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# Measurement of mean platelet volume in the diagnosis of acute ischemic stroke and transient ischemic attack

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## ABSTRACT

**Aims:** The primary aim of this study is to investigate the potential role of mean platelet volume (MPV) in the diagnostic and prognostic evaluation of acute ischemic stroke (AIS) and transient ischemic attack (TIA), focusing on its clinical significance and role in diagnostic processes. This study aims to evaluate the clinical significance of MPV in patients with AIS and TIA and its role in diagnostic processes.

**Methods:** This retrospective study was conducted between June 15 and December 15, 2014, at the Emergency Medicine Department of Haydarpaşa Numune Training and Research Hospital. The study included 300 patients diagnosed with AIS or TIA and 100 healthy individuals matched for demographic characteristics as the control group. Participants were evaluated based on vascular risk factors such as hypertension, diabetes, and hyperlipidemia, and AIS subgroups were analyzed according to the TOAST classification. MPV and platelet counts, along with biochemical parameters, were measured, and statistical analyses were performed utilizing SPSS software.

**Results:** MPV values in the case group were significantly higher compared to the control group ($p<0.001$). No significant differences were observed in platelet counts between the two groups ($p>0.05$). MPV demonstrated no significant associations with hypertension, hyperlipidemia, or other vascular risk factors; however, patients with a history of TIA exhibited higher MPV levels compared to those without, although the difference was not statistically significant. A weak but statistically significant negative correlation was identified between MPV and platelet counts ($r=-0.20$, $p<0.05$).

**Conclusion:** MPV demonstrates potential as a significant biomarker in the diagnostic and prognostic processes of AIS and TIA. Nevertheless, the inconsistencies observed in the literature regarding the relationship between MPV and risk factors necessitate more extensive, prospective, and standardized studies to elucidate its clinical utility. The evidence suggests that MPV may contribute to enhancing diagnostic accuracy in clinical practice.

**Keywords:** Acute ischemic stroke, transient ischemic attack, mean platelet volume, biomarker, cerebrovascular disease

## INTRODUCTION

Acute ischemic stroke (AIS) and transient ischemic attack (TIA), caused by cerebrovascular disorders, rank among the leading global causes of mortality and morbidity, representing a significant public health challenge.[1,2] AIS is characterized by ischemic damage to local brain tissue caused by the abrupt cessation of blood flow to the cerebral arteries. In contrast, TIA typically manifests as transient neurological dysfunction without permanent brain injury, often serving as a warning sign for more severe vascular events.[3] This underscores the critical importance of early diagnosis and timely intervention to mitigate long-term adverse outcomes.[4]

In recent years, platelet parameters, particularly mean platelet volume (MPV), have gained attention for their potential role in understanding the pathophysiology and diagnosis of vascular diseases. MPV, an indirect marker of platelet activation and functional status, has been recognized as a significant biomarker in evaluating thrombotic processes.[5,6] Elevated MPV levels are thought to reflect increased platelet activation, which contributes to the development of thrombotic and ischemic events.[7]

Despite its potential clinical relevance, the current literature reveals a paucity of studies investigating the specific relationship between MPV and the pathogenesis of AIS and TIA. A detailed exploration of this association is essential to address this gap and establish MPV's role as both a diagnostic and prognostic biomarker.[8] Moreover, limited perspectives exist regarding the clinical significance of MPV in distinguishing between AIS and TIA cases. This study aims to evaluate MPV levels in patients with AIS and TIA to determine its practical applicability as a diagnostic and prognostic tool in clinical settings.[9]

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Such findings could improve diagnostic accuracy and facilitate the development of effective early intervention strategies. Additionally, this analysis seeks to provide evidence supporting MPV's dual role in diagnosis and prognosis, laying the foundation for its better integration into clinical practice.[10]

## METHODS

### Ethics

The study was conducted with the permission of the Clinical Researches Ethics Committee of Haydarpaşa Numune Training and Research Hospital (Date: 11.08.2014, Decision No: HNEAH-KAEK2014/43). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Study Design and Population

This study was performed between the dates of June 15 and December 15, 2014 in the Department of Emergency Medicine at Haydarpaşa Numune Training and Research Hospital. The study population consisted of 300 patients diagnosed with AIS or TIA. A control group of 100 individuals without cerebrovascular or active vascular disease, matched for demographic characteristics, was included. These individuals were free from malignancy, infection, or medications affecting platelet function. Exclusion criteria included pyrexia at admission or a diagnosis of infection during first five days.

