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ASSOCIATION BETWEEN THE NEUTROPHIL-TO-LYMPHOCYTE RATIO AND THE DEGREE OF CAROTID ARTERY STENOSIS

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Abstract

Ischemic stroke accounts for the majority of instances and is mostly linked to carotid artery stenosis brought on by inflammatory atherosclerosis. This study used medical record data of hospitalized ischemic stroke patients who had digital subtraction angiography (DSA) between January and August 2025. It was an analytical observational study with a cross-sectional design that was carried out at Dr. Moewardi Hospital in Surakarta from October to November 2025. Purposive sampling was used to choose samples based on inclusion and exclusion criteria; the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria were used to determine the degree of carotid stenosis; SPSS version 25 was used for statistical analysis using Pearson or Spearman correlation tests based on data distribution. Most ischemic stroke patients were male, aged 50–64 years, with diabetes mellitus and hypertension as the main comorbidities, and the majority had mild to severe carotid stenosis, while a small proportion had critical stenosis or total occlusion. While sex, age, hypertension, diabetes mellitus, and dyslipidemia did not substantially correlate with the degree of carotid artery stenosis (p above 0.05), NLR was the only predictor that did (p below 0.001). NLR was the only independent predictor that was substantially correlated with the degree of carotid artery stenosis, according to multivariate analysis using ordinal logistic regression (B was 0.227; p was 0.012). In ischemic stroke patients at Dr. Moewardi Hospital in Surakarta, NLR is substantially correlated with and an independent predictor of the degree of carotid artery stenosis.

Keywords: *Degree of Carotid Artery Stenosis, Ischemic Stroke, Neutrophil-to-Lymphocyte Ratio*

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INTRODUCTION

Stroke is the third highest cause of death in advanced countries and a major cause of morbidity, with ischemic stroke accounting for around 85% of occurrences, which are typically triggered by emboli from the ipsilateral carotid artery. [1] Carotid artery stenosis (CAS) is a primary cause of atherosclerotic ischemic stroke.[2] CAS is a major contributing factor to ischemic stroke resulting from the atherosclerotic process. Atherosclerosis is the primary etiology of carotid stenosis, with inflammation and immune responses playing significant roles in disease development and progression.[3]

Atherosclerotic lesions are the leading cause of ischemic stroke worldwide, with inflammation serving as a key mechanism in plaque formation and progression; stroke risk is more strongly determined by plaque vulnerability to rupture than by the degree of stenosis, making early detection of neutrophil infiltration a potential predictor of plaque rupture.[4] Carotid stenosis is a narrowing of the carotid artery caused by atherosclerotic plaque that is often asymptomatic even when severe, but may lead to "transient ischemic attack" (TIA), stroke, or amaurosis fugax, with major risk factors including advanced age, hypertension, male sex, DM, dyslipidemia, chronic kidney disease, smoking, and unhealthy lifestyle.[5] Leukocyte count and its subtypes have been investigated as inflammatory biomarkers for predicting adverse cardiovascular outcomes.[6]

The "neutrophil to lymphocyte ratio" (NLR) is a simple inflammatory marker associated with the severity of carotid atherosclerosis and plaque vulnerability to rupture, and may serve as an additional indicator for assessing carotid stenosis severity and the risk of acute ischemic stroke.[7] "Doppler ultrasonography" (USG) is used for screening, with "computed tomography angiography" (CTA) or "magnetic resonance angiography" (MRA) serving as confirmatory modalities when intervention is considered; therefore, accurate early detection of carotid stenosis is crucial to prevent disabling stroke.[8,9] However, these examinations are not always available and are relatively costly. The NLR, obtained from routine blood tests, has the potential to serve as a simple, inexpensive, and easily applicable biomarker. Therefore, investigating the association between NLR and the degree of "carotid artery stenosis" (CAS) is important, particularly at Dr. Moewardi Hospital, Surakarta, as the main referral hospital in Central Java.

METHOD

This study used a quantitative analytical observational method using a "cross sectional design" observed at Dr. Moewardi Hospital in Surakarta, from October - November 2025. The sample included ischemic stroke inpatients found in medical records who received "digital subtraction angiography" (DSA) from January - August 2025 and were selected through non-random sampling guided by predetermined exclusion and inclusion criteria. Patients aged 18 years or above, either male or female, who are diagnosed with ischemic stroke and undergoing DSA for carotid stenosis evaluated according to the "North American Symptomatic Carotid Endarterectomy Trial" (NASCET) criteria were included in the study, while patients with hemorrhagic stroke, unmeasurable stenosis, severe renal dysfunction (serum creatinine exceeding three times normal), febrile condition (temperature above 38°C) or systemic inflammatory response syndrome, malignancy, autoimmune disease, hematologic or coagulation disorders, immunosuppressive treatment, or recent surgery, burns, or trauma within six months before hospital admission were excluded from the study.

