Original Research Article

INR INTERVENTIONAL NEURORADIOLOGY

Interventional Neuroradiology
1–7

DOI: 10.1177/15910199221093896
journals.sagepub.com/home/ine
SAGE

Neutrophil–Lymphocyte ratio is associated with poor clinical outcome after mechanical thrombectomy in stroke in patients with COVID-19

Fawaz Al-Mufti[1], Priyank Khandelwal[2], Tolga Sursal[1], Jared B. Cooper[1], Eric Feldstein[1], Krishna Amuluru[3], Jayaji M. Moré[1], Ambooj Tiwari[4], Amit Singla[2], Adam A Dmytriw[5], Mariangela Piano[6], Luca Quilici[6], Guglielmo Pero[6], Leonardo Renieri[7], Nicola Limbucci[7], Mario Martínez-Galdámez[8], Miguel Schüller-Arteaga[8], Jorge Galván[8], Juan Francisco Arenillas-Lara[8], Zafar Hashim[9], Sanjeev Nayak[9], Keith Desousa[10], Hai Sun[11], Pankaj K. Agarwalla[2], J Sudipta Roychowdhury[12], Emad Nourollahzadeh[12], Tannavi Prakash[2], Andrew R Xavier[13], J Diego Lozano[14], Gaurav Gupta[11], Dileep R Yavagal[15], Mohammad Elghanem[16], Chirag D. Gandhi[1] and Stephan A. Mayer[1]

Abstract

Background: The neutrophil–lymphocyte ratio (NLR) is emerging as an important biomarker of acute physiologic stress in a myriad of medical conditions, and is a confirmed poor prognostic indicator in COVID-19.

Objective: We sought to describe the role of NLR in predicting poor outcome in COVID-19 patients undergoing mechanical thrombectomy for acute ischemic stroke.

Methods: We analyzed NLR in COVID-19 patients with large vessel occlusion (LVO) strokes enrolled into an international 12-center retrospective study of laboratory-confirmed COVID-19, consecutively admitted between March 1, 2020 and May 1, 2020. Increased NLR was defined as ≥7.2. Logistic regression models were generated.

Results: Incidence of LVO stroke was 38/6698 (.57%). Mean age of patients was 62 years (range 27–87), and mortality rate was 30%. Age, sex, and ethnicity were not predictive of mortality. Elevated NLR and poor vessel recanalization (Thrombolysis in Cerebral Infarction (TICI) score of 1 or 2a) synergistically predicted poor outcome (likelihood ratio 11.65, p = .003). Patients with NLR > 7.2 were 6.8 times more likely to die (OR 6.8, CI95% 1.2–38.6, p = .03) and almost 8 times more likely to require prolonged invasive mechanical ventilation (OR 7.8, CI95% 1.2–52.4, p = .03). In a multivariate analysis, NLR > 7.2 predicted poor outcome even when controlling for the effect of low TICI score on poor outcome (NLR p = .043, TICI p = .070).

Conclusions: We show elevated NLR in LVO patients with COVID-19 portends significantly worse outcomes and increased

[1]Department of Neurosurgery, New York Medical College, Westchester Medical Center, Valhalla, New York, USA
[2]Department of Neurological Surgery, University Hospital Newark, New Jersey Medical School, Rutgers, New Jersey, USA
[3]Department of Neurointerventional Radiology, Goodman Campbell Brain and Spine, Indianapolis, Indiana, USA
[4]Department of Neurology, Brookdale and Jamaica Hospital Center, NYU School of Medicine, Brooklyn, New York, USA
[5]Neuroradiology and Neurointervention Service, Brigham & Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA
[6]Department of Neuroradiology, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
[7]Department of Radiology, Neurovascular Unit, Careggi University Hospital, Florence, Italy
[8]Department of Interventional Neuroradiology, Hospital Clínico Universitario de Valladolid, Valladolid, Spain
[9]Department of Radiology, University Hospital of North Midlands, Stoke-on-Trent, UK
[10]Department of Neurology, Northwell Health, Long Island, New York, New York, USA
[11]Department of Neurological Surgery, Rutgers Robert Wood Johnson Medical School, New Jersey Medical School, New Brunswick, New Jersey, USA
[12]Department of Neurology & Radiology, Robert Wood Johnson University Hospital, Rutgers, New Jersey, USA
[13]Department of Neurology, Saint Joseph Health, Detroit Medical Center, Detroit, Michigan, USA
[14]Department of Radiology, University of California Riverside, Riverside, California, USA
[15]Department of Neurology, Miller School of Medicine, Miami, Florida, USA
[16]Department of Neurology, University of Arizona-Tucson, Tucson, Arizona, USA