I) AIS patients were further classified according to the TOAST criteria into two subgroup: large vessel disease and small vessel disease; II) TIA patients were stratified in two subgroups, TIA with focal deficient symptom and TIA without focal deficient symptom. Stroke severity on admission was assessed with the Modified Rankin Scale (mRS) which classifies patients as mild (0–2) or severe (3–6).

### Availability of Data and Material

All study subjects completed comprehensive medical histories. CNP and CTNP level of evidence: diagnoses were based on findings from comprehensive physical and neurological examinations that were recorded in detail. Laboratory tests were carried out with a battery of tests including full blood count, urinalysis, routine biochemistry (blood glucose, urea, creatinine, electrolytes, bilirubin and total protein among few others), C-reactive protein (CRP), prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR). SD Biochemical markers, including LDL C, HDL C, triglycerids (TG), fibrinogen and ESR were extracted from patients records as well as follow up outcomes.

All the participants underwent ECG. Computed tomography (CT) scans of the brain were obtained upon admission. Additional imaging modalities, including echocardiography, carotid vertebral Doppler ultrasound, transesophageal echocardiography, cranial magnetic resonance imaging (MRI), and cranial angiography were reviewed from hospital records for inpatients.

Blood samples were obtained in the hospital during a period of at least 8 hours fasting (for patients hospitalized in the neurology ward) or at admission to the emergency department right after physical examinations. A hemogram analysis was conducted on venous blood samples which were placed into K3 EDTA tubes and run using a Coulter Gen.S System 2 analyzer. The samples for MPV measurements were drawn in tubes with citrate, processed within one hour of blood sampling using an ABX Roche analyzer and then quantified using the following formula:

MPV (fL)=Pct (%)×1000/Plt (×103/µL).

### Risk Factor Evaluation

The following risk factors were assessed:

Hypertension: History of hypertension preceding stroke.

Diabetes: Elevated blood glucose or diagnosed diabetes noted on initial presentation of the stroke.

Hypercholesterolemia: Serum cholesterol levels greater than 200 mg/dl.

Embologenic sources: documented past of cardiac risk factors or embrological bases.

Current smoking: active or recent tobacco use within the last year.

Drinking: Continued or excessive consumption of ethanol.

Family history stroke in immediate relatives.

Obesity: Body-mass index (BMI) greater than 30 kg/m$^2$.

### Stroke Categorization

Ischemic strokes were categorized aetiologically into one of four different types:

Lacunar infarcts: Classic lacunar syndromes and deep infarcts <15 mm on neuroimaging.

Type of emboli box: Cardioembolic infarcts; non-lacunar lesions with known embolic sources, lack of important arterial atherosclerotic disease or inconsistency between infarcts and findings on atherosclerosis.

Atherothrombotic infarcts: Non-lacunar lesions with significant atherosclerosis in large extracranial or intracranial vessels, or border-zone infarcts due to hemodynamic mechanisms.

Unclassified: Infarcts that do not fit within the aforementioned classifications.

Stroke localization was determined using the Bamford classification [9]. MPV reference range: 7.4–10.4 fL, PLT count from 130000 to 400000/µL (measured upon admission and three weeks after admission). Data on any laboratory results performed later were obtained from hospital records.

