Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2022;11(3):1296-9

The effect of neutrophil lymphocyte ratio on mortality in patients followed in the intensive care unit with the diagnosis of ischemic stroke from the emergency department

Hakan Aygun[1], Asli Sener[2]

[1]Bakırcay University Cigli Training and Research Hospital, Depatrment of, Anesthesia and Reanimation, Izmir, Turkey
[2]Bakırcay University Cigli Training and Research Hospital, Depatrment of, Emergency Medicine and Traumatology, Izmir, Turkey

Received 16 July 2022; Accepted 17 July 2022
Available online 25.08.2022 with doi: 10.5455/medscience.2022.06.138

Abstract

The goal of this study was to determine if the neutrophil-lymphocyte ratio (NLR) predicts mortality in patients hospitalized in the intensive care unit (ICU) with an ischemic stroke. Between January 1 and December 31, 2021, 116 patients admitted to our emergency department with the diagnosis of ischemic stroke and hospitalized in the 3rd level ICU unit were included in the study and divided into two groups: patients who died (Group 1: n=62) and patients who survived (Group 2: n=54). Patients' age, gender, presence of chronic diseases, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and neutrophil count, lymphocyte count, and NLR were obtained by dividing these two numbers in the first complete blood count taken at the time of admission to the emergency department were collected and analyzed. While 54 (46.5%) patients were discharged from the ICU, 62 (53.4%) patients died. 60 (51.7%) of the patients were female. The average age of patients was 76.85±10.70. APACHE II score was found to be correlated with mortality (AUC 0.70, 95% CI (0.616-0.802) (p=0.01). When the APACHE II cut-off value was more than 13.5, it predicted mortality with 95% sensitivity and 85% specificity. The median NLR ratio of the patients was found to be 5.08 (0.38-35.16) in the survivors and 11.68 (1.38-113.00) in patients that died. NLR was lower in survivors (p=0.002). NLR may be a valuable marker in predicting mortality in stroke patients admitted to the ICU.

Keywords: Ischemic stroke; intensive care; neutrophil-lymphocyte ratio

Introduction

Stroke is a cerebrovascular disease characterized with sudden onset of neurological symptoms and findings [1]. Approximately 85% of cases are ischemic, while 15% are hemorrhagic [2]. It is more prevalent among young men than young women, however among all age groups, women are at a higher risk of having a stroke [3]. Stroke is the leading cause of morbidity worldwide. As the extent of the affected brain tissue increases, mortality and morbidity also increase. Hypertension, smoking, diabetes, coronary artery disease, carotid artery stenosis, dyslipidemia, oral contraceptive medications, and obesity are all risk factors for stroke. Age, high hematocrit levels, homocysteine, c-reactive protein, high blood sugar, and high body heat are all risk factors for mortality. [4]. Even though stroke treatment procedures have become more effective in recent years, treatment remains a race against time. Primary therapies for acute ischemic stroke include intravenous thrombolysis and thrombectomy. In intravenous thrombolytic therapy, a 4.5 hour time restriction is established. This period is 6 hours for mechanical thrombectomy. In the first 36 hours following the onset of an acute ischemic stroke, every ten minutes of prompt treatment reduces mortality and reduces the incidence of bleeding [5].

NLR is an inexpensive and readily available parameter that allows for the determination of the inflammatory status of the body. Its predictive value for the prognosis of different cancer types, chronic inflammation, cardiac and infectious pathologies have been proven [6].

Neutrophils, created in bone marrow, have a lifespan of 24 hours. In the presence of systemic inflammatory response or systemic infection, neutrophil count increases [5]. Neutrophil count represents the severity of acute inflammation [7]. The lifespan of

*Corresponding Author: Hakan Aygun, Bakırcay University Cigli Training and Research Hospital, Depatrment of, Anesthesia and Reanimation, Izmir, Turkey
E-mail:draygunhakan@gmail.com

a lymphocyte may extend from more than a couple of weeks to a couple of years, yet lymphopenia may occur secondary to stress.

