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Trombosit İndekslerinin Trombotik ve Embolik İskemik İnme Ayırımındaki Rolü

Platelet Indices in Distinguishing Thrombotic vs Embolic Ischemic Stroke

Süleyman Alpar[1], Muhammed Furkan Ozden[2], Ali Cankut Tatliparmak[3], Gülbin Aydoğdu Umaç[4], Sarper Yılmaz[5*]

[1]İstanbul Beykent University, Department of Emergency Medicine, İstanbul /Türkiye
[2]Arnavutkoy State Hospital, Department of Emergency Medicine, İstanbul /Türkiye
[3]Uskudar University Faculty of Medicine, Department of Emergency Medicine, İstanbul /Türkiye
[4]İzmir City Hospital, Department of Emergency Medicine, İzmir/Türkiye
[5] Kartal Dr. Lutfi Kirdar City Hospital, Department of Emergency Medicine, İstanbul /Türkiye

E-mail: suleymanalpar@gmail.com, furkanozden@gmail.com, alicankut.tatliparmak@uskudar.edu.tr, dr.gulbinaydogdu@gmail.com, sarperyilmaz08@gmail.com

ORCID ID: 0000-0002-8509-0660
ORCID ID: 0000-0003-1027-0015
ORCID ID: 0000-0002-6729-5021
ORCID: 0000-0002-9874-0343
ORCID: 0000-0001-8166-659X

*Sorumlu Yazar / Corresponding Author: Sarper Yılmaz
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Öz

Giriş ve Amaç: Kritik bir klinik tablo olan iskemik inme, trombotik ve embolik alt tipler olarak sınıflandırılabilir. Bu alt tipler arasındaki trombosit indekslerindeki farklılıkların anlaşılması, önemli bilgiler sağlayabilir.

Gereç ve Yöntemler: Bu kesitsel çalışmaya, acil serviste akut iskemik inme tanısı almış hastalar dahil edilmiştir. Trombotik ve embolik alt tipler; demografik özellikler, eşlik eden hastalıklar, kan test sonuçları ve trombosit indeksleri açısından karşılaştırılmıştır. Çalışmanın birincil çıktısı, trombotik ve embolik iskemik inme hastaları arasında trombosit indekslerinin karşılaştırılmasıdır.

Bulgular: Çalışmaya toplam 233 hasta dahil edilmiş olup, bunların 130'u (%55,8) trombotik, 103'ü (%44,2) embolik iskemik inme tanısı almıştır. Trombotik inme hastaları daha ileri yaşta bulunmuş (p=0,01) ve koroner arter hastalığı sıklığı daha yüksek saptanmıştır (p=0,019). Öte yandan, embolik inme hastalarında atriyal fibrilasyon oranı anlamlı derecede daha yüksek bulunmuştur (p<0,001). Trombotik inme olgularında trombosit dağılım genişliği (PDW) [17 (16,3 – 17,8) vs. 13,7 (11,8 – 16), p<0,001] ve ortalama trombosit hacmi (MPV) [10,8 ± 1,4 vs. 9,71 ± 1,24, p<0,001] değerleri, embolik inme olgularına kıyasla anlamlı derecede yüksek bulunmuştur. Trombosit sayısı (p=0,352) ve plateletkrit (p=0,106) değerleri ise gruplar arasında anlamlı farklılık göstermemiştir.

Sonuç: Bu çalışma, trombotik ve embolik iskemik inme alt tipleri arasında belirgin trombosit indeks desenleri olduğunu ortaya koymaktadır. PDW ve MPV değerleri trombotik inme hastalarında daha yüksek saptanırken, trombosit sayısı ve plateletkrit açısından anlamlı fark gözlenmemiştir. Elde edilen bulgular, PDW ve MPV değerlerindeki artışın trombotik inmelerde artmış trombosit aktivasyonu ile ilişkili olabileceğini düşündürmektedir.