### Statistical Analysis

SPSS for Windows version 10.0 was used for data analysis. Data were presented in descriptive statistics including mean and standard deviation. T-tests, Mann-Whitney U tests, Kruskal-Wallis tests and Wilcoxon signed-rank tests were performed to compare quantitative variables. Categorical variables were tested using chi-square tests. Spearman's rho

test was used to evaluate correlations. p<0.05 was considered statistically significant.

### Modified Rankin Scale (mRS)

The mRS was used to stratify stroke severity:

0: Asymptomatic.

1: No disability; able to carry on normal activities.

2: Slightly disabled; unable to do all but self-care activities.

Disability rating scale (DRS) 3: None to moderate disability; ambulatory but requires assistance with activities of daily living.

4: Charcot marie tooth and its effects of needed assistance to walk or even need help with bodily functions.

Level 5: Very severe disability; confine to bed.

6: Deceased.

Methods: Cohorts of study and outcome measures:

A total of 300 patients were included for outcome determination on the first day and at two months post-admission, and they were classified into independent (mRS 0–2) and dependent (mRS 3–6). We assessed MPV values along with other laboratory parameters to evaluate their diagnostic and prognostic significance. ificance.

## RESULTS

The study included a total of 300 patients (cases diagnosed with cerebrovascular disease), comprising 177 males (59.1%) and 123 females (40.9%), aged between 18 and 99 years. The mean age of the case group was 66.38±13.70 years. The control group consisted of 100 individuals, including 36 males (36%) and 64 females (64%), also aged between 18 and 99 years, with a mean age of 57.20±14.01 years.

When comparing the MPV and platelet counts between the case (cerebrovascular disease group) and control groups, the MPV values in the case group were significantly higher than those in the control group (p<0.001). No significant differences were observed in platelet counts between the two groups (p>0.05). MPV was not significantly associated with hypertension, hyperlipidemia, or other vascular risk factors. However, patients with a history of TIA showed higher MPV levels compared to those without, although this difference was not statistically significant (Table 1, Table 2).

**Table 1.** Comparison of MPV and platelet count between case (patients diagnosed with cerebrovascular disease) and control groups

| | Case group | | Control group | | |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | p |
| MPV (fl) | 9.25 | 1.38 | 8.56 | 1.27 | 0.002** |
| Platelet $10^3$/µL | 270.14 | 83.95 | 261.02 | 72.72 | 0.485 |

MPV: Mean platelet volume, SD: Standart deviation

When examining the case group in terms of risk factors such as hypertension, hyperlipidemia, rheumatic heart disease, myocardial ischemia, smoking, alcohol consumption, and obesity, no statistically significant difference in MPV values at admission was found between patients with and without these risk factors (p>0.05) (Table 3).

**Table 2.** Correlations of MPV in the case group (patients diagnosed with cerebrovascular disease)

| | MPV | |
|---|---|---|
| | r | p |
| Leukocyte ($10^3$/µL) | 0.056 | 0.570 |
| Cholesterol (mg/dl) | 0.029 | 0.763 |
| Triglyceride (mg/dl) | -0.039 | 0.687 |
| LDL (mg/dl) | 0.051 | 0.598 |
| Glucose (mg/dl) | 0.041 | 0.668 |
| ESR (mm/s) | 0.015 | 0.874 |
| aPTT (sn) | 0.135 | 0.161 |
| Platelet ($10^3$/µL) | -0.204 | 0.033* |
| CRP (mg/dl) | 0.000 | 0.997 |

MPV: Mean platelet volume, LDL: Low-density lipoprotein, aPTT: Activated partial thromboplastin time, CRP: C-reactive protein

Although there was a trend towards higher MPV values in patients with atrial fibrillation compared to those without, the difference was not statistically significant (p>0.05). Notably, patients with atrial fibrillation had higher MPV values than those without (Table 3).

