American Journal of Emergency Medicine 37 (2019) 657–663

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

The diagnostic and prognostic value of platelet indices in gastrointestinal bleeding

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ARTICLE INFO

Article history:
Received 17 April 2018
Received in revised form 8 June 2018
Accepted 2 July 2018

Keywords:
Forrest classification
Gastrointestinal system hemorrhage
Platelet indices

ABSTRACT

Background: We aimed to investigate the association between platelet indices [platelet, plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW)] and gastrointestinal bleeding (GIB), as well as determine its severity and prognosis.
Method: 500 patients with GIB who were admitted to hospital between March 2014 and February 2017 and diagnosed with "Gastrointestinal System Bleeding", as well as114 healthy individuals were retrospectively included in the study. Patients' platelet indices were recorded after one week and one month from their files.
Results: Platelet, PCT, MPV and PDW levels were determined to be higher in the patients with bleeding, when compared to the control group ($p < 0.001$). Within the first week, a significant reduction was determined in patients' platelet, PCT, MPV and PDW values compared to the admission values ($p < 0.001$). In initial-month controls, a significant reduction was determined in the platelet indices compared to the initial-week values ($p < 0.001$). A significant association between bleeding severity and increased platelet indexes was determined. Increasing age, female gender, the presence of comorbidities, high levels of platelet indexes, low levels of hemoglobin, and albumin values were all found to be associated with a poor prognosis. PCT, MPV, and PDW were determined as being the independent risk factors that predict the odds of GIB, alongside the independent predictors that predict risk of bleeding severity and the prognosis.
Conclusion: We think that platelet indices may be used in diagnosis of GIB, as well as in predicting bleeding severity and the prognosis.

1. Introduction

Acute gastrointestinal bleeding (GIB) is an important cause of emergency admissions. It is an important clinical issue that may progress with high morbidity and mortality despite advanced diagnostic and treatment methods [1]. Not only may GIB originate from a superficial focus and tend to limit itself, but it also may progress to the point that it leads to hemorrhagic shock [2]. Due to the fact that early diagnosis of this clinical problem is (often) accompanied by high diagnostic and treatment costs, there is a need for the emergency endoscopy, as well as a need for cost-effective, easy-to-access, and noninvasive methods that are oriented towards predicting the need for hospitalization and intensive care.

Platelet indices include platelet count, plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW)—all of which are parameters that meet these criteria, as well as may routinely be evaluated with complete blood count. Platelet indices are known to be associated with many inflammatory, ischemic, and thrombotic events [3, 4]. When studies investigating the association between gastrointestinal system diseases and platelet indices are looked at, it has been demonstrated that the MPV value is low, that the platelet value is be high in the activation of ulcerative colitis and Crohn's disease, and that MPV levels are low during occurrence of bleeding when the disease is active [5]. Colon cancer has been determined to exhibit an association with high MPV values, while MPV values were determined to be associated with tumor stage in colon cancer. This association could not be established when it comes to stomach cancer [6, 7]. It has been revealed that patients with GIB present high MPV and low platelet values, whereby high MPV values are associated with disease severity and poor prognosis [8].

A number of the studies investigating the association between platelet indices and GIB is limited in the available literature. We aimed to

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https://doi.org/10.1016/j.ajem.2018.07.008
0735-6757/

determine the importance of these parameters, given that they are a cost-effective, easy-to-access, and noninvasive means of predicting the diagnosis of GIB, bleeding severity, and ultimately prognosis.

2. Method

This study was conducted at the Department of Internal Diseases at Ankara Numune Education and Research Hospital between June and December 2017. The study was designed as a case-control initially, and as historical cohort in the follow-up in order to examine the association of platelet indices with prognosis of gastrointestinal bleeding.

The 500 patients included in this study were admitted between March 2014 and February 2017 to the gastroenterology subdivision at the Ankara Numune Training and Research Hospital's Department of Internal Diseases as well as to the emergency ward, and registered as having "Gastrointestinal Bleeding". Moreover, 144 healthy controls were also retrospectively included in the study. Based on the reviewed literature, it was determined that at least 77 patients must be included for each group in the sample size analysis performed by PASS 15 program in order that the mean platelet level can be at least 60×10^3 μl higher in patients with GIB than those without it.

