International journal of statistics (2051-8285)

Mean Platelet Volume as a Biomarker in Acute Ischemic Stroke: Pathophysiological Associations, Prognostic Implications, and Clinical Relevance

Dr. Ananya Rao[1], **Dr. Michael J. Thompson**[2]

[1]*Department of Neurology, All India Institute of Medical Sciences, New Delhi, India*
[2]*Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, USA*

Doi https://doi.org/10.55640/ijs-03-01-01

ABSTRACT

Stroke remains a leading cause of mortality and long-term disability worldwide, with ischemic stroke constituting the majority of cases. Despite advances in neuroimaging and acute management, there is a continued need for accessible and reliable biomarkers that may assist in risk stratification, prognostication, and understanding disease mechanisms. Mean platelet volume (MPV), an index of platelet size and activity routinely reported in complete blood counts, has emerged as a potential biomarker in cerebrovascular disease. Larger platelets are metabolically and enzymatically more active, exhibit greater prothrombotic potential, and are associated with enhanced inflammatory responses, all of which are relevant to ischemic stroke pathophysiology.

This article critically examines the biological basis of MPV, its relationship with platelet function, and its association with ischemic stroke severity, subtype, lesion volume, and clinical outcomes. Evidence from epidemiological studies, hospital-based cohorts, and prognostic analyses is synthesized to evaluate whether elevated MPV is associated with worse outcomes in acute ischemic stroke. The interaction of MPV with comorbid conditions such as diabetes mellitus, metabolic syndrome, and cardiovascular disease is also explored. Methodological considerations, including preanalytical and analytical variability in MPV measurement, are discussed as important limitations affecting clinical interpretation.

Overall, current evidence suggests that MPV is associated with stroke risk and may predict severity and functional outcome in selected populations. However, heterogeneity across studies and the absence of standardized cut-off values limit its immediate clinical application. MPV should be viewed as a supportive biomarker that reflects underlying thrombo-inflammatory processes rather than a standalone diagnostic or prognostic tool. Further large-scale, standardized, and prospective studies are required to clarify its role in routine stroke care and to integrate MPV into multimarker approaches for cerebrovascular disease assessment.

Keywords: Mean platelet volume, ischemic stroke, platelet activation, cerebrovascular disease, prognostic biomarkers, thrombosis.

INTRODUCTION

Stroke represents one of the most significant global health challenges, accounting for substantial morbidity, mortality, and socioeconomic burden. The World Health Organization defines stroke as a rapidly developing clinical sign of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin [2]. Among the various stroke subtypes, ischemic stroke constitutes approximately 80–85% of all cases and arises primarily from thrombotic or embolic occlusion of cerebral arteries. Understanding the biological mechanisms underlying ischemic stroke and identifying reliable biomarkers for prediction and prognosis remain central objectives in cerebrovascular research.

Historically, the conceptualization of stroke has evolved from a purely clinical syndrome to a complex vascular and inflammatory disorder. Early historical accounts emphasized gross vascular obstruction, whereas modern perspectives integrate endothelial dysfunction, platelet activation, inflammation, and hemostatic imbalance as central contributors to ischemic injury [1]. Platelets, in particular, play a pivotal role in the initiation and propagation of thrombus formation at sites of vascular injury or atherosclerotic plaque rupture. Consequently, platelet-related indices have attracted increasing attention as potential markers of stroke risk and outcome. Mean platelet volume is a routinely available

hematological parameter that reflects the average size of circulating platelets. Larger platelets are known to be more reactive, containing higher concentrations of dense granules, thromboxane A_2, and procoagulant surface receptors. These features render them more capable of participating in thrombus formation and amplifying inflammatory cascades [4,5]. MPV has therefore been investigated as a surrogate marker of platelet activation in a range of cardiovascular and metabolic disorders, including myocardial infarction, diabetes mellitus, and metabolic syndrome [7,9,11].

In the context of ischemic stroke, multiple studies have explored the association between MPV and stroke occurrence, severity, subtype, and prognosis. Elevated MPV has been reported in patients with acute ischemic stroke compared with healthy controls and has been linked to larger infarct volumes and worse functional outcomes in some cohorts [6,10,15]. Additionally, MPV has been examined in relation to established vascular risk factors, suggesting that it may represent an integrative marker of thrombo-inflammatory burden rather than an isolated hematological abnormality.

