PROCENA ISHODA AKUTNOG ISHEMIJSKOG MOŽDANOG UDARA U ZADNJEM SLIVU U ODNOSU NA RUTINSKE PARAMETRE KRVNE SLIKE – ODNOS NEUTROFILA I LIMFOCITA, TROMBOKRIT I SREDNJI VOLUMEN TROMBOCITA

ORIGINALNI RAD

ORIGINAL ARTICLE

THE OUTCOME EVALUATION OF AN ACUTE ISCHAEMIC STROKE IN THE POSTERIOR REGION IN RELATION TO ROUTINE BLOOD COUNT PARAMETERS – NEUTROPHIL /LYMPHOCYTE RATIO, PLATELETCRIT AND MEAN PLATELET VOLUME

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SAŽETAK

Uvod: Akutni moždani udar definiše se kao fokalni ili globalni poremećaj moždane funkcije koji naglo nastaje i predstavlja treći po redu uzrok smrti u svetu. U zavisnosti od mehanizma nastanka se može klasifikovati kao akutni ishemijski moždani udar i akutni hemoragijski moždani udar.

Cilj rada je ispitivanje hipoteze da su odnos neutrofila i limfocita (NLR), trombokrit (Pct) i srednji volumen trombocita (MVP) značajnije povišeni kod bolesnika sa lošijim ishodom moždanog udara u zadnjem slivu.

Materijal i metode: Osnov metodologije je analiza laboratorijskih podataka 205 bolesnika sa ishemijskim moždanim udarom zadnjeg sliva uz podatke o modifikovanom Rankin skoru na otpustu koji su prilagođeni u rangove na tri moguća ishoda lečenja: dobar, umereno loš i loš ishod bolesti.

Rezultati: Kao najsnažniji prediktor ishoda se pokazao porast odnosa broja neutrofila i limfocita (NLR) koji korelira sa lošim ishodom bolesti ($p < 0,001$). Trombokrit pokazuje umeren stepen povezanosti sa ishodom ishemijskog moždanog udara zadnjeg sliva stepenovanog rangovima modifikovanog Rankin skora ($p = 0,002$). Srednji volumen trombocita, kod ovog uzorka ispitanika, nije pokazao ni statističku značajnost razlike medju grupama bolesnika prema ishodu bolesti stepenovanog rangovima modifikovanog Rankin skora niti korelaciju sa ishodom bolesti prema istom kriterijumu.

Zaključak: Odnos neutrofila i limfocita (NLR), kao i trombokrit (Pct) su varijable, koje su na osnovu ovog ispitivanja, ali i rezultata iz dostupne literature, značajno češće povišene kod bolesnika sa lošijim ishodom moždanog udara u zadnjem slivu gde predstavljaju prediktor lošijeg ishoda bolesti.

Ključne reči: moždani udar, akutni, trombociti, neutrofili, limfociti, odnos

ABSTRACT

Introduction: Acute stroke is defined as a focal or global disorder of brain function that occurs suddenly and is the third leading cause of death in the world. Depending on the mechanism of occurrence, it can be classified as acute ischemic stroke and acute hemorrhagic stroke.

The work aims to examine the hypothesis that the ratio of neurtophils to lymphocytes (NLR), thrombocrit (Pct) and mean platelet volume (MVP) are significantly increased in patients with a worse outcome of a stroke in the posterior basin.

Material and methods: The basis of the methodology is the analysis of laboratory data of 205 patients with ischemic stroke of the posterior basin with data on the modified Rankin score at discharge, which were adjusted into ranks for three possible treatment outcomes: good, moderately bad, and bad disease outcomes.

Results: The strongest predictor of the outcome was the increase in the ratio of neutrophils and lymphocytes (NLR), which correlates with a poor outcome of the disease ($p < 0,001$). Thrombocrit also shows a moderate degree of association with the outcome of posterior basin ischemic stroke graded by ranks of the modified Rankin score ($p = 0,002$). The mean volume of platelets, in this sample of subjects, did not show either a statistical significance of the difference between the groups of patients according to the outcome of the disease graded by the ranks of the modified Rankin score, or a correlation with the outcome of the disease according to the same criterion.