Those patients diagnosed with GIB and of whom were followed up with laboratory work, endoscopic imaging reports, and clinical findings were excluded from the study. The patients who had severe comorbidities that may influence their mortality beyond GIB (acute coronary syndrome, sepsis, trauma, malignancy, coma, severe cerebrovascular event) were also excluded from the study.

Participants' demographical, clinical and laboratory findings as well as imaging were accessed via the Fonet hospital information system. Demographical and clinical findings, including, age, gender, comorbidities, use of medications, duration of hospitalization, treatment options, and survival rates were recorded. Laboratory findings, including platelet indices (platelet, PCT, MPV, PDW), white blood cell (WBC), neutrophils, lymphocyte, monocytes, hemoglobin, erythrocyte distribution width (RDW), hematocrit, mean corpuscular volume (MCV), international normalized ratio (INR), and albumin values were also recorded. Imaging included any and all endoscopic results (localization of bleeding, Forrest classification, and type of endoscopic treatment).

First blood samples of the patients were recorded as blood samples at their admission to the emergency department. Beside baseline values, follow-up lab results both after the first week as well as the first month were also chronicled.

This study was planned in accordance with the Declaration of Helsinki and the Patient's Bill of Rights, and was approved by the Committee of Evaluation of Scientific Investigation at the Ankara Numune Training and Research Hospital.

Platelet was measured using the impedance (resistance) method, WBC using optic laser scattering (light scattering), hemoglobin using photometry, other hemogramic parameters using a Sysmex XE 2100 (Roche Diagnostics Corp., Indianapolis, Indiana, USA) hematology analyzer, INR using immunoturbimetry on a Cobas c-501 (Roche Diagnostics, Sandhofer, Mannheim, Germany) device, and albumin using the brome cresol green method on an Hitachi Modular P800 (Roche Diagnostics Corp., Indianapolis, Indiana, USA) auto-analyzer.

2.1. Statistical analysis

Statistical evaluation was performed using the Statistical (Software) Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc. Chicago, IL), Medcalc 11.4.2 (MedCalc Software, Mariakerke, Belgium), and STATA/SE 12.0 for Windows (STATAcorp LP, Texas, USA). Normal distribution of the data was evaluated using the Shapiro Wilk test. Numerical values exhibiting normal distribution were represented as mean ± standard deviation, whist values which did not exhibit normal distribution were represented as median (minimum value – maximum value). Categorical variables were expressed in terms of count and percentage. Between the two groups, the distribution of the numerical variables was evaluated using an independent sample *t*-test (for numerical variables exhibiting normal distribution), as well as the Mann Whitney *U* test (for non-normal distribution numerical variables). The distribution of the numerical variables among the three groups was calculated using the ANOVA (normal distribution) and Kruskall Wallis H tests (non-normal distribution). For comparison of categorical data, chi-square and Fisher's exact chi-square tests were used. The determination of independent predictors was carried out using retrospective step-wise multivariate logistic regression analysis. A receiver operating characteristics (ROC) curve was used for the diagnostic evaluation of independent predictors. Cut-off values of the risk factors that increase the risk of GIB were determined by using the Youden index method. In terms of statistical analyses, $p < 0.05$ value was considered to be significant.

3. Results

3.1. Clinical findings of the patients with GIB

The demographical and clinical findings of the patients with GIB are represented in detail in Table 1. In the GIB group, the upper GIB was determined in 68.2% (n:341) of patients, and lower GIB in 14.6% of the patients, while no focus was determined in 17.2% of the patients (n:86). In regard to the localization of GIB, peptic ulcer ranked first with a rate of 61.4% (n:254). A proton pump inhibitor was initiated for 89.2% of the patients. In terms of endoscopic treatment, sclerotherapy was most frequently (14.1%) performed. The most frequent accompanying chronic disease was determined to be hypertension (37.6%)

When the patients were consulted about which medications they use that may predispose them to bleeding, the use of acetylsalicylic acid was determined to be 13.6% (n:68), 9.2% were using warfarin (n:46), 7.8% were using NSAID (n:39), 4.6% were taking low molecular-weight heparin (n:23), 2% were taking a new-generation oral anticoagulant, (n:10) and 0.4% had indicated that they were using ticagrelor(n:2).