Despite growing interest, the clinical utility of MPV in stroke remains uncertain. Conflicting findings across studies, methodological variability in MPV measurement, and limited understanding of temporal changes during the acute and recovery phases of stroke have hindered definitive conclusions. Moreover, MPV is influenced by a range of biological and technical factors, including platelet turnover, cytokine activity, anticoagulant use, and laboratory processing conditions [19]. These considerations necessitate a cautious and critical appraisal of existing evidence.

The present article aims to provide a comprehensive and structured review of the role of MPV in ischemic stroke. By integrating pathophysiological insights, clinical associations, and methodological considerations, this manuscript seeks to clarify the relevance of MPV as a biomarker in acute ischemic stroke and to identify gaps that warrant further investigation.

METHODS

Study Design and Conceptual Framework

This manuscript is structured as a narrative and analytical review grounded in established clinical and experimental literature. The conceptual framework centers on the hypothesis that MPV reflects platelet activation and thrombo-inflammatory activity, which are central to ischemic stroke pathogenesis and progression. Emphasis is placed on synthesizing evidence that examines associations rather than causal relationships, in keeping with the observational nature of most available studies.

Literature Sources and Selection Criteria

Relevant literature was identified from peer-reviewed journals focusing on neurology, hematology, and cardiovascular medicine. Priority was given to studies examining MPV in the context of ischemic stroke, including epidemiological investigations, hospital-based cohort studies, and prognostic analyses. Foundational research on platelet biology and thrombopoiesis was included to support mechanistic interpretations [4,11–13]. References addressing methodological aspects of MPV measurement and normal population ranges were also incorporated [18,19].

Data Extraction and Synthesis

Key data points extracted from the literature included study design, patient population characteristics, stroke subtype classification, MPV values, outcome measures, and reported associations. Findings were synthesized qualitatively to identify consistent patterns, areas of disagreement, and methodological limitations. No quantitative meta-analysis was performed due to heterogeneity in study designs and outcome definitions.

Ethical Considerations

As this manuscript is based solely on previously published data, no new ethical approval or patient consent was required. All referenced studies were assumed to have been conducted in accordance with applicable ethical standards.

RESULTS

Biological Basis of Mean Platelet Volume

Platelet size is determined during thrombopoiesis in the bone marrow, where megakaryocytes undergo cytoplasmic fragmentation to release platelets into the circulation. Larger platelets are typically younger and exhibit enhanced metabolic and enzymatic activity. Experimental studies have demonstrated that large platelets contain increased amounts of prothrombotic mediators, including thromboxane A_2, serotonin, and platelet-derived growth factor [4]. These properties contribute to greater aggregability and adhesive capacity, particularly under high shear stress conditions relevant to cerebral circulation.

Cytokines such as interleukin-6 play a role in stimulating megakaryocyte proliferation and platelet production, potentially linking systemic inflammation with increased MPV [12,13]. This connection is particularly relevant in ischemic stroke, where inflammatory responses are activated early and may persist throughout the recovery

phase.

MPV in Acute Ischemic Stroke

Multiple clinical studies have reported elevated MPV values in patients presenting with acute ischemic stroke compared with healthy controls [6,15]. These findings suggest that increased platelet size and activity may be associated with the acute thrombotic process underlying cerebral infarction. Importantly, some studies have observed that MPV elevation is present at admission, indicating that it may reflect pre-existing platelet characteristics rather than a consequence of cerebral ischemia alone.

Greisenegger et al. reported that elevated MPV was associated with worse functional outcomes in patients with acute ischemic cerebrovascular events, as assessed by standardized neurological scales [10]. Similarly, Butterworth and Bath identified associations between MPV, stroke subtype, and clinical outcome, with higher MPV observed in patients with large artery atherosclerosis compared with other subtypes [6].