Corresponding author:
Fawaz Al-Mufti, MD, Westchester Medical Center, New York Medical College School of Medicine, 100 Woods Road, Macy Pavilion 1331, Valhalla, NY 10595, USA.
Email: Fawaz.Al-Mufti@wmchealth.org

mortality regardless of recanalization status. Severe neuro-inflammatory stress response related to COVID-19 may negate the potential benefits of successful thrombectomy.

Keywords
Neutrophil lymphocyte ratio, COVID, acute ischemic stroke, large vessel occlusion

Received 18 January 2022; final manuscript received March 15, 2022; accepted: 24 March 2022

Introduction

The current SARS-CoV-2 virus pandemic has affected 21 million individuals worldwide and has accounted for 760,000 deaths at the time of the writing of this paper. Coronavirus entry into the host cells is reportedly mediated via the angiotensin-converting enzyme ACE 2 receptor. The primary complication is acute lung injury resulting in type-1 respiratory failure, with a significant proportion of patients requiring intensive care. However, in addition to these respiratory features, the disease can affect multiple organs including the cardiovascular and gastrointestinal systems. Emerging evidence suggests neurotropism of the novel SARS-CoV-2 virus, which causes a wide range of neurologic complications.[1–3] The neutrophil–lymphocyte ratio (NLR), a marker of acute physiological stress, is an established prognostic marker in patients with cancer, cardiac disease, sepsis, and acute neurological disorders such as subarachnoid hemorrhage and acute ischemic stroke.[4–8] NLR has been demonstrated to have superior predictive value when compared to leukocyte count alone in predicting poor clinical outcomes in the aforementioned conditions.[4–8] More recently, elevated NLR has been confirmed as a negative short-term prognostic indicator for patients with COVID-19.[9,10]

We sought to describe the role of NLR in predicting poor outcome in COVID-19 patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO) undergoing mechanical thrombectomy. We hypothesize that systemic inflammation and physiological stress reflected by an elevated NLR may outweigh any potential benefit of mechanical thrombectomy. We herein examine the relationship between NLR and vessel recanalization in COVID-19 patients treated with mechanical thrombectomy for LVO stroke.

Methods

Data availability statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request

Patient selection

We conducted an international multi-center retrospective study of laboratory-confirmed COVID-19 patients with acute LVOs consecutively admitted between March 1, 2020 and May 1, 2020 in 12 stroke centers located in the US, UK, Spain, and Italy. The ethical review boards of these institutions approved the study. As this was a retrospective study, waiver of informed consent was obtained.

Data collection & analysis

We tabulated the total number of hospitalized COVID-19 patients and obtained detailed information in all consecutive LVO cases within this cohort. Per the ASA/AHA guidelines, patients met criteria for large vessel occlusion strokes if they had a common carotid occlusion, internal carotid artery occlusion, middle/ anterior cerebral artery occlusion, basilar artery occlusion, or occlusions in multiple vascular territories. All patients who had LVO in our cohort underwent mechanical thrombectomy. Collected data included demographics, past medical history, baseline clinical status, imaging results, and details of stroke treatment and complications. Details related to the diagnosis of COVID-19 included clinical presentation, laboratory findings, and pulmonary CT findings on admission, treatment regimens, and clinical outcomes. The diagnosis criteria and classification of COVID-19 severity was defined by the American Thoracic Society criteria.[11] Neutrophil (PMN) and lymphocyte counts were analyzed as percentages of the total WBC population. NLR was calculated as the ratio of the percentage of neutrophils over the percentage of lymphocytes.