Conclusion: Neutrophil to lymphocyte ratio (NLR), as well as thrombocrit (Pct), are variables that, based on this study and the results from the available literature, are significantly more often elevated in patients with a worse outcome of a stroke in the posterior basin where they represent a predictor of a worse outcome of the disease.

Keywords: stroke, acute, platelet, neutrophils, lymphocytes, ratio

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UVOD

Akutni moždani udar (AMU) definiše se kao fokalni ili globalni poremećaj moždane funkcije koji naglo nastaje, a posledica je poremećaja moždane cirkulacije ili stanja u kome protok krvi nije dovoljan da zadovolji metaboličke potrebe neurona za kiseonikom i glukozom [1,2]. AMU je bolest koja predstavlja treći po redu uzrok smrti u svetu, odmah iza kardiovaskularnih i malignih oboljenja [1]. U zavisnosti od mehanizma nastanka AMU se može klasifikovati kao: akutni ishemijski moždani udar (AIMU), koji je posledica okluzije krvnog suda i koji je značajno češći sa oko 75–80% obolelih ili kao akutni hemoragijski moždani udar (AHMU) tj. intracerebralna (ICH) ili subarahnoidalna hemoragija (SAH), a koji se javlja u preostalih 20–25% bolesnika [1,2].

U novije vreme se pojavljuju, kao prediktori lošijeg ishoda ishemijskog moždanog udara, rutinski laboratorijski parametri, koji se lako određuju iz rutinske krvne slike [3]. To su odnos neutrofila i limfocita (NLR), trombokrit (Pct) i srednji volumen trombocita (MVP).

Cilj rada je ispitivanje hipoteze da su odnos neutrofila i limfocita (NLR), trombokrit (Pct) i srednji volumen trombocita (MVP) značajnije povišeni kod bolesnika sa lošijim ishodom moždanog udara u zadnjem slivu. Analiziranje laboratorijskih parametara je vršeno na bolesnicima sa ishemijskim lezijama u zadnjem slivu, s obzirom da oni zbog lokacije generalno imaju lošiji ishod u odnosu na lezije prednjeg sliva, a kako bi se utvrdila značajnost ovih parametara i u ovoj subpopulaciji bolesnika.

METODE RADA

Osnov metodologije je analiza laboratorijskih podataka dobijenih retrospektivnom studijom relevantnih podataka istorija bolesti bolesnika sa ishemijskim moždanim udarom zadnjeg sliva. Obrada podrazumeva podatke 205 bolesnika sa ishemijskim moždanim udarom zadnjeg sliva lečenih u periodu od 01. februara 2023. godine do 01. avgusta 2023. godine u Specijalnoj bolnici "Sveti Sava". Prikupljaju se podaci o modifikovanom Rankin skoru na otpustu (mRS) kao varijabli ishoda bolesti (Tabela 1) i vrednosti odnosa broja neutrofila i limfocita (NLR), srednjeg volumena trombocita (MPV) i trombokrita (Pct). Podaci modifikovanog Rankin skora su prilagođeni analizi u rangove na tri moguća ishoda lečenja: dobar, umereno loš i loš ishod bolesti (Tabela 2). Prikupljeni su i demografski podaci o ispitanicima. Za statističku analizu su korišćeni softverski paketi IBM SPSS i Microsoft Excell, a pored metoda deskriptivne statistike je korišćen Spirmanov koeficijent korelacije, sa statističkim nivoom značajnosti manjim od 0,05.

