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Role of Lymphocyte-Monocyte Ratio in predicting the prognosis and outcome of patients with Acute Ischemic Stroke

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Abstract

Background: Acute ischemic stroke is a sudden disruption in blood flow to the brain, leading to neuronal damage that occurs secondary to inflammation. The outcome depends on the type of stroke, the duration of treatment, and the patient's physical status. Lymphocyte-to-monocyte ratio (LMR) is an emerging biomarker that can predict stroke severity and functional outcome in AIS patients.

Methods: This was a prospective, observational study including cases of ischemic stroke presenting to a tertiary care center in Kerala. Patients with neurological symptoms were evaluated according to the NIHSS score, and blood samples were sent for analysis. Patients who presented to the emergency department from July 2024 to December 2024 were included in the study, and a total of 126 patients were observed

Results: This study shows that the NIHSS score used to grade stroke severity at admission was negatively associated with LMR values. This shows that lower LMR values are associated with greater stroke severity. A cutoff value of 2.9 was used for this study, and it showed high accuracy. The result of the Spearman correlation showed that there was a very high, negative correlation between LMR and NIHSS Score. The results showed that this correlation between LMR and NIHSS Score was a statistically significant negative correlation, $r(124) = -0.71$, $p = <.001$.

Conclusion: LMR can be used as an important and effective biomarker in evaluating the severity of the disease and in predicting the outcome in patients with acute ischemic stroke.

Keywords: Acute ischemic stroke; Lymphocyte Monocyte ratio; NIHSS

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Introduction

Acute ischemic stroke is a sudden disruption in the blood flow to the brain, leading to neuronal damage secondary to inflammation. Common causes of this condition include atherosclerosis and thrombus formation.[1] A person is at a higher risk of developing ischemic stroke under the following conditions: [2] Old age, Increased blood pressure, Hyperlipidemia, Diabetes, Smoking, Obesity, Arrhythmia, Family history of stroke.

The symptoms of this situation may vary depending on the artery or branch involved in the pathology. The most common symptom of acute ischemic stroke is weakness/numbness, commonly affecting one side of the body. The patient may have difficulty standing, talking, or even smiling. Some may have dizziness or a headache, with or without the aforementioned neurological symptoms. [1] Diagnosis of a case of acute ischemic stroke is done after careful and thorough physical and neurological examination—additional tests, such as CT or MRI, further support it.

Treatment for ischemic stroke aims to restore blood flow to the brain as quickly as possible to reduce damage. Treatment options may include thrombolytic therapy, endovascular therapy, antiplatelet and anticoagulant drugs, along with rehabilitation.

The outcome of ischemic stroke depends on the type of stroke, the duration of treatment, and the patient's physical status. Recovery can take months or years and include physical, mental, and emotional recovery. [3] The first step of diagnosis occurs at the emergency department by evaluation of the symptoms and assessment of the neurological functions. The NIHSS score is allotted to each patient to grade the severity of neurological impairment.

NIHSS Score: National Institutes of Health Stroke Scale

The National Institutes of Health Stroke Scale (NIHSS) is used for assessing the severity of acute ischemic stroke. It provides a functional measure of patients' neurological status and guides treatment decisions.

The NIHSS consists of the following points: Level of Consciousness (LOC) (3 points), Gaze (3 points), Visual Fields, (3 points), Facial Palsy (3 points), Motor Strength (6

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points), Sensory (6 points), Language (3 points), Dysarthria (2 points), Extinction and Inattention (2 points), Each parameter is scored on a 0-4 scale, where 0 indicates normal function and 4 indicates severe impairment. The total score ranges from 0 to 42, higher scores indicating greater severity. NIHSS score of 0-4 indicates no significant neurological deficit, score 5-15 indicates mild stroke,16-20 indicates moderate stroke and 21-42 indicates severe stroke.[4]

A major drawback of the NIHSS scoring system is that it relies on subjective judgment and may show inter-observer variability. One notable, emerging biomarker is the lymphocyte-to-monocyte ratio (LMR). A low LMR ratio is associated with cardiovascular disease[5] and indicates a poor prognosis in malignant diseases[6] Studies have shown that LMR can predict stroke severity, functional outcome, and mortality in AIS patients. [7]

Monocytes are involved in the inflammatory response, and an increase in monocyte count indicates heightened inflammation.[8] Lymphocytes are also important mediators and reflect the resolution of inflammation.[9] A lower LMR shows an inflammatory imbalance with a relative increase in monocytes, which further indicates endothelial damage and an increase in reactive oxygen species (ROS). A lower LMR indicates oxidative stress and a weakened antioxidant defense, as well as a decrease in lymphocyte count.[10]

Prompt diagnosis and treatment are critical for a better prognosis and minimal neurological deficits. This article aims to analyze the importance of LMR in grading the severity of ischemic stroke and in predicting its outcome. We use a cutoff of 2.9 to predict patient outcomes, and we aim to evaluate the accuracy of this cutoff in our study population.