The sample size comprised all subjects who met the inclusion and exclusion criteria. Data were collected from secondary sources using patients' medical records and analyzed statistically with Statistical Product and Service Solutions (SPSS) for Microsoft Windows version 25.0. Data distribution was assessed using the Kolmogorov–Smirnov test; Pearson connection is implemented for data that has a normal distribution, while Spearman connection is implemented for data that does not have a normal distribution.

RESULTS AND DISCUSSIONS

This study involved 68 hospitalized ischemic stroke patients who underwent DSA between January and August 2025 at Dr. Moewardi Hospital, Surakarta. The analysis included univariate analysis of subject characteristics, namely sex, age, hypertension, diabetes mellitus, dyslipidemia, and the degree of CAS, with categorical data presented as frequency distributions. The descriptive results are summarized in Table 1.

Table 1. Characteristics of the Study Subjects

Characteristics	Sample total (N=68)	Percentage (%)
Gender		
Male	40	58.8
Female	28	41.2
Ages		
<50 years	10	14.7
50–64 years	35	51.5
≥65 years	23	33.8
Hypertension		
Yes	34	50
No	34	50
Diabetes mellitus		
Yes	42	61.8
No	26	38.2
Dyslipidemia		
Yes	21	30.9
No	47	69.1
Degree of carotid artery stenosis		
Mild	21	30.9
Moderate	17	25
Severe	20	29.4
Critical/Total	10	14.7

Based on Table 1, most ischemic stroke patients were male (40 patients), with the largest age group being 50–64 years (35 patients). Common comorbidities included hypertension in 34 patients (50%), diabetes mellitus in 42 patients (61.8%), and dyslipidemia in 21 patients (30.9%). Regarding the severity of carotid artery stenosis, mild stenosis was observed in 21 patients (30.9%), moderate stenosis in 17 patients (25%), severe stenosis in 20 patients (29.4%), and critical stenosis or total occlusion in 10 patients (14.7%).

For numerical data, univariate analysis of the NLR was carried out. The maximum, mean, minimum, and standard deviation (SD) of normally distributed numerical data were displayed, and the Kolmogorov-Smirnov test was used to determine the data's normality because the sample size was larger than 50. Table 2 displays the descriptive results.

Table 2. Normality Test of the Neutrophil-to-Lymphocyte Ratio

Variable	**N**	**Min.**	**Max.**	**Mean**	**SD**	**Normality test (*Kolmogorov-Smirnov*)**	
						p-value	***Note***
Neutrophil-to-lymphocyte ratio	68	1.05	18.32	3.58	2.86	0,000	Not normally distributed

Note: Kolmogorov–Smirnov test; *meets the assumption of normality (p > 0.05).*

Based on a univariate analysis of NLR in 68 samples, all data were classified as valid with no missing values. The mean NLR value was 3.58 with a median of 2.75, indicating that the data distribution tends toward lower values. The range was fairly wide, from 1.05 to 18.32, with a standard deviation of 2.86, reflecting considerable inter-subject variability. The NLR distribution appeared to be highly right- skewed, as indicated by a skewness value of 3.01 and kurtosis of 11.43, suggesting the presence of a small number of cases with very high values (outliers) compared to the majority of the sample. The 95% confidence interval indicates that the population mean is estimated to lie between 2.89 and 4.27. Overall, these findings suggest that most patients have relatively low to moderate NLR values; however, a few cases with high NLR values cause the distribution to deviate from normality.

Bivariate analysis was conducted to determine the strength of the connection between the independent variable (NLR in ischemic stroke) and the dependent variable (degree of carotid artery stenosis). Potential confounding variables (sex, age, hypertension, diabetes mellitus, and dyslipidemia) were also assessed for their connection with the dependent variable. The Kruskal-Wallis test was used for correlation analysis because the variables included both numerical and categorical data with non- normal distributions. The Chi-square test was used to assess both categorical variables. Table 3 displays the findings of the bivariate connection study.

Table 3. Bivariate analysis

Variables	N	Degree of carotid artery stenosis	
		p-value	Note
Independent Variable			
Neutrophil-to-lymphocyte ratio[a]	68	0,000*	Significant
Confounding Variable			
Gender[b]	68	0,829	Not significant
Age[b]	68	0,660	Not significant
Hypertension[b]	68	0,430	Not significant
Diabetes mellitus[b]	68	0,542	Not significant
Dyslipidemia[b]	68	0,464	Not significant

Note: [a]Kruskal–Wallis correlation test (categorical and numerical variables with non-normal distribution); [b]Chi-square test (categorical and categorical variables). Statistically significant at $\alpha = 5\%$.

According to Table 3, the following subject characteristics did not correlate with the degree of CAS: sex (p was 0.829), age (p was 0.660), hypertension (p was 0.430), diabetes mellitus (p = 0.542), and dyslipidemia (p was 0.464). Only the NLR ratio revealed a significant correlation (p below 0.001) with the degree of CAS, according to the bivariate analysis results. Other factors, including age, DM, hypertension, sex, and dyslipidemia, did not show any significant correlations (p above 0.05).