Patients' duration of hospital stay varied between 1 and 192 days, with a median of 4 days. 54.8% of patients were found to have stayed in hospital for longer than three days.

3.2. Comparison of laboratory findings of the GIB group and the control group

The distribution of the laboratory findings of the study population is summarized in detail in Table 2. Mean hemoglobin (13.1 ± 1.1 versus 15.9 ± 0.6, $p < 0.001$), mean hematocrit (29.8 ± 9.4 versus 40.2 ± 5.9, $p < 0.001$), mean MCV (84.8 ± 8.3 versus 88.2 ± 5.3, $p < 0.001$), median lymphocyte count (1600 versus 1435, $p = 0.025$) and mean albumin (3.5 ± 1 versus 4.7 ± 0.3, $p < 0.001$) levels were determined to be lower in the patients with GIB compared to the control group. Median WBC count (11 versus 7, $p < 0.001$), mean RDW (16.1 ± 3.4 versus 14.2 ± 1.6, $p < 0.001$), mean PCT (2.5 ± 0.9 versus 1,2 ± 0.4, $p < 0.001$), median platelet (255.5 versus 158, $p < 0.001$), mean MPV (8.9 ± 1.0 versus 7.4 ± 0.6, $p < 0.001$), mean PDW (16.8 ± 1.0 versus 11.6 ± 1.4, $p < 0.001$) and mean INR (1.2 versus 1.0, $p < 0.001$) levels, however, were determined to be higher in the patients with GIB compared to the control group.

3.3. Post-treatment changes in laboratory findings in patients with GIB

Within the first week following treatment, the mean platelet, mean PCT, mean MPV, and mean PDW values exhibited a reduction compared to the baseline values. However, in the first-month follow-up after

Table 1
Clinical findings of patients with GIS bleeding.

Variables	Results
	n(500)
Age (year)	64,2 ± 17,7
Gender, n(%)	
Male	331(66,2)
Localization, n(%)	
Upper GIS	341(68,2)
Lower GIS	73(14,6)
Bleeding of undetermined	86(17,2)
Presence of ulcers, n(%)	254(61,4)
Forrest classification, n(%)	
1a	6(2,4)
1b	52(20,5)
2a	50(19,7)
2b	31(12,2)
2c	55(21,7)
3	60(23,6)
Treatment option, n(%)	
Thermal coagulation	21(4.2)
Endoklip	16(3.2)
Band ligation	29(5.8)
Sclerotherapy	91(14.1)
Transarterial embolization	1(0.2)
Surgical	11(2.2)
Non-steroidal anti-inflammatory drug	433(86.6)
Follow-up without treatment	67 (13.4)
Additional disease, n(%)	
Diabetes	95(19.0)
Hypertension	188(37.6)
Arrhythmia	40(8.0)
Coronary artery disease	124(24.8)
Renal dysfunction	155(31.0)
Congestive heart failure	38(7.6)
Cerebrovascular disease	54(10.8)
Chronic liver disease	35(7.0)
Thyroid disease	14(2.8)
Malignity	110(22.0)
Chronic obstructive pulmonary disease	42(8.4)
Vasculitis	6(1.2)
Drug use, n(%)	
Acetylsalicylic acid	68(13.6)
Warfarin	46(9.2)
Low molecular weight heparin	23(4.6)
New generation oral anticoagulant	10(2.0)
Non-steroidal anti-inflammatory drug	39(7.8)
T icagrelor	2(0.4)
Proton pump inhibitor	40(8.0)
Days of hospitalization, n(%)	4(1–192)
3 days and less	226(45.2)
Over 3 days	274(54.8)

Categorical variables were expressed as number (%), numerical variables were expressed as mean ± standard deviation, numerical variables without normal distribution are shown as median (lowest value-highest value).
Abbreviations: GIS: Gastrointestinal System.

treatment, a significant reduction was determined compared to the first-week follow up values (Table 3).

