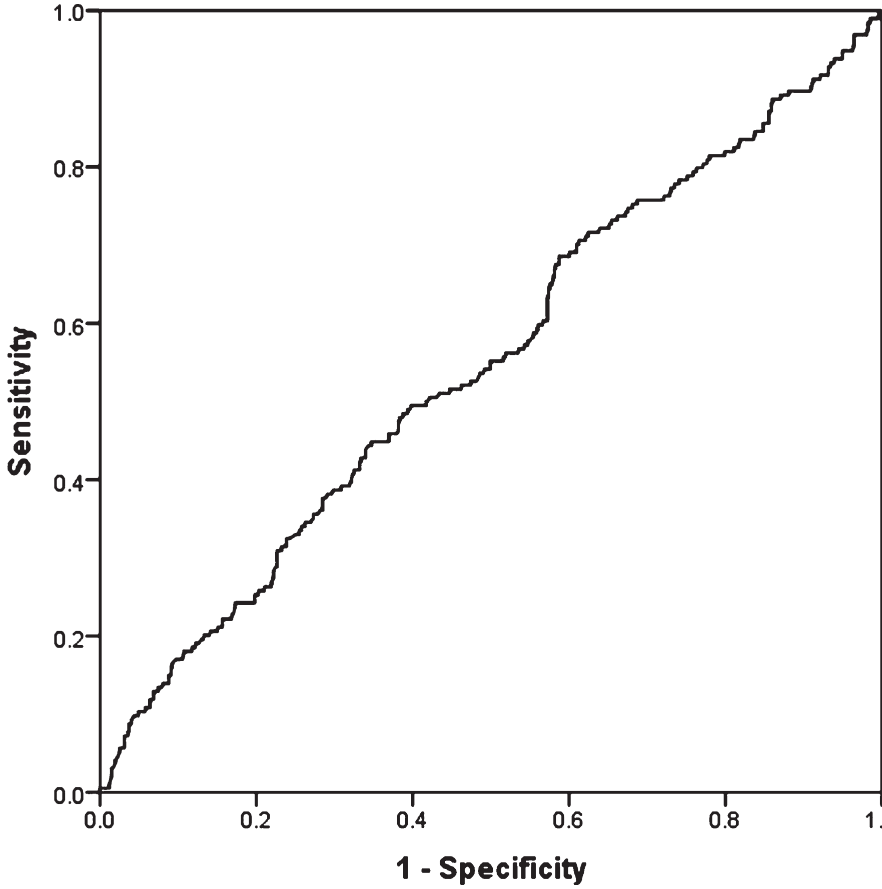

Figure 2. ROC curve for the NLR.