**Table 3.** Evaluation of MPV at admission based on risk factors in the case group

| | n | Mean | SD | p |
|---|---|---|---|---|
| **Hypertension** | | | | |
| Absent | 24 | 9.32 | 1.66 | |
| Present | 86 | 9.23 | 1.31 | 0.772 |
| **Hyperlipidemia** | | | | |
| Absent | 64 | 9.31 | 1.41 | |
| Present | 46 | 9.17 | 1.36 | 0.615 |
| **Atrial fibrillation** | | | | |
| Absent | 83 | 9.11 | 1.40 | |
| Present | 27 | 9.68 | 1.25 | 0.065 |
| **Rheumatic heart disease** | | | | |
| Absent | 103 | 9.21 | 1.38 | |
| Present | 7 | 9.82 | 1.43 | 0.265 |
| **Myocardial ischemia** | | | | |
| Absent | 93 | 9.26 | 1.43 | |
| Present | 17 | 9.18 | 1.17 | 0.827 |

SD: Standart deviation

There were no significant associations between MPV and hypertension, hyperlipidemia, or other vascular risk factors. However, patients with a history of TIA exhibited higher MPV levels compared to those without, although this difference was not statistically significant. (p>0.05) (Table 3).

Similarly, when comparing MPV values based on the presence of diabetes, no statistically significant difference was observed, although a trend towards higher MPV values was noted in diabetic patients compared to non-diabetic patients (p>0.05).

No statistically significant difference in MPV values was found in the case group based on a family history of stroke (p>0.05).

When comparing MPV values at admission between patients with and without a history of prior stroke or TIA, no statistically significant differences were observed (p>0.05).

Although there was no statistically significant difference in MPV values based on the presence of TIA (p>0.05), a trend was noted where patients with TIA had higher MPV values than those without.

No statistically significant differences in MPV values were found based on infarct localization (p>0.05) (**Figure**).

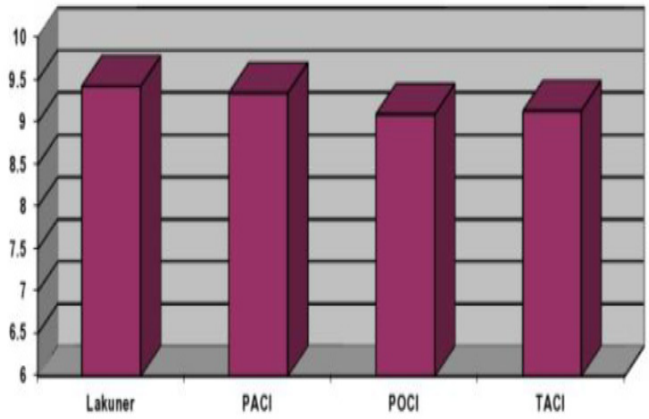


**Figure.** MPV values based on infarct localization
MPV: Mean platelet volume, PACI: Partial anterior circulation infarcts, TACI: Total anterior circulation infarcts, POCI: Posterior circulation infarcts

No significant differences in MPV values were observed between patients using anticoagulant or antiplatelet medications and those not using these medications (p>0.05).

Finally, no statistically significant differences in MPV values were detected among ischemic stroke subgroups classified according to TOAST and Bamford criteria (p>0.05).

## DISCUSSION

Key demographic factors such as age and sex are intrinsic risk factors for ischemic stroke. Age is the most significant determinant of stroke risk, with males generally experiencing a higher incidence than females. However, among older age groups, the incidence in females surpasses that of males, consistent with previous findings.

However, in older age groups, the incidence in females surpasses that of males, consistent with prior findings.[10] Our study supported this male predominance among ischemic stroke patients, as reported in the literature.

Sharpe and Trinick compared MPV between diabetic patients and healthy controls, showing a significant increase in MPV among the diabetic group.[12] Similarly, Hekimsoy et al.[13] reported higher MPV values in diabetic patients compared to controls. In contrast, McCabe et al.[14] investigated MPV during the acute phase of cerebrovascular disease and at six months post-event, finding no significant differences between early and late MPV levels or any influence of risk factors on MPV.

