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Original Article

Relationship Between Platelet Indices with Severity of Hemorrhage, Prognosis and Scoring Systems for Nonvariceal Upper GIS Bleeding

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ABSTRACT

Objective: We aimed to determine the place of platelet indices [platelet (PLT), platelet crit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW)] in predicting the severity of hemorrhage and prognosis in non-variceal upper gastrointestinal system (GIS) bleeding.

Methods: The study included 210 patients hospitalized due to non-variceal upper GIS bleeding. Full blood count values were recorded when the patients were admitted to hospital, on the 5th day and at discharge. The Rockall and Blatchford scores were calculated according to the clinical and endoscopic findings of patients and Forrest classification was made.

Results: Blatchford and Rockall scores for patients whose hospitalization period is more than 5 days and who require transfusion was higher than the group without ($p<0.001$). When the groups with a hospital stay of more than 5 days and less than 5 days and the groups with and without transfusion were compared, no significant difference was found between PLT, PCT, MPV and PDW values ($p>0.05$). There was a very weak positive correlation between MPV at time of admission and MPV and PDW values at discharge with Blatchford score. There was a very weak positive correlation between MPV and PDW values at discharge with Rockall score. To predict the risk of admission of 5 days or more, forward selection logistic regression was performed and platelet indexes were not identified to be independent predictors.

Conclusion: It was observed that platelet indices were not independent predictors in determining bleeding severity and prognosis in upper GIS hemorrhage, but MPV and PDW were very weakly related to scoring systems.

INTRODUCTION

Upper gastrointestinal (GI) hemorrhage is one of the most frequent causes of emergency department visits and represents a significant clinical challenge, with mortality rates reported to be as high as 10% despite advances in diagnostic and therapeutic endoscopic methods.[1,2] The most common cause of GI bleeding is hemorrhage from the upper part of the GI tract, located proximal to the ligament of Treit.[3] The incidence of GI hemorrhage in males is approximately twice that in females.[4]

While GI bleeding risk scoring is generally based on treatment requirements, some scoring systems take into account the probability of mortality and recurrent hemorrhage. The Rockall score includes age, the presence of shock, comorbidities, endoscopic diagnosis, and signs of recent bleeding observed during endoscopy.[5] The Blatchford score uses levels of urea and hemoglobin, systolic blood pressure, pulse rate, and the presence of melena, syncope, hepatic disease, and heart failure to determine whether intervention is required to control the bleeding.[6] Early identification of this clinical problem, which is associated with high mortality and morbidity, and the assessment of bleeding severity and risk are important for deciding on hospitalization to continue treatment and managing patient costs. The use of low-cost and non-invasive parameters in daily practice to guide the management and clinical decision-making processes for patients with up-

per GI bleeding offers great advantages.[7,8] Platelet count (PLT), plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) —known collectively as platelet indices — meet these criteria and are routinely measured as part of a complete blood count.

In our study, we aimed to investigate the role of non-invasive, low-cost platelet indices (PLT, PCT, MPV, and PDW) in diagnosing GI bleeding and in predicting bleeding severity and prognosis. Furthermore, we evaluated the correlation between these platelet indices and the Rockall and Blatchford scores.

MATERIALS AND METHODS

This retrospective study included 210 patients admitted to the internal medicine clinic with a diagnosis of non-variceal upper GI hemorrhage between 2016 and 2019. The study protocol was approved by the Taksim Clinical Research Ethics Committee on 13 November 2019 (Decision No. 160) and was conducted in accordance with the principles of the Declaration of Helsinki. All patients were over 18 years of age, were non-pregnant, had no malignancy, and had undergone endoscopy. The patient medical histories, initial physical examination findings, medications, and comorbidities were retrieved from the hospital's SARUS system. At admission, urea and creatinine levels were measured using a Beckman Coulter AU2700 (Beckman Coulter, Inc., USA) autoanalyzer with spectrophotometric methods. Hemoglobin, PLT, PCT, MPV, and PDW levels were analyzed using an ABX Pentra DX120 analyzer (Horiba Medical, USA). These parameters were recorded at three time points: At admission, on the 5th day of hospitalization, and at discharge. Endoscopic findings and the amount of erythrocyte transfusion administered during hospitalization were retrieved for all patients. The Forrest classification was applied to patients with peptic ulcers. The Rockall and Blatchford scores were calculated for all patients included in the study.

