



Research

# Neutrophil Lymphocyte Ratio of Ischemic Stroke Based on Region of Lesion

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## ARTICLE INFORMATION

Received: August 15, 2023  
Revised: August 30, 2023  
Accepted: September 27, 2023  
Available online: November 01, 2023

## KEYWORDS

Ischemic stroke; CT scan; Neutrophil Lymphocyte Ratio (NLR)

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## A B S T R A C T

**Background:** Ischemic stroke is a type of stroke that occurs when blood arteries get blocked as a result of embolic or thrombotic events. Brain imaging tools, particularly CT Scans, are the gold standard for diagnosing stroke. Blood tests were also performed, focusing on neutrophils and lymphocytes in particular. The prognosis for stroke can be determined by the neutrophil lymphocyte ratio (NLR). However, based on CT Scan imaging, it is currently unknown how the NLR and brain region of ischemic stroke are related.

**Purpose :** This study investigates the correlation between CT scan images in ischemic stroke patients with Neutrophil Lymphocyte Ratio (NLR).

**Methods:** It is a cross-sectional design study with observational method, this study involved 36 patients that were selected based on inclusive and exclusive criteria. Data was collected from medical records in Royal Prima Hospital and analyzed with Mann-Whitney Test.

**Results:** The result shows that CT scan images in ischemic stroke patients does not have a significant correlation to NLR, with p value > 0,05.

**Conclusion:** This study reveals that there is no significant correlation between CT scan images in patients with ischemic stroke and NLR. There may be other factors that influence the NLR such as age, stress level, obesity and medication. Further research needs to be conducted to study those other factors.

## INTRODUCTION

Stroke is a major cause of disability and death characterized by neurological deficit[1]. It is classified as ischemic stroke and hemorrhagic stroke, and even though a report from American Health Organization (2016) shows that the prevalence of ischemic stroke is higher[2], deaths from hemorrhagic stroke demonstrate a bigger number[3]. Meanwhile, according to data from the Ministry of Health's 2018 Riset Kesehatan Dasar (Riskesdas), the prevalence of stroke in Indonesia has reached 10.9 per million, or in other words, there are 11 stroke incidents for every 1000 people. It is interesting to note that the tendency of stroke survivors, which had previously been in the older age range, has changed to be in the younger age range. This disease

began to increase in the age of 10-14 years[4]. In North Sumatera, particularly in Medan, exhibits a same trend[5]. This high prevalence needs serious attention because in addition of it reducing the quality of life[6], it burdens the nation's economy[7], and also threatens the vision of Indonesia Gold 2045[8].

The pathophysiology of an ischemic stroke includes an important event called inflammation, which occurs when immune cells called neutrophils are the first to enter the wounded area of the brain[9]. Research by Herz et al. (2015) demonstrated that blocking neutrophil entrance helped reverse neurological impairments in experimental mice with a stroke-like condition. This shows that neutrophils have a negative effect and the accumulation of them may be a sign of poor prognosis of ischemic stroke[10]. The Neutrophil Lymphocyte Ratio (NLR) can be used as an indicator to determine the prognosis of ischemic stroke[11]. Patients who have suffered an ischemic stroke are at an increased risk of having a poor prognosis if their NLR is high[12]. Brain imaging tools, notably CT scans, are typically used to diagnose strokes, whether they are ischemic or hemorrhagic[13]. Even though high NLR is marked by the volume of cerebral infarction[13], it is not yet known whether there is a correlation between NLR and the region of the brain of ischemic stroke. Therefore, this study tried to find the correlation between NLR and brain lesion regions on CT scan images of ischemic stroke patients.

## **METHOD**

### **Research Design**

This study is an observational analytic study using cross-sectional design to find out the correlation between lesion location in CT scan images in ischemic stroke patients with NLR.

### **Time and Place of Research**

Data was collected from medical records in Royal Prima Hospital and continued by data analysis in University of Prima Indonesia from June to July 2023.

### **Population and Sample**

The number of research objects that met the requirements was obtained through sample calculation using the Slovin formula from the population of ischemic stroke patients at Royal Prima Hospital from January to December 2022. The sample in this study is 36 ischemic stroke patients.

### **Sample Criteria**

The inclusion criteria in this study were ischemic stroke patients with complete CT scan and blood test data. The exclusion criteria included ischemic stroke patients with other diseases such as infections, epilepsy, and others that could affect the CT scan and blood tests.