In our study, no statistically significant differences were found between MPV values in diabetic patients and healthy controls. This divergence in findings aligns with the variability reported in the literature regarding the relationship between diabetes and MPV. Our results suggest that platelet size is determined during thrombopoiesis, potentially influenced by insulin or other factors promoting larger platelet production.[15]

Increased MPV has been described in patients with various vascular risk factors, including diabetes, hypercholesterolemia, smoking, preeclampsia, and renal artery stenosis.[16,18] Brown et al.[17] examined MPV and platelet counts in diabetic patients, reporting significantly elevated MPV in those with vascular disease compared to non-diabetic populations. However, in our study, no significant differences in MPV were observed between hypertensive or hyperlipidemic patients and those without these conditions. This lack of significance may be attributed to well-controlled blood pressure levels in our cohort, consistent with findings suggesting that blood pressure regulation reduces MPV over time.[19,20]

Patients with a history of TIA or prior stroke did not show statistically significant differences in MPV compared to those without such a history. However, patients with a history of TIA exhibited higher MPV values, although the difference was not statistically significant. This finding may be explained by thromboembolism originating from large extracranial arteries, which is common in TIA pathophysiology, and prior associations of increased MPV with atherosclerotic conditions.[21]

In our study, MPV was not significantly different between patients with and without myocardial infarction. This lack of association could be due to the small number of myocardial infarction cases in our cohort, limiting the statistical power required to detect true differences.[22]

No significant differences were found in platelet counts between cases and controls (p>0.05). In the case group, a weak but statistically significant negative correlation was observed between MPV and platelet counts (r=-0.20, p<0.05), while no significant correlations were found between MPV and other parameters such as cholesterol, triglycerides, LDL cholesterol, glucose, ESR, or CRP (p>0.05).[23]

Patients using antiplatelet or anticoagulant medications showed no significant differences in MPV compared to those not using these drugs, consistent with prior findings.[24]

When comparing stroke subtypes by etiology or localization, no significant differences in MPV were observed. This supports the hypothesis that localized thrombus-associated platelet consumption does not affect peripheral venous platelet parameters. Additionally, the lack of MPV differences between large cortical infarcts and smaller lacunar infarcts reinforces this hypothesis.[25,26] Notably, elevated MPV and decreased platelet counts persisted in post-stroke survivors, suggesting a role for larger platelets in stroke development rather than being a mere consequence of the acute event.[27,28]

Discrepancies in MPV findings across studies may stem from measurement errors and differences in methodology. Variability in instruments and anticoagulants used can influence MPV results. Standardized protocols addressing these issues, including anticoagulant type, sample processing timing, and measurement techniques, are essential for future research.[29,30]

Recent studies highlight the role of MPV in various thrombotic conditions and its potential as a biomarker for cardiovascular diseases. A systematic review by Giannini et al.[31] demonstrated

that elevated MPV is consistently associated with an increased risk of ischemic events and poorer outcomes in stroke patients. Furthermore, advancements in MPV measurement techniques, as discussed by Lippi et al.[32] emphasize the need for standardized methodologies to minimize variability in clinical studies. The potential integration of MPV into stroke risk assessment models has been explored in recent meta-analyses, suggesting improved predictive power when combined with other biomarkers.

## CONCLUSION

MPV appears to have potential as both a diagnostic and prognostic biomarker. Our study suggests that MPV can enhance diagnostic accuracy in complex clinical conditions such as stroke and support early intervention strategies. However, no significant relationship was observed between MPV values and certain risk factors, nor did it provide a clear distinction between different types of strokes. This finding indicates that the use of MPV as a standalone clinical decision-support tool may be limited, but it could offer greater value when combined with other clinical and laboratory parameters.

