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Research article

From Basic Blood Counts to Functional Outcomes: Neutrophil–Lymphocyte Ratio as a Predictor of Disability in Acute and Subacute Ischemic Stroke

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Abstract: Inflammation plays a pivotal role in the pathophysiology of ischemic stroke, influencing neuronal injury and recovery. The neutrophil–lymphocyte ratio (NLR), a simple marker derived from routine blood tests, has emerged as a potential predictor of stroke severity and outcome. This study aimed to evaluate the relationship between NLR and functional disability in patients with acute and subacute ischemic stroke. This analytical, prospective cohort study included 32 patients with confirmed ischemic stroke admitted between October 2024 and October 2025. Stroke severity was assessed using the NIHSS, and functional outcomes by the modified Rankin Scale (mRS). Admission NLR values were obtained from complete blood counts. Given non-normal variable distributions, Spearman correlation analysis was applied. The median age was 71.09 years (IQR: 15.3). NLR showed a moderate positive correlation with mRS (Spearman r = 0.313), but this association did not reach statistical significance (p = 0.0809). Despite this, the direction and magnitude of the observed trend were consistent with previously reported associations between heightened inflammatory response and poorer outcomes. Although elevated NLR tended to associate with greater functional disability, the correlation was not statistically significant, likely reflecting the limited sample size. These preliminary findings support the biological plausibility of NLR as a prognostic marker but underscore the need for larger, adequately powered, multicenter studies to confirm this relationship and explore complementary indices such as PLR and SII.

Keywords: neutrophil–lymphocyte ratio (NLR), ischemic stroke, inflammation, functional outcomes, modified Rankin Scale (mRS), prognostic biomarker, systemic immune response, neuroinflammation, acute stroke, stroke recovery

1. Introduction

Ischemic stroke remains a major cause of mortality and long-term disability worldwide, despite advances in reperfusion therapies and neuroprotective strategies [1,2]. Early identification of simple and reliable prognostic markers is important for guiding acute management and informing rehabilitation planning. Among the biological processes shaping stroke evolution, inflammation plays a central role: ischemia triggers vascular dysfunction, oxidative stress, and activation of innate and adaptive immune pathways, contributing to blood–brain barrier disruption and secondary neuronal injury [3,4].

Given this inflammatory basis, hematologic biomarkers have gained interest for their potential to reflect the extent of immune activation after stroke. The neutrophil–lymphocyte ratio (NLR), derived from a routine complete blood count, has emerged as one of the most accessible tools in this regard. Elevated NLR at admission has been associated with greater stroke severity, larger infarct volumes, early neurological deterioration, and poorer functional outcomes measured by NIHSS and mRS [1,2,5]. Studies also suggest that NLR predicts prolonged hospitalization, reduced functional independence, and adverse outcomes in both acute and subacute phases [3,6].

Beyond isolated measurements, NLR contributes to composite inflammatory indices such as the platelet–lymphocyte ratio (PLR) and the systemic immune-inflammation index (SII), which may enhance prognostic discrimination [4,7]. Importantly, elevated NLR has been linked to increased long-term vascular and all-cause mortality among stroke survivors [8]. Because NLR is inexpensive, rapidly available, and universally obtained in emergency settings, it offers practical advantages compared with more specialized inflammatory or imaging biomarkers [9–11]. Integrating NLR into prognostic models may therefore help clinicians anticipate disability and individualize rehabilitation intensity [12,13].

However, variability in cut-off thresholds, timing of measurement, and study design has limited standardization of NLR use in clinical practice [14]. Moreover, most existing evidence comes from retrospective or large multicenter cohorts, whereas fewer prospective studies have evaluated NLR specifically at discharge—a time point directly relevant for early functional prognostication.

To address this gap, the present study examines whether admission NLR correlates with functional disability at discharge in a real-world, prospective cohort of acute and subacute ischemic stroke patients. This approach provides insight into the utility of NLR under routine clinical conditions and supports ongoing efforts to refine inflammation-based prognostic tools in stroke care.

2. Materials and Methods

Study Design

This is an analytical, prospective, cohort study (32 patients), conducted on acute and subacute ischemic stroke patients, over a period of 12 months, between October 2024 and October 2025, in the Neurology Department of Ilfov County Clinical Emergency Hospital.

The study aimed to evaluate the correlation between the neutrophil–lymphocyte ratio (NLR) and functional disability in patients diagnosed with acute and subacute ischemic stroke.

