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Evaluation of the MAPH Score in Predicting Acute Ischemic Stroke Severity and Major Vessel Occlusion in the Emergency Department

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Abstract

Objective: This study aimed to evaluate the utility of the MAPH score, a biomarker combining blood viscosity indicators such as mean platelet volume (MPV), total protein (TP), and hematocrit (Hct), in differentiating acute ischemic stroke (AIS) from transient ischemic attack (TIA) and predicting major vessel occlusion in patients presenting to the emergency department with suspected stroke.

Materials and Methods: A retrospective analysis was conducted on 226 patients presenting to the emergency department with focal neurological symptoms. Patients were categorized into AIS and TIA groups based on diffusion-weighted magnetic resonance imaging findings. Data collected included demographic characteristics, vital signs, laboratory parameters, and imaging results. MPV, age, Hct, and TP levels were recorded. High-shear rate and low-shear rate were calculated from total TP and Hct values. Receiver operating characteristic (ROC) curve analysis was performed to evaluate diagnostic performance.

Results: The ROC analysis demonstrated the diagnostic accuracy of the MAPH score in differentiating AIS from TIA and predicting major vessel occlusion. Additionally, the score showed a significant correlation with National Institutes of Health Stroke Scale ≥20, indicating its association with stroke severity.

Conclusion: The MAPH score is a simple and practical tool that aids in distinguishing AIS from TIA and predicting major vessel occlusion, thus improving stroke management in emergency settings.

Keywords: MAPH score, acute ischemic stroke, transient ischemic attack, major vessel occlusion, emergency medicine

Introduction

Cerebrovascular diseases continue to be a significant cause of mortality and disability in public health. Acute stroke occurs as a result of neuronal damage caused by reduced blood flow to the brain and is a common medical emergency encountered in emergency departments [1]. Globally, approximately 80% of strokes are ischemic, while 20% are hemorrhagic [2]. Following cardiovascular diseases and cancer, stroke ranks as the third leading cause of death worldwide and is the most prevalent cause of disability [3].

Acute ischemic stroke (AIS) occurs due to causes such as thrombosis, embolization, and lacunar infarction, resulting from small vessel disease. Increased whole blood viscosity (WBV) and the subsequent formation of thrombus are among the primary risk factors for ischemia [4]. The severity of ischemia may vary depending on the persistence and size of the thrombus, as well as underlying risk factors such as the patient's gender, age,

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and smoking habits. In some cases, the patient's symptoms may be transient. When symptoms resolve within 24 hours without evidence of tissue infarction on diffusion-weighted magnetic resonance imaging (MRI), the condition is referred to as a transient ischemic attack [5]. Factors such as the patient's clinical condition, the size of the ischemic area, and eligibility for reperfusion strategies necessitate treatment decisions to be made in the emergency department as quickly as possible. The first hours in AIS are critical for preserving brain tissue. While thrombolytic therapies can be administered to eligible patients within the first 4-5 hours of symptom onset, endovascular thrombectomy may be considered in selected patients during extended time windows of up to 24 hours. Clinical criteria are required to grade the severity of ischemic stroke, assess changes during the follow-up process, ensure uniform communication among healthcare professionals, and predict prognosis. One of the most commonly used scales, the National Institutes of Health Stroke Scale (NIHSS), evaluates neurological findings by assigning scores and provides valuable information about long-term prognosis. The MAPH score, defined by Abacioglu et al. [6] incorporates blood viscosity biomarkers such as mean platelet volume (MPV), total protein (TP), hematocrit (Hct), and age, and has been used to assess thrombus burden in myocardial infarction (MI) patients. This score was later investigated in the context of thrombus risk in pulmonary thromboembolism (PTE) [7]. Similarly, increased plasma viscosity and alterations in blood rheology can be associated with thrombus formation in ischemic strokes.

The aim of this study is to evaluate the relationship between major vessel occlusion, AIS, less critical TIA in patients presenting to the emergency department with suspected ischemic stroke. Furthermore, this practical score is aimed to contribute to the management protocols for AIS in the emergency department.