Statistical Analysis

Quantitative variables were summarized as mean and standard deviation, while qualitative variables were summarized as frequency (percentage). The chi-square test was used to evaluate qualitative variables. The normality assumption for variables was assessed using the Kolmogorov-Smirnov test for sample sizes greater than 50 and the Shapiro-Wilk test for sample sizes less than 50. When the assumptions for parametric testing were met, differences between the means of two independent variables were analyzed using the Student's t-test. When these assumptions were not met, the Mann-Whitney U test was applied. The correlation between two variables was assessed using the Pearson test for normally distributed data and the Spearman correlation test for non-normally distributed data. Additionally, explanatory variables affecting the categorized length of hospital stay were analyzed using the logistic regression method. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 25.0, and a p-value of <0.05 was considered statistically significant.

Table 1. Demographic characteristics of patients

	n	%
Gender		
Female	72	34.28
Male	138	65.72
Total	210	100
Age (Mean± Standard deviation)	62.29±21.38	
Comorbidities	**Yes (%)**	**No (%)**
Diabetes	17%	83%
Hypertension	39%	61%
Coronary artery disease	25%	75%
Congestive heart failure	12%	88%
Atrial fibrillation	10%	90%
Neurological disorders	9%	91%
Chronic renal failure	9%	91%
Respiratory disease	9%	91%
Valvular heart disease	4%	96%
Thyroid disorders	6%	94%
Other	5%	95%
Drugs	**Yes (%)**	**No (%)**
Acetylsalicylic acid	16%	84%
Coumadin	14%	86%
Clopidogrel	5%	95%
NOAC	6%	94%
P2Y12 inhibitors	1%	99%
NSAID	16%	84%
Heparin	1%	99%
Beta blocker	12%	88%
Antibiotic	1%	99%
ACE inhibitor	9%	91%
ARB	4%	96%
Digoxin	2%	98%
Calcium channel blocker	6%	94%
Aldosterone	4%	96%
Diuretic	8%	92%
Statin	3%	97%
Nitrate	1%	99%
Neurological drugs	2%	98%
Oral antidiabetic	2%	98%
Insulin	1%	99%
Thyroid drugs	3%	97%

RESULTS

Our study included a total of 210 patients, of whom 34.28% were female (n=72) and 65.72% were male (n=138). The

Table 2. The relationship between the Rockall, Blatchford, and Forrest scoring systems and the platelet indices obtained at admission, on the 5th day of hospitalization, and at discharge

Platelet indices	Scoring variables					
	Forrest		Rockall		Blatchford	
	r	p	r	p	r	p
Admission						
Platelet	-0.102	0.298	0.051	0.459	0.009	0.911*
Plateletcrit	-0.087	0.371	0.044	0.527	0.027	0.694*
Mean platelet volume	0.043	0.658	0.062	0.375	0.143	0.038*
Platelet distribution width	0.021	0.831	0.076	0.273	0.121	0.080*
Day 5						
Platelet	-0.143	0.143	-0.082	0.239	-0.041	0.550*
Plateletcrit	-0.131	0.180	-0.050	0.469	-0.020	0.772*
Mean platelet volume	-0.001	0.992	0.115	0.096	0.133	0.055*
Platelet distribution width	0.071	0.466	0.103	0.139	0.095	0.156*
Discharge						
Platelet	-0.200	0.039	-0.047	0.494	-0.039	0.571*
Plateletcrit	-0.219	0.016	0.016	0.818	0.001	0.999*
Mean platelet volume	-0.029	0.764	0.154	0.025	0.159	0.021*
Platelet distribution width	0.038	0.697	0.145	0.035	0.144	0.037*

*The normality assumption was violated for all variables. The Spearman correlation coefficient was used.

