Predictive Potential of Platelet Mass Index for 30-Day Mortality in Acute Ischemic Stroke

Akut İskemik İnmede Platelet Kütlesi İndeksinin 30 Günlük Mortaliteyi Tahmin Etme Gücü

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ABSTRACT

Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide, with early mortality risk prediction essential for guiding treatment decisions. Platelet Mass Index (PMI), a composite measure derived from platelet count and mean platelet volume (MPV), has shown promise as a biomarker in cardiovascular conditions. This study aimed to assess the predictive value of PMI for 30-day mortality in AIS patients. This retrospective cohort study included patients diagnosed with AIS who presented to the emergency department of a tertiary hospital between January 1, 2019, and January 1, 2024. The primary outcome was 30-day mortality. To determine the optimal PMI cutoff for predicting mortality, we calculated sensitivity, specificity, and likelihood ratios and the area under the curve (AUC) was obtained for overall diagnostic accuracy. A total of 117 AIS patients were analyzed, with a mean age of 68,2±14,6 years, and 58,1% were female. The 30-day mortality rate was 27,4%, with deceased patients being significantly older than survivors. PMI values were notably lower in deceased patients, and the ROC analysis yielded an AUC of 0,775. The optimal PMI cutoff provided a sensitivity of 71,8% and a specificity of 75%, with higher values associated with decreased survival. PMI may serve as a valuable prognostic tool for predicting 30-day mortality in AIS patients. These findings support the potential utility of PMI in early risk stratification, though further prospective studies are needed to validate its use in diverse clinical settings.

Keywords: Acute ischemic stroke, Mortality, Platelet mass index

ÖZ

Akut iskemik inme (Aİİ), dünya çapında morbidite ve mortalitenin önde gelen nedenlerinden biri olup, erken mortalite risk tahmini tedavi kararlarını yönlendirmek için önemlidir. Platelet Mass İndeks (PMİ), platelet sayısı ve mean platelet volume (MPV) kullanılarak hesaplanan bileşik bir ölçüdür ve kardiyovasküler hastalıklar gibi durumlarda biyomarker olarak umut verici sonuçlar göstermiştir. Bu çalışma, Aİİ hastalarında PMİ'nin 30 günlük mortaliteyi öngörücü değerini değerlendirmeyi amaçlamıştır. Bu retrospektif kohort çalışmasına, 1 Ocak 2019 ile 1 Ocak 2024 tarihleri arasında bir üçüncü basamak hastanenin acil servisine başvuran Aİİ tanısı almış hastalar dahil edilmiştir. Birincil sonlanım noktası 30 günlük mortalite olarak belirlendi. Mortalitenin tahmin edilmesinde optimal PMİ kesiş noktasını belirlemek için duyarlılık, özgüllük ve olasılık oranları hesaplanmış ve genel tanısal doğruluğun ölçülmesi için eğri altındaki alan hesaplanmıştır. Toplamda 117 Aİİ hastası analiz edilmiştir, ortalama yaş 68,2±14,6 yıl olup, hastaların %58,1'i kadındı. 30 günlük mortalite oranı %27,4 olup, ölen hastalar hayatta kalanlardan belirgin şekilde yüksek yaştaydı. Ölen hastalarda PMİ değerleri anlamlı şekilde düşüktü ve EAA 0,775 olarak bulunmuştur. Optimal PMİ kesiş noktası, %71,8 duyarlılık ve %75 özgüllük sağlamakta olup, yüksek değerlerin daha düşük sağkalımla ilişkilendirildiği görülmüştür. PMİ, Aİİ hastalarında 30 günlük mortaliteyi öngörebilecek değerli bir prognostik araç olabilir. Bu bulgular, PMİ'nin erken risk sınıflandırmasındaki potansiyel faydasını desteklemekte olup, farklı klinik ortamlarda kullanımının doğrulanması için ileriye dönük çalışmalar gerekmektedir.