3.4. Distribution of laboratory findings of the patients according to Forrest classification

In Forrest I patients, the median WBC level was determined to be higher, while the mean hemoglobin level was determined to be lower compared when compared with the Forrest II and III patients. In Forrest I patients, the median platelet, mean PCT, mean MPV, and mean PDW levels were determined to be higher compared to the Forrest II and III patients. Among Forrest III patients, median INR level was determined to be lower than their Forrest I and II counterparts. Among Forrest II patients, WBC levels were determined to be higher and, moreover, mean hemoglobin level was determined to be lower compared to Forrest III patients. The median platelet, mean PCT, mean MPV, and mean PDW levels of Forest II patients were determined to be higher compared to the Forrest III patients. No significant difference in regard to other laboratory findings was determined (Table 4).

Table 2
Distribution of laboratory findings for study population.

Variables	GIS bleeding	Control	p
	n(500)	n(144)	
WBC ($\times10^3$)	11(5.0–46.5)	7(4.4–11.0)	<0.001*
Neutrophils ($\times10^3$)	7.4(1.1–55)	7.3(1.2–19)	0.202
Lymphocytes ($\times10^3$)	1.6(0.1–10.9)	1.4(0.5–3.6)	0.025*
Monocytes ($\times10^3$)	0.6(0.1–7.3)	0.6(0.3–1.0)	0.179
Hemoglobin (g/dL)	13.1 ± 1.1	15.9 ± 0.6	<0.001*
Hematocrit (%)	29.8 ± 9.4	40.2 ± 5.9	<0.001*
Mean corpuscular volume (fL)	84.8 ± 8.3	88.2 ± 5.3	<0.001*
Red cell distribution width (%)	16.1 ± 3.4	14.2 ± 1.6	<0.001*
Plateletcrit (%)	2.5 ± 0.9	1.2 ± 0.4	<0.001*
Platelet ($\times10^3$)	255.5(164–945)	158(150–551)	<0.001*
Mean platelet volume (fL)	8.9 ± 1	7.4 ± 0.6	<0.001*
Platelet distribution width (%)	16.8 ± 1	11.6 ± 1.4	<0.001*
Albumin (g/dL)	3.5 ± 1	4.7 ± 0.3	<0.001*
International normalized ratio	1.2(0.8–28)	1.0 (0.8–1.1)	<0.001*

Categorical variables were expressed as number (%), numerical variables were expressed as mean ± standard deviation.
Abbreviations: GIS: Gastrointestinal System, WBC: White Blood Cell.
* $p < 0.05$ is statistically significant.

3.5. Distribution of patients' demographical and clinical characteristics according to duration of hospital stay

Mean age and ratio of female gender were higher in patients with a hospital stay duration of more than three days compared to those who had stayed in hospital for three or fewer days. Median WBC (18 versus 11, $p < 0.001$), median platelet (275.5 versus 203, $p < 0.001$), mean PCT (2.7 ± 10.9 versus 2.1 ± 0.6, $p < 0.001$), mean MPV (9.1 ± 1.1 versus 8.8 ± 0.8, $p < 0.001$), and mean PDW (17.0 ± 0.7 versus 16.6 ± 1,1, $p < 0.001$) levels were determined to be higher, while the mean hemoglobin (12.8 ± 1.0 versus 13.3 ± 1.2, $p < 0,001$) and mean albumin (3.3 ± 0.9 versus 3.6 ± 1.0, $p < 0.001$) were determined to be lower in patients who had stayed in hospital for longer than three days versus those who stayed in hospital for three days or less. No significant difference in regard to other laboratory findings was determined.

Table 3
Changes in laboratory findings of patients after treatment.