Materials and Methods

This was a prospective, observational study including all cases of clinically confirmed ischemic stroke presenting to the Emergency Medicine Department of a Tertiary Care Center in Kerala, India.

Patients who presented to the emergency department from July 2024 to December 2024 were included in the study, and a total of 126 patients were included by convenience sampling. Patients with neurological symptoms were evaluated using the NIHSS score, and blood samples were sent for analysis. Blood samples were collected within 4 hours of symptom onset and within 1 hour of hospital admission. Patients on immunosuppressants, patients with severe sepsis, hepatic or renal dysfunction, and known cases of malignancies were excluded from the study. Blood cell indices were obtained from the ABX Penta XL hematology analyser. Total leukocyte count, absolute lymphocyte count, and absolute monocyte count were obtained from the analyzer. The lymphocyte/monocyte ratio was calculated by dividing the absolute lymphocyte count by the absolute monocyte count.

The treatment of all patients followed the same protocol. All patients received dual antiplatelet therapy and later single antiplatelet therapy, along with physiotherapy. Thrombolysis was initiated if indicated (NIHSS score >5) and started within 4 hours of symptom onset. Other comorbidities were managed and kept under control.

Follow-up of the patients was done at 1-month post-admission by phone to enquire about any persisting complaints or loss of function, and to evaluate the patient's general condition. The majority of patients were unable to attend the hospital for re-evaluation due to personal reasons, and thus, a clinical evaluation of progress could not be obtained. The improvement in symptoms, quality of life, and the ability to carry out daily and basic activities were enquired into and noted. Data were entered in Microsoft Excel, and analysis was performed using SPSS software version 22.0. Spearman rank correlation was calculated to evaluate the relationship between LMR and NIHSS score. An ANCOVA was performed to assess LMR's ability to predict the outcome.

Results

A total of 126 patients were included in the study. The study showed a slight male predominance with 62 female patients and 64 male patients. The age distribution of the study population is depicted in Figure 1.

The age of the patients ranged from 41 to 93 years, with a mean age of 68.43 and a standard deviation of 13.04. The 95% confidence interval for the mean was 66.12-70.13. Age distribution of the study population is depicted in Figure 2.

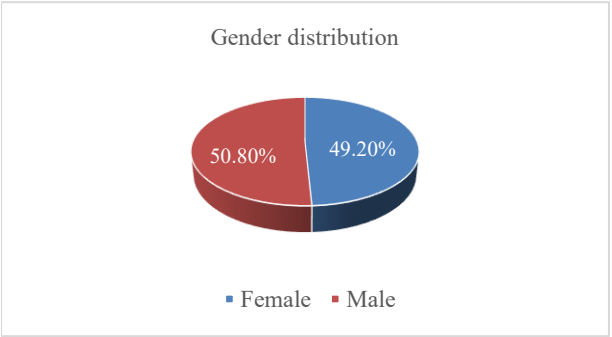

Figure 1. Gender distribution of the study population.

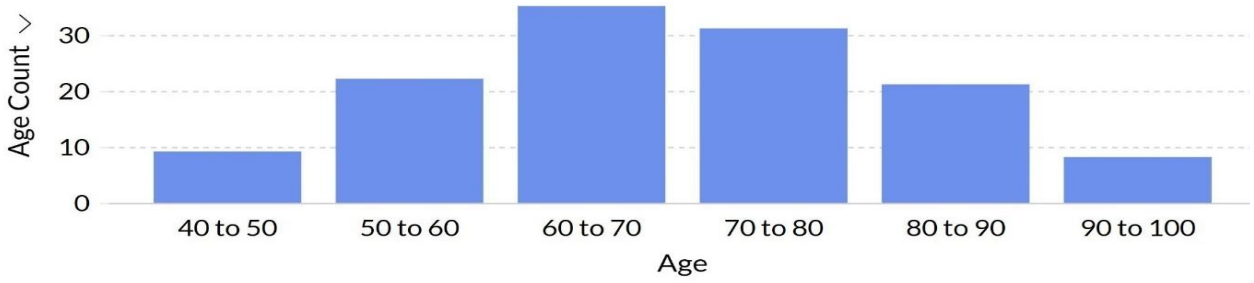

Figure 2. Age distribution of the study population.