Materials and Methods

Study Design and Setting

This retrospective study was conducted at the Emergency Medicine Clinic of University of Health Sciences Türkiye, Ankara Etlik City Hospital between December 1, 2023, and May 1, 2024. Inclusion criteria were as follows: Focal neurological symptoms that started within the last 24 hours (such as asymmetric weakness, sensory changes, speech impairment, facial asymmetry, altered mental status, dizziness, and visual disturbances with sudden onset) or all male and female patients aged 18 years and older.

Exclusion criteria were as follows: Individuals under 18 years of age, pregnant patients, those diagnosed with cerebrovascular disease, PTE, or acute coronary syndrome within the past month, patients using anticoagulants, and those with incomplete laboratory results. During triage, a critical pathway was activated to ensure rapid communication with the neurology team for patients suspected of having a stroke. A total of 412 patients presenting with suspected acute stroke were evaluated during the specified dates. Stroke was ruled out in 101 of these patients. Additionally, 45 patients who did not meet the inclusion criteria and 40 patients diagnosed with hemorrhagic stroke were excluded from the study. Consequently, a total of 226 patients were included in the study. The study was conducted with approval from the Ethics Committee of University of Health Sciences Türkiye, Ankara Etlik City Hospital (approval number: AEŞH-BADEK-2024-891, date: 25.09.2024). As this was a retrospective file review and did not involve patient identification, informed consent was not required. The study was conducted in accordance with the Declaration of Helsinki.

Data Collection and Research Protocol

All patient data were obtained from the hospital database and patient records. Sociodemographic characteristics (age, gender, comorbidities), vital parameters [systolic and diastolic blood pressure, body temperature, heart rate, respiratory rate, peripheral oxygen saturation (SpO_2)], Glasgow Coma Scale (GCS), complete blood count parameters [leukocyte, hemoglobin, Hct, platelet, MPV], glucose, blood urea nitrogen, creatinine, TP, albumin, aspartate aminotransferase, alanine aminotransferase, sodium, cholesterol, triglycerides, NIHSS, MAPH score, low-shear rate (LSR), high-shear rate (HSR), brain computed tomography (CT), brain computed tomography angiography (CTA), diffusion MRI findings, admission status, and 30-day mortality data were recorded. All data were reviewed and verified by two emergency medicine specialists. Patients were initially divided into two groups based on diffusion MRI findings: those with pathological findings were classified as the AIS group, while those without pathological findings were classified as the TIA group. The MAPH score, LSR, and HSR values were compared between these two groups. Additionally, in the AIS group, subgroups were formed based on brain CTA findings into patients with and without major vessel occlusion, and the MAPH scores of these subgroups were compared.

Definition

The diagnosis of AIS is supported by radiological imaging and confirmed by the presence of vascular occlusion or detection of diffusion restriction. On the other hand, TIA is defined as a transient episode of neurological dysfunction, caused by focal ischemia of the brain, spinal cord, or retina, which resolves rapidly within 24 hours and shows no evidence of tissue infarction on diffusion-weighted MRI [5].

In AIS, major vessel occlusion includes the middle cerebral artery (M1, M2), posterior cerebral artery (P1, P2), anterior cerebral artery (A1, A2), internal cerebral artery, basilar artery, and vertebral arteries, as identified on brain CTA.

The MAPH score consists of four parameters: MPV, Age (A), TP, and Hct [6]. Cut-off values for each parameter of the score were determined using receiver operating characteristic (ROC) curve analysis and the Youden Index. A score of 1 was assigned for values equal to or above the cut-off, and a score of 0 was assigned for values below the cut-off. The total MAPH score was calculated by summing the scores of each parameter.

The NIHSS is a scale used to assess neurological status and determine stroke severity [8]. It consists of an 11-step evaluation system, including parameters such as level of consciousness, eye movements, visual fields, facial paralysis, motor strength (upper and lower extremities), ataxia, sensation, speech, dysarthria, and neglect.