### **Data Collected**

Patient's medical record included patient CT scan images which explained the lesion region in brain and blood test which showed the numbers of neutrophil and lymphocyte. The lesion region in ischemic stroke patient divided into 3 parts: Anterior Cerebral Artery (ACA), Middle Cerebral Artery (MCA), and Posterior Cerebral Artery (PCA).

### **Data Analysis**

After the data was collected, analysis using statistic tests was conducted. Normality data was firstly tested using Kolmogorov-Smirnov with a result of p-value <0.001 which is less than 0,05. This shows that the data was not normally distributed (p<0,05). Thus, the analysis was done using Mann-Whitney test to determine the correlation between CT scan images of ischemic stroke patients and NLR.

### **Ethic Research**

This study was ethically approved by the Health Research Ethics Committee University Of Prima Indonesia No 008/KEPK/UNPRI/VI/2023.

## RESULT DAN DISCUSSION

There were 36 medical record data after being selected through inclusion and exclusion criteria. The subject characteristics is shown in this following table.

**Table 1.** Subject Characteristics

Characteristic	Frequency (%)
<b>Gender</b>	
Male	23 (63,9%)
Female	13 (36,1%)
<b>Age</b>	
26-35	1 (2,8%)
36-45	0 (0%)
46-55	8 (22,2%)
56-65	11 (30,6%)
≥66	16 (44,44%)
<b>Lesion Location</b>	
Anterior Cerebral Artery	7 (19,4%)
Middle Cerebral Artery	19 (52,8%)
Posterior Cerebral Artery	10 (27,8%)

**Table 2.** Mean range of neutrophil, lymphocyte and neutrophil lymphocyte ratio

	Mean	Median
Neutrophil	71,7861%	73,1500%
Lymphocyte	18,6806%	17,35%
Neutrophil Lymphocyte Ratio	8,2767%	4,29%

**Table 3.** Correlation between CT Scan images in ischemic stroke patients with NLR

	Anterior Cerebral Artery	Middle Cerebral Artery	Posterior Cerebral Artery
<b>Neutrophil Lymphocyte Ratio</b>	+	7	19
	-	29	17
<b>p value</b>	0.826	0.318	0.191

The table shows that there were 23 male patients (63,9%) and 13 female patients (36,1%). The age range of the subjects was 26 to ≥66 years with the highest frequency being the patients with age ≥66 years, for about 16 people (44,4%). It is followed by the patients with age between 56-65 for about 11 people (30,6%) and there is only 1 people (2,8%) for the age group between 26-35. Based on the lesion location, MCA occupied the largest portion with 19 people (52,8%) and the lowest being ACA with 7 people (19,4%). The average number of neutrophils in the study subjects was 71,7861%, lymphocytes 18,6806% and 8,2767% for NLR.

Data analysis using Mann-Whitney showed p value = 0,826 for ACA lesion, 0,318 for MCA lesion, and 0,191 for PCA lesion. Based on the p values of 0,826; 0,318 and 0.191 (p value>0.05), this shows that there is no significant correlation between the lesion location in CT scan images of ischemic stroke patients with NLR.

## 1. Characterization of Subjects

### a. Gender

In this study, the gender that most often suffered from ischemic stroke was the male group, namely 23 people (63,9%). This is consistent with earlier research that found that men experienced ischemic stroke more frequently than women [14]. According to a study by Keller et al. also demonstrated that men had a higher prevalence of ischemic stroke than women did. One of the reasons that causes more men to be diagnosed with ischemic stroke is due to the delay of diagnosis in women. It is reported that women delay three times longer than men in seeking care once stroke symptoms have appeared [14].

### b. Age

The age group that most often suffered from ischemic stroke is the group age  $\geq 66$  years with 16 people (44,4%) which then followed by the group age 56-65 years namely 11 people (30,6%). Based on research by Yousufuddin and Young (2019) showed that about  $\frac{3}{4}$  cases of ischemic stroke happened to a group with age  $\geq 65$  years [15]. Earlier research also showed that stroke incident will increase twice after the age of 55 [16].

### c. Neutrophil, Lymphocyte and Neutrophil Lymphocyte Ratio (NLR)

The mean of the neutrophil counts in this sample is 71,7861% which is slightly increased from its normal level (40-60%) [17]. The increase of this neutrophil happened because of infection or inflammation process. Additionally, the average percentage of lymphocytes in the sample, which is 18,6806% on average, is slightly lower than the typical range of 20-40%. Based on earlier research, lymphocyte counts tended to drop in ischemic stroke patients. Lowered lymphocyte count later on is linked to bad prognosis [18]. However, the sample's average NLR was 8,2767% which is greater above the typical range of 0,78 to 3,53. Based on earlier research revealing the correlation between elevated NLR levels with increased risk of short-term death and poor functional outcome [19].