Anahtar kelimeler: İskemik inme, trombotik inme, embolik inme, trombosit indeksleri, inme sınıflandırması, ortalama trombosit hacmi, trombosit dağılım genişliği, inme patofizyolojisi

Abstract

Aim; Ischemic stroke, a critical condition, can be categorized into thrombotic and embolic subtypes. Understanding the differences in platelet indices between these subtypes can provide valuable insights.

Method; This cross-sectional study included patients diagnosed with acute ischemic stroke in the emergency department. Thrombotic and embolic subtypes were compared in terms of demographics, comorbidities, blood results and platelet indices. The primary outcome of the study was comparison of platelet indices between thrombotic and embolic ischemic stroke patients.

Results; The study included a total of 233 patients, with 130 (55.8%) diagnosed with thrombotic ischemic stroke and 103 (44.2%) with embolic ischemic stroke. Thrombotic stroke patients were older in age ($p=0.01$), had higher rates of coronary artery disease ($p=0.019$). But the embolic stroke patients and higher rate of atrial fibrillation ($p<0.001$). Thrombotic stroke cases demonstrated significantly higher platelet distribution width (PDW) values (17 [16.3 – 17.8] vs. 13.7 [11.8 – 16], $p < 0.001$) and mean platelet volume (MPV) values (10.8 ± 1.4 vs. 9.71 ± 1.24, $p < 0.001$) compared to embolic stroke cases. The platelet count ($p=0.352$) and plateletcrit ($p=0.106$) did not differ significantly among groups.

Conclusion; This study reveals distinctive platelet index patterns between thrombotic and embolic ischemic stroke subtypes. While PDW and MPV were higher in thrombotic patients, platelet count and plateletcrit were not significantly different between groups. The findings suggest a potential association between elevated PDW and MPV values and heightened platelet activation in thrombotic strokes.

Keywords: Ischemic stroke, thrombotic stroke, embolic stroke, platelet indices, stroke classification, mean platelet volume, platelet distribution width, stroke pathophysiology

1. Introduction

Stroke, a medical condition acknowledged as an ailment throughout history, has endured for over two millennia. However, as per the 2022 report published by the World Stroke Organization (WSO), it currently maintains its position as the second leading cause of global mortality and holds the third rank in terms of Disability-Adjusted Life Years (DALY), a metric encompassing both fatalities and disability rates [1]. Despite advancements in medical technology, the formulation of societal strategies targeting strokes, and substantial economic investments, the aforementioned report underscores a noteworthy surge in stroke cases between 1990 and 2019. Within this temporal span, there was a conspicuous 70.0% upswing in the incidence of stroke cases and a corresponding 43.0% escalation in stroke-associated fatalities. While the prevalent explanation attributes this rapid escalation to an aging demographic, it is pertinent to note that the impact extends to the younger population in developing nations as well [2]. These rapid upsurges necessitate a comprehensive reevaluation, demanding innovative paradigms and policies that encompass medical, socio-cultural, and economic dimensions, to effectively address the multifaceted aspects of mortality, morbidity, and impaired functionality in stroke patients. This exigency further underscores the imperative of delving more profoundly into the intricate nuances of this clinical landscape.

While the term "stroke" is clinically applied based on patient presentations, it fundamentally encapsulates a clinical framework rooted in diverse etiological underpinnings. In contrast to hemorrhagic and subarachnoid bleed-induced occurrences, the vast majority of cases—approximately 90%—originate from an ischemic genesis. However, under closer pathophysiological scrutiny, ischemic antecedents can be parsed into three elemental subtypes: thrombosis (atherothrombosis), emboli (thromboemboli), and systemic hypoperfusion [3]. Thrombotic strokes transpire due to the aftermath of a pathological process instigating thrombus formation within an artery, resulting in diminished distal blood flow (low flow). Conversely, embolic strokes delineate impediments arising from extraneous particles, stemming from disparate locales, which obstruct arterial access to distinct cerebral regions [4]. Irrespective of contributory etiologic factors, the prospects of restoring an individual's pre-incident state post-stroke hinge on a confluence of factors. These encompass timely patient presentation, swift embrace of diagnostic and therapeutic modalities, precise clinical and radiological evaluations, and the collaborative endeavors of a diversified cohort of specialists encompassing emergency medicine practitioners, neurologists, and interventional radiologists [5]. Although the initial patient encounter transpires within the confines of the Emergency Department—signifying a pivotal locus during the critical "golden hours" of stroke management—the holistic and efficacious management of stroke pivots on an accurate apprehension of its variegated subtypes. Moreover, the crux of the matter resides in preemptive measures preceding the onset of stroke, thereby engendering a proactive milieu for averting its incidence.