Table 1. Total WBC count and Absolute lymphocyte and monocyte counts of the study population.

	Total leukocyte count (cells/mm^3)	Absolute lymphocyte count (cells/mm^3)	Absolute monocyte count (cells/mm^3)
Mean	9063.49	2033.73	617.22
Std. Deviation	3362.56	923.45	505.38
Minimum	4500	640	100
Maximum	21300	5410	3200
95% confidence interval for the mean	8469.35-9657.64	1870.56-2196.9	527.93-706.52
Mean ± Std. Deviation	9063.49± 362.56	2033.73 ± 923.45	617.22 ± 505.38

The absolute counts of the study population are depicted in Table 1. The absolute Lymphocyte counts of the study population ranged from 640 cells/mm^3 to 5410 cells/mm^3, while the absolute monocyte counts ranged from 100 cells/mm3 to 3200 cells/mm3.

Table 2 shows the mean NIHSS and LMR scores, along with their standard deviations and 95% confidence intervals. LMR was calculated by dividing the absolute lymphocyte count by the absolute monocyte count, and the values ranged from 0.25 to 22.2, with a mean of 5.57.

The result of the Spearman correlation showed that there was a high, negative correlation between LMR and NIHSS Score. The results showed that this correlation between LMR and NIHSS score was a statistically significant negative correlation, $r(124)=0.71$, $p<.001$. As the NIHSS Score increases, the LMR tends to decrease. Figure 3 shows a scatter diagram depicting the negative relationship between LMR and NIHSS score.

Out of 126 patients, 66 patients were better at the 1-month follow-up,46 patients were worse, and 14 patients had passed away. Figure 4 summarizes the follow-up outcome.

Table 2. Mean values of NIHSS score and LMR of the study population.

	NIHSS score	LMR
Mean	14.56	5.57
Std. Deviation	11.58	4.93
Minimum	1	0.25
Maximum	41	22.2
95% confidence interval for the mean	12.52-16.61	4.7-6.44

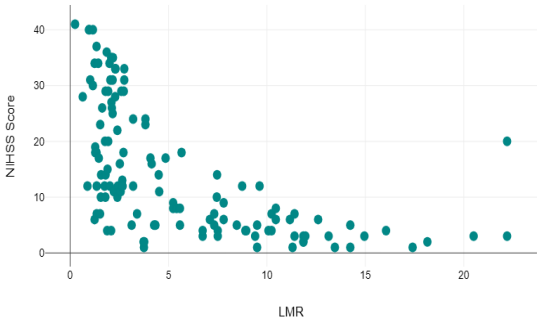

Figure 3. Scatter diagram showing the relationship between LMR and NIHSS score.

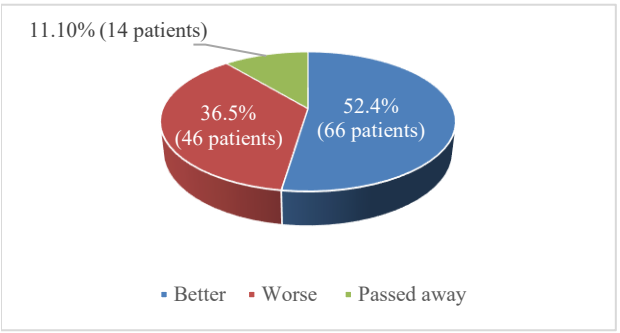

Figure 4. General outcome of the patients at one-month follow-up.

Figure 5 shows an analysis of LMR with the clinical outcome at 1-month follow-up. It is seen that the majority of cases with LMR more than 2.9 were better at follow-up, and the majority of patients with LMR less than 2.9 were worse or had passed away.

A one-way analysis of variance (ANOVA) showed a significant difference between the categorical variable, Follow-up, and the variable, LMR ($F=21.48$, $p<.001$), after adjusting for the presence of comorbidities, including hypertension, dyslipidemia, diabetes mellitus, and seizures.