INTRODUCTION

Acute stroke (AS) is defined as a focal or global disturbance of brain function that abruptly arises due to disruptions in the cerebral circulation, leading to insufficient blood flow to meet neuronal metabolic demands for oxygen and glucose [1,2]. AS ranks as the third leading cause of death worldwide, following cardiovascular and malignant diseases [1]. Depending on the underlying mechanism, AS can be classified as acute ischemic stroke (AIS), resulting from vascular occlusion and accounting for approximately 75–80% of cases, or as acute hemorrhagic stroke (AHS), encompassing intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH), which occurs in the remaining 20–25% of patients [1,2].

In recent times, routine laboratory parameters easily obtainable from complete blood count have emerged as predictors of worse outcomes in ischemic stroke [3]. These parameters include the neutrophil-to-lymphocyte ratio (NLR), plateletcrit (Pct), and mean platelet volume (MPV).

This study aims to investigate the hypothesis that the neutrophil-to-lymphocyte ratio (NLR), plateletcrit (Pct), and mean platelet volume (MPV) are significantly elevated in patients with poorer outcomes of posterior circulation stroke. Laboratory parameter analysis was performed on patients with ischemic lesions in the posterior circulation, considering that these patients generally exhibit worse outcomes due to lesion location compared to anterior circulation lesions, aiming to establish the significance of these parameters within this specific patient subgroup.

MATERIALS AND METHODS

The primary methodology involved analyzing laboratory data obtained from a retrospective study of relevant medical records of patients with posterior circulation ischemic stroke. The dataset comprised information from 205 patients with posterior circulation ischemic stroke treated at the Special Hospital "Sveti Sava" from February 1, 2023, to August 1, 2023. Data included the modified Rankin Scale (mRS) score at discharge as an outcome variable (Table 1), and values of the neutrophil-to-lymphocyte ratio (NLR), mean platelet volume (MPV), and plateletcrit (Pct). The mRS scores were categorized into ranks representing three possible treatment outcomes: good, moderately poor, and poor disease outcomes (Table 2). Demographic data of the participants were also collected.

Statistical analysis was performed using IBM SPSS and Microsoft Excel software. Descriptive statistics methods were applied, and Spearman's correlation coefficient was used with a statistical significance level set at less than 0.05.

Tabela 1. Modifikovan Rankin skor

Table 1. Modified Rankin Scale

mRS	Opis / *Description*
0	Bez simptoma / *No symptoms*
1	Bez značajne onesposobljenosti – sposoban za obavljanje svih aktivnosti / *No significant disability - able to carry out all usual activities*
2	Laka onesposobljenost – sposoban za samozbrinjavanje ali ne i za sve premorbidne aktivnosti / *Slight disability - able to look after own affairs but unable to carry out all pre-morbid activities*
3	Umerena onesposobljenost – zahteva pomoć ali sposoban za samostalni hod / *Moderate disability - requires some help but able to walk unassisted*
4	Umereno teška onesposobljenost – nije sposoban za samostalni hod / *Moderately severe disability - unable to walk unassisted*
5	Teška onesposobljenost – nepokretan i kompletno zavistan od tuđe nege i pomoći / *Severe disability - bedridden, incontinent, and requiring constant nursing care and attention*
6	Smrt / *Death*

Tabela 2. Modifikovan Rankin skor iskazan po rangovima ishoda bolesti.

Table 2. Modified Rankin Scale expressed by outcome ranges

Dobar ishod bolesti / *Good Disease Outcome*	0 – 2
Umereno loš ishod bolesti / *Moderately Poor Disease Outcome*	3 – 5
Loš ishod bolesti / *Poor Disease Outcome*	6

Tabela 3. Raspodela bolesnika prema vrednostima modifikovanog Rankin skora

Table 3. Distribution of patients according to modified Rankin Scale values

Skor / *Score*	Učestalost / *Frequency*	Procenat / *Percentage*
0	12	5.9
1	43	21
2	28	13.7
3	32	15.6
4	32	15.6
5	23	11.2
6	35	17.1
Ukupno / *Total*	205	100

REZULTATI

Od 205 bolesnika čiji su rezultati analizirani njih 35 je imalo smrtni, odnosno loš ishod bolesti što čini 17,1 % ispitanika. Dobar i umereno loš ishod bolesti je imalo otprilike podjednako bolesnika (Tabela 3 i 4). 57,6% uzorka, odnosno 118 ispitanika je bilo muškog pola a prosečna starost uzorka je bila 71,7 godina sa standardnom devijacijom od 10,1 godinu (Tabela 5 i 6).