Anahtar kelimeler: Akut iskemik inme, Mortalite, Platelet kütlesi indeksi

Highlights

* This study evaluates the predictive value of Platelet Mass Index for 30-day mortality in acute ischemic stroke patients.
* Platelet Mass Index was found to be a significant predictor, with an AUC of 0.775, sensitivity of 71.8%, and specificity of 75%.
* Platelet Mass Index can serve as an effective prognostic tool for early risk stratification in acute ischemic stroke, aiding clinical decision-making.

The study received approval from the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (decision no: 2024/010.99/10/55, date: 29.11.2024).

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INTRODUCTION

Acute ischemic stroke (AIS) is a leading cause of death and disability worldwide and is considered a significant health issue, particularly in older populations. Globally, approximately 13.7 million stroke cases occur each year, with about 84.4% being ischemic in origin.[1-3] This condition not only decreases individuals' quality of life but also imposes substantial economic and societal burdens. Risk factors such as advancing age, hypertension, diabetes mellitus, dyslipidemia, and atrial fibrillation increase the risk of AIS and play a critical role in the disease's pathophysiology.[4,5] Although these risk factors have been identified, they do not fully account for all AIS cases, and the incidence of stroke is rising, particularly in younger age groups. Early diagnosis and risk prediction in AIS management have thus become crucial for improving patient outcomes.

Platelet mass index (PMI), calculated using platelet count and mean platelet volume (MPV), is considered a biomarker capable of reflecting thrombotic and inflammatory processes.[6-8] The capacity of PMI to indicate levels of thrombotic activity and inflammation in the vascular system suggests its potential as a prognostic marker, especially in cardiovascular events.[9] Given the role of platelets in clot formation in AIS, PMI's predictive power for disease prognosis is noteworthy. Studies in the literature have shown that PMI yields significant prognostic results in critical illnesses.[10]

The aim of this study is to evaluate the potential of PMI in predicting 30-day mortality in patients with acute ischemic stroke.

MATERIALS AND METHODS

Study Design

This study is a monocentric, retrospective cohort analysis conducted on patients presenting with acute ischemic stroke (AIS) to the emergency department of a tertiary hospital between January 1, 2022, and January 1, 2024.

Ethical Considerations

Data collection and analysis were performed following approval from the Kartal Dr. Lütfi Kirdar City Hospital Ethics Committee (decision no: 2024/010.99/10/55, date: 29.11.2024). Given the retrospective nature of the study, the ethics committee waived the requirement for written informed consent.

Population Selection

Patients eligible for inclusion were those aged 18 years or older, presenting with a confirmed diagnosis of AIS based on clinical and radiological findings. Exclusion criteria included patients diagnosed with hemorrhagic stroke, transient ischemic attack (TIA), or other neurological conditions, those with a known history of platelet disorders, patients receiving anticoagulant or antiplatelet therapy, and patients with incomplete data on key clinical and laboratory variables required for analysis.

Data Collection

Data were extracted from the hospital's electronic medical records. Collected data included demographic information (age, sex), clinical characteristics (blood pressure, Glasgow Coma Scale score), and laboratory values (platelet count, mean platelet volume, and derived PMI). Platelet counts and volumes were obtained from the first complete blood count test performed upon admission to the emergency department. PMI was calculated using the formula:

PMI = platelet count × mean platelet volume/ 10,000.[11]

The primary outcome of this study was 30-day mortality, defined as death occurring within 30 days of admission for AIS. Mortality data were obtained through electronic medical records, cross-referenced with the national patient registry, and, if

needed, verified by contacting patients' families.