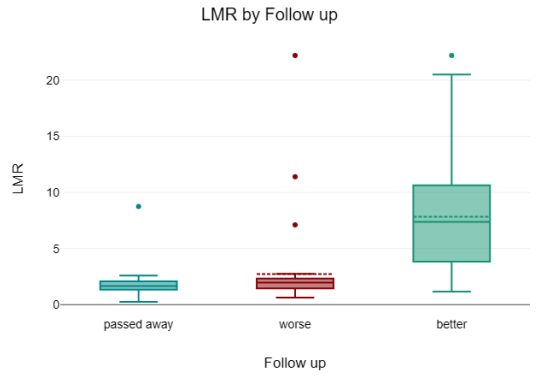

Figure 5. Box plot depicting the relationship between LMR and the outcome of the patients.

Thus, with the available data, the null hypothesis (i.e., there is no correlation) was rejected (Table 3).

The mean LMR values for patients who had passed away and were symptomatically worse were 2.07 and 2.73, respectively, whereas patients who were symptomatically better after 1 month showed a mean LMR value of 7.84, which was significantly higher than those of the other two groups (Figure 6). This shows that a lower LMR value is linked to a worse prognosis.

Table 3. Results of ANCOVA analysis done to analyze the predictive ability of LMR.

	Sum of Squares	df	Mean Square	F	p
Follow up	786.6	2	393.3	21.48	<0.001
Residual	2252.27	123	18.31	-	-
Total	3038.88	125	-	-	-

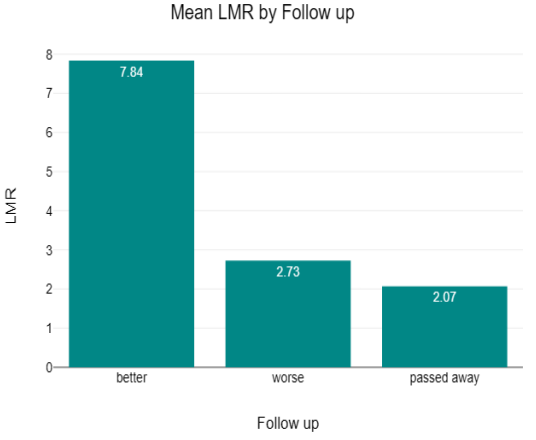

Figure 6. Mean LMR values of patients who were symptomatically better, worse or had passed away.

Discussion

This study shows that the NIHSS score used to grade stroke severity at admission was negatively associated with LMR values. Lower LMR values were observed in patients with higher NIHSS scores. This shows that lower LMR values are associated with greater stroke severity. This is in accordance with the study conducted by Hao Ren et al. [7] The study showed that a lower LMR value was closely associated with stroke severity and poor outcome, and that LMR values less than 2.9 were associated with increased stroke severity, with a sensitivity of 69.3% and specificity of 86.6%.

A study conducted by Shifa Prabhu et al showed a similar correlation between LMR and stroke severity.[11]

The pathophysiology of acute ischemic stroke shows an increase in the release of inflammatory mediators. This, in turn, leads to neuronal damage secondary to ischemic changes. Following a stroke, systemic stress activates the renin-angiotensin system, which, in turn, leads to cortisol release and, thereby, lymphocyte apoptosis.[9] Lymphocytes have a neuroprotective effect, while peripheral monocytes are a source of MMP-9, which aggravates the damage to neuronal tissue.[10] Therefore, LMR, which combines lymphocyte count and monocyte count, can be seen as a useful parameter in assessing stroke severity.

A study conducted by Bonifacic et al. showed that a higher monocyte count was associated with a poor outcome.[12]

This study also shows that LMR at admission can predict the patient's clinical outcome. In this study, the majority of patients with LMR more than 2.9 were clinically better at the one-month follow-up as compared to the patients with LMR less than 2.9 who were clinically worse or had passed away. These findings are similar to the study conducted by Zhang Y et al [13] and Park M G et al [14]which suggested that a low LMR value is related to poor functional outcome in acute ischemic stroke patients. In the study by Park M G et al., LMR was calculated on days 1 and 7 of admission. The study concluded that lower LMR values at day 1 were associated with increased risk of infections, including pneumonia. In contrast, lower LMR at day 7 was associated with a poorer functional outcome at the 3-month evaluation.