A thorough examination of the existing literature reveals a plethora of studies focused on distinguishing between hemorrhagic and ischemic strokes. Notably, the thrombotic and embolic subtypes of ischemic stroke, despite harboring distinct etiologies, outcomes, and treatment strategies, are unfortunately underrepresented in the body of research concerning their management [6, 7]. Clinicians, however, employ a range of diagnostic and investigative approaches, including patient symptomatology, to effectively differentiate between these two subtypes. The objective of these methods is to elucidate the underlying cause of occlusion post-restoration of intravascular flow, thereby preemptively addressing the occurrence of subsequent occlusions (re-infarction) [8]. Acknowledging the heightened mortality rates and comprehensive physical, cognitive, and emotional repercussions experienced by stroke patients, there has been a growing emphasis on research aimed at prognosticating early-stage outcomes. In this context, it has been posited that a multitude of factors influence stroke prognosis, encompassing stroke subtype, patient age, stroke severity, and infarction localization [9]. Notably, recent literature has examined the relationship between platelet indices and both ischemic and hemorrhagic stroke etiologies, yet a noticeable gap exists in research that elucidates the correlation between thrombocyte indices and specific ischemic stroke subtypes [10–12].

As commonly recognized, platelets serve as initiators of hemostatic plug formation, exerting a pivotal influence along the coagulation cascade and representing a critical constituent in thrombotic processes. These platelets, subject to activation triggered by factors such as thrombosis rupture and inflammation, occupy a particularly crucial role in the context of thrombosis [13, 14]. While the function of platelets in atherosclerosis pathogenesis and their incorporation as integral components of atheromatous plaques are comprehensively understood, their involvement in the fundamental pathologies underpinning ischemic stroke etiology, namely atherothrombosis and thromboemboli, remains an area warranting further illumination. In atherothrombosis, platelets contribute to both the structural narrowing of the vascular lumen within atheromatous plaques and the formation of occlusive clots in the constricted lumen. In contrast, in the realm of thromboembolism, thrombi originating from diverse anatomical locales take on the role of impeding central flow by occluding the vascular lumen [15]. At this juncture, a salient differentiation comes into focus: atherothrombosis, directly associated with vascular sources, impacts central flow, whereas thromboembolism predominantly emerges from peripheral vessels. Thus, it becomes evident that ischemic stroke manifests shared and distinctive etiologies within its two subtypes.

Given their limited practical application in daily clinical settings, methods like flow cytometry or platelet aggregometry have led to ongoing reliance on complete blood count parameters to access information about platelet function and structure. Among these parameters are indicators such as platelet count, mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW) [16–18]. These indicators provide a means to assess the biochemical and morphological characteristics of platelets, while also serving the purpose of understanding distinctions between the thrombotic and embolic subtypes in individuals presenting with acute ischemic stroke. Unveiling these differences holds particular importance as it contributes to an enhanced understanding of the conditions, thereby facilitating the development of efficacious and individualized therapeutic approaches. In light of this context, the primary aim of this study is to compare the platelet indices of thrombotic and embolic subtypes in patients who present to the emergency department with a confirmed diagnosis of ischemic stroke, ultimately shedding light on potential divergences.

2. Methods

2.1. Study Design and Settings:

This study was designed as an observational cross-sectional investigation conducted at a single center. The primary aim of the study is to compare platelet indices in thrombotic and embolic subtypes of acute ischemic stroke patients who presented at the emergency department. Ethical approval for the study was obtained from the Medipol Non-Invasive Clinical Research Ethics Committee (Approval no: E-10840098-604.01.01-1306, Date: February 20, 2023). All research protocols were followed in accordance with the Helsinki Declaration, and written consent was obtained from all participating patients or their next of kin.

