VIA MEDICA

ORIGINAL ARTICLE

Disaster and Emergency Medicine Journal
2022, Vol. 7, No. 4, 203–208
DOI: DEMJ.a2022.0036

ISSN 2451–4691, e-ISSN 2543–5957

INVESTIGATION OF THE RELATIONSHIP BETWEEN HALP SCORE AND MORTALITY IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Erdem Kurt[1], **Sebnem Zeynep Eke Kurt**[2]

[1]Departmant of Emergency Medicine Istanbul Training And Research Hospital Eme, Istanbul, Turkey
[2]Taksim Training and Research Hospital, Turkey

ABSTRACT

INTRODUCTION: Acute ischemic stroke (AIS) is the leading cause of death and long-term disability worldwide. The aim of this study is to examine the relationship between HALP (hemoglobin, albumin, platelet, lymphocyte) score and mortality in patients diagnosed with AIS who visited the emergency department (ED).

MATERIAL AND METHODS: Data of AIS patients aged 18 years and older who visited ED during the study period were analyzed retrospectively. Data were obtained from an electronic-based hospital information system. The area under the receiver operating characteristic (ROC) curve and the area under the curve (AUC) were used to evaluate each discriminant cut-off value to estimate mortality.

RESULTS: A total of 138 patients were included in this study, the median age of the patients was 66, and 74 (54%) were male. While the average hospital stay of the patients was 5 days, 30 patients were admitted to the intensive care units. As a result of the ROC analysis of the HALP score to predict the presence of in-hospital mortality, the area under the curve was calculated as 0.701 (95% CI: 0.553–0.849), the Youden index was 0.334, and the p-value was 0.001. When the cut-off value of the HALP score in determining the presence of in-hospital mortality is > 29.44, the sensitivity is 58.4%, the specificity is 75.0%, the positive predictive value is 96.05%, and the negative predictive value is 14.75%.

CONCLUSIONS: In our study, we concluded that the HALP score can be a good predictor of mortality in stroke patients. We recommend the use of the score because it is cheap, practical, and useful.

KEY WORDS: Acute ischemic stroke; HALP score; mortality

Disaster Emerg Med J 2022; 7(4): 203–208

INTRODUCTION

The World Health Organization (WHO) defines stroke as "a clinical syndrome lasting 24 hours or longer, resulting in focal or global cerebral dysfunction as a result of impaired cerebral blood flow, for no other than vascular cause" [1]. Stroke is the third leading cause of death worldwide, after cardiovascular diseases and cancer, and is the first cause of disability [2]. According to the data from the United States of America, a person has a stroke almost every 1 minute in the United States. Each year, more than 700 000 people experience a new or recurrent stroke, with approximately 22% of these cases resulting in death [3].

Creating new scores showing stroke prognosis can be used for early diagnosis of high-risk patients

ADDRESS FOR CORRESPONDENCE:
Erdem Kurt, Departmant Of Emergency Medicine Istanbul Training And Research Hospital Eme, Istanbul, Turkey
e-mail: erdemkurt@live.com
Received: 6.07.2022 Accepted: 15.09.2022 Early publication date: 20.10.2022

and may be beneficial in secondary prevention. There are multiple scoring systems developed for stroke. Although scoring systems are not used in the diagnosis, they provide many advantages such as specifying the severity of the neurological deficit, creating a common language among doctors, determining the location of vascular occlusion and early prognosis [4].

Recent studies have shown that hemoglobin, albumin, platelet, and lymphocyte (HALP) score can be used to determine inflammation and nutritional status [5]. It is thought to have an important effect on prognosis, especially in cancer patients [6, 7]. Few studies have examined the prognostic effect of the HALP score on acute ischemic stroke [8].

The aim of this study is to examine the relationship between HALP score and mortality in patients with acute ischemic stroke visited the emergency department (ED).

MATERIAL AND METHODS

This single-center, retrospective, and observational study was carried out in the ED of a tertiary care teaching hospital between June 1, 2021 and June 1, 2022. The institutional review board approved the analysis and the requirement for written informed consent was waived (Ethics Committee Ruling number: 2011-KAEK-50-191).

All patients over the age of 18 who visited ED within the period determined for the study and were diagnosed with acute ischemic stroke were included in the study. Patients with a diagnosis other than acute ischemic stroke, patients transferred from another hospital, patients who died in ED, and patients with missing laboratory data were excluded from the study. The vital parameters, laboratory values, and outcomes of the patients included in the study were recorded in a pre-created dataset. The HALP score was calculated according to the formula: hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L)/ /platelets (/L). The primary study outcome was all-cause in-hospital mortality.