Increases in inflammation and stress are proportional to the size of the affected tissue. In the acute phase of inflammation, the neutrophil-lymphocyte ratio (NLR) rises as a result of elevated neutrophils and reduced lymphocyte numbers caused by the suppression of acute stress. It is reported that a high NLR is associated with a bad prognosis in acute coronary syndromes [8].

In this study, we aimed to determine whether NLR is useful in predicting the mortality of patients hospitalized for ischemic stroke in the intensive care unit.

Material and Methods

Study design and data collection

Our study is a cross-sectional descriptive study. Patients who were admitted to ICU due to ischemic stroke following emergency room presentation between 1st January –31st December 2021 were included to the study. Patient data was obtained from a hospital database and the data was retrospectively analyzed. The age, gender, length of ICU stay, outcome of ICU treatment, APACHE II score, neutrophil and lymphocyte levels were retrieved. NLR was calculated by dividing the neutrophil levels by lymphocyte levels. The following patients were excluded: those <18y age, those with non-ischemic strokes or ischemic stroke cases who weren't hospitalized, cases where all data was unavailable, those with a diagnosis, of cancer, those who underwent immunosuppressive treatment in the last month, patients who had cardiac arrest during hospital stay, history of steroid use, and cases who received blood transfusions.

Patients were divided into two groups: those who were deceased during ICU admission (Group 1) and those who survived (Group 2) (Table 1). Age, gender, presence of chronic diseases, APACHE II scores, neutrophil and lymphocyte levels at admission and NLR were recorded (Table 2). In order to calculate the Charlson Comorbidity Index (CCI) score, each patient's medical history was obtained during admission to the emergency department and admission diagnoses and systemic diseases were recorded according to the 19 types of diagnostic groups in the CCI score. The sum of the points assigned to these diagnostic groups was accepted as the CCI score. Laboratory results, screening and interventional radiological studies, and pathology reports were also documented.

Bakircay University Ethical Committee's approval was sought for this project (Date: 17.05.2022 and Decision Number: 608)

Statistical Analysis

SPSS 26.0 (IBM Corporation, Amonk, New York, United States) was used to analyze the variables. Demographics were reported as numbers and ratios. For parametric tests, the conformance of groups to a normal distribution was initially evaluated. Median and standard deviation were used for reporting normally distributed data while median, minimum and maximum were used to report non-normally distributed data. Chi-square was used to compare non-parametric data. If the predictive values in the cells were less than 5, the Fisher exact test was employed. For comparing the medians between groups, the Student-t test was utilized. If the group variables were less than 30, the Mann-Whitney U test was used. $p<0.05$ was considered as statistically significant.

Results

A total of 116 patients were included in the study. Of these, 60 were female (51.7%) and 56 were male (48.2%). There was no statistically significant difference between groups with regards to gender ($p>0.05$). There were 62 patients in group 1 and 54 in group 2. Statistically significant difference was found between the groups in terms of CCI values, group 1 was 5.84±1.58 and in group 2 was 4.07±1.57, ($p<0.05$). The average age of patients in group 1 was 79.74±10.13 and in group 2 it was 73.54±10.46 ($p=0.915$).

The median (min-max) NLR value for all patients was 7.50±0.38-113. When NLR values were compared between groups, median NLR was found to be significantly higher in group 1(11.68**[**1.38 –113.00**]**) when compared to group 2(5.08±0.38–35.16**]**) ($p=0.002$).