mean age of the patients was 62.29±21.38 years. Among patients with chronic diseases, 39% had hypertension (HT), 25% ischemic heart disease (IHD), 17% diabetes mellitus (DM), 12% congestive heart failure (CHF), 10% atrial fibrillation (AF), 10% neurological disorders, 9% chronic renal failure (CRF), 9% respiratory diseases, 6% thyroid disorders, and 4% valvular heart disease. The most commonly used medications were acetylsalicylic acid (ASA) and nonsteroidal anti-inflammatory drugs (NSAIDs). Among the patients, 16% used aspirin, 16% used NSAIDs, 14% used warfarin, 6% used novel oral anticoagulants (NOACs), and 5% used clopidogrel (Table 1).

The correlations between the Blatchford, Rockall, and Forrest scores and platelet indices were examined at admission, on the 5th day of hospitalization, and at discharge. Since the score variables were not normally distributed, the Spearman correlation coefficient was used. For the Blatchford score, a very weak positive correlation was found with MPV at admission (r=0.143, p=0.038; 14.03%), with MPV at discharge (r=0.159, p=0.021; 15.90%), and with PDW at discharge (r=0.144, p=0.037; 14.40%). For the Rockall score, very weak positive correlations were also observed with MPV (r=0.154, p=0.037; 15.40%) and PDW at discharge (r=0.145, p=0.035; 14.50%). The Forrest score showed very weak negative correlations with PLT (r=-0.200, p=0.039; 20.00%) and PCT at discharge (r=-0.219, p=0.016; 21.90%) (Table 2).

Since platelet indices were not normally distributed, the Mann-Whitney U test was used to evaluate whether differences in mean platelet indices were statistically significant according to transfusion requirements. Comparing the groups with and without transfusion, no statistically significant differences were found in PLT, PCT, MPV, or PDW levels (p>0.05). In contrast, the differences in mean HGB levels were statistically significant: Patients who required transfusion had lower mean HGB levels compared to those who did not (Table 3).

The differences in laboratory values were examined in relation to the length of hospital stay. For this purpose, the independent two-sample Student's t-test was used for PLT, as it was normally distributed, while the Mann-Whitney U test was applied for PCT, MPV, PDW, and HGB, which did not follow a normal distribution. Comparing the patient groups by the length of hospital stay (<5 days vs. >5 days), no statistically significant differences were found in PLT, PCT, MPV, or PDW levels (p>0.05). Lower hemoglobin levels, advanced age, and the presence of comorbidities (CHF, valvular heart disease, AF, and CRF) were significantly associated with longer hospital stays (p<0.001). Patients hospitalized for more than 5 days had significantly lower HGB values compared to those hospitalized for less than 5 days (p<0.001). In addition, the patients with a hospital stay longer than 5 days had significantly higher mean Rockall and Blatchford scores compared to those with a hospital stay less than 5 days (p<0.001) (Table 4).

A forward selection logistic regression analysis was performed to identify the risk factors associated with hospitalization longer than 5 days compared to hospitalization shorter than5 days. According to the Hosmer-Lemeshow and Omnibus test results, the logistic regression model

Table 3. Comparison of platelet indices by transfusion requirement

Variables	Transfusion need		p-value
	No	Yes	
Admission			
Hemoglobin	9.34±2.11	7.98±1.46	<0.001*
Platelet	233.79±100.37	244.88±81.04	0.114*
Plateletcrit	0.21±0.08	0.22±0.07	0.190*
Mean platelet volume	9.31±1.13	9.24±1.19	0.511*
Platelet distribution width	16.07±1.95	15.75±1.6	0.158*
Day 5			
Hemoglobin	121.75±169.54	111.28±136.59	0.530*
Platelet	252.46±98.2	233.48±78.14	0.194*
Plateletcrit	0.23±0.08	0.22±0.07	0.179*
Mean platelet volume	9.32±1.16	9.46±1.29	0.598*
Platelet distribution width	16.16±2.04	16.03±1.6	0.582*
Discharge			
Hemoglobin	10.6±1.66	10.43±1.3	0.767*
Platelet	256.23±102.51	245.55±79.97	0.561*
Plateletcrit	0.23±0.08	0.23±0.07	0.601*
Mean platelet volume	9.29±1.15	9.63±1.87	0.368*
Platelet distribution width	15.98±1.88	16.18±1.73	0.503*

*The normality assumption was violated for all variables. The Mann-Whitney U test was used.