Variables	Bazal	1. Week	1. Month	p
	n(500)	n(500)	n(500)	
WBC ($\times10^3$)	11(5.0–46.5)	7.4(1.0–46.3)	7.4(0.7–31.0)	<0.001*
Neutrophils ($\times10^3$)	7.4(1.1–55)	4.6 (0.2–36.6)	4.6(0.3–28.6)	<0.001*
Lymphocytes ($\times10^3$)	1.6(0.1–10.9)	1.7(0.1–7)	1.7(0.1–7)	0.452
Monocytes ($\times10^3$)	0.6(0.1–7.3)	0.5(0.1–14.2)	0.5(0.1–5.6)	<0.001*
Hemoglobin (g/dL)	13.1 ± 1.1	15.0 ± 3.7	15.6 ± 4.0	<0.001*
Hematocrit (%)	29.8 ± 9.4	33.7 ± 7.6	34.4 ± 7.6	<0.001*
Mean corpuscular volume (fL)	84.8 ± 8.3	85.7 ± 5.7	85.6 ± 5.7	0.068
Red cell distribution width (%)	16.1 ± 3.4	15.8 ± 3.3	16 ± 2.3	0.100
Plateletcrit (%)	2.5 ± 0.9	1.6 ± 0.5	1.2 ± 0.4	<0.001*
Platelet ($\times10^3$)	255.5(164–945)	205(150–645)	165.5(150–495)	<0.001*
Mean platelet volume (fL)	8.9 ± 1.0	8.3 ± 1.0	7.6 ± 1.1	<0.001*
Platelet distribution width (%)	16.8 ± 1.0	14.8 ± 1.5	12.9 ± 1.0	<0.001*

Categorical variables were expressed as number (%), numerical variables were expressed as mean ± standard deviation, numerical variables without normal distribution are shown as median (lowest value-highest value).
Abbreviations: GIS: Gastrointestinal System.
* $p < 0.05$ is statistically significant.

Table 4
Distribution of laboratory findings of patients according to Forrest classification.

Variables	Forrest classification			p
	I	II	III	
	n(58)	n(136)	n(60)	
WBC ($\times 10^3$)	21.5(19–46.5)	15(12.9–19.0)	11(5–12.9)	<0.001*
Neutrophils ($\times 10^3$)	7.4(1.4–23)	7.8(1.2–55)	7.7(1.1–25.9)	0.703
Lymphocytes ($\times 10^3$)	1.8(0.1–4.4)	1.8(0.1–7.7)	1.7(0.2–6.7)	0.569
Monocytes ($\times 10^3$)	0.5(0.1–3.1)	0.6(0.1–7.2)	0.6(0.1–2)	0.568
Hemoglobin (g/dL)	11.3 ± 0.2	12.2 ± 0.4	12.9 ± 0.4	<0.001*
Hematocrit (%)	29.8 ± 9.7	28.3 ± 8.9	31.8 ± 10.1	0.075
Mean corpuscular volume (fL)	85.6 ± 6.7	85 ± 7.9	85 ± 7.6	0.876
Red cell distribution width (%)	15.1 ± 2.8	15.1 ± 3.5	15.3 ± 2.5	0.431
Plateletcrit (%)	4.0 ± 1.3	2.9 ± 0.3	2.0 ± 0.3	<0.001*
Platelet ($\times 10^3$)	473(246–945)	318(219–397)	209(200–259)	<0.001*
Mean platelet volume (fL)	10.9 ± 1.2	9.4 ± 0.5	9.0 ± 0.5	<0.001*
Platelet distribution width (%)	18.5 ± 0.5	17.3 ± 0.4	16.9 ± 0.5	<0.001*
Albumin (g/dL)	3.6 ± 0.9	3.5 ± 0.9	3.5 ± 0.9	0.600
International normalized ratio	1.2(1–18.4)	1.2(0.9–14)	1.1(1–5.5)	0.039*

Categorical variables were expressed as number (%), numerical variables were expressed as mean ± standard deviation, numerical variables without normal distribution are shown as median (lowest value-highest value).
Abbreviations: GIS: Gastrointestinal System.
* $p < 0.05$ is statistically significant.