Statistical analysis

The descriptive statistics were presented in median values and interquartile ranges (IQR; 25% to 75%) for the quantitative variables; and frequencies and percentages for the categorical variables. Normality tests were carried out by using one-sample Kolmogorov–Smirnov and Shapiro-Wilk tests and through histogram graphs. The patients were divided into two groups survivors and non-survivors, and all variables were compared according to the groups. The frequencies of categorical variables were compared using Pearson's chi-square test. The median values of the quantitative variables were compared using the Mann-Whitney U test. The correlations of HALP score and mortality variables were evaluated using point-biserial correlation and phi coefficient. Receiver operating characteristic (ROC) analysis was performed to evaluate the predictive power of the HALP score in terms of mortality. In light of the ROC analysis, the optimum cut-off points of the HALP score were calculated for mortality according to Youden's index. A 2-sided p-value of 0.05 was regarded as statistically significant (except for the phi coefficient in correlation analysis -correlation is significant at the 0.01 level-). All data analyses were performed using SPSS statistical software (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

RESULTS

A total of 137 patients were included in our study after evaluating the inclusion and exclusion criteria. The median (IQR) age of the patients was 66.0 (58.0–79.0) years and 63 (46.0) were female. Thirty (21.9%) of the patients required ICU admission and 12 (8.8%) died.

The study population was divided into two groups based on mortality. The characteristics of the patients such as age, gender, vital signs, laboratory results, HALP score, length of hospital stay, and ICU admission were compared according to the groups (Tab.1). There was no difference between the groups in age and gender variables ($p > 0.05$ for both). Among the vital findings, there was a significant difference only in SBP, the median SBP value was 142 (130–156) mmHg in the survivor group and 127 (116–142) mmHg in the non-survivor group ($p = 0.047$). There was no significant difference between the groups in terms of other vital signs ($p > 0.05$ for all three). In the laboratory results, the median value of white blood cell (WBC) was 9.21 (7.38–10.77) 10^3/uL in the survivor group, it was found to be significantly higher with 11.85 (10.49–16.06) 10^3/uL in the non-survivor group ($p = 0.001$). Troponin-I median was also higher in the non-survivor group with 0.006 (0.003––0.013) μg/L versus 0.015 (0.006–0.089) μg/L,

Table 1. Baseline characteristics of patients according to survivors and non-survivors

Variables, median (IQR) or n (%)	**Total**, n = 137	**Survivors**, n = 125 (91.2)	**Non-survivors**, n = 12 (8.8)	p
Age [years]	66.0 (58.0–79.0)	66.0 (58.0–79.0)	66.5 (60.8–82.5)	0.594*
Gender				0.132**
Female	63 (46.0)	55 (44.0)	8 (66.7)	
Male	74 (54.0)	70 (56.0)	4 (33.3)	
Vital Signs				
Systolic BP [mmHg]	141 (130–156)	142 (130–156)	127 (116–142)	**0.047***
Diastolic BP [mmHg]	84 (74–93)	84 (74–92)	77 (70–95)	0.368*
Pulse [bpm]	80 (72–90)	80 (72–88)	83 (77–102)	0.170*
Body temperature [°C]	36.5 (36.4–36.7)	36.5 (36.4–36.6)	36.5 (36.3–36.7)	0.972*
Laboratory				
WBC [10^3/uL]	9.49 (7.65–10.98)	9.21 (7.38–10.77)	11.85 (10.49–16.06)	**0.001***
Hemoglobin [g/L]	129 (119–143)	129 (119–143)	127 (112–143)	0.488*
Lymphocyte [10^3/uL]	1.44 (1.09–1.82)	1.45 (1.12–1.86)	1.23 (0.90–1.45)	0.103*
HCT [%]	40.0 (37.4–43.9)	40.0 (37.7–43.9)	39.9 (36.6–44.3)	0.796*
Platelet [10^3/uL]	236 (204–286)	235 (204–279)	275 (202–396)	0.208*
Glucose [mg/dL]	128 (102–177)	125 (101–176)	142 (113–189)	0.520*
BUN [mg/dL]	17 (14–23)	16 (14–23)	21 (16–37)	0.077*
Creatinine, mg/dL	0.94 (0.80–1.21)	0.94 (0.80–1.19)	0.93 (0.77–1.60)	0.852*
ALT [u/L]	15 (11–21)	15 (11–21)	18 (11–21)	0.846*
AST [u/L]	18 (14–24)	18 (14–24)	21 (17–33)	0.085*
Albumin [g/L]	40.4 (38.4–42.5)	40.6 (38.5–42.5)	39.4 (36.6–41.0)	0.186*
CRP [mg/L]	4.0 (1.0–14.0)	3.0 (1.0–10.0)	7.5 (2.0–38.0)	0.070*
Sodium [mmol/L]	139 (138–141)	139 (138–141)	140 (138–141)	0.598*
Potassium [mmol/L]	4.3 (4.1–4.7)	4.3 (4.1–4.7)	4.0 (3.9–4.3)	0.064*
Troponin I [µg/L]	0.006 (0.003–0.016)	0.006 (0.003–0.013)	0.015 (0.006–0.089)	**0.019***
PT (INR)	1.06 (0.98–1.13)	1.06 (0.98–1.12)	1.09 (1.02–1.14)	0.311*
APTT [seconds]	27.5 (25.8–29.3)	27.6 (26.0–29.4)	25.3 (24.5–27.0)	**0.025***
HALP score	30.7 (22.4–40.7)	31.7 (23.7–42.3)	23.0 (11.6–30.3)	**0.022***
LOS [days]	5 (3–7)	5 (3–7)	11 (6–15)	**0.012***
ICU admission	30 (21.9)	20 (16.0)	10 (83.3)	**< 0.001****