2.2. Selection of Participants:

The study included patients aged 18 and above, diagnosed with acute ischemic stroke, who presented to the Arnavutköy State Hospital Emergency Department between January 1, 2018, and December 31, 2022. Patients with etiologies other than cardioembolic or large artery atherosclerosis, as per the TOAST classification (such as small vessel occlusion [lacunar infarct], strokes attributed to other etiologies, or undetermined etiology ischemic strokes), were not included in the study [19].

2.3. Data Collection:

The demographic characteristics of participating patients (age, gender), vital parameters at admission (blood pressure, pulse rate, peripheral oxygen saturation), existing comorbidities (hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation), medication history (antiplatelet, anticoagulant medications), infarct areas based on MRI results conducted in the emergency department, complete blood count parameters (white blood cell

[WBC] count, neutrophil count, lymphocyte count, hemoglobin, red cell distribution width [RDW], albumin, C-reactive protein [CRP], urea, creatinine, lactate dehydrogenase [LDH]), blood gas parameters (actual base excess [aBE], anion gap, bicarbonate, lactate), and platelet indices (platelet count, MPV, PCT, PDW were documented as part of the study. All blood parameters were assessed based on test results obtained at the time of patients' admission to the emergency department

2.4. Statistics

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS v29., IBM Corp. Armonk, NY). Descriptive statistics were employed to characterize the data, using counts and percentages for categorical variables and mean ± standard deviation or median [IQR 25th-75th] values for continuous variables. The normal distribution of the data was assessed through the Shapiro-Wilk test and histograms. Inter-group comparisons employed the Pearson chi-square test for categorical variables (Fisher's exact test when conditions were not met), and Student's t-test or Mann-Whitney U test for continuous variables. All comparisons were performed two-sided, with a significance level of <0.05 considered as the alpha level of significance.

3. Results and Discussion

3.1. Results

A total of 233 patients were enrolled in the study, with the patient population divided into two distinct groups based on the subtypes of ischemic stroke: embolic (44.2%, n=103) and thrombotic (55.8%, n=130). The median age of the thrombotic group (72 [IQR 62.75-77]) was observed to be significantly higher compared to the embolic group (64 [IQR 56-75]) (p=0.01). Sex distribution between the groups did not reveal any statistically significant differences (p=0.124) (Table1). Notably, no significant disparities were identified in mean systolic and diastolic blood pressure within the two groups (p=0.984, p=0.711, respectively). Likewise, median pulse rate and peripheral oxygen saturation exhibited no statistically significant differences across the groups (p=0.584, p=0.062, respectively).

Concerning comorbidities, the prevalence of hypertension was not significantly different between the embolic (63.1%, n=65) and thrombotic (74.6%, n=97) groups (p=0.058). Similarly, the incidence of diabetes mellitus comorbidity demonstrated no statistically significant difference between the embolic (54.4%, n=56) and thrombotic (51.5%, n=67) subtypes (p=0.667). However, a notable finding was the significantly higher frequency of coronary artery disease in the thrombotic group (43.1%, n=56) compared to the embolic group (28.1%, n=29) (p=0.019). Furthermore, atrial fibrillation prevalence was markedly higher in the embolic group (35.9%, n=37) compared to the thrombotic group (9.4%, n=12) (p<0.001).

Medication usage data indicated that the rate of antiplatelet medication usage was notably higher in the thrombotic group (40.8%, n=53) than in the embolic group (23.3%, n=24) (p=0.005), while no statistically significant difference was observed in terms of anticoagulant medication usage between the groups (p=0.534). The incidence of infarcts larger than 4 cm was significantly higher in the thrombotic group (35.5%, n=46) than in the embolic group (2.9%, n=3) (p<0.001).