Association with Infarct Volume and Severity

Advances in neuroimaging have enabled more precise quantification of infarct volume, facilitating correlations with biological markers. Liu and Che demonstrated that retinol-binding protein 4 and MPV were associated with lesion volume determined by magnetic resonance imaging in acute ischemic stroke [3]. These findings support the notion that MPV may be linked to the extent of ischemic injury, potentially through enhanced thrombus stability or microvascular obstruction.

However, not all studies have reported consistent associations between MPV and stroke severity. Ciancarelli et al. suggested that while MPV may function as a pro-inflammatory biomarker during the acute phase and neurorehabilitation, it was not directly linked to clinical outcome measures [14]. Such discrepancies underscore the complexity of interpreting MPV in heterogeneous patient populations.

MPV and Stroke Prognosis

The prognostic value of MPV has been evaluated in several observational studies. Elevated MPV has been associated with increased risk of recurrent stroke and poorer long-term outcomes in patients with a history of cerebrovascular disease [8]. Mayda-Domaç et al. reported that MPV and platelet count together provided prognostic information in both ischemic and hemorrhagic stroke, although the strength of association varied by stroke type [16].

Lok et al. further examined the predictive role of MPV in first-ever acute ischemic stroke, identifying associations with early neurological deterioration and functional outcome [17]. These findings suggest that MPV may contribute incremental prognostic information when considered alongside clinical and imaging parameters.

Interaction with Comorbid Conditions

MPV is influenced by several cardiovascular and metabolic conditions that are themselves risk factors for ischemic stroke. Patients with diabetes mellitus exhibit larger, more reactive platelets, a phenomenon attributed to chronic hyperglycemia, oxidative stress, and low-grade inflammation [11]. Similarly, individuals with metabolic syndrome have been shown to exhibit elevated MPV, which correlates with the presence and severity of coronary artery disease [7].

These associations complicate the interpretation of MPV in stroke populations, as elevated values may reflect the cumulative burden of vascular risk factors rather than stroke-specific processes alone. Nonetheless, this integrative characteristic may also enhance the utility of MPV as a global marker of thrombotic risk.

DISCUSSION

Interpretation of Findings

The available evidence indicates that MPV is associated with ischemic stroke occurrence, severity, and outcome in a substantial proportion of studies. The biological plausibility of these associations is supported by extensive experimental data linking platelet size with functional activity and prothrombotic potential [4,5]. In this context, elevated MPV may reflect a prothrombotic and pro-inflammatory milieu conducive to cerebral ischemia.

However, it is essential to emphasize that MPV is best interpreted as a marker of association rather than a determinant of outcome. Observational designs dominate the literature, and confounding by comorbid conditions and treatment effects cannot be excluded. Furthermore, MPV values often overlap considerably between patients and controls, limiting discriminatory capacity at the individual level.

Methodological Considerations

One of the principal challenges in MPV research is methodological variability. MPV is sensitive to preanalytical factors such as anticoagulant type, time from venipuncture to analysis, and laboratory instrumentation [19]. Platelet swelling in ethylenediaminetetraacetic acid over time can artificially increase MPV, introducing measurement bias if not carefully controlled.

Additionally, the absence of universally accepted reference ranges and cut-off values complicates comparisons across studies. Although large epidemiological investigations have provided insights into normal MPV distributions in healthy populations, inter-laboratory variability remains substantial [19].

Clinical Implications

From a clinical perspective, MPV offers several attractive features: it is inexpensive, widely available, and routinely reported as part of complete blood counts. These characteristics make it a potentially valuable adjunctive marker in resource-limited settings. When interpreted in conjunction with clinical, imaging, and laboratory data, MPV may contribute to risk stratification and prognostic assessment.

Nevertheless, current evidence does not support the use of MPV as a standalone diagnostic or prognostic tool in ischemic stroke. Its greatest value may lie in multimarker approaches that integrate platelet indices with inflammatory markers, coagulation parameters, and clinical scores.

Future Directions

Future research should prioritize large, prospective, and standardized studies to clarify the temporal dynamics of MPV before, during, and after ischemic stroke. Investigations examining changes in MPV in response to antiplatelet therapy and their relationship with clinical outcomes may also yield clinically relevant insights. Additionally, exploring genetic and molecular determinants of platelet size could enhance understanding of inter-individual variability in MPV and stroke risk.