Među praćenim parametrima, u ovoj analizi, kao najsnažniji prediktor ishoda se pokazao odnos broja neutrofila i limfocita (NLR). Porast odnosa broja neutrofila i limfocita korelira sa lošim ishodom bolesti ($p < 0,001$) i ukazuje na umereno jaku povezanost događaja, tj. odnosa ćelija i ishoda ishemijskog moždanog udara u zadnjem slivu (Tabela 7).

Trombokrit, takođe, pokazuje umeren stepen povezanosti sa ishodom ishemijskog moždanog udara zadnjeg sliva stepenovanog rangovima modifikovanog

RESULTS

Out of 205 patients whose results were analyzed, 35 had a fatal or poor disease outcome, representing 17.1% of the study participants. Approximately an equal number of patients had good and moderately poor disease outcomes (Tables 3 and 4). Within the sample, 57.6%, or 118 participants, were male, with a mean age of 71.7 years and a standard deviation of 10.1 years (Tables 5 and 6).

Among the monitored parameters, the neutrophil-to-lymphocyte ratio (NLR) emerged as the strongest predictor of outcome in this analysis. An increase in the neutrophil-to-lymphocyte ratio correlated with a poor disease outcome ($p < 0.001$) and indicated a moderately strong association between cell ratios and the outcome of posterior circulation ischemic stroke (Table 7).

Tabela 4. Distribucija ispitanika prema rangovno modifikovanom Rankin skoru

Table 4. Distribution of participants according to modified Rankin Scale ranking

Dobar ishod bolesti / *Good Disease Outcome*	83
Umereno loš ishod bolesti / *Moderately Poor Disease Outcome*	87
Loš ishod bolesti / *Poor Disease Outcome*	35
Ukupno / *Total*	205

Tabela 5. Distribution of participants by gender

Table 5. Distribucija ispitanika po polu

	Broj / *Number*	Procenat / *Percentage*
Muški pol / *Male gender*	118	57,6
Ženski pol / *Female gender*	87	42,4
Ukupno / *Total*	205	100,0

Tabela 6. Distribucija ispitanika po godinama starosti

Table 6. Distribution of participants by age

Srednja vrednost / *Mean*	71.72
Standardna devijacija / *Standard Deviation*	10.149
Minimum / *Minimum*	35
Maksimum / *Maximum*	96

Rankin skora ($p = 0,002$), ali nižeg stepena povezanosti sa ishodom bolesti u poređenju sa odnosom apsolutnog broja neutrofila i limfocita (Tabela 7).

Srednji volumen trombocita, kod ovog uzorka ispitanika, nije pokazao korelaciju sa ishodom bolesti prema ishodu bolesti stepenovanog rangovima modifikovanog Rankin skora ($p = 0,427$) (Tabela 7).