Outcome assessment

The primary outcome measure was poor outcome, defined as death or discharge to a skilled nursing facility. Good outcome was defined as discharge to home or an acute rehabilitation facility. These definitions have been previously used in the literature, both as clinically significant definitions of outcome as well as helpful divisions for statistical analysis.[12–14] Our secondary outcomes were relationships between NLR, TICI score, and mechanical ventilation.

Statistical analysis

Data analyses were performed with Stata statistical software (Stata Version 16.1, Statacorp LLC). P values of $\leq .05$ were considered significant. Individual variables were analyzed using chi-square or t-test, followed by logistic regression. Univariate associations with a P < .05 were then tested further to assess in multivariable models to assess interactions and combined predictive capabilities. Initial analysis of outcome was performed using individual variables NLR, TICI, and mechanical ventilation, using an ordered logistic regression. Each individual variable was predictive of outcome. While other inflammatory biomarkers were ran on our multivariate model, such as white blood cell count, d-dimer, serum ferritin, C-reactive protein, fibrinogen, procalcitonin, and platelet count, only elevated NLR remained an individual predictor of outcome and mortality.

Receiver operating characteristic (ROC) analysis was undertaken to determine if a particular cutoff for NLR, TICI, or ventilator days may be more helpful in predicting outcomes. compare the predictive value of NLR and the TICI score on outcome (Table 1, Figure 1). The NLR cutoff was determined to be >= 7.272 with 78.57% of patients correctly classified with this cutoff (AUC .7427). TICI score (TICI 0, 1, and 2a in one group and TICI 2b, 2c, and 3 in the other) correlated with outcome in 73.68% of cases (AUC .6462). There was no statistical significance between the AUC of the NLR and TICI score (AUC: .7427 vs. .6462; p = .51).

After cutoffs were identified on ROC curve, outcome was converted to binary where variables were still predictive in a logistic regression. Dichotomous outcomes helped to achieve sufficient statistical significance for analysis.

Table 1. ROC curves for NLR and TICI.

	Obs	ROC Area	Std. Error	[95% Confidence Interval]
NLR	28	0.74	0.11	0.54–0.95
-TICI	28	0.65	0.12	0.42–0.89

P = 0.51.

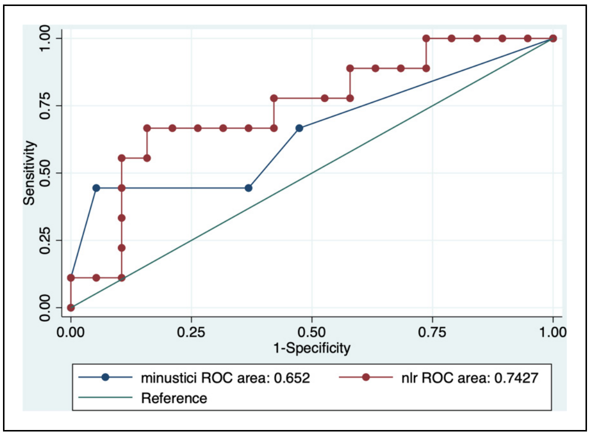

Figure 1. ROC curves for NLR and TICI: comparative predictive value of NLR and TICI score on outcome compared to reference curve.

Results

Demographic and clinical features

Out of a total of 6698 patients admitted with COVID-19 to 12 stroke centers during the study period, the incidence of LVO stroke was 38/6698 (.57%). Mean age of the patients with LVO stroke was 62 years (range 27–87), 50% were female, and the hospital mortality rate was 29% (11/38). Of these 38 patients, 28 had NLR measured on admission and were included in the subsequent analysis. There were no major differences between LVO patients with or without an admission NLR with regard to demographics, stroke characteristics, or mortality (Table 2). Eight of 38 patients (21.1%) had internal carotid artery-middle cerebral artery tandem occlusions. Three out of nine patients with NLR >7.2 had tandem occlusions (p = .11).