Analysis

All statistical analyses were performed using SPSS version 30.0 (IBM Corp, Armonk, NY, USA) for clinical and demographic comparisons, and MedCalc version 20.218 (MedCalc Software Ltd., Ostend, Belgium). Descriptive statistics for continuous variables were expressed as means ± standard deviations or medians (interquartile ranges [IQR]) depending on the distribution, while categorical variables were presented as counts (percentages). The normality of continuous variables was assessed using both the Kolmogorov-Smirnov test and visual inspection of histograms. For comparisons between the survivor and deceased groups, Student's t-test was used for normally distributed continuous variables, and the Mann-Whitney U test was employed for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate, based on expected frequencies. The significance level was set at $p<0.05$. Receiver Operating Characteristic (ROC) curve analysis was conducted to assess the diagnostic accuracy. The area under the ROC curve (AUC) was calculated with 95% confidence intervals (CI) using the binomial exact method. The optimal cutoff value was determined using the Youden Index (J = sensitivity + specificity – 1).[12] Sensitivity, specificity, positive likelihood ratio (+LR), and negative likelihood ratio (-LR) were calculated at the optimal cutoff point.

RESULTS AND DISCUSSION

A total of 117 AIS patients were included in the study, with 72.6% (n=85) being survivors and 27.4% (n=32) deceased. The mean age in the deceased group (76.6 ± 16.9 years) was 13 years older than in the survivor group (63.6 ± 11.4 years, 95% CI 6.4 - 19.5, $p<0.001$). There was no statistically significant difference in the proportion of males between the groups (60.0%, n=51 vs. 62.5%, n=20, p=0.805), and smoking status was also similar between survivors and deceased (28.2%, n=24 vs. 28.1%, n=9, p=0.991).

Diabetes mellitus was significantly more frequent in the deceased group (56.2%, n=18) compared to survivors (31.8%, n=27, p=0.015). No statistically significant differences were observed for hypertension (43.8%, n=14 vs. 50.6%, n=43, p=0.509), coronary artery disease (37.5%, n=12 vs. 22.4%, n=19, p=0.09), atrial fibrillation (12.5%, n=4 vs. 3.5%, n=3, p=0.09), or previous TIA or stroke (9.4%, n=3 vs. 2.4%, n=2, p=0.125).

The mean systolic blood pressure in the deceased group (183.2 ± 48.7 mmHg) was 30 mmHg higher (95% CI 14.9 - 45.1) than in the survivor group (153.2 ± 31.1 mmHg, $p<0.001$). No statistically significant differences were observed for diastolic blood pressure (102.1 ± 29.2 mmHg vs. 93.2 ± 20.3 mmHg, p=0.066) or pulse rate (80.6 ± 27.9 bpm vs. 72.2 ± 20.9 bpm, p=0.081).

The Glasgow Coma Scale (GCS) score was significantly lower in the deceased group [median GCS 8.0 (IQR 5.8 - 9.0)] compared to survivors [median GCS 15.0 (IQR 13.0 - 15.0), $p<0.001$].

For laboratory values, the platelet count was significantly lower in the deceased group (180.3 ± 49.4 x10^9/L) compared to the survivors (214.5 ± 52.8 x10^9/L), with a mean difference of 34.2 (95% CI 13.3 - 55.1, p=0.002). The mean platelet volume (MPV) was also significantly lower in the deceased group (8.7 ± 2.5 fL) compared to the survivors (10.5 ± 1.6 fL), with a mean difference of 1.75 (95% CI 0.98 - 2.52, $p<0.001$). There were no statistically significant differences in red cell distribution width (RDW) (15.1 ± 2.5% vs. 15.0 ± 1.9%, p=0.836).

The PMI was significantly lower in the deceased group (1.57 ± 0.61) than in the survivors (2.25 ± 0.65), with a mean difference of 0.68 (95% CI 0.42 - 0.94, $p<0.001$) (Figure 1).

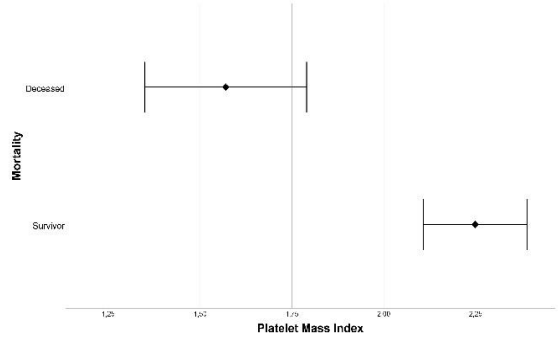

Figure 1. Comparison of Platelet Mass Index between Survivor and Deceased Patients

The cardioembolic etiology was significantly more prevalent in the deceased group (50.0%, n=16) compared to the survivors (22.4%, n=19, p=0.004).