Study Population

Eligible participants were consecutive adult patients (aged ≥18 years) admitted with a confirmed diagnosis of acute or subacute ischemic stroke, established by clinical assessment and neuroimaging (brain computed tomography and/or magnetic resonance imaging).

Inclusion Criteria

- Age ≥18 years;
- Stroke onset within 3 days prior to admission;
- Availability of complete clinical and laboratory data at baseline;
- Signed informed consent.

Exclusion Criteria

- Hemorrhagic stroke or transient ischemic attack;
- Active infection, autoimmune disease, malignancy, or chronic inflammatory condition;
- Recent major surgery or trauma (within 3 months);
- Immunosuppressive or corticosteroid therapy;
- Incomplete follow-up or missing data relevant to study variables.

Clinical and Laboratory Data Collection

Upon admission, demographic data (age, sex), vascular risk factors (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, smoking status), and medication history were recorded. Stroke severity was evaluated using the National Institutes of Health Stroke Scale (NIHSS) at presentation. Functional outcome was assessed using the modified Rankin Scale (mRS) at discharge, presented in Table 1.

Table 1. Modified Rankin Scale (mRS) – Scoring Table

Score	Description
0	No symptoms at all.
1	No significant disability despite symptoms; able to carry out all usual duties and activities.
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.
3	Moderate disability; requires some help, but able to walk unassisted.
4	Moderately severe disability; unable to attend to own bodily needs without assistance and unable to walk without help.
5	Severe disability; bedridden, incontinent, requiring constant nursing care and attention.
6	Dead.

Peripheral venous blood samples were collected at the moment of admission, before the initiation of any stroke treatment. The complete blood count (CBC) was analyzed using a standardized automated hematology analyzer. The neutrophil–lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the lymphocyte count. All analyses were performed in the hospital's central laboratory following standardized internal quality control procedures.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR) depending on data distribution, while categorical variables were presented as frequencies and percentages. The Spearman rank correlation coefficient was used to assess relationships between NLR and clinical outcomes (NIHSS, mRS). A p-value < 0.05 was considered statistically significant. All variables included in the analysis were complete for the final sample, and no missing data were present; therefore, no imputation or additional handling procedures were required.

No a priori sample size or formal power calculation was performed for this study. The final sample of 32 patients reflects the total number of consecutive, eligible cases admitted to our single tertiary center within the predefined 12-month recruitment window and was therefore determined by feasibility rather than by a target effect size. The study was conceived as exploratory and hypothesis-generating, aiming to provide real-world preliminary data on the relationship between NLR and functional disability at discharge.

Previous studies investigating inflammatory markers and functional outcome in ischemic stroke have generally reported small-to-moderate correlations between NLR and clinical scales such as NIHSS or mRS. Under these conditions, a modest sample size

like ours is expected to have limited power to detect statistically significant associations in the lower range of effect sizes (e.g., correlations around r ≈ 0.2–0.3), while being more suitable for identifying only larger effects. Consequently, the absence of a statistically significant correlation in our cohort should be interpreted with caution, as it may primarily reflect restricted power rather than the absence of a biologically relevant association. For this reason, our findings are best viewed as preliminary and supportive of the need for larger, prospectively designed, multicenter studies with formal sample size estimation based on anticipated effect sizes.

3. Results

Participant characteristics

A total of 32 patients diagnosed with acute or subacute ischemic stroke were prospectively included in the study between October 2024 and October 2025. The cohort comprised both male (19) and female (13) participants aged between 41 and 83 years (median age 71.09). All patients had confirmed ischemic stroke on neuroimaging and available hematological parameters at admission. Table 2 shows the basseline clinical characteristics of the study cohort.

Table 2. Baseline clinical characteristics of the study cohort (N = 32)