NLR, TICI score, and outcome

Seven patients (7/28, 25%) had a normal NLR of ≤3, whereas nine patients (9/28, 32.1%) had an admission NLR ≥ 7.2, indicative of moderate-to-severe physiologic stress (Table 3). Among the patients who had NLR data, seven patients (7/28, 25%) died. Mean NLR was similarly higher in those who died compared to those who lived (9.2 vs. 4.7, P = .015) (Table 4). Mean NLR was higher in the population that had poor outcome (discharge to SNF or death) compared to those with good outcome (discharge to home or ARF, 8.7 vs. 4.8, P = .019) (Table 3). Among the patients with poor recanalization score (TICI 0, 1, or 2a) three patients died [3/7 (43%) versus 7/31 (23%), p = .27]. Five patients with TICI 0, 1, or 2a scores had poor outcome (nursing home, death) [5/7 (71%) versus 8/31 (26%), p = .02] (Table 5). Logistic

Table 2. comparison of patients with and COVID-19 With and without admission NLR data.

Variables	Without NLR Data (N = 10)	With NLR Data (N = 28)	P-value
Age (years)	60.8 ± 5.7	62.9 ± 2.9	0.36
Female	5 (50)	14 (50)	1.0
Ethnicity			0.125
White	5 (50)	17 (61)	
Black	2 (20)	7 (26)	
Hispanic	1 (10)	4 (5)	
Other	2 (20)	0 (0)	
NIHSS score	20.1 ± 2.3	18.8 ± 1.4	0.31
TICI Score			0.73
TICI 1	0 (0)	1 (4)	
TICI 2a	2 (20)	4 (14)	
TICI 2b	5 (50)	10 (36)	
TICI 3	3 (30)	13 (46)	
Mechanical Ventilation	1 (33)	7 (30)	0.92
Discharge to SNF	2 (20)	1 (4)	0.11
Died in hospital	3 (30)	7 (26)	0.80

Table 3. NLR and outcome.

Group	Obs	Mean	Std. Error	Std. Dev.	[95% Confidence Interval]
Good Outcome	19	4.76	0.82	3.56	3.05–6.48
Poor Outcome	9	8.66	1.94	5.83	4.17–13.14
Combined	28	6.01	0.89	4.68	4.20–7.83

Table 4. NLR and mortality.

Group	Obs	Mean	Std. Error	Std. Dev.	[95% Confidence Interval]
Survival	20	4.73	0.77	3.46	3.11–6.35
Mortality	7	9.15	2.44	6.45	3.19–15.11
Combined	27	5.88	0.91	4.72	4.01–7.75

regression suggests that patients with poor outcome (nursing home or death) are 7.2 times more likely to be in the cohort with poor TICI scores (TICI 0, 1, or 2a), (OR 7.2, CI95% 1.2–44.7, p = .034).

Patients with a NLR > 7.2 were 6.8 times more likely to die (OR 6.8, CI95% 1.2–38.6, p = .03) and approximately 6 times more likely to have a poor outcome (OR 5.9, CI95% 1.3–27.3, p = .02). Ordered logistic regression of outcome and TICI score is statistically significant and suggests that patients with better TICI grade tend to have better outcomes, and it also predicts that patients with worse TICI scores (TICI 0, 1, or 2a) are more likely to have worse outcomes than those with better TICI scores (TICI 2b, 2c, or 3), (OR 5.6, CI95% 1.2–26.0, p = .029). When added to our model as a covariate, both NLR (OR 1.24, 95% CI 1.02–1.50, P = .03) and a TICI score of 0, 1 or 2a (OR 10.78, 95% CI 1.30–89.63, P = .03) independently predicted poor outcome. In a multivariate analysis, the predictive significance of TICI grade on poor outcome was lost when an NLR > 7.2 cutoff was included (NLR > 7.2 p = .043, TICI p = .070).

Mechanical ventilation, ventilator days, and outcome

In our COVID-19 LVO cohort, invasive mechanical ventilation (>24 h) was a highly significant predictor of mortality [7/8 (88%) ventilated patients versus 3 of 30 (10%) non-ventilated patients, P = .001] and poor outcome [7/8 (88%) ventilated patients versus 6/30 (20%) non-ventilated patients, P = .001]. These were all patients ventilated in the setting of severe COVID-19 pneumonia. Note that there were 2 of 30 non-ventilated patients that were intubated for <24 h. Average number of ventilator days was significantly higher in patients who died compared with patients who survived (5.3 vs. 1.1, days, p = .02), as well as those with poor outcomes compared to better outcomes (4.7 vs. 1.2, p = .03). ROC analysis was undertaken to assess the predictive value

Table 5. TICI grade and outcome.