A study conducted by Mao et al [15] stated that LMR was an independent predictor of progressive infarction in patients with acute ischemic stroke. A study conducted by Danielle Lux et al [16] showed that lower LMR values were related to poor functional outcome, but with a lower cutoff of 2.0

Other studies have shown the importance of LMR in cardiovascular diseases, dementia, and malignancies.[17-20] Study conducted by Cai et al [21] showed that lower LMR was associated with increased mortality and major adverse events in patients with ST elevation Myocardial Infarction. Studies conducted by Zhu JY et al.[6] and Song W et al.[22] showed that LMR values were associated with

poor outcomes in malignancies.

Sadeghi F et al [23] showed that a combination of higher NLR and lower LMR values has a greater predictive value in the functional outcome of patients with acute ischemic stroke. A study conducted by Song Q. [24] et al showed that lower LMR values were related to increased risk of hemorrhagic transformation in acute ischemic stroke patients. Other studies by Li et al. [25] and Chen C et al.26 emphasize the importance of LMR as a biomarker.

This study showed no significant gender predominance. The majority of patients were in the 60-70-year age group. This study is limited by its small sample size, and further research is needed to establish standardized reference ranges. It is important to note that the prognostic value of LMR may be affected by factors including the timing of LMR measurement, the presence of comorbidities, and other factors such as age, sex, and race. Further studies are needed to determine the prognostic value of LMR in a larger population and to evaluate the exact underlying pathophysiology.

Conclusion

This study concludes that LMR can be used as an important biomarker in evaluating the severity and predicting the outcome in acute ischemic stroke patients. A cutoff value of 2.9 showed high accuracy, sensitivity, and specificity. As LMR gains wider recognition, it is likely to become an important tool in personalized medicine and precision health.

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Ethical consideration

No additional tests were performed on the patients. Institutional ethical clearance was obtained. Ref No: IECKMCT/26/24-28.11.2024.

Competing Interests

The authors declare no conflict of interest.

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None.

References

1. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. Harrison's Principles of Internal Medicine. 20th ed. New York: McGraw-Hill Education; 2018. p. 3068.
2. Boehme AK, Esenwa C, Elkind MS. Stroke risk factors, genetics, and prevention. Circ Res. 2017;120(3):472-495. doi: 10.1161/CIRCRESAHA.116.308398
3. Kalkonde YV, Deshmukh MD, Sahane V, Puthran J, Kakarmath S, Agavane V, et al. Stroke is the leading cause of death in rural Gadchiroli, India: A prospective community-based study. Stroke. 2015;46(7):1764-1768. doi: 10.1161/STROKEAHA.115.008067
4. Ram CVS, Kumar S, Renjen PN, Kumar GP, Swaminathan J, Reddy CR, et al. Risk factors predisposing to acute stroke in India: A prospective study. J Hypertens. 2021;39(11):2183-2189. doi: 10.1097/HJH.0000000000002915
5. Ji H, Li Y, Fan Z, et al. Monocyte/lymphocyte ratio predicts the severity of coronary artery disease: a syntax score assessment. BMC Cardiovasc Disord. 2017;17:90. doi: 10.1186/s12872-017-0512-6
6. Zhu JY, Liu CC, Wang L, et al. Peripheral blood lymphocyte-to-monocyte ratio as a prognostic factor in advanced epithelial ovarian cancer: a multicenter retrospective study. J Cancer. 2017;8(5):737-743. doi: 10.7150/jca.17199
7. Ren H, Liu X, Wang L, et al. Lymphocyte-to-monocyte ratio: a novel predictor of the prognosis of acute ischemic stroke. J Stroke Cerebrovasc Dis. 2017;26(11):2595-2602. doi: 10.1016/j.jstrokecerebrovasdis.2017.06.019
8. ElAli A, Jean LeBlanc N. The role of monocytes in ischemic stroke pathobiology: new avenues to explore. Front Aging Neurosci. 2016;8:29. doi: 10.3389/fnagi.2016.00029
9. Liesz A, Suri-Payer E, Veltkamp C, et al. Regulatory T cells are key cerebroprotective immunomodulators in acute experimental stroke. Nat Med. 2009;15(2):192-199. doi: 10.1038/nm.1927
10. Li P, Mao L, Zhou G, et al. Adoptive regulatory T-cell therapy preserves systemic immune homeostasis after cerebral ischemia. Stroke. 2013;44(12):3509-3515. doi: 10.1161/STROKEAHA.113.002637
11. Prabhu S, Harshavardhan L. Role of platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio and lymphocyte-to-monocyte ratio in acute ischaemic stroke severity: a prospective cohort study. J Clin Diagn Res. 2023;17(10):OC12-OC16. doi: 10.7860/JCDR/2023/64152/18614
12. Bonifacic D, Toplak A, Benjak I, et al. Monocytes and monocyte chemoattractant protein-1 (MCP-1) as early predictors of disease outcome in patients with cerebral ischemic stroke. Wien Klin Wochenschr. 2016;128(Suppl 7):20-27. doi: 10.1007/s00508-015-0864-1
13. Zhang Y, Xing Z, Zhou K, et al. The predictive role of systemic inflammation response index (SIRI) in the prognosis of stroke patients. Clin Interv Aging. 2021;16:1997-2007. doi: 10.2147/CIA.S339221
14. 1Park MG, Kim MK, Chae SH, et al. Lymphocyte-to-monocyte ratio on day 7 is associated with outcomes in acute ischemic stroke. Neurol Sci. 2018;39(2):243-249. doi: 10.1007/s10072-017-3163-7
15. Mao X, Yu Q, Liao Y, et al. Lymphocyte-to-monocyte ratio is independently associated with progressive infarction in patients with acute ischemic stroke. Biomed Res Int. 2022;2022:2290524. doi: 10.1155/2022/2290524
16. Lux D, Alakbarzade V, Bridge L, et al. The association of neutrophil-lymphocyte ratio and lymphocyte-monocyte ratio with 3-month clinical outcome after mechanical thrombectomy following stroke. J Neuroinflammation. 2020;17:60. doi: 10.1186/s12974-020-01739-y
17. Grimm RH Jr, Neaton JD, Ludwig W. Prognostic importance of the white blood cell count for coronary, cancer, and all-cause mortality. JAMA. 1985;254(14):1932-1937. doi: 10.1001/jama.254.14.1932
18. Shankar A, Wang JJ, Rochtchina E, et al. Association between circulating white blood cell count and cancer mortality: a population-based cohort study. Arch Intern