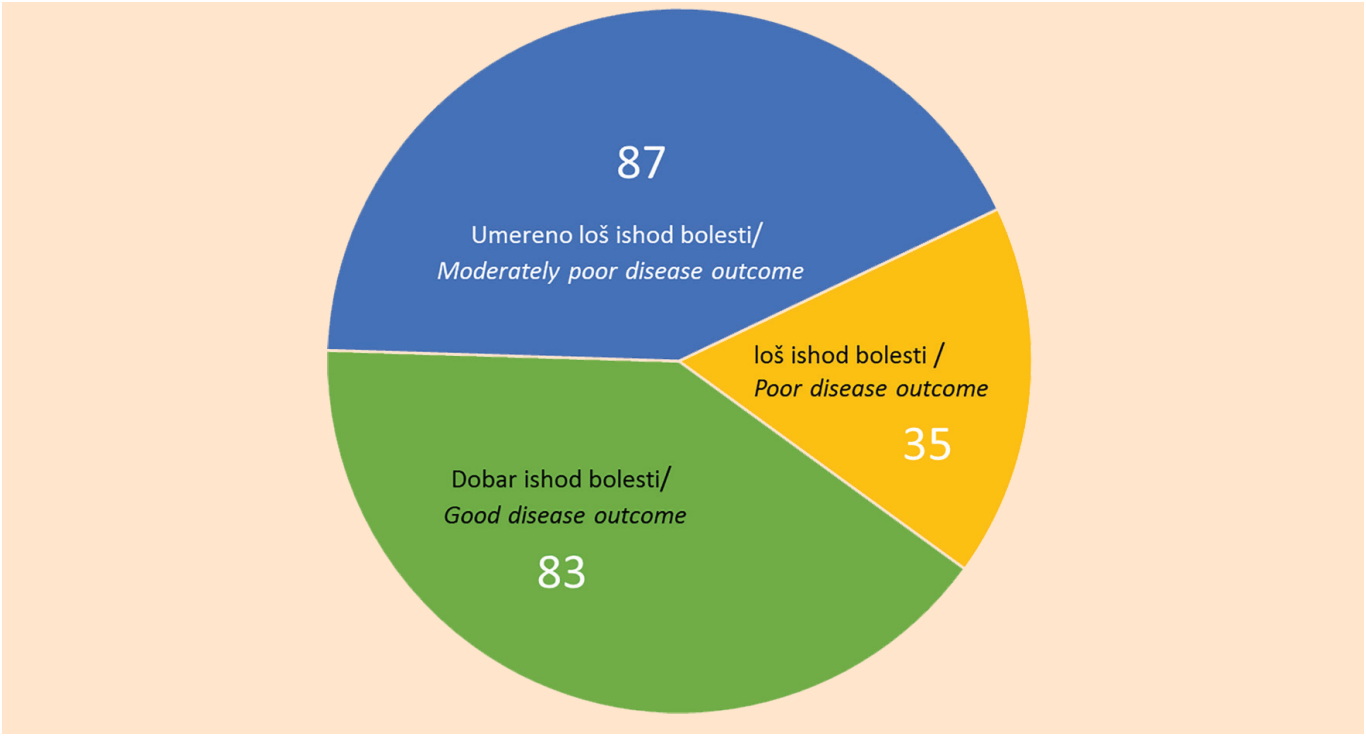
Tabela 7. Spirmanova korelacija NLR, Pct i MPV i ishoda bolesti po rangovima mRS

Table 7. Spearman Correlation of NLR, Pct, and MPV with disease outcome by mRS rankings

Spirmanova korelacija / Spearman Correlation		NLR	Pct	MPV
mRS	Koeficijent korelacije / *Correlation Coefficient*	0.420	0.211	0.056
	Značajnost razlike / *Significance Level*	<0.001	0.002	0.427
	Broj ispitanika / *Number of Participants*	205	205	205

NLR – Odnos broja neutrofila i limfocita; Pct – trombokrit; MPV – srednji volumen trombocita; mRS – modifikovani Rankin skor.

NLR – Neutrophil-to-Lymphocyte Ratio; Pct – Plateletcrit; MPV – Mean Platelet Volume; mRS – Modified Rankin Scale.