Variable	Value
Demographics	
Age, years — median (IQR)	71.09 (15.3)
Sex, n (%)	Male: 19 (59.4%), Female: 13 (40.6%)
Vascular Risk Factors, n (%)	
Hypertension	29 (90.62%)
Diabetes Mellitus	14 (43.75%)
Dyslipidemia	17 (53.12%)
Atrial Fibrillation	6 (18.75%)
Ischemic Heart Disease	30 (93.75%)
Smoking Status	18 (56.25%)
Prior Stroke/TIA	4 (12.5%)
Comorbidities, n (%)	
Chronic Kidney Disease	8 (25%)
Heart Failure	12 (37.5%
Peripheral Artery Disease	7 (21.87%)
Obesity (BMI ≥30 kg/m²)	2 (6.25%)
Active Malignancy (excluded per criteria)	–
Autoimmune/Inflammatory Disease (excluded per criteria)	–
Stroke Characteristics	
Stroke subtype, n (%)	Cardioembolic: 6 (18.75%); Large artery atherosclerosis: 10 (31.25%) Small vessel disease: 14 (43.75); Other: 2 (6.25%)
Onset-to-admission time ≤3 days, n (%)	32 (100%)
NIHSS at admission — median (IQR)	6.5 (2–26)
mRS at discharge — median (IQR)	2.5 (1–5)
Treatment Modalities, n (%)	
Dual antiplatelet therapy	21 (65.62%)
Single antiplatelet therapy	5 (15.62%)
Anticoagulation (e.g., AF-related)	6 (18.75%)
Statin therapy	32 (100%)
In-hospital complications (e.g., pneumonia, UTI)	12 (37.5%)

Descriptive statistics

The neutrophil–lymphocyte ratio (NLR) displayed a wide range of values, consistent with the heterogeneity of systemic inflammatory activation following ischemic stroke. The National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) scores indicated that most patients presented with mild to moderate neurological impairment and functional disability at discharge.

Normality testing using the Shapiro–Wilk test demonstrated that all three key variables deviated significantly from a normal distribution:

- NLR: $W = 0.502$, $p < 0.001$
- NIHSS: $W = 0.667$, $p < 0.001$
- mRS: $W = 0.899$, $p = 0.0058$

Consequently, non-parametric methods were employed in subsequent correlation analyses. A summary of descriptive statistics for the main study variables is presented in Table 3.

Because all key variables violated assumptions of normality on the Shapiro–Wilk test, nonparametric methods were applied. Spearman's rank correlation was used because it assesses monotonic rather than strictly linear relationships, making it appropriate for skewed or ordinal data distributions.

Table 3. Descriptive statistics of study variables (N = 32)

Variable	Median (IQR)	Minimum	Maximum	Shapiro–Wilk p-value
NLR	4.66 (2.93-8.1)	0.4	33.55	<0.001
NIHSS	6.5 (4.00-11.00)	2	26	<0.001
mRS	2.5 (2.00-4.00)	0	5	0.0058

Spearman correlation between NLR and mRS: r = 0.313, p = 0.0809.

Given the non-normal distribution of the analyzed variables, Spearman's rank correlation coefficients were used to assess the relationships between hematological inflammatory indices and clinical outcomes, as presented in Figure 1.

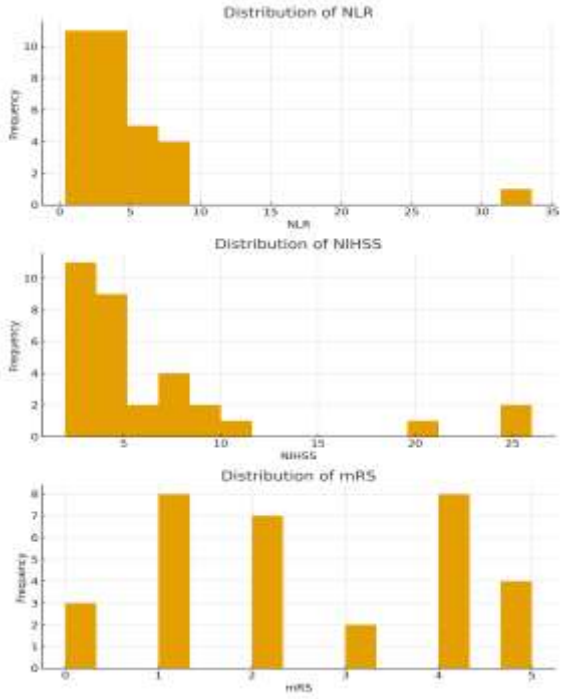

Figure 1. Distribution of the neutrophil–lymphocyte ratio (NLR), NIH Stroke Scale (NIHSS), and modified Rankin Scale (mRS) in the study cohort. All three variables show right-skewed, non-normal distributions, supporting the use of nonparametric statistical methods.

A positive correlation was observed between the neutrophil–lymphocyte ratio (NLR) and the modified Rankin Scale (mRS) at discharge, suggesting that higher inflammatory activity at admission tended to associate with greater functional disability. The correlation coefficient indicated a moderate effect size (Spearman's $r = 0.313$, $p = 0.0809$, $N = 32$), though this did not reach conventional statistical significance. The directionality of this relationship aligns with prior evidence linking systemic inflammation to poorer neurological recovery after ischemic stroke.