In terms of outcomes, the length of hospital stay was significantly shorter in the deceased group [median 4.0 days (IQR 3.3 - 4.5)] compared to the survivor group [median 6.3 days (IQR 5.1 - 7.0), p<0.001] (Table 1).

Table 1. Clinical and Laboratory Characteristics of Stroke Patients

Parameter	Survivor (n=85)	Deceased (n=32)	p	Mean difference (95% CI)
Demographics				
Age (years)	63.6±11.4	76.6±16.9	<0.001[1]	13 (6.4-19.5)
Sex (male)	51 (60.0%)	20 (62.5%)	0.805[2]	
Smoking	24 (28.2%)	9 (28.1%)	0.991[2]	
Comorbidities				
Diabetes Mellitus	27 (31.8%)	18 (56.2%)	0.015[2]	
Hypertension	43 (50.6%)	14 (43.8%)	0.509[2]	
Coronary Artery Disease	19 (22.4%)	12 (37.5%)	0.09[2]	
Atrial Fibrillation	3 (3.5%)	4 (12.5%)	0.09[3]	
Previous TIA or Stroke	2 (2.4%)	3 (9.4%)	0.125[3]	
Vital Signs				
Systolic Blood Pressure (mmHg)	153.2±31.1	183.2±48.7	<0.001[1]	30 (14.9-45.1)
Diastolic Blood Pressure (mmHg)	93.2±20.3	102.1±29.2	0.066[1]	
Pulse Rate (beats per minute)	72.2±20.9	80.6±27.9	0.081[1]	
Glasgow Coma Scale	15.0 (13.0-15.0)	8.0 (5.8-9.0)	<0.001[4]	
Laboratory Values				
Hemoglobin (g/dL)	11.7±3.8	12.3±4.7	0.445[1]	
Platelet Count (x10^9/L)	214.5±52.8	180.3±49.4	0.002[1]	34.2 (13.3-55.1)
Mean Platelet Volume (fL)	10.5±1.6	8.7±2.5	<0.001[1]	1.75 (0.98–2.52)
Red Cell Distribution Width (%)	15.0±1.9	15.1±2.5	0.836[1]	
Risk Score				
Platelet Mass Index	2.25±0.65	1.57±0.61	<0.001[1]	0.68 (0.42-0.94)
Etiology				
Cardioembolic	19 (22.4%)	16 (50.0%)	0.004[2]	
Outcomes				
Length of Hospital Stay (days)	6.3 (5.1-7.0)	4.0(3.3-4.5)	<0.001[4]	

[1] Student's t-test [2] Chi-square test. [3] Fisher's exact test [4] Mann-Whitney U test CI: Confidence Interval

The diagnostic performance of the PMI in predicting mortality was evaluated using ROC analysis. The area under the ROC curve (AUC) for PMI was 0.775 (95% CI 0.689 - 0.847) (Figure 2).

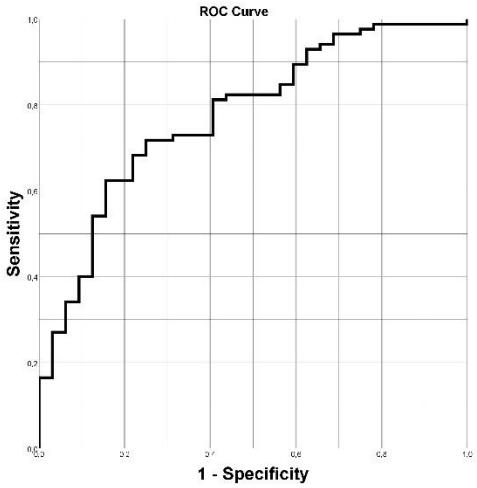

Figure 2. Receiver Operating Characteristic Curve for Platelet Mass Index in Predicting Mortality

The Youden index was 0.467, with an associated criterion of >1.90, yielding a sensitivity of 71.8% (95% CI 61 - 81%) and a specificity of 75% (95% CI 56.6 - 88.5%) (Table 2).