The calculation of WBV was performed using LSR and HSR values. These were determined based on Hct and TP using previously validated formulations by de Simone et al. [9].

$$HSR = (0.12 \times Hct) + 0.17 \times (TP-2.07)$$

$$LSR = (1.89 \times Hct) + 3.76 \times (TP-78.42)$$

Statistical Analysis

Descriptive statistics were presented as frequencies (percentages) for categorical variables and as means with standard deviations for numerical variables. The normality assumption for numerical variables was evaluated both analytically and graphically. Comparisons of patient characteristics were performed using the chi-square test for categorical variables and either the Independent Samples t-test or the Mann-Whitney U test for numerical variables. The diagnostic ability of laboratory parameters with statistically significant p-values from group comparison tests was assessed using the area under the ROC curve. Cut-off values for potential biomarkers were determined using the Youden Index and diagnostic performance metrics. Sensitivity, specificity, and corresponding 95% confidence intervals calculated. Pairwise comparison of ROS properties of scoring systems was performed using paired-sample area difference under the ROC curves. Statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS, Version 23, Inc., Chicago, IL), and a $p<0.05$ was considered statistically significant.

Results

A total of 226 patients were included in the study. Based on clinical findings and diffusion MRI results, 154 patients with acute diffusion restriction were classified as the AIS group, while 72 patients were classified as the TIA group. Sociodemographic data, symptom and examination findings, scores such as NIHSS and GCS, and other findings related to the patients are presented in detail in Table 1. In the AIS group, Hct and MPV values were found to be higher, and this difference was statistically significant (Table 1).

Based on brain CTA findings, major vessel occlusion was detected in 61 patients (39.6%) in the AIS group. Intravenous thrombolytic therapy with recombinant tissue plasminogen activator was administered to 12 patients (5.3%), and mechanical thrombectomy was performed on 31 patients (13.7%). Among all patients, 44 (19.5%) were discharged from the emergency department, 106 (46.9%) were admitted to the ward, and 76 (33.6%) were transferred to the intensive care unit. In-hospital mortality occurred in 34 patients (19.9%).

In the ROC analysis performed for the MAPH score, the cut-off values were determined according to the Youden index as follows: 11 for MPV, 60 for age, 6.49 for total plasma protein, and 43.1 for Hct. The cut-off value for the MAPH score was found to be 3. Comparisons of MAPH, LSR, and HSR values between AIS and TIA patients based on these cut-off values are presented in Table 2.

The ROC analysis demonstrated that the MAPH score, LSR, and HSR could predict the diagnosis of AIS. Table 3 presents all potential cut-off points for the continuous variables (MAPH, LSR, and HSR) that could be used for AIS diagnosis, along with their predictive performance metrics. A comparison of the ROC curves for the continuous variables revealed that the MAPH score was significantly superior to the others in predicting AIS based on the dataset, followed by LSR and HSR (Figure 1).

Comparisons of MAPH, LSR, and HSR values with the presence of major vessel occlusion in the AIS group are presented in Table 4. ROC analysis demonstrated that the MAPH score, LSR, and HSR could predict the presence of major vessel occlusion in AIS patients. Table 5 details all potential cut-off points for the continuous variables (MAPH, LSR, and HSR) used to determine the presence of major vessel occlusion, and the accuracy of these variables in prediction. A comparison of the ROC curves for the continuous variables revealed that MAPH, LSR, and HSR were statistically significant in predicting the presence of major vessel occlusion based on the dataset (Figure 2).

In the ROC analysis, the MAPH score was compared with NIHSS and showed a significant correlation in patients with NIHSS ≥20 ($p=0.018$). A comparison of the ROC curves for the continuous variables demonstrated that the MAPH score was statistically significant in predicting NIHSS ≥20 based on the dataset (Figure 3).