Table 1. Study flowchart

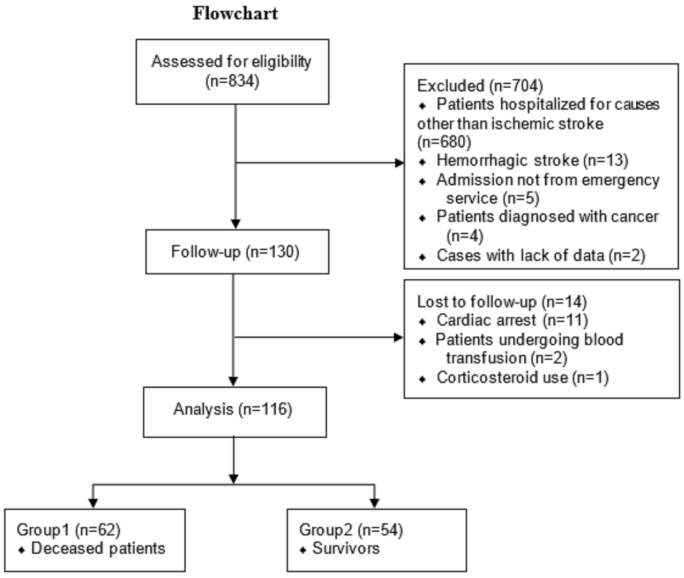

Table 2. Comparison of data between groups.

	Group 1 (deceased)n:62	Group 2 (survivors) n:54	p-value
Female	29 (46.8%)	31 (57.4%)	0.169
Male	33 (53.2%)	23 (42.6%)	
Age	79.74±10.13	73.54±10.46	0.915
NLR*	11.68 (1.38-113.00)	5.08 (0.38-35.16)	0.002
APACHE II	23.77±6.63	19±5.18	0.087
Outcome time	17.5±14.5	25.13±14.9	0.313
CCI#	5.84±1.58	4.07±1.57	($p<0.05$)

*median value (min-max), # Charlson Comorbidity Index

For NLR, the receiver processing characteristics (ROC) curve analysis area under the curve (AUC) value was 0.57 (95% CI (0.465-0.677, $p=0.18$ (Figure 1). Average APACHE II score was similar between groups (23.77±6.63 vs 19.50±18.00, $p>0.05$). For APACHE II, AUC value was 0.70, (%95 CI 0.616-0.802, $p<0.01$) (Figure 2). A cutoff value of 13.5 for APACHE II had a 95% sensitivity and 85% specificity for predicting mortality.

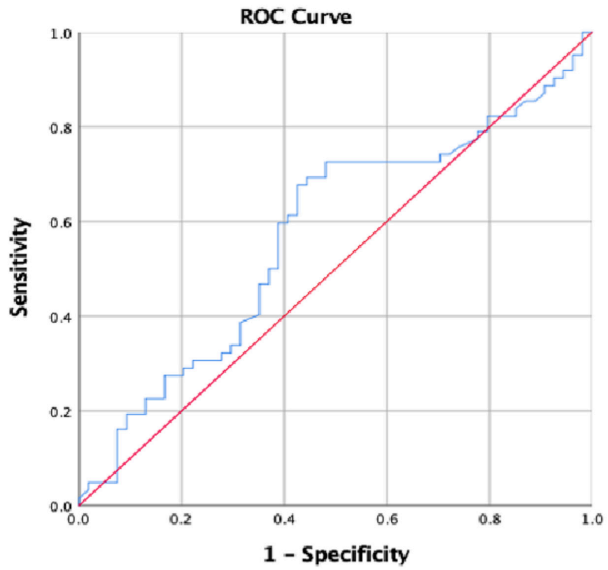

Figure 1. NLR¥ survival ROC† analysis graph ¥: Neutrophil-lymphocyte ratio, †: Receiver Operating Characteristic