Table 4. Comparison of laboratory findings, scoring system results, and comorbidities by length of hospital stay

Variables	Length of hospital stay		p-value
	<5 days	>5 days	
Platelet	229.34±81.24	245.8±100.81	0.400*
Plateletcrit	0.21±0.07	0.23±0.08	0.202**
Mean platelet volume	9.2±1.13	9.35±1.17	0.225**
Platelet distribution width	15.79±1.94	16.06±1.7	0.264**
Hemoglobin	9.58±2.06	8.11±1.65	<0.001**
Rockall	3.30±1.83	5.04±2.074	<0.001**
Blatchford	7.14±3.65	11.56±3.231	<0.001**
Diabetes	12 (16)	24 (20)	0.138***
Hypertension	30 (35.4)	50 (44.6)	0.122***
Coronary artery disease	18 (22.7)	33 (28.3)	0.128***
Congestive heart failure	5 (10.7)	19 (13.3)	0.013***
Atrial fibrillation	5 (9.3)	16 (11.7)	0.044***
Neurological disorders	4 (8)	14 (10)	0.047***
Chronic renal failure	4 (8)	14 (10)	0.049***
Respiratory disease	7 (8)	11 (10)	0.616***
Valvular heart disease	1 (4)	8 (5)	0.039****
Thyroid disorders	4 (5.3)	8 (6.7)	0.423***
Other	2 (4.9)	9 (6.1)	0.071****

*Independent sample t-test, **Mann-Whitney U, ***Pearson chi-square, ****Fisher's exact test

was found to be statistically significant. The Nagelkerke R^2 value was calculated as 0.334. Examining the parameter estimates, HGB level, comorbidities, and BUN level were identified as independent risk factors (Table 5).

Table 5. Logistic regression results for predicting hospitalization of 5 days or more

Variables	Parameter Estimation	Standard Error	p	Hosmer Lemeshow Test		Omnibus Test		Nagelkerke R^2
				Test statistic	p	Test statistic	p	
Hemoglobin	-0.338	0.095	<0.001	7.234	0.512	60.016	<0.001	0.334
Comorbidities (0=None)	-0.711	0.340	0.037					
BUN	0.035	0.011	0.001					
Constant term	2.436	0.956	0.011					

DISCUSSION

Upper GI hemorrhage is a serious clinical condition with a mortality rate ranging from 2% to 10% and an annual incidence of 103 to 172 per 100,000, despite advances in diagnostic and therapeutic endoscopic methods.[9] Various risk factors, including advanced age, liver cirrhosis, heart failure, and the use of antiplatelet or anticoagulant agents, affect both the occurrence of bleeding and mortality.[10] The incidence is higher among men, individuals with low socioeconomic status, and the elderly.

Medication use plays a significant role in the etiology of upper GI hemorrhage. The increasing prevalence of comorbidities in elderly patients particularly contributes to increased medication use. Medications such as NSAIDs, ASA, and warfarin are well-known etiological factors. NSAIDs and ASA disrupt the gastrointestinal mucosal barrier by inhibiting the synthesis of prostaglandins through cyclooxygenase inhibition; additionally, they impair platelet function and are considered causative agents of GI bleeding.[11] Bor et al.[12] reported that among patients presenting with upper GI hemorrhage, 43.2% had used NSAIDs and aspirin, 7% had used steroids, and 6.6% had received anticoagulant therapy. A study by Paspatis et al.[13] found that half of the patients with GI hemorrhage had used ASA or NSAIDs. Similarly, Ateş et al.[14] reported that 27% of patients had used ASA, 23% NSAIDs, 5% oral anticoagulants, and 1% steroids. In our study, the most frequently used medications were ASA (16%), NSAIDs (16%), and coumadin (14%).