Table 1. Sociodemographic data and laboratory values

Total (n=226)		Acute ischemic stroke (n=154)	Transient ischemic attack (n=72)	p
Age-mean (±SD)		73±11	72±12	0.751
Gender (n,%)	Female	84 (54%)	39 (54%)	0.958
	Male	70 (46%)	33 (46%)	
Vital signs (median ± SD)				
Systolic blood pressure (mmHg)		169±26	153±27	<0.001*
Diastolic blood pressure (mmHg)		95±14	88±15	0.002*
Heart rate (beats/min)		84±48	80±13	0.955
Oxygen saturation (SpO_2, %)		93±3	94±3	0.026*
Body temperature (°C)		36.7±0.4	36.7±0.4	0.618
Respiratory rate (breaths/min)		17±4	16±3	0.096
NIHSS-median (IQR)		6 (3-12)	2 (1-4)	<0.001*
GCS scores (median, IQR)				
Eye response		4 (4-4)	4 (4-4)	0.039*
Verbal response		5 (4-5)	5 (5-5)	0.013*
Motor response		6 (5-6)	6 (6-6)	<0.001*
Comorbidities (n, %)				
Hypertension		140 (90.3%)	60 (84.5%)	0.203
Diabetes mellitus		58 (37.4%)	30 (42.3%)	0.489
Atrial fibrillation		73 (47.4%)	23 (31.9%)	0.028*
Smoking habit		49 (31.6%)	12 (16.9%)	0.021*
Laboratory findings				
White blood cell count (10^3/µL)		9.7±3.7	8.6±2.9	0.054
Hemoglobin (g/dL)		13±2.3	12.8±1.7	0.602
Hematocrit (%)		41±6	39±4	0.001*
Platelet fount (10^3/µL)		240±79	265±156	0.254
Mean platelet volume (fL)		11±0.8	10.4±0.7	<0.001*
Glucose (mg/dL)		150±56	136±47	0.101
Total protein (g/dL)		6.5±0.6	6.5±0.4	0.580
Albumin (g/dL)		4.1±3	3.8±0.4	0.816
Blood urea nitrogen (mg/dL)		46±30	40±16	0.437
Creatinine (mg/dL)		1.1±0.9	0.9±0.3	0.364
Total cholesterol (mg/dL)		180±52	169±52	0.077
Low-density lipoprotein (mg/dL)		115±43	109±41	0.156
High-density lipoprotein (mg/dL)		48±15	48±13	0.727
Triglycerides (mg/dL)		129±73	123±61	0.779

*Chi-square test, Mann-Whitney U/t-test.

GCS: Glasgow Coma Scale, NIHSS: National Institutes of Health Stroke Scale, SD: Standard deviation, IQR: Interquartile range

Table 2. Comparison of MAPH, LSR, and HSR between acute ischemic stroke and transient ischemic attack patients

Parameters	Acute ischemic stroke	Transient ischemic attack	p
MAPH-MPV	0.77±0.4	0.19±0.3	<0.001*
MAPH-Age	0.90±0.2	0.76±0.4	0.005*
MAPH-Protein	0.81±0.3	0.81±0.3	0.995
MAPH-Hematocrit	0.64±0.4	0.18±0.3	<0.001*
MAPH	3.11±0.8	1.94±0.7	<0.001*
LSR	25±12	22±9	0.005*
HSR	4±0.7	3.8±0.5	0.003*

*Mann-Whitney U/t-test.

MPV: Mean platelet volume, MAPH: MPV, age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate

Table 3. ROC analysis of MAPH, LSR, and HSR in acute ischemic stroke and transient ischemic attack patients

Parameters	AUC	Cut-off	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV, %)	Negative predictive value (NPV, %)
MAPH	0.825	3	76	81	89	61
LSR	0.617	25.9	60	69	81	45
HSR	0.621	4.2	54	80	85	45

MAPH: MPV, age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate, PPV: Positve predictive value

Table 4. Comparison of MAPH, LSR, and HSR in patients with and without major vessel occlusion