Visual inspection of the scatter plot (Figure 2) confirms the positive association between NLR and mRS, with a clear upward trend across the range of NLR values. The dispersion of data points reflects clinical heterogeneity within the cohort, which may account for the borderline significance observed.

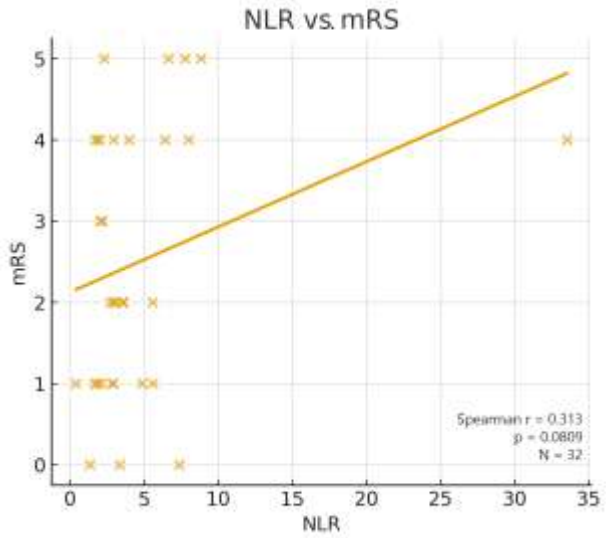

Figure 2. Correlation between neutrophil–lymphocyte ratio (NLR) and functional disability (mRS). Scatter plot showing the relationship between NLR and mRS at discharge. The regression line (least-squares fit) demonstrates a positive trend between inflammatory status and functional outcome.

In addition to reporting the Spearman correlation coefficient and p-value, we calculated a 95% confidence interval (CI) for the correlation estimate using a bootstrap resampling approach (5,000 iterations), providing additional context regarding the precision and uncertainty of the effect size.

The correlation between NLR and mRS was positive but not statistically significant (Spearman r = 0.313, p = 0.0809). The 95% confidence interval ranged from –0.09 to 0.65, indicating substantial uncertainty around the effect size and reflecting the limited sample size.

Given the clinical relevance of early neurological status, we also explored the association between NLR and NIHSS at admission. The correlation was weak and not statistically significant (Spearman r = 0.114, p = 0.535), indicating that in this cohort NLR did not strongly reflect initial stroke severity. This finding contrasts with several larger studies reporting moderate positive associations between NLR and admission NIHSS, and may reflect the limited sample size, heterogeneity of stroke subtypes, or restricted range of NIHSS values in our population.

Sensitivity Analysis

To evaluate the influence of extreme NLR values (range 0.4–33.55) on the primary association, a sensitivity analysis was performed using the Tukey interquartile range method to remove outliers. In the full dataset, the correlation between NLR and

mRS was Spearman r = 0.313 (p = 0.0809). After excluding outliers, the correlation remained positive but slightly attenuated (r = 0.278), and the p-value increased (p = 0.1300). These findings indicate that while extreme values contribute modestly to the effect size, the overall direction of association between inflammatory activation and functional disability remains consistent.

Interpretation

These results suggest that the neutrophil–lymphocyte ratio, a readily obtainable parameter from the complete blood count, may serve as a potential biomarker of disability in ischemic stroke, particularly in the acute and subacute phases. Although the correlation in this cohort did not reach significance, the magnitude and direction of association are consistent with existing literature. A larger sample size and inclusion of additional inflammatory indices (PLR, CRP) are warranted to validate these findings and to establish clinically meaningful thresholds for prognostication.

4. Discussion

The present study investigated whether the neutrophil–lymphocyte ratio (NLR) at admission correlates with functional disability at discharge in patients with acute and subacute ischemic stroke. Although we observed a positive association between higher NLR values and worse mRS outcomes, this correlation did not reach statistical significance. As such, our findings should be viewed as exploratory and hypothesis-generating. Nonetheless, the direction of the observed trend is consistent with previous work demonstrating that inflammatory biomarkers—including NLR—may reflect the extent of neurological impairment and functional prognosis after stroke [15].