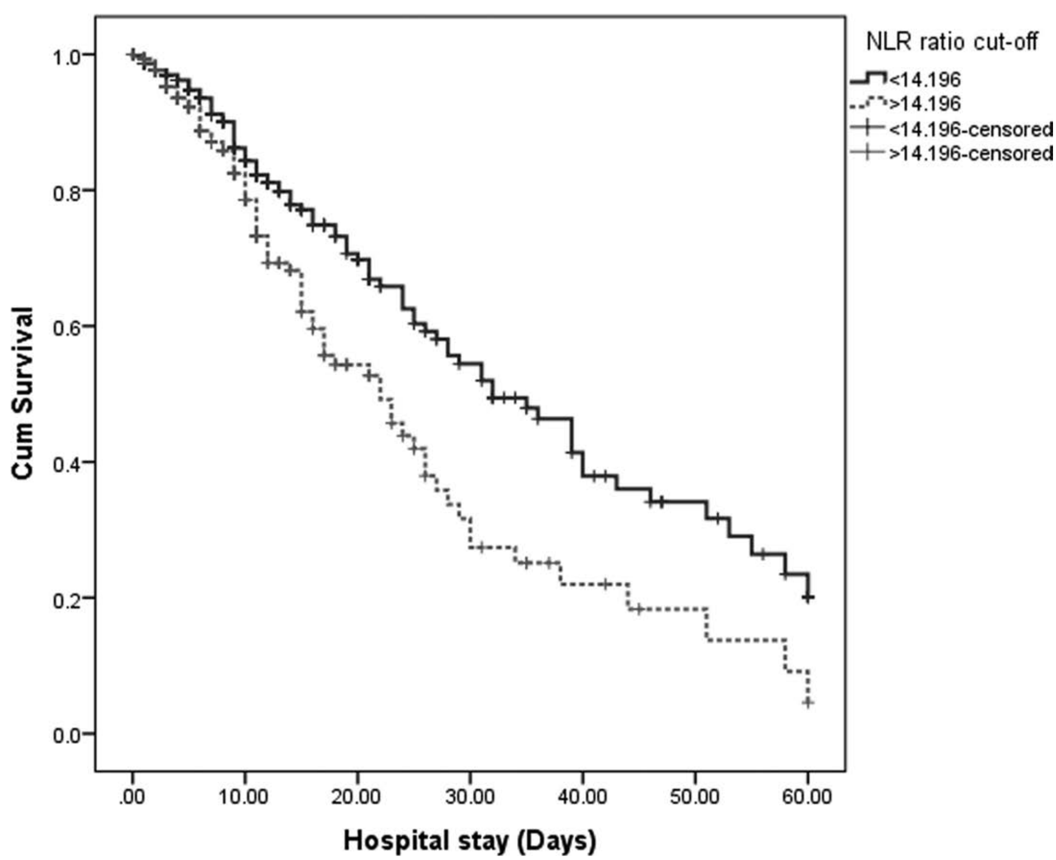

Figure 3. Kapan–Meier curves (Below the cutoff vs above the cutoff). *P* value by log rank:<.001.

Table 2

Baseline characteristics of the patients presenting to the Emergency Department with neutrophil to lymphocyte ratio above vs below the cutoff.

	Neutrophil to lymphocyte ratio		
	Below the cutoff N = 545 Mean ± SD N (%)	Above the cutoff N = 320 Mean ± SD N (%)	*P* value
Age	72.91 ± 15.41	74.22 ± 14.44	.22
Male	306 (56.1)	203 (63.4)	.04
Smoking	238 (43.7)	142 (44.4)	.84
Chronic kidney disease	133 (24.4)	80 (25.0)	.84
Hypertension	356 (65.3)	213 (66.6)	.71
Dyslipidemia	230 (42.2)	133 (41.6)	.85
Atrial fibrillation	98 (18.0)	78 (24.4)	.02
Coronary artery disease	188 (34.5)	112 (35.0)	.88
Congestive heart failure	137 (25.1)	80 (25.0)	.96
Malignancy	181 (33.2)	129 (40.3)	.04
Receiving any treatment	92 (53.2)	57 (48.3)	.41
History of stroke	49 (9.0)	20 (6.3)	.15
History of TIA	6 (1.1)	4 (1.3)	.84
History of vascular disease	50 (9.2)	32 (10.0)	.70
Diabetes mellitus	231 (42.4)	136 (42.5)	.97
Chronic obstructive Pulmonary disease	103 (18.9)	47 (14.7)	.11

Zahorec et al reported an association between NLR and disease severity and mortality in septic patients.[12] The pooled results of a meta-analysis showed that increases in NLR were linked to worse prognosis in sepsis (HR = 1.75, 95% CI = [1.56–1.97], $P < .01$).[11] Multiple studies showed NLR to be an independent predictor of in hospital mortality in septic patients with one of them showing that increases in NLR from day 1 to day 5 of hospital admission are associated with worse outcomes.[6,13,14] In patients admitted for community acquired pneumonia NLR was found to be a useful tool in predicting mortality.[15] Sepsis induced tissue injury causes an acute inflammatory response where neutrophils play an important role. Septic patients tend to have increased cortisol levels and be in a state of neuroendocrine stress which were found to be associated with lymphopenia. The above could be a possible explanation to why NLR would be higher in non-survivors compared to survivors because of systemic inflammation.[6]

In our study, the optimal neutrophil to lymphocyte ratio cutoff was not associated with in-hospital mortality (OR = 1.451, 95% CI = [0.927–2.270], $P = .103$). In a cohort study involving critically ill patients the NLR ratio was not associated with 28-day mortality in the sepsis group. The study

Table 3

Vital signs and lab parameters of patients presenting to the Emergency Department with neutrophil to lymphocyte ratio above vs below the cutoff.