Parameters	Major Vessel Occlusion (+)	Major Vessel Occlusion (-)	p-value
MAPH-MPV	0.80±0.4	0.50±0.5	<0.001*
MAPH-Age	0.85±0.3	0.86±0.3	0.738
MAPH-Protein	0.78±0.4	0.81±0.3	0.618
MAPH-Hematocrit	0.72±0.4	0.40±0.4	<0.001*
MAPH	3.15±0.8	2.5±0.9	<0.001*
LSR	27±11	22±11	<0.001*
HSR	4±0.7	3.8±0.7	<0.001*

*Mann-Whitney U/t-test; MPV: Mean platelet volume, MAPH: MPV age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate

Table 5. ROC Analysis of MAPH, LSR, and HSR in patients with major vessel occlusion

Parameters	AUC	Cut-off	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV, %)	Negative predictive value (NPV, %)
MAPH	0.661	4	45	80	47	78
LSR	0.644	27.8	61	68	44	81
HSR	0.650	4.25	58	72	46	81

MAPH: MPV, age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate, PPV: Positve predictive value

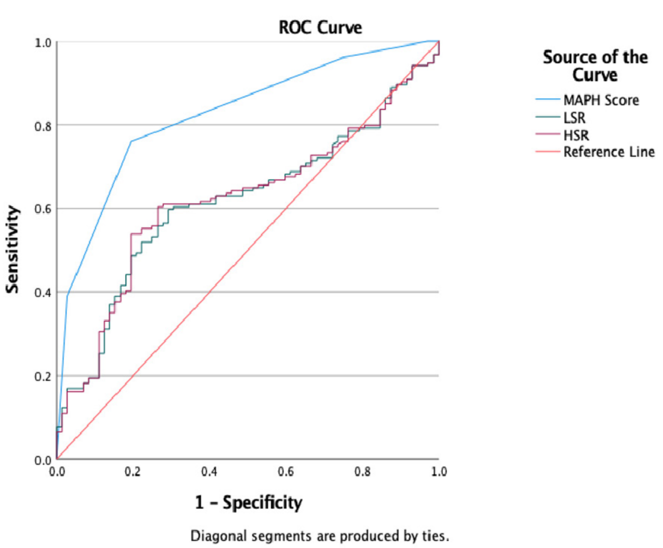

Figure 1. ROC curve of MAPH for patients diagnosed with acute ischemic stroke major vessel occlusion