3.6. Factors associated with GIB, Forrest classification and risk for >3 days of hospital stay

Factors associated with GIB, Forrest classification, and risk for >3 days of hospital stay are summarized in Table 5. In the multivariate logistic regression model involving potential risk factors that may increase possibility of GIB; increased platelets (OR = 1.11; $p < 0.001$), increased PCT (OR = 16.63; $p < 0.001$), increased MPV (OR = 8.44; $p < 0.001$), increased PDW (OR = 9.66; $p < 0.001$) and decreased albumin (OR = 0.18; $p < 0.001$) levels were determined to be independent risk factors that increase likelihood of GIB. Diagnostic performance evaluation of the independent risk factors in predicting likelihood of GIB is given in Fig. 1. According to this, performance ranking of the independent risk factors that could predict the odds of GIB was determined to be PDW > PCT > MPV > platelet = Albumin. Plateletcrit levels over 1.98 were determined to increase likelihood of development of GIB, with a sensitivity of 93.4% and specificity of 94.4% (+PV: 99.7%; −PV: 43%). Platelet levels over 171 were determined to increase likelihood of development of GIB, with a sensitivity of 96.8% and specificity of 74.3% (+PV: 98.6%; −PV: 55%). Mean platelet volume over 7.6 was determined to increase likelihood of development of GIB, with a sensitivity of 98.4% and specificity of 69.4% (+PV: 98.4%; −PV: 69.6%). Platelet distribution width over 13.95 was determined to increase likelihood of development of GIB, with a sensitivity of 99.2% and specificity of 100% (+PV: 100%; −PV: 86.8%). Albumin levels of 4 and below were determined to increase likelihood of development of GIB, with a sensitivity of 68.4% and specificity of 98.6% (+PV: 99.9%; −PV: 14.1%). In terms of the retrospective step-wise logistic regression model involving potential risk factors, the platelet (OR = 1,48, p = 0,010) and PCT (OR = 1,16, p = 0,003) levels were determined to be independent risk factors involving the prediction of a Forrest II versus a Forrest I risk. Moreover, platelet (OR = 1,09, $p < 0,001$) and PCT (OR = 2,03, $p < 0,001$) levels were determined to be independent risk factors involving the prediction of a Forrest III versus a Forrest II risk.

In terms of predicting the risk of a duration of hospital stay of more than three days versus the group with three or fewer days, hypertension (OR = 1.91, p = 0,002), platelet (OR = 1.05, p = 0.014), PCT (OR = 6.51, $p < 0.001$), MPV (OR = 2.91, $p < 0.001$), PDW (OR = 2.25, p = 0.024), and albumin (OR = 0.70, $p < 0.001$) levels were all determined to be independent risk factors.

Table 5
Factors associated with GIB, Forrest classification, and >3 days hospitalization.

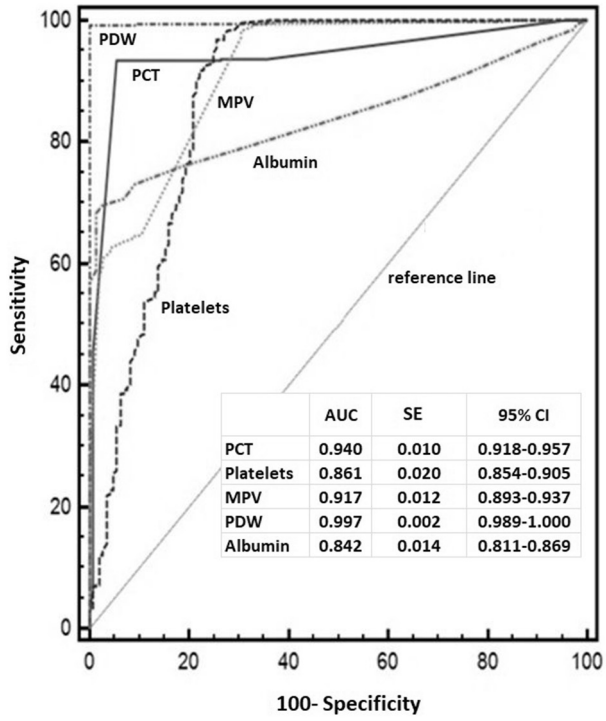
Risk factors	OR	%95 C.I.	p
Independent risk factors that increase the likelihood of GIB			
Plateletcrit	16.63	6.43–43.03	<0.001*
Platelet	1.11	1.03–1.19	<0.001*
Mean platelet volume	8.66	4.22–17.78	<0.001*
Platelet distribution width	9.66	5.33–17.51	<0.001*
Albumin	0.18	0.10-0.33	<0.001*
Nagelkerke $R^2 = 0.797$; $p < 0.001$*			
Independent risk factors for Forrest classification			
Forrest II (ref: I)			
Plateletcrit	1.16	1.05–1.29	0.003*
Platelet	1.48	1.08–2.24	0.010*
Nagelkerke $R^2 = 0.453$; $p < 0.001$*			
Forrest III (ref: II)			
Plateletcrit	2.03	1.67–2.47	<0.001*
Platelet	1.09	1.05–1.13	<0.001*
Nagelkerke $R^2 = 0.874$; $p < 0.001$*			
Independent risk factors that predict >3-day risk of hospitalization			
Hypertension	1.91	1.26–2.88	0.002*
Plateletcrit	6.51	3.45–12.24	<0.001*
Platelet	1.05	1.01–1.08	0.014*
Mean platelet volume	2.91	1.92–4.39	<0.001*
Platelet distribution width	2.25	1.11–4.55	0.024*
Albumin	0.70	0.57-0.86	0.001*
Nagelkerke $R^2 = 0.632$; $p < 0.001$*			