In this study, PMI was found to provide significant predictive value in estimating 30-day mortality risk among AIS patients. The findings suggest that PMI holds potential as a tool for clinical risk stratification.

Table 2. Diagnostic Performance of Mass Platelet Index in Predicting Mortality

Variable	p	AUC (95% CI)	Youden Index J	Associated Criterion	Sensitivity (95% CI)	Specificity (95% CI)
Mass Platelet Index	<0.001	0.775 (0.689-0.847)	0.467	>1.90	71.8 (61-81)	75 (56.6-88.5)

CI: Confidence interval; AUC: Area under the curve

Acute ischemic stroke is a disease with high rates of mortality and complications, imposing a substantial burden on healthcare systems worldwide.[13,14] Prognostic assessment in these patients not only improves survival rates but also facilitates the development of targeted and effective treatment strategies. Early identification of high-risk patients enhances emergency intervention processes and allows for the optimal utilization of intensive care resources. Therefore, the identification of reliable biomarkers for short-term mortality prediction in AIS patients is essential for both patient management and efficient resource allocation. Biomarkers such as PMI have the potential to fulfill this role, contributing to prognostic assessments while adding value to clinical decision-making processes.

The components of PMI, namely platelet count and mean platelet volume (MPV), play a central role in the pathophysiological processes of acute ischemic stroke (AIS). Platelets are fundamental to hemostatic processes as well as inflammatory responses, and high thrombotic activity with clot formation is a critical mechanism in the development of AIS.[15] MPV reflects the activation state of platelets, providing insight into thromboembolic risk. While a high MPV indicates the presence of larger, more reactive platelets, the combination of low platelet count and low MPV observed in AIS patients may reflect both an inflammatory response and thrombotic tendency, contributing to

prognosis prediction.[16] Therefore, the effectiveness of PMI as a mortality predictor in AIS patients aligns with its comprehensive nature as a biomarker reflecting both thrombotic and inflammatory processes.

In this study, it was concluded that the PMI provides significant value in predicting 30-day mortality in patients with AIS. Similar findings exist in the literature; for example, Mohamed et al. demonstrated that MPV and PMI are effective in predicting short-term outcomes in AIS patients, with MPV acting as an independent predictor.[17]. Similarly, Dağar et al. reported that PMI is associated with prognosis in patients with hemorrhagic stroke, although its predictive power for 30-day survival is limited.[18] The data from these studies highlight the clinical importance of evaluating PMI as a prognostic marker in AIS patients.

CONCLUSION AND RECOMMENDATIONS

This study suggests that PMI could be a valuable prognostic biomarker for predicting 30-day mortality in patients with AIS. Our findings indicate that PMI, as a composite index reflecting both platelet count and platelet size, may help clinicians stratify risk and guide early intervention strategies in AIS management.

Limitations

This study has several limitations. First, its retrospective design may introduce bias, as data were collected from existing medical records, which might lack some details relevant to prognosis. Second, as a single-center study conducted in a single center, the generalizability of our findings to other populations or healthcare settings may be limited. Finally, while PMI demonstrated potential as a predictor of 30-day mortality, prospective studies with larger, diverse patient populations are needed to validate these results and establish clinical thresholds.

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Conflict of interest

None

Author Contributions

The concept and design of the study were developed by İ.U. and N.B. Data acquisition, as well as the analysis and interpretation of the results, were carried out by İ.U. and N.B. Statistical analysis was performed by İ.U., who also drafted the manuscript. İ.U. and N.B. were responsible for the critical revision of the manuscript for important intellectual content. Both authors contributed to the final approval of the manuscript and supervised the study. All authors read and approved the final version of the manuscript.

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