Group	TICI 0, 1, 2a	TICI 2b, 2c, 3	Total
Good Outcome	2	23	25
Poor Outcome	5	8	13
Total	7	31	38

of a longer intubation period on outcomes. The ventilator days optimal cutoff for both mortality and poor outcome was determined to be > = 3 days, and with this cutoff 92% (AUC .88) of patients correctly classified with mortality and 88.5% (AUC .83) of patients correctly classified with poor outcome. While number of ventilator days alone was not found in our cohort to be predictive of poor outcome or mortality, invasive mechanical ventilation (>24 h) is a highly significant predictor of mortality (OR 119, p = .001) and also of poor outcome (OR 56, p = .002). Also, patients with NLR > 7.2 were almost 8 times more likely to be in the cohort of patients who underwent prolonged (>24hr) invasive mechanical ventilation (OR 7.8, CI95% 1.2–52.4, p = .03). When we applied multivariate logistic regression analysis to the 3 variables of NLR, TICI, and mechanical ventilation, mechanical-ventilation(>24hr) had such a strong correlation with mortality [mortality: mechanical-ventilation(>24hr) p = 0.002, NLR(>7.2) p = .14, TICI(0,1,2a) p = .72] and poor outcome [mortality: mechanical-ventilation(>24 h) p = .01, NLR(>7.2) p = .10, TICI(0,1,2a) p = .12] in our cohort that it overpowered the effects of NLR and TICI on outcome, both of which lost their significance.

Discussion

Immune dysregulation has long been purported to be involved in pathophysiology of acute ischemic stroke, and more recently COVID-19. Severe inflammatory responses induced by COVID-19 have been shown to contribute to weak immune adaption, and consequently imbalanced immune responses. Evidence has shown that patients with stroke and COVID-19 have a higher mortality rate, as well as a prolonged hospital length of stay.[15] Circulating biomarkers may be surrogate markers for inflammatory and immune status in COVID-19, and have furthered the understanding of the rapidly evolving pandemic.

An elevated NLR represents an immune dysregulation state, manifested as an elevated innate immune response (represented by higher neutrophil counts) and a decreased adaptive immune response (represented by lower lymphocyte counts), causing immunosuppression by lowering the cytolytic activities of lymphocytes.[1–3,16] As a marker of systemic subclinical inflammation, the NLR has been demonstrated to predict worse clinical outcomes in patients with cancer, cardiac disease and sepsis. The NLR has also been implicated in a number of neurological conditions including subarachnoid hemorrhage and stroke. Studies examining NLR in hemorrhagic stroke have shown that NLR is an independent predictor of worse functional outcome after acute intraparenchymal hemorrhage.[17] Prior studies have also defined a relationship between NLR and the development of delayed cerebral ischemia in subarachnoid hemorrhage.[18] The NLR, easily calculated by routine blood counts, can be a potentially powerful tool in the prognostication of patients with COVID-19 suffering from AIS due to LVO. In addition to predicting a higher risk of hemorrhage and mortality, elevated NLR values may also identify patients who are at risk for other complications especially other post-stroke infection. Given these recent data, the NLR may present itself as an appealing candidate to assess the neurotropic inflammatory component of COVID-19.[4–8,19–22]

Though elevated NLR was linked with increased mortality and poor outcome in our cohort, this was a result ultimately dwarfed by the relationship of mechanical ventilation on mortality. When controlling for mechanical ventilation in our model, all effect of NLR on outcome disappeared. Mechanical ventilation may thus fill the role of a mediating variable between elevated NLR and outcome, where elevated NLR might predict outcome through its prediction of mechanical ventilation status.