The multivariate analysis in this study “aimed to determine whether the NLR ratio is a dominant

variable influencing the degree of carotid artery stenosis." In the analysis, potential confounding variables were also tested to assess whether they had a significant association with the degree of carotid CAS. Accordingly, the multivariate analysis included sex, age, hypertension, diabetes mellitus, and dyslipidemia as confounding variables in the relationship between the NLR ratio and the degree of CAS, with the results as follows.

Table 4. Multivariate Analysis Using Ordinal Logistic Regression on the Degree of Carotid Artery Stenosis

Variables	*Estimate (B)*	*Std. Error*	*Wald*	*p-value*	Interpretation
NLR	**0.227**	0.090	6.372	**0.012***	**Significant**
Gender	0.436	0.479	0.827	0.363	Not significant
Age	0.170	0.720	0.056	0.813	Not significant
Hypertension	–0.808	0.478	2.860	0.091	Not significant
Diabetes mellitus	0.145	0.486	0.089	0.765	Not significant
Dyslipidemia	0.183	0.511	0.128	0.721	Not significant

Note: Ordinal logistic regression analysis (link function: logit). The reference category was automatically set by SPSS (indicated as 0^{a}). *Statistically significant at $\alpha < 0.05$.

Multivariate analysis using ordinal logistic regression confirmed these findings, with NLR remaining the only factor that had a significant effect on the degree of stenosis (B was 0.227; p was 0.012). Other variables tested—including sex, age, DM, dyslipidemia, and hypertension—did not show a significant independent effect in predicting the severity of stenosis (p above 0.05). Overall, this study demonstrates that NLR is an independent estimates of the degree of CAS, regardless of other clinical factors.

Discussions

The study's findings demonstrate that NLR (r was 0.573; p was 0.000) has a positive and substantial link with the degree of CAS. This data reveals that greater NLR levels are associated with larger degrees of CAS in individuals with ischemic stroke, implying that NLR may act as an inflammatory signal related to the advancement of CAS.

A study conducted in Lanzhou, China, reported that the NLR value at the time of initial hospital admission is a novel and significant biomarker for assessing carotid plaque vulnerability, and that the degree of vulnerability can be evaluated through carotid ultrasonography in patients with acute ischemic stroke.[10] A systematic review reported that NLR has the potential to be used as a predictive indicator for detecting subclinical atherosclerosis as well as monitoring the progression of atherosclerosis in the carotid arteries.[11] Similar findings were also reported in a study conducted in Nice, France, which showed that elevated NLR values during the preoperative period there is a crucial connection with occurrence of symptomatic internal CAS.[12] A study conducted in South Korea reported that NLR has clinical predictive value for the degree of CAS, particularly in male patients with ischemic stroke.[13]

A study in northern Taiwan reported that the accumulation of cardiovascular comorbidities is the strongest predictor for the onset and worsening of atherosclerosis, with hypertension being the most consistently associated factor with plaque formation and progression. These findings underscore that blood pressure control should be a primary focus in the elderly population.[14] A study in Rome, Italy, reported that individuals under 70 years of age are more likely to experience plaque instability compared to older age groups. The risk of plaque destabilization increases when accompanied by higher levels of low-density lipoprotein (LDL), total cholesterol, or triglycerides.[15] These findings are consistent with a study in Taiwan, which reported that hypertension and hypercholesterolemia are significantly associated with the accelerated progression of carotid artery stenosis.[16] A multicenter study reported that the presence of carotid artery plaques is significantly associated with age under 60 years and is more frequently observed in women.[17]

A study in Busan, South Korea, reported that patients with type 2 DM who have high levels of inflammation exhibit significantly greater susceptibility to carotid artery atherosclerosis as well as coronary heart disease.[18] A study in Novosibirsk, Russia, reported that male sex, higher body mass index, longer duration of diabetes, and decreased glomerular filtration rate are predictive factors for the occurrence of carotid artery stenosis.[19] This study is similar to an observation in Taiwan, which showed that diabetes mellitus has a linear relationship with carotid plaque formation and is associated with a greater degree of carotid atherosclerosis compared with patients without diabetes..[20]

The limitations of this study include that the observed relationship between NLR and the degree of stenosis is associative, not causal. In addition, the limited number of respondents may reduce the statistical power and essential skills for research findings in larger populations. Other limitations of the study include variables such as smoking, history of heart disease, physical activity, central obesity, body mass index, duration of hypertension/diabetes, and medication use (statins, antihypertensives, antiplatelets), which may have an effect but were not analyzed. Finally, classic risk factors (hypertension, dyslipidemia, diabetes) were not significant—possibly due to the small sample size, uneven distribution, or lack of additional clinical data.

CONCLUSION

There is an association between NLR and the degree of CAS in ischemic stroke patients at Dr. Moewardi Hospital, Surakarta.

RESEARCH ETHICS

"This study has received ethical approval from the Health Research Ethics Committee of Dr. Moewardi Hospital", as documented in approval letter number 2.273/X/HREC/2025.

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