Moving to laboratory parameters, analyses revealed no statistically significant differences between the groups in terms of median white blood cell (WBC) count, neutrophil count, and lymphocyte count (p=0.529) (Table 2). The mean hemoglobin levels were comparable between the embolic group (13.9±1.6 g/dL) and the thrombotic group (14±1.9 g/dL) (p=0.652). An interesting observation was the statistically significant higher median red cell distribution width (RDW) in the embolic group (14 [IQR 13.3-14.8]) compared to the thrombotic group (13.5 [IQR 13.2-14.5]) (p=0.043). Analyses of median albumin, CRP, and urea values did not reveal any statistically significant differences between the groups (p=0.729, p=0.663, p=0.284, respectively). Median creatinine levels were found to be significantly higher in the thrombotic group (1 [IQR 0.8-1.2] mg/dL) compared to the embolic group (0.7 [IQR 0.6-1] mg/dL) (p<0.001). No significant disparities were observed between the groups in terms of median lactate dehydrogenase (LDH), actual base excess (aBE), anion gap, bicarbonate, and lactate (p=0.987, p=0.297, p=0.242, p=0.159, p=0.541, respectively).

Turning our attention to platelet indices, the median platelet count in the embolic group was 271 [IQR 167-356] x 103/µL, while in the thrombotic group, it was 244 [IQR 163-325] x 103/µL, with no statistically significant difference (p=0.352) (Table 3). The mean mean platelet volume (MPV) in the embolic group was 9.71±1.24 fL, which was notably lower than the value in the thrombotic group (10.8±1.43 fL), with a statistically significant difference of -1.09 (95% CI 0.75-1.45) (p<0.001). There were no statistically significant differences between the groups in terms of median plateletcrit value (p=0.106). The median platelet distribution width (PDW) was significantly lower in the embolic group (13.7 [IQR 11.8-16]%) than in the thrombotic group (17 [IQR 16.3-17.8]%), with a statistically significant difference (p<0.001)

Table 1. Demographic and clinical characteristics of embolic and thrombotic ischemic stroke patients

Parameters	Embolic (n=103, 44,2%)	Thrombotic (n=130, 55,8%)	*p* value
Age (years)	64 (56-75)	72 (62.75-77)	0.01
Sex (female)	54 (52.4%)	55 (42.3%)	0.124
Systolic BP (mmHg)	159±32	159±30	0.984
Diastolic BP (mmHg)	89±18	88±13	0.711
Pulse Rate	84 (74-91)	82.5 (73.8-92.3)	0.584
Oxygen saturation	97 (95-98)	97 (95-99)	0.062
Hypertension	65 (63.1%)	97 (74.6%)	0.058
Diabetes Mellitus	56 (54.4%)	67 (51.5%)	0.667
Coronary Artery Disease	29 (28.1%)	56 (43.1%)	0.019
Atrial Fibrillation	37 (35.9%)	12 (9.4%)	<0.001
Antiplatelet therapy	24 (23.3%)	53 (40.8%)	0.005
Anticoagulant therapy	19 (18.4%)	20 (15.4%)	0.534
Infarct size >4cm	3 (2.9%)	46 (35.4%)	<0.001

Values are presented as mean ± standard deviation, median (interquartile range), or count (percentage) as appropriate. BP: Blood pressure

Table 2. Comparison of laboratory parameters between embolic and thrombotic stroke patients.