Recently, the NLR has been shown to be a potential predictor of prognosis in COVID-19.[23] Specifically, an increased neutrophil count has been shown to be associated with heightened risk of ARDS in COVID-19 patients, while lymphopenia has been associated with worse outcomes.[24] An elevated NLR was found to be an independent predictor of poor clinical outcome with an AUC of 0.841, specificity 63.6% and sensitivity of 88%.[23] Liu et al. demonstrate that patients with COVID-19, aged ≥50 and with an NLR ≥3.13 are predicted to develop critical illness, and should thus have rapid access to an intensive care if necessary.[25] In a study of 74 hospitalized patients with confirmed COVID-19, an NLR of >4 ($P = .046$) predicted admission to the ICU, reinforcing the theory of a close association between a hyper-inflammatory state and COVID-19 pathogenesis.[26] Our results confirm these prior data and lend increasing evidence towards using the NLR as a consistent prognosticator in COVID-19. In our multivariate analysis, patients with a NLR >7.2 were 6.8 times more likely to die, and approximately 6 times more likely to have a poor outcome. Patients with NLR > 7.2 were almost 8 times more likely to be in the cohort of patients who underwent prolonged (>24hr) invasive mechanical ventilation, which was heavily predictive of mortality and poor outcome.

This is not the first paper to attempt to identify risk factors for mortality in LVO patients with COVID-19, and, indeed, it has been previously shown that there is an association of elevated NLR values on development of poor outcome in this patient population: Goyal et. al demonstrated that higher admission NLR values are independent predictors of symptomatic intracranial hemorrhage and 3-month mortality in LVO patients treated with mechanical thrombectomy.[27–29] In an observational study of 60 patients with acute ischemic stroke, Lin et. al showed that patients with the SARS-Cov-2 virus had a higher NLR compared to those without infection.[30] In a retrospective analysis of 116 patients with AIS secondary to LVO, a NLR≥5.9 predicted poor outcome and death at 90 days that remained significant when controlling for age, treatment with IV tPA, and recanalization.[31] In our study we found that patients with an elevated NLR >7.2 were more likely to die and have a poor outcome, even when controlling for the effect of poor recanalization. Our results confirm the well-known association between poor angiographic recanalization and outcome. Patients in our cohort with TICI 0–2a were approximately 7 times more likely to have poor outcome. Furthermore, our finding of the synergistically predictive ability of an elevated NLR and low TICI score on worse outcome improves prognostication. Patients with elevated NLR and TICI 0–2a are nearly 12 times more likely to do poorly.

While recanalization determined by TICI scores are a simple and immediate post-angiographic metric to guide treatment and provide some prognostication, when examined in isolation, they are not always reliable. This is evidenced by the fact that several patients fail to do well despite TICI 3 recanalization (i.e "futile recanalization"), and identifying these patients is the subject of ongoing research.[32] In our multivariate analysis, patients with elevated NLR went on to have poor clinical outcome, despite favorable recanalization. This finding is significant as it suggests that in certain patients, the neuro-inflammatory process in COVID-19 may outweigh the potential benefit of a successful thrombectomy. This idea is corroborated by a recent study introducing the Poor Outcome of Endovascular Treatment With Successful Recanalization (PREDICT) scale. Notably, one of the individual components of PREDICT scale is admission NLR.[33] PREDICT has been shown to have good discrimination and satisfactory calibration in a multi-center cohort of 332 LVO patients treated with thrombectomy. Identification of patients with perhaps both elevated PREDICT scores and NLR, may lead to improved prognostication, both for patient and family counseling, and for allocation of resources. As the allocation of healthcare resources continues to be an ever-present dilemma during this pandemic, NLR can be incorporated as a scoring variable, to predict response after such a procedure. Accurate identification of patients with COVID-19 who would reliably do poorly despite successful thrombectomy may also lead to more efficient ICU utilization.

Several limitations of this study deserve mention. This is a retrospective evaluation of prospectively databases maintained during the height of the pandemic. We were unable to compare baseline demographic and disease-related features between the patients with LVO and the main cohort of COVID-19 patients. Similarly, we also were unable to provide an estimated frequency of stroke among the overall cohort of COVID-19 patients who did not undergo brain imaging due to being too ill to transfer or under sedation. Due to the fact that all of our patients were sick enough to be admitted to the hospital, multiple confounding factors could have contributed to the observed complications and outcomes. This includes the inability to attribute NLR as a marker for neuro-specific inflammatory stress versus a systemic inflammatory response in the setting of COVID-19. Furthermore, while we know that the data for this study was collected in pre-Omicron and pre-Delta phases of the pandemic, we do not have granular data on the specific subtype of COVID-19 these patient's had. Finally, the small number of included patients may limit the generalizability of our findings to other regions throughout the world.