MAPH: MPV, age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate

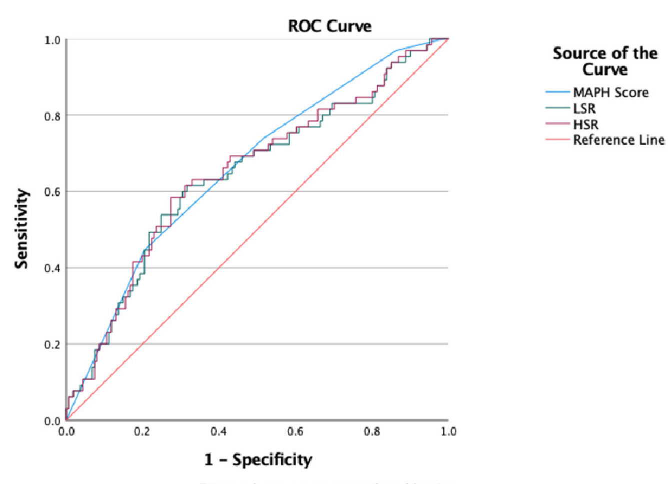

Figure 2. ROC Analysis curves of MAPH, LSR and HSR for major vessel occlusion

MAPH: MPV, age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate

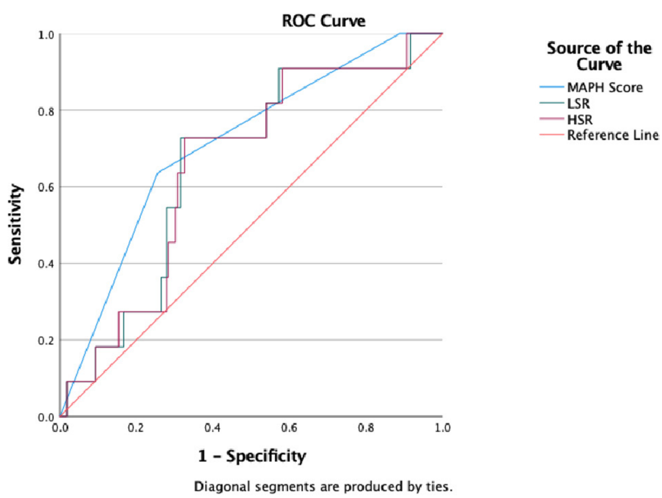

Figure 3. ROC analysis of MAPH, LSR and HSR for NIHSS ≥20

NIHSS: National Institutes of Health Stroke Scale, MAPH: MPV, age, total protein, and hematocrit, LSR: Low shear rate, HSR: High shear rate

Discussion

This study demonstrated that the MAPH score exhibited significant performance in differentiating AIS from TIA in patients presenting with suspected stroke and provided high diagnostic accuracy in predicting major vessel occlusion associated with disease severity. By combining parameters such as Hct and TP, which affect blood viscosity, with factors like MPV, reflecting systemic inflammation, and age, the MAPH score can be considered a biomarker aligned with the mechanisms involved in thrombus formation in AIS pathophysiology.

Platelets play an active role in the mechanism of AIS development. The production of thromboxane A2 by activated platelets and the surface presence of glycoprotein IIb/IIIa receptors constitutes the primary mechanism of thrombosis formation. This mechanism explains how aspirin and clopidogrel provide antiplatelet effects by inhibiting thromboxane A2 synthesis and glycoprotein IIb/IIIa receptor activity, offering a significant therapeutic approach to reducing the risk of stroke. Although platelet aggregation is a specific method for evaluating platelet function, parameters such as MPV and platelet distribution width also play an important role in the pathophysiology of AIS [10]. MPV is a measure of platelet size and is considered a key indicator of platelet activity [11]. In our study, ROC analysis identified an MPV cut-off value of 11 fL, determined based on the Youden index, which was significantly higher in the AIS group compared to the TIA group, and in patients with major vessel occlusion compared to those without. This finding suggests that increased MPV values may be associated with thrombus burden. In another study, MPV was shown to be an independent predictor of stroke risk in 3,134 patients with cerebrovascular disease. A positive association was also observed between MPV and stroke risk in patients with a history of stroke or TIA [12]. Similarly, a meta-analysis conducted by Sadeghi et al. [13] identified higher MPV values in AIS patients.

In this study, the ROC analysis identified a Hct cut-off value of 43.1%, determined based on the Youden index. This value was found to be higher in the AIS group compared to the TIA group and significantly higher in patients with major vessel occlusion compared to those without occlusion. One of the fundamental mechanisms of ischemic stroke is arterial thrombus formation. Increased WBV is a known risk factor for thrombosis, and elevated Hct levels are generally associated with increased WBV [14]. While viscosity increases exponentially with Hct in large vessels, it shows a linear increase in small vessels [15]. In this context, the observed elevation in Hct in the AIS group may be associated with the greater thrombus burden in this group compared to the TIA group. Studies on the MAPH score have shown that Hct levels are elevated in patients who have experienced MI and have a high thrombus grade [6,16].

TP, consisting of albumin, fibrinogen, and globulins, is one of the most important serum components regulating plasma viscosity [17]. In one study, higher serum protein levels were found in patients with acute stroke who had a higher degree of spontaneous echo contrast, indicating an increased risk of cardioembolic events [18]. However, in our study, no significant difference was found between the AIS and TIA groups regarding the determined cut-off value. This may be due to the characteristics of the patient population included in our study and due to the inability to clearly distinguish factors such as inflammation, hydration status, or nutritional deficiencies that could affect protein levels.