Parameters	Embolic (n=103, 44,2%)	Thrombotic (n=130, 55,8%)	*p* value
WBC (x10^3 cells/μL)	8.3 (7.6-10)	8.3 (6.4-11.1)	0.529
Neutrophil Count (x10^3 cells/μL)	5.2 (4.2-6.3)	5.3 (3.8-8.5)	0.862
Lymphocyte Count (x10^3 cells/μL)	2.1 (1.4-3)	2 (1.6-2.6)	0.501
Hemoglobin (g/dL)	13.9±1.6	14±1.9	0.652
Red cell distribution width (%)	14 (13.3-14.7)	13.5 (13.2-14.5)	0.043
Albumin (g/dL)	4.2 (3.9-4.5)	4.3 (4.1-4.4)	0.729
C-reactive protein (mg/L)	4.9 (1.7-18.2)	4.2 (1.9-10.4)	0.663
Urea (mg/dL)	33.9 (29.1-50.1)	38.6 (29.9-48.3)	0.284
Creatinine (mg/dL)	0.7 (0.6-1)	1 (0.8-1.2)	<0.001
Lactate dehydrogenase (U/L)	196 (180 - 273)	192 (155.5-226.5)	0.987
Actual base excess (mEq/L)	-1 (-4.8 - 2.6)	-0.3 (-2.7 - 1.3)	0.297
Anion gap (mEq/L)	15 (11.6 - 16.5)	14.9 (14.1-17.4)	0.242
Bicarbonate (mEq/L)	24.7 (20.7 - 27.6)	25.2 (22.8 - 27.4)	0.159
Lactate (mmol/L)	1.87 (1.46-2.95)	1.61 (1.37-3.34)	0.541

Values are presented as mean ± standard deviation, median (interquartile range), or count (percentage) as appropriate.

Table 3. Comparison of platelet indices between embolic and thrombotic stroke patients

	Embolic (n=103, 44,2%)	Thrombotic (n=130, 55,8%)	*p* value
Platelet count (x10^3 cells/μL)	271 (167-356)	244 (163-325)	0.352
Mean platelet volume (fL)	9.71±1.24	10.8±1.43	<0.001
Plateletcrit (%)	0.25 (0.21-0.29)	0.26 (0.22-0.30)	0.106
Platelet distribution width (fL)	13.7 (11.8-16)	17 (16.3-17.8)	<0.001

Values are presented as mean ± standard deviation, median (interquartile range)

3.2. Discussion

In the realm of ischemic stroke research, a subset of studies has honed in on unraveling the distinct pathophysiological nuances characterizing diverse stroke subtypes, directing their focus towards nuanced aspects of stroke categorizations [20, 21]. Nevertheless, our existing literature presents only a handful of studies delving into the broader involvement of platelets and platelet indices—an integral facet of hemostasis—across an array of pathophysiological processes extending beyond hemostasis. These encompass congenital and adaptive immune responses, atherosclerosis, angiogenesis, lymphatic vessel development, liver regeneration, and tumor metastasis [22, 23]. Concurrently, perusal of investigations scrutinizing the influence of "stroke subtypes" on stroke patient prognosis reveals an ongoing ambiguity regarding whether hematological traits exert comparable influence across all forms of ischemic stroke.[24] Notably, the prevailing discourse in research has chiefly centered around dissimilarities between ischemic and hemorrhagic stroke cohorts, stemming from the understanding that thrombogenesis factors intertwined with the platelet system orchestrate the inception and evolution of atherogenesis and clot formation [25]. However, a noteworthy gap exists in the current literature—a dearth of studies probing the interplay of platelet indices between thrombotic and embolic subtypes within the realm of ischemic stroke.

The exploration of the pathophysiology underlying intravascular thrombus formation traces its roots back to the early 1900s, laying the groundwork for Virchow's triad theory, which encompasses three fundamental factors: intravascular endothelial injury, alterations in hemodynamics, and a heightened state of hypercoagulability [26]. As Virchow sought to elucidate the causes of thromboembolism, he posited that arterial embolisms often stemmed from peripheral or distant thrombosis. The hypercoagulability aspect of the triad entails endeavors to comprehend the mechanisms initiating peripheral clotting or to pinpoint specific conditions that facilitate this phenomenon. In the contemporary context, this theory significantly shapes the foundational dynamics of various thrombosis-related disorders, including thromboembolic strokes. Within the realm of atherothrombotic strokes, Virchow's theory of intravascular endothelial injury comes to the fore, with the other two components—hemodynamic alterations and hypercoagulability—converging with the primary element to yield their respective effects. Essentially, while ischemic strokes manifest with distinct etiological triggers, both subtypes share a common thread in their pathophysiology: the presence of thrombotic occlusion. However, unraveling the nuances between these etiologies by scrutinizing variations in platelet indices holds immense significance. In this light, the analysis of platelet indices in ischemic stroke subtypes plays a pivotal role in advancing our understanding of these diverse pathophysiological mechanisms and in laying the groundwork for future personalized therapeutic strategies.