Conclusion

An elevated NLR in patients with COVID-19 and AIS due to LVO is a significant indicator of mechanical ventilation which portents significantly worse outcomes and increased mortality regardless of the TICI score. This suggests that clinical scenarios may exist where the inflammatory response in COVID-19 outweighs any potential benefit of a successful thrombectomy. Further study is necessary to characterize the details of this relationship.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Fawaz Al-Mufti https://orcid.org/0000-0003-4461-7005
Jared B. Cooper https://orcid.org/0000-0003-4737-3026
Eric Feldstein https://orcid.org/0000-0002-1952-4555
Krishna Amuluru https://orcid.org/0000-0002-8859-8574
Adam A Dmytriw https://orcid.org/0000-0003-0131-5699
Nicola Limbucci https://orcid.org/0000-0002-0432-5414
Mario Martínez-Galdámez https://orcid.org/0000-0002-8024-4712
Miguel Schüller-Arteaga https://orcid.org/0000-0003-3351-668X
Sanjeev Nayak https://orcid.org/0000-0002-9616-1188

References

1. Petrie HT, Klassen LW and Kay HD. Inhibition of human cytotoxic t lymphocyte activity in vitro by autologous peripheral blood granulocytes. *J. Immunol* 1985; 134: 230–234.
2. el-Hag A and Clark RA. Immunosuppression by activated human neutrophils. Dependence on the myeloperoxidase system. *J. Immunol* 1987; 139: 2406–2413.
3. Provencio JJ. Inflammation in subarachnoid hemorrhage and delayed deterioration associated with vasospasm: a review. *Acta Neurochir* 2013; 115: 233–238.
4. Kumar R, Geuna E, Michalarea V, et al. The neutrophil-lymphocyte ratio and its utilisation for the management of cancer patients in early clinical trials. *Br J Cancer* 2015; 112: 1157–1165.
5. Nunez J, Nunez E, Bodi V, et al. Usefulness of the neutrophil to lymphocyte ratio in predicting long-term mortality in st segment elevation myocardial infarction. *Am J Cardiol* 2008; 101: 747–752.
6. Akpek M, Kaya MG, Lam YY, et al. Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with st-elevated myocardial infarction undergoing primary coronary intervention. *Am J Cardiol* 2012; 110: 621–627.
7. Cho KH, Jeong MH, Ahmed K, et al. Value of early risk stratification using hemoglobin level and neutrophil-to-lymphocyte ratio in patients with st-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Am J Cardiol* 2011; 107: 849–856.
8. Yalcinkaya E, Yuksel UC, Celik M, et al. Relationship between neutrophil-to-lymphocyte ratio and electrocardiographic ischemia grade in stemi. *Arq Bras Cardiol* 2015; 104: 112–119.
9. Kalemci S, Sarıhan A and Zeybek A. Association between NLR and COVID-19. *Int Immunopharmacol* 2020; 88: 106917.
10. Haghjooy Javanmard S, Vaseghi G, Manteghinejad A, et al. Neutrophil-to-lymphocyte ratio as a potential biomarker for disease severity in COVID-19 patients. *J Glob Antimicrob Resist* 2020; 22: 862–863.
11. Jamil S, Mark N, Carlos G, et al. Diagnosis and management of COVID-19 disease. *Am J Respir Crit Care Med* 2020; 201: 19–27.
12. Al-Mufti F, Amuluru K, Sahni R, et al. Cerebral venous thrombosis in COVID-19: a New York Metropolitan Cohort Study. *American Journal of Neuroradiology* 2021; 42: 1196–1200. doi:10.3174/ajnr.A7134
13. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area. *JAMA* 2020; 323: 2052–2059. doi:10.1001/jama.2020.6775
14. Stein LK, Mocco J, Fifi J, et al. Correlations between physician and hospital stroke thrombectomy volumes and outcomes: a nationwide analysis. *Stroke* 2021; 52: 2858–2865. doi:10.1161/STROKEAHA.120.033312
15. Yaghi S, Ishida K, Torres J, et al. SARS-CoV-2 and stroke in a New York healthcare system. *Stroke* 2020; 51: 2002–2011.
16. Bianchi ME. Damps, pamps and alarmins: all we need to know about danger. *J Leukoc Biol* 2007; 81: 1–5.
17. Liu S, Liu X, Chen S, et al. Neutrophil-lymphocyte ratio predicts the outcome of intracerebral hemorrhage: a meta-analysis. *Medicine (Baltimore)* 2019; 98: e16211.
18. Al-Mufti F, Amuluru K, Damodara N, et al. Admission neutrophil-to-lymphocyte ratio predicts delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. *J Neurointerv Surg* 2019; 11: 1135–1140.
19. Halazun HJ, Mergeche JL, Mallon KA, et al. Neutrophil-lymphocyte ratio as a predictor of cognitive dysfunction in carotid endarterectomy patients. *J Vasc Surg* 2014; 59: 768–773.
20. Demirci S, Demirci S, Kutluhan S, et al. The clinical significance of the neutrophil-to-lymphocyte ratio in multiple sclerosis. *Int J Neurosci* 2016; 126: 700–706.
21. Tokgoz S, Kayrak M, Akpinar Z, et al. Neutrophil lymphocyte ratio as a predictor of stroke. *J Stroke Cerebrovasc Dis* 2013; 22: 1169–1174.
22. Tokgoz S, Keskin S, Kayrak M, et al. Is neutrophil/lymphocyte ratio predict to short-term mortality in acute cerebral