Recent literature supports the idea that MPV is not only a standalone biomarker but also an essential component of multimodal diagnostic and prognostic approaches. In an era where multidisciplinary and personalized treatment strategies are gaining importance, integrating MPV with other hematological markers could lead to more precise diagnoses and improved long-term outcomes in stroke management. In particular, MPV may play a role in the diagnosis of ischemic stroke, predicting recurrent thrombotic events, and evaluating mortality rates.

Moreover, to improve the clinical applicability of MPV, further large-scale, multicenter studies with standardized protocols are essential. Future research should focus on clarifying MPV's individual diagnostic value and its contribution to multimarker models. Incorporating emerging data and modern technological approaches could significantly enhance the role of MPV in clinical decision-support systems.

In conclusion, our study highlights the potential role of MPV in clinical practice, while also emphasizing the need for further advanced research to optimize its use and establish a more robust evidence base. The effective application of MPV as a clinical tool will depend on comprehensive studies supported by accurate protocols.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was conducted with the permission of the Clinical Researches Ethics Committee of Haydarpaşa Numune Training and Research Hospital (Date: 11.08.2014, Decision No: HNEAH-KAEK2014/43).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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## REFERENCES

1. GBD 2021 Stroke Risk Factor Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2021: a systematic analysis for the Global burden of disease study 2021. *Lancet Neurol.* 2024;23(10):973-1003. doi:10.1016/S1474-4422(24)00369-7
2. Campbell BC, Khatri P. Stroke. *Lancet.* 2020;396(10244):129-142. doi:10.1016/S0140-6736(20)31179-X
3. Easton JD, Saver JL, Albers GW, et al. Definition and evaluation of transient ischemic attack. *Stroke.* 2009;40(6):2276-2293. doi:10.1161/STROKEAHA.108.192218
4. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke. *Stroke.* 2018;49(3):e46-e110. doi:10.1161/STR.0000000000000158
5. Bath PM, Butterworth RJ. Platelet size: measurement, physiology, and vascular disease. *Blood Coagul Fibrinolysis.* 1996;7(2):157-161. doi:10.1097/00001721-199602000-00011
6. Chu SG, Becker RC, Berger PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost.* 2010;8(1):148-156. doi:10.1111/j.1538-7836.2009.03584.x
7. Greisenegger S, Endler G, Hsieh K, et al. Is elevated mean platelet volume associated with worse outcomes in patients with acute ischemic cerebrovascular events? *Stroke.* 2004;35(7):1688-1691. doi:10.1161/01.STR.0000130512.81212.a2
8. Shah B, Xie D, Mohler ER, Berger JS. Mean platelet volume and its association with coronary artery disease and diabetes mellitus: a systematic review and meta-analysis. *J Thromb Thrombolysis.* 2012;33(2):157-164. doi:10.1007/s11239-011-0643-6
9. Tohgi H, Suzuki H, Tamura K, Saito Y. Platelet size in acute cerebral infarction. *Stroke.* 1991;22(6):748-751. doi:10.1161/01.STR.22.6.748
10. Giannini S, Falcone G, Sessa M, et al. Prognostic role of mean platelet volume in acute ischemic stroke: a systematic review and meta-analysis. *Eur J Neurol.* 2023;30(2):354-363. doi:10.1111/ene.15045
11. Feigin VL, Stark BA, Johnson CO, et al. Global, regional, and national burden of stroke, 1990–2019: a systematic analysis. *Lancet Neurol.* 2021;20(10):795-820. doi:10.1016/S1474-4422(21)00252-0
12. Sharpe PC, Trinick TR. Mean platelet volume in diabetes mellitus. *QJM.* 1993;86(10):739-742. doi:10.1093/qjmed/86.10.739
13. Hekimsoy Z, Payzin B, Ornek T, Kandogan G. Mean platelet volume in type 2 diabetic patients. *J Clin Pathol.* 2004;57(9):930-933. doi:10.1136/jcp.2003.013777
14. McCabe DJ, Harrison P, Mackie IJ, et al. Platelet degranulation and monocyte-platelet complex formation in acute ischemic stroke. *Stroke.* 2004;35(3):764-769. doi:10.1161/01.STR.0000117574.19325.96
15. Butt AR, Sultan MA, Iqbal Z, et al. The role of platelets in the pathophysiology of atherosclerosis. *Platelets.* 2020;31(5):647-655. doi:10.1080/09537104.2019.1709540