### d. Lesion Location

The most frequently involved lesion location was the MCA, namely 19 people (52,8%). This shows that the Middle Cerebral Artery is the target of the majority of ischemic strokes. According to Nogles *et al.* (2023) of 85% of ischemic stroke patients, more than half are ischemic strokes that attacks MCA. The frontal, temporal, and parietal lobes of the brain areas like the caudate, internal capsule and thalamus receive blood flow via the MCA [20].

## 2. Relationship between CT scan images of ischemic stroke patients with Neutrophil Lymphocyte Ratio (NLR)

In this study, researchers examined whether there was a correlation between CT scan images of ischemic stroke patients with NLR and based on statistic analysis using Mann-Whitney test resulting in p value>0,05 which means there is no significant correlation between CT scan images of ischemic stroke patients and NLR. The results of this study are not in line with the hypothesis which states that there is a correlation between CT scan images of ischemic stroke patients and NLR. The CT scan images in form of infarct volumes may be related to NLR, because based on previous study, it is shown that higher the NLR level, the wider the infarction [21]. However, this study did not examine the lesion location.

Earlier research that was done by Keskinbalta *et al.* (2023) who assessed the evaluation of laboratory results on 189 ischemic stroke patients showed that there was no significant correlation between the CT scan images and NLR with p value = 0,082) [22]. The results obtained in this study were the same as the previous study, which showed that there is no significant

correlation. NLR was obtained by dividing the neutrophil count by lymphocytes. Several studies used NLR as a prognostic indicator in ischemic stroke and found that elevated NLR was associated with early onset delirium, mortality and poor functional outcome [23]. NLR in this study was not caused by the location of the lesion, but may be due to other factors that not examined in this study. Other factors that can affect NLR in patients include age, medication, obesity, and stress level [23].

## CONCLUSION

This study shows that there is no significant correlation between CT scan images of ischemic stroke patients specifically the lesion location with neutrophil lymphocyte ratio (NLR). There may be other factors that influence the NLR such as age, medication, obesity and stress level. Those factors could be an investment for future research in studying the correlation with NLR on larger sample and different methods or procedure.

## ANNOUNCEMENTS

We would like to thank to everyone especially Royal Prima Hospital and University of Prima Indonesia for the help and support for this research.

## REFERENCE

- [1] R. L. Sacco *et al.*, “An updated definition of stroke for the 21st century: A statement for healthcare professionals from the American heart association/American stroke association,” *Stroke*, vol. 44, no. 7, pp. 2064–2089, 2013, doi: 10.1161/STR.0b013e318296aeca.
- [2] D. Mozaffarian *et al.*, “Heart Disease and Stroke Statistics-2016 Update A Report From the American Heart Association,” 2015. [Online]. Available: <http://my.americanheart.org/statements>
- [3] S. M. Fernando *et al.*, “Intracerebral Hemorrhage Incidence, Mortality, and Association with Oral Anticoagulation Use: A Population Study,” *Stroke*, pp. 1673–1681, 2021, doi: 10.1161/STROKEAHA.120.032550.
- [4] Kementerian Kesehatan RI, “Penyakit Tidak Menular Kini Ancam Usia Muda,” 2020. Accessed: Aug. 29, 2023. [Online]. Available: <https://p2ptm.kemkes.go.id/kegiatan-p2ptm/dki-jakarta/penyakit-tidak-menular-kini-ancam-usia-muda>
- [5] Riskesdas, “Laporan Riskesdas Indonesia 2018,” 2018. Accessed: Aug. 15, 2023. [Online]. Available: <https://repository.badankebijakan.kemkes.go.id/id/eprint/3514/>
- [6] Nicholas. Sprigg, “Very Low Quality of Life After Acute Stroke,” in *Stroke*, Lippincott Williams and Wilkins, 2013. doi: 10.1161/STROKEAHA.
- [7] H. Fadhilah and V. Y. Permanasari, “Economic Burden Bore by Patients and Families because of stroke: Policy Assessment,” 2020.
- [8] Kementerian PPN Indonesia, “Indonesia 2045,” 2019, Accessed: Aug. 15, 2023. [Online]. Available: [https://perpustakaan.bappenas.go.id/e-library/file\\_upload/koleksi/migrasi-data-publikasi/file/Policy\\_Paper/Ringkasan%20Eksekutif%20Visi%20Indonesia%202045\\_Final.pdf](https://perpustakaan.bappenas.go.id/e-library/file_upload/koleksi/migrasi-data-publikasi/file/Policy_Paper/Ringkasan%20Eksekutif%20Visi%20Indonesia%202045_Final.pdf)
- [9] R. Chen *et al.*, “New Insight Into Neutrophils: A Potential Therapeutic Target for Cerebral Ischemia,” *Frontiers in Immunology*, vol. 12. Frontiers Media S.A., Jul. 14, 2021. doi: 10.3389/fimmu.2021.692061.
- [10] J. Herz, P. Sabellek, T. E. Lane, M. Gunzer, D. M. Hermann, and T. R. Doeppner, “Role of neutrophils in exacerbation of brain injury after focal cerebral ischemia in hyperlipidemic mice,” *Stroke*, vol. 46, no. 10, pp. 2916–2925, 2015, doi: 10.1161/STROKEAHA.115.010620.