	Neutrophil to lymphocyte ratio		
	Below the cutoff N = 545 Mean ± SD	Above the cutoff N = 320 Mean ± SD	*P* value
Systolic blood pressure upon presentation (mmHg)	121.96 ± 26.03	118.90 ± 27.56	.10
Diastolic blood pressure upon presentation (mmHg)	68.60 ± 15.49	66.62 ± 15.93	.07
Heart rate upon presentation (beats/min)	98.44 ± 25.37	100.10 ± 25.21	.35
O_2 saturation upon presentation (%)	93.48 ± 9.59	93.64 ± 9.52	.08
Temperature upon presentation (C)	37.39 ± 1.78	37.39 ± 1.58	.97
Respiratory rate upon presentation (Breaths/min)	21.71 ± 8.24	21.64 ± 7.15	.90
White blood cell count (cu.mm)	10801.62 ± 7651.71	14877.80 ± 8492.98	
Neutrophil count (cu.mm)	8026.47 ± 4479.79	13514.00 ± 7530.05	
Lymphocyte count (cu.mm)	1661.41 ± 3417.68	520.08 ± 323.66	
Neutrophil to lymphocyte ratio	6.95 ± 3.60	33.68 ± 25.31	
Hematocrit (%)	35.15 ± 7.61	35.76 ± 5.99	.22
Hemoglobin (g/dL)	11.45 ± 2.30	11.68 ± 2.06	.15
Platelets (cu.mm)	228970.64 ± 129269.39	237883.64 ± 140994.58	.34
Lactate (mmol/L)	2.80 ± 2.00	3.21 ± 2.69	.01
C-reactive protein(mg/L)	119.33 ± 100.81	146.37 ± 103.80	.004
Albumin (g/L)	33.95 ± 6.52	31.92 ± 7.05	
Procalcitonin (ng/L)	5.05 ± 16.76	6.19 ± 15.16	.45
Glucose (mg/dL)	159.52 ± 83.90	177.13 ± 106.65	.02
BUN (mg/dL)	31.48 ± 22.93	38.54 ± 27.85	
Creatinine (mg/dL)	1.52 ± 1.34	1.64 ± 1.37	.21
Bicarbonate (mmol/L)	24.48 ± 10.33	22.64 ± 8.09	.007
Ph_arterial	7.39 ± 0.10	7.39 ± 0.10	.92

Table 4

Therapeutic measures undergone by patients presenting to the Emergency Department and outcomes with neutrophil to lymphocyte ratio above vs below the cutoff.

	Neutrophil to lymphocyte ratio		P value
	Below the cutoff N = 545 Mean ± SD N(%)	Above the cutoff N = 320 Mean ± SD N(%)	
Vasopressor use in the first 24 h	87 (16.0)	71 (22.2)	.02
Dobutamine use in the_first_24 h	5 (0.9)	1 (0.3)	.42
Steroid use during hospital stay	162 (29.7)	100 (31.3)	.64
Intubation within the first 24 h	59 (10.8)	35 (10.9)	.96
Intubation within the first 48 h	32 (5.9)	22 (6.9)	.56
Iv fluids in first 6 hours	1.22 ± 0.97	1.43 ± 1.10	.004
Iv fluids in first 24 h	1.98 ± 1.43	2.32 ± 1.48	.001
Development of septic shock	110 (20.2)	101 (31.6)	
ICU admission	215 (39.4)	152 (47.5)	.02
Required mechanical ventilation	76 (13.9)	57 (17.8)	.13
Hospital length of stay (days)	10.83 ± 13.10	9.62 ± 9.77	.13
Hospital mortality	107 (19.6)	87 (27.2)	.01

Table 5

Stepwise logistic regression for mortality.