One of the early investigations conducted on stroke patients involves assessing complete blood count parameters, such as red cell distribution width (RDW) and mean platelet volume (MPV), to predict prognosis [27–29]. Platelets play a vital role in the early thromboembolic phase of ischemic stroke, contributing to coagulation, inflammation, thrombosis, and atherosclerosis processes. Numerous researchers propose that both MPV and PDW act as indicators of factors contributing to thrombosis and stroke, as these indices can reflect the release of thromboxane A2 and high-expressing glycoprotein Ib and glycoprotein IIb / IIIa receptors, which are indicative of platelet activation [30]. In our study, we observed a significant increase in MPV in the thrombotic stroke subtype compared to embolic stroke. MPV is recognized as an indicator of platelet activity and aggregation capacity. Larger platelets have a higher likelihood of contributing to thrombotic events and are associated with conditions like atherothrombotic disorders [31]. Consequently, our study investigated the expected link between thrombotic stroke and a higher MPV value than embolic stroke. However, a study by Noris and his colleagues emphasized the considerable variability in the role of MPV in diagnosing and predicting disease prognosis due to factors like platelet count, gender, age, and ethnicity. The lack of standardized measurement methodologies also hampers the determination of an individual patient's normal range [32]. Our study found a statistically significant difference in MPV between the two groups, but the clinical implications await further clarification.

Within the existing body of literature, an additional hypothesis has emerged to elucidate the connection between thromboembolism and mean platelet volume (MPV). This proposition suggests that molecules present in the thrombin and thrombus formation region activate circulating platelets, leading to an increase in their volume and consequently resulting in elevated MPV values. Thus, it posits that a high MPV value is an outcome of vascular occlusion rather than a causal factor for occlusion itself [33]. n a comprehensive systematic review and meta-analysis conducted by Shemirani et al., the role of MPV in acute stroke patients was scrutinized, yielding findings that lend credence to this hypothesis. Their investigation demonstrated a noteworthy elevation in MPV values among stroke patients in comparison to healthy controls (mean difference: 0.51 fL; 95% confidence interval: 0.27-

0.74 fL). Furthermore, the outcomes of analyses specifically targeting different ischemic stroke subtypes corroborated these findings, albeit differing from our study (mean difference: 0.55 fL; 95% CI: 0.29-0.81 fL) [34]. Our study, in contrast, presents two scenarios that both corroborate and challenge this hypothesis. These contrasting circumstances unfold as follows: Primarily, our investigation did not yield MPV values surpassing the previously established average range (7.2 to 11.7 fL) documented in healthy individuals within the Turkish populace, regardless of the stroke subtype [35]. Furthermore, in light of the shared outcome of vascular occlusion in both stroke subtypes, irrespective of etiology, the alignment of average values across the two groups and their alignment with the range observed in healthy individuals contradicts the conjecture of "Elevated MPV as a consequence, not a cause of vascular occlusion." This incongruity may be particularly associated with the heightened prevalence of atrial fibrillation (AF) among embolic patients. Remarkably, Weymann and co-authors underscored in their research that patients with AF exhibited elevated MPV values in comparison to other patient groups [36]. An additional corroborating observation for the hypothesis surfaced within our study: patients with an infarct area exceeding 4 cm in size demonstrated significantly augmented MPV values within the context of the thrombotic stroke subtype.

In the domain of investigating the association between mean platelet volume (MPV) and embolic events, it is apparent that the prevailing focus has been on studies primarily examining venous thromboembolism [37]. However, conclusive evidence directly assessing the correlation between thromboemboli and stroke through the lens of MPV remains notably absent in the existing literature. While several studies have delved into this matter, certain research endeavors have underscored the potential predictive role of platelet-related factors in the genesis of atrial fibrillation (AF), positing that these factors could contribute to the onset of AF.[36] In the context of our present study, an intriguing observation surfaces—embolic stroke patients exhibit a heightened prevalence of AF. Remarkably, the MPV values within this subgroup align with the average range observed in the general healthy population and, intriguingly, even trend lower than the mean MPV values exhibited by their thrombotic stroke counterparts [35].