Grafikon 1. Raspodela ispitanika po rangiranom modifikovanom Rankin skoru ishoda bolesti

Figure 1. Distribution of participants according to ranked Modified Rankin Scale disease outcomes

DISKUSIJA

U studiju je uključeno 205 ispitanika oba pola prosečne strarosti oko 71 godinu, a koji su bolovali od akutnog ishemijskog moždanog udara u zadnjem slivu, uz laku dominaciju muškog pola koji čini nešto preko polovine uzorka (57,6%). Manje od petine uzorka je imalo loš ishod bolesti po modifikovanom Rankinom skoru (6 bodova), odnosno smrtni ishod (17,1%). Dve petine lečenih, odnosno 40,4% uzorka, je imalo dobar ishod

Plateletcrit also showed a moderate degree of association with the outcome of posterior circulation ischemic stroke as measured by ranks of the modified Rankin Scale ($p = 0.002$), albeit with a lower degree of association compared to the neutrophil-to-lymphocyte ratio (Table 7).

The mean platelet volume did not correlate with disease outcome as measured by ranks of the modified Rankin Scale within this sample of participants ($p = 0.427$) (Table 7).

bolesti po rangiranom modifikovanom Rankin skoru (0, 1 ili 2 boda) i približno isto toliko (42,5%) umereno loš ishod bolesti po rangiranom modifikovanom Rankin skoru (3, 4 ili 5 bodova).

Što se tiče, analiziranih laboratorijskih parametara, kao prediktora ishoda kod bolesnika sa ishemijskim moždanim udarom zadnjeg sliva, kao najkorelabilniji se pokazao odnos broja neutrofila i limfocita. Bolesnici sa povećanim odnosom, u ovoj kohorti, imaju upadljivo lošiji ishod. Ovo je skladno podacima iz dostupne literature koja se bavi ovom vrstom problematike [4-7]. Moguće objašnjenje za ovaj fenomen je da favorizovanje neutrofilije bude objašnjeno većim stepenom nekroze tkiva kod većeg odnosno opsežnijeg moždanog udara i potrebom za borbu organizma sa debrisom. Takođe bolesnici sa lošijim ishodom bolesti, često imaju i komorbiditetne bakterijske infekcije praćene neutrofilijom, a sam tok infekcije je takođe skopčan sa nepovoljnijim tokom i ishodnom osnovne bolesti. Nažalost, infekcije kao varijable ishoda nisu uzete u obzir pri dizajnu ovog istraživanja te to ostaje kao budući zadatak. Ovakav odnos subtipova belih krvnih zrnaca važi i kod primene savremene reperfuzione terapije, hemijske ili mehaničke [8,9].

Nadalje, trombokrit je pokazao umerenu povezanost sa ishodom oboljenja u smislu lošijeg ishoda bolesti kod većeg trombokrita, ali nižeg stepena u komparaciji sa odnosom neutrofila i limfocita što je delimično u saglasnosti sa literaturom gde se opisuje snažna veza [10-12], dok srednji volumen trombocita nije pokazao sposobnost predikcije ishoda, što je u suprotnosti sa dostupnim podacima iz literature [13-16]. Ovo se može objasniti malom veličinom uzorka kao i činjenicom da Bolnica poseduje više hematoloških analizatora koji imaju različite tehnike odredjivanja parametra te je i ovde potrebna provera promenom dizajna istraživanja za ovu varijablu.

ZAKLJUČAK

Odnos neutrofila i limfocita (NLR) kao i trombokrit (Pct) su varijable, koje su na osnovu ovog ispitivanja ali i rezultata iz dostupne literature, značajno češće povišene kod bolesnika sa lošijim ishodom moždanog udara u zadnjem slivu gde i predstavljaju prediktor lošijeg ishoda bolesti. Srednji volumen trombocita (MVP) ne pokazuje statističku značajanost u razlici distribucije među podgrupama bolesnika po ishodu u okviru ishemijske lezije moždanog parenhima u teritoriji zadnjeg sliva, niti korelaciju sa ishodom oboljenja.