It is well known that AIS is more common particularly in individuals aged 65 and older, and that mortality and morbidity increase with age. In our study, the >60 years cut-off value determined for predicting AIS was found to be higher in the acute AIS group compared to the TIA group. This finding is consistent with the literature, which identifies increasing age as a risk factor for thrombus formation and thromboembolic events [19].

Changes in WBV are thought to play an important role in the development of ischemic stroke [20]. High WBV in HSR and LSR has been reported to be associated with apical thrombus, stent thrombosis, poor outcomes in patients with ST-elevation MI undergoing percutaneous coronary intervention, and an increased risk [21]. Additionally, elevated WBV has been shown to be a risk factor for both primary and secondary stroke [14]. High WBV at both shear rates has been associated with an independent predictor of high thrombus burden in patients with non-ST-elevation MI [22]. de Simone et al. [9] formulated simple equations using Hct and TP levels to determine WBV at various shear rates [9]. In this study, the comparison of LSR, HSR, and MAPH scores between the TIA and AIS groups revealed that these values were significantly higher in the AIS group. Furthermore, in the AIS group, patients with major vessel occlusion had higher LSR, HSR, and MAPH scores compared to those without occlusion.

One of the most significant findings of the study emerged from the comparison of continuous variables using ROC analyses. The MAPH score, created by incorporating age into the parameters affecting viscosity, such as Hct and TP, demonstrated superior performance compared to known biomarkers like HSR and LSR, as well as its individual components-Hct, age, TP, and MPV. This superiority was evident in both the differentiation of AIS and TIA and its association with a high thrombus burden in patients presenting with suspected stroke.

In the ROC analysis, the MAPH score was compared with the NIHSS. It showed a significant correlation with patients having an NIHSS score of NIHSS ≥20 (p=0.018). A comparison of the ROC curves for continuous variables, revealed that the MAPH score was statistically significant in predicting NIHSS ≥20 based on the dataset. The NIHSS is graded on a scale of 0-42, with scores of 0-11 classified as “mild”, 12-22 as “moderate”, and ≥23 as “severe”. In this study, the MAPH score was found to be significantly higher in the patient group classified as severe (NIHSS ≥20). This finding is highly significant, as treatment decisions are largely based on stroke severity and the site of involvement. The severity of the disease varies depending on the site of involvement and thrombus burden. The MAPH score has the potential to correlate with thrombus burden [6,16,23].

Study Limitations

This study has several limitations. One of the limitations of the study is the retrospective design and single-center nature, which limits the generalizability of the results to different patient populations and geographic regions. Additionally, as the MAPH score is a novel biomarker, its validation in larger patient groups and various clinical settings is necessary. The study did not thoroughly evaluate factors such as inflammation, hydration status, and nutritional deficiencies, which could influence TP levels, potentially restricting a comprehensive understanding of this parameter’s impact. One of the limitations of our study is the lack of systematic records on morbidity outcomes, such as post-stroke complications, functional status, and disability. Although we reported 30-day mortality rates, the absence of comprehensive data on the long-term clinical course of patients remains a significant limitation.

Conclusion

This study demonstrated that the MAPH score, a novel indicator of WBV, provides high diagnostic accuracy in both differentiating between AIS and TIA groups, and identifying major vessel occlusion. These findings suggest that the MAPH score, which is simple to calculate, could aid in determining disease severity and contribute to patient management in individuals presenting to the emergency department with suspected stroke. However, MAPH needs to be validated in larger patient cohorts before it can be recommended as an independent diagnostic method.

Ethics

Ethics Committee Approval: The study was conducted with approval from the Ethics Committee of University of Health Sciences Türkiye, Ankara Etlik City Hospital (approval number: AEŞH-BADEK-2024-891, date: 25.09.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: E.S., Design: E.S., M.Y., Data Collection or Processing: E.S., M.Y., Analysis or Interpretation: M.Y., Literature Search: E.S., M.Y., Writing: E.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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