BP — blood pressure; WBC — white blood cell; HCT — hematocrit; BUN — blood urea nitrogen; AST — aspartate aminotransferase; ALT — alanine aminotransferase; CRP — C-reactive protein; PT — prothrombin time; INR — international normalized ratio; APTT — activated partial thromboplastin time; HALP — hemoglobin-albumin-lymphocyte-platelet; LOS — length of hospital stay; ICU — intensive care unit; *Mann-Whitney U test; **Pearson's chi-squared test

(p = 0.019). The third and final significant difference in laboratory results was in activated partial thromboplastin time (APTT), which was higher in the survivor group with 27.6 (26.0–29.4) seconds versus 25.3 (24.5–27.0) seconds, (p = 0.025). There was no significant difference between the groups in laboratory results except for WBC, troponin-I, and APTT (p > 0.05 for all). HALP scores of the patients were calculated according to hemoglobin, albumin, lymphocyte, and thrombocyte values. It was significantly higher in the survivor group with 31.7 (23.7–42.3) versus 23.0 (11.6–30.3), (p = 0.022). There was also a significant difference between the groups in terms of length of hospital stay (LOS) and the median value of the non-survivor group was longer with 11 (6–15) days versus 5 (3–7) days (p = 0.012). Last, 83.3% of the patients in the non-survivor group required ICU admission, this rate was 16.0% in the survivor group (p < 0.001).

ROC analysis was performed to determine the power of the HALP score to predict mortality (Fig. 1). The predictive power of the HALP score

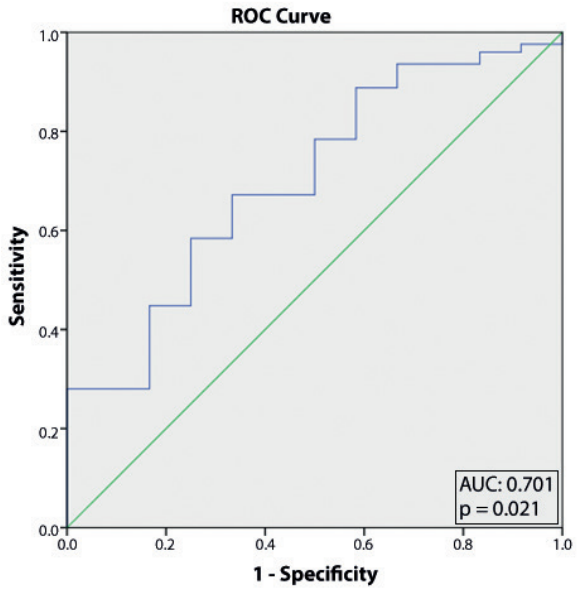

FIGURE 1. Receiver Operating Characteristic (ROC) analysis of hemoglobin-albumin-lymphocyte-platelet score in terms of mortality; Area Under the Curve (AUC): 0.701 ± 0.075 (95% CI: 0.553–0.849), (p= 0.021).

was fair with an area under the curve (AUC) of 0.701 ± 0.075 (95% CI: 0.553–0.849), (p= 0.021). According to the result of the ROC analysis, the optimum cut-off points of the HALP score were determined using Youden's index (Tab. 2). The cut-off point with the highest Youden's index was found to be 25.25. In this cut-off value, sensitivity was 67.2%, specificity 66.67%, positive predictive value (PPV) 95.45% and negative predictive value (NPV) 16.33%.