		95% C.I.		
	OR	Lower	Upper	P value
Neutrophil to lymphocyte ratio cutoff	1.451	0.927	2.270	.103

Variables included in the model:Imposed: Neutrophil to lymphocyte ratio cutoffStepwise: Age; gender (reference: male); Chronic kidney disease; hypertension; dyslipidemia; coronary artery disease; atrial fibrillation; malignancy history of stroke; history of TIA; diabetes mellitus; chronic obstructive pulmonary disease; SBP upon presentation; HR upon presentation; O2 saturation upon presentation; WBC; hemoglobin; platelets; lactate at presentation; albumin; bun; creatinine; bicarbonate; Bilirubin total; Vasopressor use in the first 24 h; dobutamine use in the first 24 h; patient received steroids; intubation within the first 24 h; intubation within the first 48 h; IV fluid in first 6 h; IV fluid in first 24 h

categorized patients by quartiles based on the NLR ratio.[16] Another study also showed no association between NLR and 28-day mortality in septic patients with a *P* value of .988.[4] Bermejo-Martín et al showed a link between mortality and low neutrophil count.[17] Septic patients with a low neutrophil count may have suboptimal innate immune response to infection. Sepsis may enhance adhesion between neutrophils and the endothelium of blood vessels causing endothelial damage and a decrease in measured circulating neutrophils.[17] In addition, Brown et al suggested that neutrophils can exist in a variety of functional states thus an assessment of the NLR ratio at 1 point in time may be insufficient to evaluate the effect of this ratio on disease states like sepsis that last for days to weeks.[8]

Studies have also investigated the prognostic utility of the NLR in septic patients with regards to outcomes other than mortality. Septic patients with a high NLR had increased disease severity, longer ICU stay, higher Acute Physiology and Chronic Health Evaluation score (APACHE II) and higher SOFA score.[12,18] Velissaris et al found a positive correlation between NLR and disease severity on admission (SOFA, $r = 0.497$, $P < .001$; APACHE II, $r = 0.411$, $P = .006$).[19] Another study showed that increased NLR levels were associated with increased risk of an unfavorable outcome after adjusting for confounders (OR = 1.043 95% CI = [1.012–1.083] $P = .016$).[13] In our study we found that septic patients that had an NLR above the optimal cutoff were more likely to develop septic shock and be admitted to the ICU (31.6% vs 20.2, $P < .0001$ and 47.5% vs 39.4%, $P = .02$ respectively). However, in a study done by Pantzaris et al, no statistically significant association was found between NLR and disease severity (SOFA score and APACHE II score) as well as length of hospital stay.[15] The authors noted that their small sample size may be why there were not able to find a statistically significant relationship.

5. Limitations

Our study has several limitations. It was conducted at a in a single tertiary-care center which limits the generalizability of our data. The NLR was taken at 1 point in time (upon hospital admission). Serial measurements to trend NLR during hospital stay could have shown an association with in-hospital mortality similar to the findings of a previously mentioned study.[14] We did not investigate the association between NLR and severity scores such as SOFA and APACHE II scores. In addition, we did not compare the prognostic ability of NLR to other inflammatory biomarkers; this would be our aim in future prospective studies and endeavors. Future studies including multiple tertiary care centers with a larger sample size should be done to further evaluate the prognostic value of NLR in septic patients. In addition, studies examining the association between NLR trends during hospital stay and in-hospital mortality should be done. The association between NLR and disease severity in septic patients should be studied by comparing it to validated scoring systems such as APACHE II and SOFA scores and clinical outcomes such as development of septic shock and ICU admission. Finally comparing NLR to other inflammatory biomarkers in predicting in-hospital mortality would be the next step.

6. Conclusion

In conclusion, the optimal cutoff for the neutrophil to lymphocyte ratio that predicts mortality was found to be 14.20 with a sensitivity of 44.8% and a specificity of 65.3% (with PPV = 0.27 and NPV = 0.80). The area under the curve for the ratio was 0.552 with a 95% CI = [0.504–0.599] with a *P* value = .03. Patients that have a NLR above the cutoff were less likely to survive with time compared to patients below the cutoff.

However, after adjusting for confounders, the neutrophil to lymphocyte ratio cutoff was not associated with in-hospital mortality (OR = 1.451, 95% CI = [0.927–2.270], *P* = .103). Further studies, preferably prospective with a larger sample size should be done to determine the optimal NLR cutoff and its prognostic role in septic patients (mortality and other clinically significant outcomes).

Acknowledgments

We would like to acknowledge the role of the Emergency Medicine Department at the American University of Beirut for their help in the study.