Multimorbidna stanja mogu uticati na vrstu lečenja neophodnog za bolesnika koji je preživeo moždani udar, stoga je imperativ razumeti kako svi ovi uslovi utiču na buduću terapiju pacijenata sa moždanim udarom,

DISCUSSION

The study included 205 participants of both sexes with an average age of around 71 years, who suffered from acute ischemic stroke in the posterior circulation, with a slight male predominance accounting for just over half of the sample (57.6%). Less than one-fifth of the sample had a poor disease outcome according to the modified Rankin Scale (6 points), representing a fatal outcome (17.1%). Two-fifths of the treated sample, or 40.4%, had a good disease outcome based on the ranked modified Rankin Scale (0, 1, or 2 points), and a similar proportion (42.5%) had a moderately poor disease outcome based on the ranked modified Rankin Scale (3, 4, or 5 points).

Regarding the analyzed laboratory parameters as predictors of outcome in patients with posterior circulation ischemic stroke, the neutrophil-to-lymphocyte ratio (NLR) emerged as the most correlated. Patients with an increased ratio in this cohort had notably worse outcomes. This is consistent with data from available literature on this issue [4-7]. One possible explanation for this phenomenon is that the favoring of neutrophilia may be explained by greater tissue necrosis in larger or more extensive strokes, necessitating the body's response to debris. Additionally, patients with poorer disease outcomes often have comorbid bacterial infections accompanied by neutrophilia, and the course of infection is also associated with a more unfavorable outcome of the underlying disease. Unfortunately, infections as outcome variables were not considered in the design of this study and remain a future task. This relationship between subtypes of white blood cells holds true even with the application of modern reperfusion therapies, whether chemical or mechanical [8,9].

Furthermore, plateletcrit showed a moderate association with disease outcome in terms of poorer disease outcomes with higher plateletcrit, but to a lesser degree compared to the neutrophil-to-lymphocyte ratio, which is partially consistent with literature describing a strong association [10-12]. However, mean platelet volume did not demonstrate predictive ability for outcomes, contrary to available literature [13-16]. This could be explained by the small sample size and the fact that the hospital has multiple hematology analyzers with different techniques for parameter determination, necessitating further investigation and potentially a change in study design for this variable.

CONCLUSION

The neutrophil-to-lymphocyte ratio (NLR) and plateletcrit (Pct) are variables that, based on this study and results from available literature, are significantly more frequently elevated in patients with poorer outcomes

koja zahteva individualizovani pristup ali uz poštovanje principa dobre kliničke prakse lečenja kako moždanog udara tako i svih pratećih komorbiditeta paralelno.

SPISAK SKRAĆENICA

AMU – Akutni moždani udar
AIMU – Akutni ishemijski moždani udar
AHMU – Akutni hemoragijski moždani udar
ICH – Intracerebralna hemoragija
SAH – Subarahnoidalna hemoragija
NLR – Odnos neutrofila i limfocita
PCT – Trombokrit
MVP – Srednji volumen trombocita
mRS – Modifikovan Rankin skor na otpustu

Sukob interesa: Nije prijavljen.

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of posterior circulation stroke, where they serve as predictors of worse disease outcomes. Mean platelet volume (MPV) does not demonstrate statistical significance in distribution differences among patient subgroups based on outcome within the ischemic lesion of the posterior cerebral parenchyma territory, nor does it correlate with disease outcome.

Multimorbid conditions can influence the type of treatment necessary for a patient surviving a stroke; therefore, it is imperative to understand how all these conditions impact the future therapy of stroke patients, requiring an individualized approach while respecting the principles of good clinical practice in treating both stroke and all accompanying comorbidities simultaneously.

LIST OF ABBREVIATIONS

AS – Acute stroke
AIS – Acute ischemic stroke
AHS – Acute hemorrhagic stroke
ICH – Intracerebral hemorrhage
SAH – Subarachnoid hemorrhage
NLR – Neutrophil-to-lymphocyte ratio
PCT – Plateletcrit
MPV – Mean platelet volume
mRS – Modified Rankin Scale at discharge

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