One of the factors affecting the mortality and morbidity of patients with GI bleeding is the presence of chronic diseases. In our study, the prevalence of chronic conditions was 39% for HT, 25% for IHD, 17% for DM, and 12% for CHF. A study by Erkuş et al.[15] reported HT (32.3%) as the most common comorbidity, with 19.1% of patients having chronic IHD, 14.1% having DM, and 9.1% having CHF. Okutur et al.[16] found that 46.2% of patients had HT, 22% had DM, and 16.5% had IHD in their study. Consistent with our study, HT was the most common comorbidity among patients with upper GI bleeding in the literature, and the most commonly used medications were ASA and NSAIDs, followed by warfarin.[10-17]

Patient scores were calculated using the Rockall and Blatchford scoring systems, which are utilized to predict the prognosis and severity of bleeding in cases of non-variceal upper GI hemorrhage. In our study, higher scores on both the Rockall and Blatchford scoring systems were significantly associated with longer hospitalization durations. Prolonged hospital stays were associated with poor prognosis. We also found that low hemoglobin levels, advanced age, and comorbidities (CHF, valvular heart disease, AF, and CRF) were associated with longer hospital stays and thus appeared to correlate with poor prognosis. Several studies have found that male gender, advanced age, and the use of antiplatelet and anticoagulant medications are associated with poor prognosis.[18-20]

A variety of scoring systems are used to identify high-risk patients and distinguish them from those at low risk. Risk factors include the need for erythrocyte transfusion, monitoring in the intensive care unit, endoscopic intervention, recurrent hemorrhage, and mortality. In the literature, there are many studies evaluating the predictive accuracy of these scoring systems in assessing such risk factors. The Rockall and Blatchford scoring systems are commonly used to assess the prognosis and severity of bleeding.[6,21] Our study is the first to examine the correlation between these scoring systems and platelet indices. PLT, PCT, MPV, and PDW levels were recorded on the first and fifth days of hospitalization and at discharge. In our study, elevated MPV levels at admission, as well as elevated MPV and PDW levels at discharge, showed a weak correlation with higher scores on both the Rockall and Blatchford scoring systems.

No significant correlation was found between hospitalization duration and the mean levels of these platelet indices in our study. In the literature, there are very few studies investigating the correlation between platelet indices (PLT, PCT, MPV, PDW) and the prognosis of GI hemorrhage. A study by Şenel et al.[22] found that elevated levels of these indices were associated with longer hospital stays and poor prognosis. Similarly, a study by Makay et al.[23] investigating the correlation between MPV and GI hemorrhage in patients with Henoch-Schönlein purpura found that mean MPV was significantly lower in patients with GI hemorrhage compared to those without hemorrhage. In another study, Tanoğlu et al.[24] found that higher MPV values were associated with increased erythrocyte transfusion requirements and longer hospital stays.

To assess the prognosis and severity of bleeding, the need for erythrocyte transfusion was evaluated. There are several studies in the literature investigating the predictive performance of scoring systems in estimating the need for erythrocyte transfusion.[25,26] In a study by Chen et al.,[27] the Blatchford scoring system was found to be superior to the Rockall scoring system in predicting the need for blood transfusion. In our study, the mean Blatchford and Rockall scores were significantly higher in patients who required transfusion compared to those who did not ($p<0.001$). The need for erythrocyte transfusion is considered an indicator of poor prognosis. However, no significant correlation was found between PLT, PCT, MPV, and PDW levels and the need for transfusion.

The Forrest classification is used to determine the severity of bleeding in patients. No significant correlation was observed between PLT, PCT, MPV, PDW, or HGB levels across the Forrest groups. Independent predictors of bleeding severity were found to be comorbidities, peak heart rate, and BUN levels. In our study, hospitalization duration was used as a marker of prognosis. The independent predictors of poor prognosis were identified as low HGB levels, comorbidities, and BUN levels. Previous studies have reported various independent predictors of poor prognosis, including hematemesis,[28,29] signs of hypovolemia,[29,30] low HGB and HCT levels,[28-30] hypoalbuminemia,[30] erythrocyte transfusion,[28] and prolonged hospitalization.[31]

Study Limitations

The limitations of our study include the unavailability of some data due to its retrospective design. In addition, being a single-center study limited the sample size. Larger-scale, multicenter, and comprehensive studies are needed to further investigate this topic.