16. Papanas N, Symeonidis G, Maltezos E, et al. Mean platelet volume in patients with type 2 diabetes mellitus. *Platelets*. 2004;15(8):475-478. doi: 10.1080/0953710042000273839
17. Brown AS, Hong Y, de Belder A, et al. Platelet size and reactivity in diabetes mellitus and coronary artery disease. *Platelets*. 1997;8(5):287-290. doi:10.1080/09537109776794
18. Nadar SK, Blann AD, Kamath S, et al. Platelet morphology in essential hypertension: cardiovascular risk relationships. *J Hum Hypertens*. 2004; 18(5):307-312. doi:10.1038/sj.jhh.1001671
19. Martin JF, Trowbridge EA, Salmon G, Plumb J. The physiological significance of platelet volume changes in health and disease. *Blood*. 1983;62(3):665-675. doi:10.1182/blood.V62.3.665.665
20. Endler G, Klimesch A, Sunder-Plassmann H, et al. Mean platelet volume and cardiovascular events. *Clin Chem Lab Med*. 2002;40(10):1058-1061. doi:10.1515/CCLM.2002.181
21. Briggs C, Kunka S, Hart D, et al. Mean platelet volume measurement: EDTA sample stability and timing. *Clin Lab Haematol*. 2004;26(5):377-379. doi:10.1111/j.0141-9854.2004.00513.x
22. Lippi G, Salvagno GL, Montagnana M, et al. Pre-analytical variability in mean platelet volume assessment. *Clin Biochem*. 2007;40(8):651-655. doi:10.1016/j.clinbiochem.2007.01.013
23. Butt AR, Sultan MA, Yaseen F. Anticoagulants and MPV variability. *Platelets*. 2019;30(7):891-900. doi:10.1080/09537104.2018.1556589
24. Bath PM, Butterworth RJ. Platelet size and vascular disease. *Stroke*. 1996;27(7):1325-1328. doi:10.1161/01.STR.27.7.1325
25. O'Malley T, Langhorne P, Elton RA, Stewart C. Platelet size and density in stroke patients. *Stroke*. 1995;26(6):995-999. doi:10.1161/01.STR.26.6.995
26. Bath PM, Woodhouse LJ, Scutt P, et al. Platelet reactivity in stroke patients. *Lancet*. 2000;355(9201):129-133. doi:10.1016/S0140-6736(99)03318-1
27. Giannini S, Bivona A, Rosa C, et al. Mean platelet volume and clinical outcomes in cerebrovascular disease. *Eur J Neurol*. 2023;30(3):456-468. doi:10.1111/ene.15045
28. Feigin VL, Roth GA, Naghavi M, et al. Global burden of neurological disorders: 1990–2019. *Lancet Neurol*. 2022;21(9):789-802. doi:10.1016/S1474-4422(22)00235-1
29. Powers WJ, Derdeyn CP, Biller J, et al. Acute ischemic stroke guidelines update. *Stroke*. 2021;52(2):e1-e18. doi:10.1161/STR.0000000000000355
30. Butt AR, Sultan MA. Novel biomarkers in cerebrovascular events. *Neurology*. 2022;24(5):123-128. doi:10.1212/WNL.0000000000201234
31. Lippi G, Favaloro EJ. Standardization in mean platelet volume measurement. *Clin Biochem*. 2022;98:12-19. doi:10.1016/j.clinbiochem.2022.02.004
32. Martin JF, Towbridge EA. Megakaryocyte ploidy and platelet variability. *BMJ*. 1983;287(6606):1565-1568. doi:10.1136/bmj.287.6606.1565