DISCUSSION

In this study, the relationship between HALP score and mortality in patients visited the emergency department and were diagnosed with acute ischemic stroke was investigated. It was concluded that the HALP score can be a good predictive tool for mortality estimation.

HALP score has been defined as a prognostic factor in patients with gastrointestinal, genitourinary, and various malignant cancer types [9, 10]. There are 4 parameters in the score: hemoglobin, albumin, lymphocyte, and thrombocyte. There are many studies examining the relationship between each of these parameters and acute ischemic stroke.

Besides being a risk factor for ischemic stroke, anemia is also associated with high mortality [11, 12]. There is a relationship between low hemoglobin levels and oxygen transport, inflammatory response, changes in blood viscosity, and impaired cerebral autoregulation [13, 14]. The prevalence of anemia in acute stroke patients ranges from 17% to 29% [15]. In a cohort where patients with acute stroke were followed for 1 year, anemia was found to be common in both men and women and was associated with poor prognosis, according to WHO anemia criteria. This relationship; did not differ between men and women or by type of ischemic stroke. The relationship between hemoglobin and mortality is not linear, and the risk of death was found to be high at low and high hemoglobin levels. In the study, approximately 20% of the patients had anemia and it was stated that it was valuable in the 1-year mortality estimation [16].

Albumin is a non-glycosylated plasma protein synthesized in the liver. It plays an important role in the transport of molecules in the blood and in the prevention of fluid leakage from the vascular tissue [17]. In studies on animal models, albumin exerts neuroprotective effects with antioxidants, thrombosis, and leukocyte adhesion antagonism. Serum albumin is a multifunctional protein that contains many physiological features that will have a positive effect on brain damage [18]. Hemodilution has been investigated over the years as a treatment modality in ischemic stroke. In a study conducted in experimental animals, it was shown that in transient cerebral ischemia caused by middle cerebral artery occlusion, a decrease in hematocrit, infarct volume, cerebral edema and brain damage was observed with albu-

Table 2. Optimum cut-off points* of hemoglobin-albumin-lymphocyte-platelet score in terms of mortality

Cut-off point	Sens [%]	Spec [%]	PPV [%]	NPV [%]	AUC	Youden's Index
25.25	67.2	66.67	95.45	16.33	0.701	0.339
29.44	58.4	75.00	96.05	14.75	0.701	0.334
25.56	66.4	66.67	95.40	16.00	0.701	0.331

HALP — hemoglobin-albumin-lymphocyte-platelet; Sens — sensitivity; Spec — specificity; PPV — positive predictive value; NPV — negative predictive value AUC — area under the curve; *Cut-off points with the three highest Youden's index value were shown

min therapy applied initially [19]. Protein malnutrition is a risk factor for poor prognosis after acute stroke. In the study of Davalos et al. [20], serum albumin levels in patients who died after stroke were found to be lower than those who survived.

Low lymphocyte count is associated with physiological stress [21]. Although the number of lymphocytes is low after an ischemic event in animal experiments, it has been found that the number of lymphocytes accumulates in the lesion within 7 to 15 days after the stroke and increases up to 30 days [22]. It was observed that the size of the lesion was larger in middle cerebral artery occlusion formed in mice with interleukin-10 deficiency, and stroke damage was reduced when IL-10 was administered to animals with deficiency [23].

Platelets play a role in cardiocerebrovascular diseases by being activated in some conditions such as atherosclerosis, inflammation, and hematological changes and participating in the formation of thrombus and embolism [24]. In a prospective study conducted with the participation of 16,823 patients with normal platelet counts among 21,592 stroke and transient ischemic attack patients in China, a J-shaped relationship was found between platelet count and stroke recurrence and all-cause mortality, and a U-shaped relationship between platelet count and poor functional outcomes [25].

There are few studies examining the relationship between HALP score and stroke. Tian et al. concluded that the HALP score was successful in estimating 90-day and 1-year mortality in 1337 stroke patients [8]. In our study, we found that the HALP score is a good predictor of in-hospital mortality. In light of this information, our study was found to be compatible with the studies in the literature.