The biological rationale for examining NLR is supported by the well-established role of post-stroke inflammation in driving secondary neuronal injury. Neutrophil activation and infiltration promote blood–brain barrier disruption and tissue damage, while lymphopenia reflects a systemic immunosuppressive state that may worsen outcomes. These processes provide a plausible mechanistic basis for associations reported between elevated NLR and functional impairment [16]. Previous studies have shown that higher NLR values are linked to mortality, worse cardiovascular outcomes, and greater disability among stroke survivors [17,18]. Dynamic changes in NLR have also been shown to predict 90-day outcomes, indicating that the temporal trajectory of systemic inflammation is clinically relevant [18,19].

Beyond isolated measurements, incorporating NLR into composite inflammatory indices has demonstrated added prognostic utility. Combinations such as NLR with the platelet–lymphocyte ratio (PLR) or the systemic immune-inflammation index (SII) improve discrimination of poor outcomes, early neurological deterioration, and long-term morbidity [20,21]. Elevated NLR has also been associated with the severity of intracranial atherosclerosis and vascular stenosis, suggesting a link between systemic inflammation and underlying vascular pathology [22]. Other studies have reported that persistent elevations in NLR during hospitalization predict unfavorable outcomes and may reflect ongoing inflammatory activation [23,24]. Collectively, this evidence supports the investigation of NLR as a prognostic biomarker, although not all studies have demonstrated uniform results [25–27].

Despite this supportive framework, our study did not demonstrate a statistically significant association between NLR and functional outcome. This likely reflects methodological constraints, most notably the small sample size, which limits statistical power to detect moderate correlations. Similar modest associations have been observed in other small or single-center cohorts, whereas larger studies have more consistently reported statistically robust findings [23,24,26–28]. The non-significant result in our analysis therefore does not contradict previous literature but instead underscores the importance of adequate sample size when evaluating biomarkers with moderate effect sizes.

Emerging studies have also explored the role of NLR in relation to stroke progression, treatment response, and long-term outcomes. Elevated NLR has been associated with worse progression of ischemic injury, poorer functional outcomes, and increased mortality in older adults [29–32]. Furthermore, NLR has shown value in stratifying severity and predicting outcomes in patients with large-vessel occlusion and in those undergoing reperfusion therapies [33,34]. Associations between NLR and other vascular risk markers, including hyperhomocysteinemia, also highlight its potential relevance to stroke-related systemic inflammation [35]. Retrospective analyses and population-based cohorts similarly support the prognostic role of NLR and related indices [36,37]. Finally, older patient cohorts have shown that elevated NLR reliably predicts poor short-term outcomes, reinforcing its potential value across diverse clinical contexts [38].

Several limitations of the present study should be noted. The sample size was limited, and no a priori power calculation was performed, increasing the risk of type II error. The single-center design may reduce generalizability, and single-time-point NLR measurements do not account for dynamic inflammatory changes known to influence prognosis. Unmeasured confounders—such as occult infection, comorbid inflammatory conditions, or variability in treatment modality—may also influence NLR independently of stroke severity.

Several potential confounders must be considered when interpreting the association between NLR and functional disability. First, although patients with active infection were excluded by design, subclinical or early-stage infectious processes may still elevate neutrophil counts and thereby inflate NLR independently of stroke severity. Even mild respiratory or urinary symptoms not meeting diagnostic thresholds can alter leukocyte profiles and obscure true neuroinflammatory signals. Second, stroke subtype is an important biological modifier of inflammatory response. Large artery atherosclerosis and cardioembolic strokes often involve more extensive tissue injury and heightened innate immune activation compared with small vessel disease, potentially producing higher NLR values regardless of functional outcome. Without subtype-stratified analysis, these differences may confound the observed correlations.

Systemic comorbidities—such as chronic kidney disease, diabetes, heart failure, and chronic inflammatory conditions—may also influence baseline leukocyte dynamics and contribute to elevated NLR independent of acute neurological injury. Metabolic stress, sympathetic activation, and endothelial dysfunction in these conditions can amplify neutrophil release and lymphocyte suppression, complicating interpretation of NLR as a stroke-specific biomarker. Similarly, treatment differences may act as confounders. Reperfusion therapies (IV thrombolysis or mechanical thrombectomy) modulate reperfusion injury and inflammatory cascades, while antiplatelet agents, anticoagulation, and statins have known immunomodulatory properties that could lower or stabilize NLR values. Variation in time-to-treatment or therapeutic intensity may therefore shape NLR trajectories independent of disability outcomes.