Conclusion

In our study, we aimed to investigate the correlation between platelet indices and the prognosis and severity of upper GI hemorrhage. We used the Rockall and Blatchford scoring systems to assess patient prognosis. The relationships between scoring systems and platelet indices were examined. Higher MPV levels at initial presentation and elevated PDW and MPV levels after treatment showed weak correlations with both the Blatchford and Rockall scoring systems, which are commonly used to predict clinical outcomes.

A significant correlation was found between prolonged hospitalization and the need for erythrocyte transfusion using the prognostic scoring systems. When length of hospital stay and the need for erythrocyte transfusion were used as prognostic criteria, platelet indices did not appear to be significant prognostic predictors.

In our study, platelet indices were not identified as independent predictors of prognosis and severity of hemorrhage. Larger, multicenter studies are warranted to further elucidate the role of platelet indices in predicting the prognosis and severity of hemorrhage in non-variceal upper GI bleeding.

Ethics Committee Approval

The study was approved by the Taksim Training and Research Hospital Clinical Research Hospital Ethics Committee (Date: 13.11.2019, Decision No: 160).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: B.B.; Design: O.M.; Supervision: B.B.; Fundings: F.B.D.; Materials: F.B.D.; Data collection &/or processing: O.M.; Analysis and/or interpretation: K.K.; Literature search: F.B.D.; Writing: O.M., F.B.D.; Critical review: K.K.

Conflict of Interest

None declared.

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Varis Dışı Üst Gis Kanamalarında Trombosit İndekslerinin Kanama Ciddiyeti, Prognoz ve Skorlama Sistemleri ile İlişkisi

Amaç: Trombosit indekslerinin [trombosit (PLT), trombositkrit (PCT), ortalama trombosit hacmi (MPV), trombosit dağılım genişliği (PDW)] varis dışı üst gastrointestinal sistem (GİS) kanamalarında kanama ciddiyeti ve prognozu öngörmedeki yerini belirlemeyi amaçladık.

Gereç ve Yöntem: Varis dışı üst GİS kanaması nedeniyle yatırılmış 210 hasta çalışmaya alındı. Hastaların başvuru anındaki, 5. gündeki ve taburculuklarındaki tam kan sayımı değerleri kaydedildi. Hastaların Rockall ve Blatchford skorları hesaplandı ve Forrest sınıflaması yapıldı.

Bulgular: Yatış süresi 5 gün üzeri ve transfüzyon ihtiyacı olan hastaların Blatchford ve Rockall skorları; olmayan gruba göre daha yüksekti ($p<0.001$). Yatış süresi 5 gün üzeri ve altında olan gruplar ve transfüzyon yapılan ve yapılmayan gruplar karşılaştırıldığında PLT, PCT, MPV ve PDW değerleri arasında anlamlı fark saptanmadı ($p>0.05$). İlk başvuru esnasındaki MPV ve taburculuk esnasındaki MPV ve PDW değerleri ile Blatchford skoru arasında aynı yönlü çok zayıf bir ilişki bulundu. Taburculuk esnasındaki MPV ve PDW değerleri ile Rockall skoru arasında aynı yönlü çok zayıf bir ilişki bulundu. Yatış süresinin 5 gün ve üzeri olması riskini öngörmede, ileriye doğru seçimli lojistik regresyon analizi yapıldığında trombosit indeksleri bağımsız prediktör olarak saptanmadı.

Sonuç: Üst GİS kanamalarında kanama ciddiyeti ve prognozu belirlemede trombosit indekslerinin bağımsız prediktor olarak yer almadığı, ancak MPV ve PDW nin skorlama sistemleri ile çok zayıf ilişkili olduğu gözlendi.

Anahtar Sözcükler: Blatchford skorlama; Rockall skorlama; trombosit indeksleri; varis dışı üst GİS kanama.