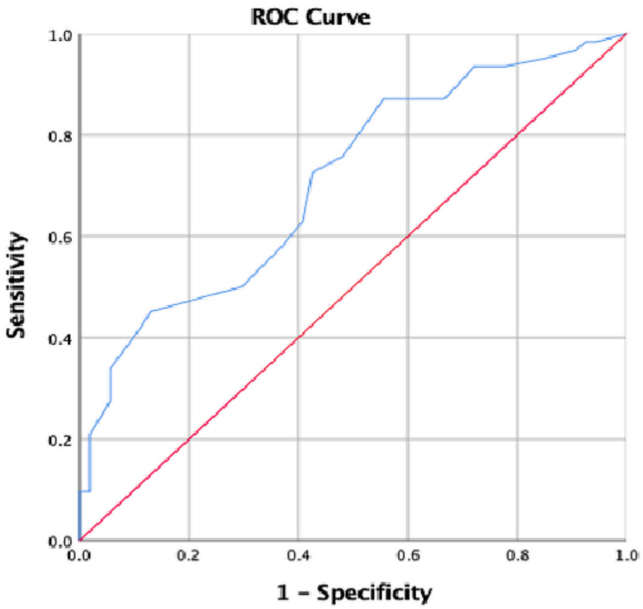

Figure 2. APACHE II‡ survival ROC† analysis graph ‡: APACHE II Acute Physiology and Chronic Health Evaluation, †: Receiver Operating Characteristic

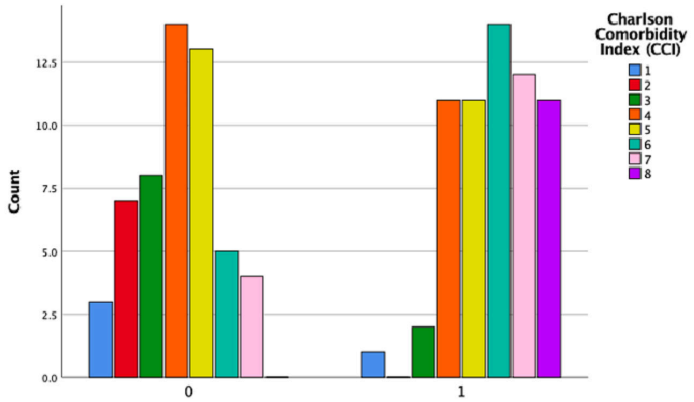

Figure 3. Survivors deceased-CCI± graph 0: Survivors, 1: Deceased, ±: Charlson Comorbidity Index

Discussion

Ninety-nine percent of strokes seen in clinical practice are secondary to arterial occlusion, manifesting as thrombotic or embolic events. Experimental stroke models have demonstrated that increasing lymphocyte counts generate anti-inflammatory cytokines while suppressing inflammatory cytokines, thereby reducing neuronal damage [9]. In the early phase, the increase in neutrophil levels has been associated with the severity of the stroke, whereas the drop in lymphocytes has been associated with poor functional recovery [10]. In a meta-analysis of prognostic variables in acute ischemic stroke, high NLR values were found to be predictive of outcome and a major risk factor for cerebral hemorrhage [11].

Numerous risk factors play a role in ischemic stroke. Increased age, male gender, hypertension, diabetes, coronary artery disease, and smoking are all risk factors. A rise in cholesterol levels also raises the likelihood of thromboembolic events [12]. The exact mortality rate of ischemic stroke patients in ICU is difficult to predict. The 30-day mortality rate for first stroke is reported to be 10-17% [13] and the five-year survival rate is projected to be 40% [14].

The mortality rate in our study was 53.4%. Similarly, Arslan et al. reported a 74.4% mortality rate for stroke patients in a third-grade ICU [13]. The CCI values of patients who died versus those who survived were significantly different. Analysis revealed that this was likely due to the high prevalence of comorbidities among the deceased (Figure 3). The median age of patients in our group was 76.85±10.70 years and there was no statistically significant correlation between age and mortality. Age, which is the key risk factor for mortality and morbidity, is crucial in stroke cases. Mortality and morbidity rise proportionally with age [15]. In our study, the high average age was thought to be one of the causes of the high mortality rate we report.

Recently, the use of accessible and inexpensive hematological markers as prognostic indicators has expanded in ischemic strokes [16]. Qun et al. found an association between elevated NLR and poor prognosis in ischemic stroke [17]. In a meta-analysis of the predictors of the course of acute ischemic stroke, a high NLR was identified as a risk factor for symptomatic intracranial bleeding and an indicator of prognosis [11].