Within the context of this investigation, a distinct feature between the two subcategories of ischemic stroke is evident in the analysis of platelet distribution width (PDW), a parameter recognized for its indication of activated platelets. Notably, this study delves into PDW, revealing a notably elevated value among patients with thrombotic strokes[30]. Research has unveiled connections of PDW with conditions such as hypertension, heart failure, and upper gastrointestinal bleeding [38–40]. While prior research has established the correlation between mean platelet volume (MPV) and stroke outcomes, certain studies in the field of previous thromboembolic disorders have occasionally disregarded a platelet index like PDW when compared to MPV [30, 41, 42]. In fact, some studies have even proposed that PDW might serve as a more sensitive marker for platelet size variation, offering more comprehensive insights into thrombocyte reactivity compared to MPV, particularly concerning carotid stenosis [43]. Consistent with the proposition of Gao and colleagues, heightened PDW values could signify an increased production of larger, more active platelets, while lower PDW values might suggest the presence of previously formed thromboses [30]. In this context, an alignment emerges between our study and these findings. While thrombo-emboli that arise from ischemic strokes typically originate from regions of thrombosis distal to the central circulation, occlusions associated with atherothrombosis generally stem from recently formed thromboses within the central circulation. Given these insights, a key inference from our study suggests that higher PDW values are expected when identifying cases of the atherothrombotic stroke subtype. Nevertheless, it is crucial to acknowledge that parameters like age, atrial fibrillation, and infarct area could potentially influence PDW and should not be overlooked when interpreting the outcomes of these two subtypes of ischemic stroke.

The management of stroke patients within the emergency department aligns with the triage, diagnosis, and monitoring protocols recommended in stroke management guidelines. The updated 2022 module on Acute Stroke Management, in its seventh edition, underscores the significance of promptly addressing triage, assessment, vital parameter evaluation, and expeditious acute blood tests. As an integral facet of the initial assessment, rapid evaluation of electrolytes, random glucose levels, complete blood count (CBC), coagulation profile (INR, aPTT), and creatinine levels is advocated [44]. This insight reflects the presence of research that highlights the potential for parameters like PDW and MPV to undergo changes following a patient's presentation at the emergency department [45]. At this juncture, comprehending the evolution of these parameters during acute stroke, particularly in hypercoagulable contexts, assumes paramount importance. This study is grounded in the immediate test outcomes procured upon the patient's admission to the emergency department. The notable distinctions observed in PDW between two distinct ischemic stroke subtypes are attributed to this setting. However, while this divergence holds promise as compelling evidence for delineating the

two ischemic stroke subtypes, its validation necessitates broader-scale investigations.

4. Limitations

While this study has yielded significant findings, it is important to acknowledge certain limitations that might impact the interpretation of the results and the generalizability of the study's findings. There could be uncontrolled variables that, due to the study's design and methodology, could not be fully accounted for. Thus, a cautious approach is needed when interpreting the results, considering potential alternative explanations. It is worth noting that the study's single-center nature might limit the generalizability of the results to different geographical or healthcare settings. Although the study focused on platelet indices, it omitted consideration of other pertinent biological factors that could impact the outcomes, which is a point to be mindful of.

5. Conclusion

This study has provided valuable insights into the pathophysiology of thrombotic and embolic ischemic strokes in patients presenting with acute ischemic stroke at the emergency department. The findings have elucidated the impact of both etiological factors on platelet indices. Notably, in the thrombotic ischemic stroke subtype, both PDW and MPV values exhibited a statistically significant increase when compared to the embolic ischemic stroke subtype. These results emphasize the differential effects of these two etiologies on platelet activation and aggregation.

6. References:

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