There were some limitations to this study. First, this was a single-center retrospective study. In addition, in our study, only the values of hemoglobin, albumin, lymphocyte, and thrombocyte values, which are components of the HALP score, at the time of application to ED were used, and dynamic changes were not examined. Multicenter prospective studies are needed to adapt the results of our study to the general population.

CONCLUSIONS

Acute ischemic stroke is an important cause of mortality and morbidity worldwide. It is important to identify early patients who may have a poor outcome in these patients. In our study, we concluded that the HALP score can be a good predictor of mortality in stroke patients. We recommend the use of the score because it is cheap, practical, and useful.

Author contributions

Conceptualization, E.K. and S.Z.E.K.; Methodology, E.K.; Software, E.K.; Validation, E.K. and S.Z.E.K.; Formal Analysis, S.Z.E.K.; Investigation, E.K.; Resources, S.Z.E.K.; Data Curation, E.K.; Writing — Original Draft Preparation, E.K..; Writing — Review & Editing, E.K. and S.Z.E.K.; Visualization, S.Z.E.K.; Supervision, E.K.; Project Administration, E.K.; Funding Acquisition, S.Z.E.K.

Funding

This research received no specific grant from any funding agency in the public, commercial, or non-profit sectors.

Conflict of interest

The author(s) declare(s) that there is no conflict of interest.

Ethical approval

The study was approved by the ethical review board. (Istanbul Education and Research Hospital- non-interventional clinical trials ethics committee, number: 2011-KAEK-50-191 and date:17/06/2022)

Written or verbal informed consent was not obtained from the patients because it was a retrospective study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Availability of data and materials

The authors agree to the conditions of the publication including the availability of data and materials in our manuscript.

Human rights

The principles outlined in the Declaration of Helsinki have been followed.

Informed consent

Written informed consent was not necessary because no patient data has been included in the manuscript.