- [11] Y. Ying *et al.*, “Neutrophil-to-Lymphocyte Ratio as a Predictive Biomarker for Stroke Severity and Short-Term Prognosis in Acute Ischemic Stroke With Intracranial Atherosclerotic Stenosis,” *Front Neurol*, vol. 12, Jul. 2021, doi: 10.3389/fneur.2021.705949.
- [12] K. Quan *et al.*, “Neutrophil to lymphocyte ratio and adverse clinical outcomes in patients with ischemic stroke,” *Ann Transl Med*, vol. 9, no. 13, pp. 1047–1047, Jul. 2021, doi: 10.21037/atm-21-710.
- [13] M. P. Lin and D. S. Liebeskind, “Imaging of Ischemic Stroke,” 2016. [Online]. Available: [www.ContinuumJournal.com](http://www.ContinuumJournal.com)
- [14] C. L. Gibson, “Cerebral ischemic stroke: Is gender important?,” *Journal of Cerebral Blood Flow and Metabolism*, vol. 33, no. 9, pp. 1355–1361, Sep. 2013. doi: 10.1038/jcbfm.2013.102.
- [15] M. Yousufuddin and N. Young, “Aging and Ischemic Stroke,” *Aging*, vol. 11, no. 9, pp. 1–3, 2019.
- [16] R. Soto-Cámara, J. J. González-Bernal, J. González-Santos, J. M. Aguilar-Parra, R. Trigueros, and R. López-Liria, “Age-related risk factors at the first stroke event,” *J Clin Med*, vol. 9, no. 7, pp. 1–12, Jul. 2020, doi: 10.3390/jcm9072233.
- [17] L. K. Riley and J. Rupert, “Evaluation of Patients with Leukocytosis,” 2015. [Online]. Available: [www.aafp.org/afp](http://www.aafp.org/afp).
- [18] C. Juli *et al.*, “The lymphocyte depletion in patients with acute ischemic stroke associated with poor neurologic outcome,” *Int J Gen Med*, vol. 14, pp. 1843–1851, 2021, doi: 10.2147/IJGM.S308325.
- [19] K. Quan *et al.*, “Neutrophil to lymphocyte ratio and adverse clinical outcomes in patients with ischemic stroke,” *Ann Transl Med*, vol. 9, no. 13, pp. 1047–1047, Jul. 2021, doi: 10.21037/atm-21-710.
- [20] T. E. Nogles and M. A. Galuska, “Middle Cerebral Artery,” *StatPearls*, 2023.
- [21] I. Hunaifi and T. D. Cahyawati, “Korelasi Antara RNL dengan Volume Infark Serebri pada Penderita Stroke Iskemik Akut,” *Neurona*, 2019.
- [22] D. Keskinbalta, D. Öztürk, A. Melekoğlu, E. Uysal, and E. Altınbilek, “Evaluation of Laboratory Findings for Treating Acute Ischemic Stroke,” *Global Emergency and Critical Care*, vol. 2, no. 1, pp. 8–12, Apr. 2023, doi: 10.4274/globecc.galenos.2023.57966.
- [23] R. Zahorec, “Neutrophil-to-lymphocyte ratio, past, present and future perspectives,” *Bratislava Medical Journal*, vol. 122, no. 7, pp. 474–488, 2021, doi: 10.4149/BLL\_2021\_078.