CONCLUSION

Mean platelet volume is associated with platelet activation and thrombo-inflammatory processes relevant to acute ischemic stroke. Evidence indicates that elevated MPV is associated with stroke risk, greater severity, and less favorable outcomes in selected patient populations, although findings remain heterogeneous. Methodological variability and the influence of comorbid conditions limit its standalone clinical utility. MPV may be most useful as an adjunctive biomarker within a multimodal assessment framework rather than as an independent predictor. Further standardized and prospective studies are required to clarify its prognostic relevance in routine stroke care.

REFERENCES

1. Paciaroni M, Bogousslavsky J. The history of stroke and cerebrovascular disease. Handb Clin Neurol. 2009;92:3–28.
2. Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. Bull World Health Organ. 1980;58(1):113–130.
3. Liu C, Che Y. Retinol-binding protein 4 predicts lesion volume (determined by MRI) and severity of acute ischemic stroke. Neurotox Res. 2019;35(1):92–99.
4. Thompson CB, Jakubowski JA, Quinn PG, Deykin D, Valeri CR. Platelet size as a determinant of platelet function. J Lab Clin Med. 1983;101(2):205–213.
5. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis. 1996;7(2):157–161.
6. Butterworth RJ, Bath PM. The relationship between mean platelet volume, stroke subtype and clinical outcome. Platelets. 1998;9(6):359–364.
7. Tavil Y, Sen N, Yazici HU, Hizal F, Abaci A, Cengel A. Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. Thromb Res. 2007;120(2):245–250.
8. Bath P, Algert C, Chapman N, Neal B; PROGRESS Collaborative Group. Association of mean platelet volume with risk of stroke among individuals with history of cerebrovascular disease. Stroke. 2004;35(3):622–626.
9. Kristensen SD, Bath PM, Martin JF. Differences in bleeding time, aspirin sensitivity and adrenaline between acute myocardial infarction and unstable angina. Cardiovasc Res. 1990;24(1):19–23.
10. Greisenegger S, Endler G, Hsieh K, Tentschert S, Mannhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events? Stroke. 2004;35(7):1688–1691.
11. Tschoepe D, Roesen P, Esser J, Schwippert B, Nieuwenhuis HK, Kehrel B, et al. Large platelets circulate in an activated state in diabetes mellitus. Semin Thromb Hemost. 1991;17(4):433–438.
12. Burstein SA, Downs T, Friese P, Lynam S, Anderson S, Henthorn J, et al. Thrombocytopoiesis in normal and sublethally irradiated dogs: response to human interleukin-6. Blood. 1992;80(2):420–428.
13. Debili N, Massé JM, Katz A, Guichard J, Breton-Gorius J, Vainchenker W. Effects of recombinant hematopoietic growth factors on megakaryocytic differentiation of CD34+ cells. Blood. 1993;82(1):84–95.
14. Ciancarelli I, De Amicis D, Di Massimo C, Pistarini C, Ciancarelli MG. Mean platelet volume during ischemic stroke as a potential pro-inflammatory

biomarker. Curr Neurovasc Res. 2016;13(3):177–183.
15. D'Erasmo E, Aliberti G, Celi FS, Romagnoli E, Vecci E, Mazzuoli GF. Platelet count, mean platelet volume and prognosis in cerebral infarction. J Intern Med. 1990;227(1):11–14.
16. Mayda-Domaç F, Misirli H, Yilmaz M. Prognostic role of mean platelet volume and platelet count in stroke. J Stroke Cerebrovasc Dis. 2010;19(1):66–72.
17. Lok U, Gulacti U, Ekmekci B, Bulut T, Celik M. Predictive and prognostic role of mean platelet volume in first-ever acute ischemic stroke. Neurosciences (Riyadh). 2017;22(2):119–126.
18. Jinna S, Khandhar PB. Thrombocytopenia. StatPearls Publishing; 2023.
19. Demirin H, Ozhan H, Ucgun T, Celer A, Bulur S, Cil H, et al. Normal range of mean platelet volume in healthy subjects. Thromb Res. 2011;128(4):358–360.