REFERENCES

1. The world health organization monica project (monitoring trends and determinants in cardiovascular disease): A major international collaboration. J Clin Epi 1988; 41(2): 105–114, doi: 10.1016/0895-4356(88)90084-4.
2. Weinberger J. Stroke. 2nd. ed. Handbooks in Health Care Co, Pennsylvania 2002: 1–80.
3. Ferris A, Robertson RM, Fabunmi R, et al. American Heart Association, American Stroke Association. American Heart Association and American Stroke Association national survey of stroke risk awareness among women. Circulation. 2005; 111(10): 1321–1326, doi: 10.1161/01.CIR.0000157745.46344.A1, indexed in Pubmed: 15769775.
4. Sakal C, Ak R, Taşçı A, et al. Admission blood lactate levels of patients diagnosed with cerebrovascular disease effects on short- and long-term mortality risk. Int J Clin Pract. 2021; 75(8): e14161, doi: 10.1111/ijcp.14161, indexed in Pubmed: 33759312.
5. Peng D, Zhang CJ, Tang Qi, et al. Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy. BMC Urol. 2018; 18(1): 20, doi: 10.1186/s12894-018-0333-8, indexed in Pubmed: 29544476.
6. Yang N, Han X, Yu J, et al. Hemoglobin, albumin, lymphocyte, and platelet score and neutrophil-to-lymphocyte ratio are novel significant prognostic factors for patients with small-cell lung cancer undergoing chemotherapy. J Cancer Res Ther. 2020; 16(5): 1134–1139, doi: 10.4103/jcrt.JCRT_1066_19, indexed in Pubmed: 33004760.
7. Shen XB, Zhang YX, Wang W, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score in Patients with Small Cell Lung Cancer Before First-Line Treatment with Etoposide and Progression-Free Survival. Med Sci Monit. 2019; 25: 5630–5639, doi: 10.12659/MSM.917968, indexed in Pubmed: 31356586.
8. Tian M, Li Y, Wang X, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score Is Associated With Poor Outcome of Acute Ischemic Stroke. Front Neurol. 2020; 11: 610318, doi: 10.3389/fneur.2020.610318, indexed in Pubmed: 33510706.
9. Jiang H, Li H, Li A, et al. Preoperative combined hemoglobin, albumin, lymphocyte and platelet levels predict survival in patients with locally advanced colorectal cancer. Oncotarget. 2016; 7(44): 72076–72083, doi: 10.18632/oncotarget.12271, indexed in Pubmed: 27765916.
10. Peng D, Zhang CJ, Gong YQ, et al. Prognostic significance of HALP (hemoglobin, albumin, lymphocyte and platelet) in patients with bladder cancer after radical cystectomy. Sci Rep. 2018; 8(1): 794, doi: 10.1038/s41598-018-19146-y, indexed in Pubmed: 29335609.
11. Seiffge DJ, Werring DJ, Paciaroni M, et al. Timing of anticoagulation after recent ischaemic stroke in patients with atrial fibrillation. Lancet Neurol. 2019; 18(1): 117–126, doi: 10.1016/S1474-4422(18)30356-9, indexed in Pubmed: 30415934.
12. Milionis H, Papavasileiou V, Eskandari A, et al. Anemia on admission predicts short- and long-term outcomes in patients with acute ischemic stroke. Int J Stroke. 2015; 10(2): 224–230, doi: 10.1111/ijs.12397, indexed in Pubmed: 25427291.
13. Cappellini MD, Motta I. Anemia in Clinical Practice-Definition and Classification: Does Hemoglobin Change With Aging? Semin Hematol. 2015; 52(4): 261–269, doi: 10.1053/j.seminhematol.2015.07.006, indexed in Pubmed: 26404438.
14. Ferrucci L, Guralnik JM, Woodman RC, et al. Proinflammatory state and circulating erythropoietin in persons with and without anemia. Am J Med. 2005; 118(11): 1288, doi: 10.1016/j.amjmed.2005.06.039, indexed in Pubmed: 16271918.
15. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in The Atherosclerosis Risk in Communities (ARIC) study. J Am Coll Cardiol. 2002; 40(1): 27–33, doi: 10.1016/s0735-1097(02)01938-1, indexed in Pubmed: 12103252.
16. Tanne D, Molshatzki N, Merzeliak O, et al. Anemia status, hemoglobin concentration and outcome after acute stroke: a cohort study. BMC Neurol. 2010; 10: 22, doi: 10.1186/1471-2377-10-22, indexed in Pubmed: 20380729.
17. He P, Curry FE. Albumin modulation of capillary permeability: role of endothelial cell [Ca2+]i. Am J Physiol. 1993; 265(1 Pt 2): H74–H82, doi: 10.1152/ajpheart.1993.265.1.H74, indexed in Pubmed: 8342667.
18. Babu MS, Kaul S, Dadheech S, et al. Serum albumin levels in ischemic stroke and its subtypes: correlation with clinical outcome. Nutrition. 2013; 29(6): 872–875, doi: 10.1016/j.nut.2012.12.015, indexed in Pubmed: 23422540.
19. Belayev L, Pinard E, Nallet H, et al. Albumin therapy of transient focal cerebral ischemia: in vivo analysis of dynamic microvascular responses. Stroke. 2002; 33(4): 1077–1084, doi: 10.1161/hs0402.105555, indexed in Pubmed: 11935064.
20. Dávalos A, Ricart W, Gonzalez-Huix F, et al. Effect of malnutrition after acute stroke on clinical outcome. Stroke. 1996; 27(6): 1028–1032, doi: 10.1161/01.str.27.6.1028, indexed in Pubmed: 8650709.
21. Usage of the Ranson criteria and neutrophil-lymphocyte ratio measured on presentation to the emergency department in the prediction of mortality in acute pancreatitis. Signa Vitae. 2022, doi: 10.22514/sv.2022.033.
22. Stubbe T, Ebner F, Richter D, et al. Regulatory T cells accumulate and proliferate in the ischemic hemisphere for up to 30 days after MCAO. J Cereb Blood Flow Metab. 2013; 33(1): 37–47, doi: 10.1038/jcbfm.2012.128, indexed in Pubmed: 22968321.
23. Ooboshi H, Ibayashi S, Shichita T, et al. Postischemic gene transfer of interleukin-10 protects against both focal and global brain ischemia. Circulation. 2005; 111(7): 913–919, doi: 10.1161/01.CIR.0000155622.68580.DC, indexed in Pubmed: 15710762.
24. Alexandru N, Andrei E, Dragan E, et al. Interaction of platelets with endothelial progenitor cells in the experimental atherosclerosis: Role of transplanted endothelial progenitor cells and platelet microparticles. Biol Cell. 2015; 107(6): 189–204, doi: 10.1111/boc.201400071, indexed in Pubmed: 25763472.
25. Yang M, Pan Y, Li Z, et al. Platelet Count Predicts Adverse Clinical Outcomes After Ischemic Stroke or TIA: Subgroup Analysis of CNSR II. Front Neurol. 2019; 10: 370, doi: 10.3389/fneur.2019.00370, indexed in Pubmed: 31031698.