infarct independently from infarct volume? *J Stroke Cerebrovasc Dis* 2014; 23: 2163–2168.
23. Yang A-P, Liu J-P, Tao W-Q, et al. The diagnostic and predictive role of NLR, d-NLR, and PLR in COVID-19 patients. *Int Immunopharmacol* 2020; 84: 106504.
24. Terpos E, Engelhardt M, Cook G, et al. Management of patients with multiple myeloma in the era of COVID-19 pandemic: a consensus paper from the European myeloma network (EMN). *Leukemia* 2020; 34: 2000–2011.
25. Liu J, Liu Y, Xiang P, et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 novel coronavirus in the early stage. *J Transl Med* 2020; 18: 206.
26. Cicculo A, Borghetti A, Lombardi F, et al. Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front line. *Int J Antimicrob Agents* 2020; 56: 106017.
27. Altschul DJ, Esenwa C, Haranhalli N, et al. Predictors of mortality for patients with COVID-19 and large vessel occlusion. *Interv Neuroradiol* 2020; 26: 623–628. doi:10.1177/1591019920954603
28. Esenwa C, Cheng NT, Luna J, et al. Biomarkers of coagulation and inflammation in COVID-19–associated ischemic stroke. *Stroke* 2021; 52: e706–e709. doi:10.1161/STROKEAHA.121.035045
29. Goyal N, Tsivgoulis G, Chang JJ, et al. Admission neutrophil-to-lymphocyte ratio as a prognostic biomarker of outcomes in large vessel occlusion strokes. *Stroke* 2018; 49: 1985–1987.
30. Lin C, Arevalo YA, Nanavati HD, et al. Racial differences and an increased systemic inflammatory response are seen in patients with COVID-19 and ischemic stroke. *Brain Behav Immun Health* 2020; 8: 100137.
31. Brooks SD, Spears C, Cummings C, et al. Admission neutrophil-lymphocyte ratio predicts 90 day outcome after endovascular stroke therapy. *J Neurotinterv Surg* 2014; 6: 578–583.
32. van Horn N, Kniep H, Leischner H, et al. Predictors of poor clinical outcome despite complete reperfusion in acute ischemic stroke patients. *J Neurointerv Surg* 2021; 13: 14–18.
33. Wang H, Zhang M, Hao Y, et al. Early prediction of poor outcome despite successful recanalization after endovascular treatment for anterior large vessel occlusion stroke. *World Neurosurg* 2018; 115: e312–e321.