Finally, the timing of blood sampling—restricted to admission—captures only an initial snapshot of inflammation and may not fully represent patients with delayed immune activation or post-stroke immunosuppression. Dynamic changes in NLR during hospitalization might better reflect evolving injury and recovery processes. Taken together, these confounding factors underscore the complexity of using single-time-point inflammatory markers as prognostic tools and highlight the need for larger, stratified, and treatment-adjusted analyses in future studies.

The correlation between NLR and mRS was positive but did not reach statistical significance (Spearman $r = 0.313$, $p = 0.0809$). This result indicates a trend toward an association; however, the p-value exceeds the conventional alpha level of 0.05, and therefore the relationship cannot be considered statistically significant.

It is important to note that functional outcome in this study was assessed using the mRS at discharge rather than the conventional 90-day endpoint used in most large clinical trials and observational cohorts. The mRS at discharge primarily reflects early neurological status and the immediate impact of acute care, including complications, early rehabilitation availability, and length of hospitalization. In contrast, 90-day mRS incorporates the broader trajectory of spontaneous neurological recovery, neuroplasticity, and structured rehabilitation, and therefore serves as a more stable and widely accepted measure for long-term functional outcome. As a result, discharge mRS values may underestimate eventual recovery or overestimate disability in patients who continue to improve substantially during the subacute and chronic phases. This difference limits direct comparability with larger studies that rely on 3-month outcomes and may partly explain the modest strength of association observed between admission NLR and functional disability in our cohort. Nevertheless, discharge mRS remains clinically relevant for early prognostication, discharge planning, and rehabilitation triage, supporting its use in real-world prospective studies such as ours.

Although an upward trend was observed between admission NLR and functional disability at discharge, the association did not reach statistical significance in this cohort. Consequently, these findings should not be interpreted as evidence supporting the immediate use of NLR in standalone prognostic algorithms or clinical decision-making. At best, our results provide preliminary, exploratory insight into inflammation–outcome relationships and reinforce biological plausibility rather than clinical applicability. The modest effect sizes, lack of statistical significance, and potential influence of confounders highlight the need for large, adequately powered prospective studies before NLR can be reliably incorporated into routine prognostic workflows. Until such evidence is available, NLR should be viewed as a supportive research marker rather than a validated tool for predicting functional outcomes in individual patients.

In summary, this study identified a non-significant trend toward higher disability with elevated NLR in acute and subacute ischemic stroke. While compatible with prior evidence, the findings are insufficient to validate NLR as a prognostic marker in this cohort. Future multicenter, adequately powered studies incorporating serial inflammatory measurements and comprehensive adjustment for confounders are needed to clarify the prognostic utility of NLR and to determine its potential integration into clinical decision-making frameworks.

Future Directions

Building on these findings, several avenues for future research are proposed. Larger, multicenter prospective studies should be undertaken to validate the prognostic value of NLR and establish standardized cut-off thresholds for clinical use. Such studies should include diverse populations and stratify analyses by stroke subtype, treatment modality, and comorbidities to enhance applicability across clinical settings. Longitudinal monitoring of NLR and other inflammatory indices (PLR, SII, CRP) throughout the acute and subacute phases may provide insight into the temporal evolution of immune activation and its impact on recovery. Combining dynamic hematological markers with neuroimaging biomarkers (e.g., infarct volume, perfusion deficit, or white matter hyperintensities) could yield a more comprehensive prognostic framework [39].

Future studies should explore the integration of NLR into multivariate predictive models alongside clinical (NIHSS, age, comorbidities) and radiological parameters to improve the precision of disability prediction. Research should also investigate the therapeutic implications of modulating post-stroke inflammation. Interventional trials assessing anti-inflammatory or immunomodulatory strategies (e.g., IL-1 or IL-6 blockade, colchicine, or statins) could evaluate whether reductions in NLR correspond to improved neurological outcomes [40-41]. In this context, NLR may serve not only as a prognostic biomarker but also as a monitoring tool for therapeutic efficacy.

5. Conclusions

This study examined the relationship between admission NLR and functional disability at discharge in patients with acute and subacute ischemic stroke. Although NLR showed a positive but non-significant association with mRS, the direction of the trend was consistent with the biologically plausible role of inflammation in early stroke outcomes. Exploratory analyses, including sensitivity testing and correlation with NIHSS, showed similarly modest effect sizes. These findings indicate that while NLR may reflect elements of the inflammatory response to ischemia, its prognostic utility in this small, real-world cohort was limited. Overall, the results offer preliminary insight into early inflammatory profiles after stroke and provide a basis for further investigation into how dynamic inflammatory markers may contribute to clinical assessment and patient stratification.

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