In our study, the NLR value of patients with ischemic stroke admitted to our ICU from the emergency room was statistically greater in the deceased group when compared to the survivors ($p<0.05$). ROC analysis revealed that NLR was a substantial predictor of mortality in the ICU ($p=0.001$). The results of our investigation are consistent with other studies that have been examined this correlation in the literature [18].

Study limitations

Our research is restricted by its retrospective, single-center design and small sample size. There is a need for prospective, multicenter studies that analyze the outcomes of a greater number of cases with a variety of factors.

Conclusion

In patients admitted to the ICU with ischemic stroke, neutrophil

to lymphocyte ratio is a cheap and effective indicator for the prediction of mortality. Since there are limited studies in the literature on the neutrophil-lymphocyte ratio in ischemic stroke, more clinical studies with more patients are needed in the future.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
Bakircay University Ethical Committee's approval was sought for this project (Date: 17.05.2022 and Decision Number: 608).

References

1. Boursin P, Paternotte S, Dercy B, et al. Semantics, epidemiology and semiology of stroke. Soins. 2018;63:24-7.
2. Guzik A, Bushnell C. Stroke Epidemiology and risk factor management. Continuum (Minneap Minn). 2017;23:15-39.
3. Seshadri S, Beiser A, Kelly-Hayes M, et al. The lifetime risk of stroke: estimates from the Framingham study. Stroke. 2006;37:345-50.
4. Aksoy D, İnanır A, Ayan M, et al. Predictors of mortality and morbidity in acute ischemic stroke. Arch Neuropsychiatry. 2013;50:40-4.
5. Ministry of Health ischemic stroke diagnosis and treatment guide,Turkey. 07.10.2020
6. Forget P, Khalifa C, Defour JP, et al. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Res Notes. 2017;10:2.
7. Aydın İ, Ağıllı M, Aydın F, et al. The reference ranges of neutrophil-lymphocyte ratio in different age groups. Gülhane Med J, 2015;57:414.
8. Celikbilek A, Ismailogullari S, Zararsiz G. Neutrophil to lymphocyte ratio predicts poor prognosis in ischemic cerebrovascular disease. J Clin Lab Anal. 2014;28:27-31.
9. Ren H, Liu X, Wang L, et al. Lymphocyte-to-monocyte ratio: a novel predictor of the prognosis of acute ischemic stroke. J Stroke Cerebrovasc Dis. 2017;26:2595–602.
10. Kim JY, Park J, Chang JY, et al. Inflammation after ischemic stroke: the role of leukocytes and glial cells. Exp Neurobiol. 2016;25:241–51.
11. Jing Zhang, Qingqing Ren, Yanlin Song, et al. Prognostic role of neutrophil–lymphocyte ratio in patients with acute ischemic stroke. Medicine. 2017;96:e8624.
12. Şahin D, Yusuf Ü, Derya I. Management of preventable risk factors in cerebrovascular diseases. Ankara Med J, 2015;15(2).
13. Arslan Z, Özmen Ö, Çömez M. Factors affecting the mortality of the patients with ischemic stroke in reanimation intensive care unit. Mustafa Kemal Univ Med J. 2016;7:23-31.
14. Martinez-Garcia MA, Soler-Cataluna JJ, Ejarque- Martinez L, et al. Continuous positive airway pressure treatment redu- ces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. Am J Respir Crit Care Med. 2009;180:36-41.
15. Goldstein LB, Bushnell CD, Adams RJ, et al. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42:517-84.
16. Luo Fan, Li Gui, Er-Qing Chai, et al. Routine hematological parameters are associated with short-and long-term prognosis of patients with ischemic stroke. J Clin Lab Anal. 2018;32:e22244.
17. Qun S, Tang Y, Sun J, et al. Neutrophil-to-lymphocyte ratio predicts 3-month outcome of acute ischemic stroke. Neurotox Res. 2017;31:444-52.
18. Xue J, Huang W, Chen X, et al. Neutrophil-to-lymphocyte ratio is a prognostic marker in acute ischemic stroke. J Stroke Cerebrovasc Dis. 2017;26:650–7.