Author contributions

Conceptualization: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Data curation: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Formal analysis: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Nadim Kattouf, Ralph Bou Chebl.
Funding acquisition: Mohamed Khamis, Saadeddine Haidar.
Investigation: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Methodology: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Project administration: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Resources: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Software: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Supervision: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Validation: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Visualization: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Writing – original draft: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.
Writing – review & editing: Gilbert Abou Dagher, Hani Tamim, Karim Abdeldaem, Maha Makki, Mohamad Assaf, Mohamed Khamis, Nadim Kattouf, Ralph Bou Chebl, Saadeddine Haidar.

References

[1] Prescott HC, Osterholzer JJ, Langa KM, Angus DC, Iwashyna TJ. Late mortality after sepsis: propensity matched cohort study. BMJ 2016;353:i2375.
[2] Lippi G, Montagnana M, Balboni F, et al. Academy of Emergency Medicine and Care-Society of Clinical Biochemistry and Clinical Molecular Biology consensus recommendations for clinical use of sepsis biomarkers in the emergency department. Emerg Care J 2017;13. https://doi.org/10.4081/ecj.2017.6877.
[3] PRISM Investigators, Rowan KM, Angus DC, Bailey M, et al. Early, goal-directed therapy for septic shock—a patient-level meta-analysis. N Eng J Med 2017;376:2223–34.
[4] Ni J, Wang H, Li Y, Shu Y, Liu Y. Neutrophil to lymphocyte ratio (NLR) as a prognostic marker for in-hospital mortality of patients with sepsis: a secondary analysis based on a single-center, retrospective, cohort study. Medicine 2019;98:e18029.
[5] Kumarasamy C, Sabarimurugan S, Madurantakam RM, et al. Prognostic significance of blood inflammatory biomarkers NLR, PLR, and LMR in cancer—a protocol for systematic review and meta-analysis. Medicine 2019;98:e14834.
[6] Liu Y, Zheng J, Zhang D, Jing L. Neutrophil-lymphocyte ratio and plasma lactate predict 28-day mortality in patients with sepsis. J Clin Laborat Analy 2019;33:e22942.
[7] Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:801–10.
[8] Brown KA, Brain SD, Pearson JD, Edgeworth JD, Lewis SM, Treacher DF. Neutrophils in development of multiple organ failure in sepsis. Lancet 2006;368:157–69.
[9] Taneja R, Parodo J, Jia SH, Kapus A, Rotstein OD, Marshall JC. 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.
[10] Vidal AC, Howard LE, de Hoedt A, et al. Neutrophil, lymphocyte and platelet counts, and risk of prostate cancer outcomes in white and black men: results from the SEARCH database. Cancer Causes Control 2018;29:581–88.
[11] Huang Z, Fu Z, Huang W, Huang K. Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: a meta-analysis. Am J Emerg Med 2020;38:641–7.
[12] 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.
[13] Liu X, Shen Y, Wang H, Ge Q, Fei A, Pan S. Prognostic significance of neutrophil-to-lymphocyte ratio in patients with sepsis: a prospective observational study. Med Inflammation 2016;2016.
[14] Riché F, Gayat E, Barthélémy R, Le Dorze M, Matéo J, Payen D. Reversal of neutrophil-to-lymphocyte count ratio in early versus late death from septic shock. Crit Care 2015;19:439.
[15] Pantzaris ND, Platanaki C, Pierrako C, Karamouzos V, Velissaris D. Neutrophil-to-lymphocyte ratio relation to sepsis severity scores and inflammatory biomarkers in patients with community-acquired pneumonia: a case series. J Translat Internal Med 2018;6:43–6.
[16] Salciccioli JD, Marshall DC, Pimentel MA, et al. The association between the neutrophil-to-lymphocyte ratio and mortality in critical illness: an observational cohort study. Crit Care 2015;19:13.
[17] Bermejo-Martín JF, Tamayo E, Ruiz G, et al. Circulating neutrophil counts and mortality in septic shock. Crit Care 2014;18:407.
[18] Kaushik R, Gupta M, Sharma M, et al. Diagnostic and prognostic role of neutrophil-to-lymphocyte ratio in early and late phase of sepsis. Indian J Crit Care Med 2018;22:660–3.
[19] Velissaris D, Pantzaris ND, Bountouris P, Gogos C. Correlation between neutrophil-to-lymphocyte ratio and severity scores in septic patients upon hospital admission. A series of 50 patients. Rom J Intern Med 2018;56:153–7.