Med. 2006;166(2):188–194. doi: 10.1001/archinte.166.2.188
19. Margolis KL, Manson JE, Greenland P, et al. Leukocyte count as a predictor of cardiovascular events and mortality in postmenopausal women: The Women's Health Initiative Observational Study. Arch Intern Med. 2005;165(5):500–508. doi: 10.1001/archinte.165.5.500
20. Kabat GC, Kim MY, Manson JE, et al. White blood cell count and total and cause-specific mortality in the Women's Health Initiative. Am J Epidemiol. 2017;186(1):63–72. doi: 10.1093/aje/kww226
21. Cai M, Liang D, Gao F, Hong X, Feng X, Yang Y, et al. Association of lymphocyte-to-monocyte ratio with the long-term outcome after hospital discharge in patients with ST-elevation myocardial infarction: a retrospective cohort study. Coron Artery Dis. 2020;31(3):248–254. doi: 10.1097/MCA.0000000000000837
22. Song W, Tian C, Wang K, et al. The pretreatment lymphocyte-to-monocyte ratio predicts clinical outcome for patients with hepatocellular carcinoma: a meta-analysis. Sci Rep. 2017;7:46601. doi: 10.1038/srep46601
23. Sadeghi F, Sarkady F, Zsóri KS, et al. High neutrophil-lymphocyte ratio and low lymphocyte-monocyte ratio combination after thrombolysis is a potential predictor of poor functional outcome of acute ischemic stroke. J Pers Med. 2022;12(8):1221. doi: 10.3390/jpm12081221
24. Song Q, Pan R, Jin Y, et al. Lymphocyte-to-monocyte ratio and risk of hemorrhagic transformation in patients with acute ischemic stroke. Neurol Sci. 2020;41(9):2511–2520. doi: 10.1007/s10072-020-04355-z
25. Li G, Hao Y, Wang C, et al. Association between neutrophil-to-lymphocyte ratio/lymphocyte-to-monocyte ratio and in-hospital clinical outcomes in ischemic stroke treated with intravenous thrombolysis. J Inflamm Res. 2022;15:5567–5578. doi: 10.2147/JIR.S382876
26. Chen C, Gu L, Chen L, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as potential predictors of prognosis in acute ischemic stroke. Front Neurol. 2020;11:525621. doi: 10.3389/fneur.2020.525621