Abbreviations: GIB: Gastrointestinal System Bleeding, OR: odd ratio, CI: confidence interval.
* $p < 0.05$ is statistically significant.

4. Discussion

Acute GIBs are an important cause of morbidity and mortality. Despite high diagnostic and treatment costs, early diagnosis of GIB, the determination of risks and bleeding severity, and the prediction of prognosis are all of vital importance. Therefore, cost-effective, easy-to-access and noninvasive parameters are required. We examined the association between platelet indices and GIB, which may be evaluated routinely with complete blood count, and which is cost-effective.

At present, there are a limited number of studies examining the association between GIB and platelet indices. In a study conducted by Balahan et al. [9] involving a pediatric patient population, it was reported that the MPV value was determined to be lower in patients with Henoch Schönlein Purpura suffering from GIB complications when compared with the normal population. In a study conducted by Tanoğlu et al. [8], however, MPV levels were determined to be significantly higher, whist PLT levels were determined to be significantly lower in patients with upper GIB compared to the healthy control group. In our study, all platelet indices were determined to be significantly higher in patients with GIB compared to the control group. However, in acute blood loss, it is well-known that while PLT increases, MPV proportionally decreases (albeit indirectly) [10]. In our study, and contrary to the literature, MPV was shown to increase together with other platelet indices in patients with bleeding. This condition was thought to be associated with sympathetic activity due to hypovolemia and hypotension. Increased sympathetic activity is known to cause an increase in MPV with two different mechanisms. One of these mechanisms is the development of platelet activation, resulting in alterations in shape, size, and function of platelets with alpha-2 adrenoreceptor stimulation [11-13]. In the second one, however, it is release of large and active platelets sequestered in the spleen into bloodstream through adrenalin discharge [14].



	AUC	SE	95% CI
PCT	0.940	0.010	0.918-0.957
Platelets	0.861	0.020	0.854-0.905
MPV	0.917	0.012	0.893-0.937
PDW	0.997	0.002	0.989-1.000
Albumin	0.842	0.014	0.811-0.869

Pairwise comparison of ROC Curve

	ΔAUC	SE	p
PCT			
vs Platelets	0.079	0.019	<0.001
vs MPV	0.022	0.013	0.100
vs PDW	0.057	0.010	<0.001
vs Albumin	0.097	0.017	<0.001
Platelets			
vs MPV	0.056	0.021	0.031
vs PDW	0.136	0.020	<0.001
vs Albumin	0.019	0.022	0.178
MPV			
vs PDW	0.079	0.012	0.001
vs Albumin	0.075	0.018	0.001
PDW			
vs Albumin	0.155	0.014	<0.001

Fig. 1. Diagnostic performance of the independent predictors predicting the GIB.

In our study, laboratory results at admission were compared with both post-first week and first month control values. Within the first week, a significant reduction in patients' WBC, neutrophil, monocyte, platelet, PCT, MPV, and PDW values, alongside a significant increase in hemoglobin and hematocrit were determined. In our hospital, early-term bleeding control can be guaranteed in many patients with GIB with an early diagnosis of patients with bleeding, an initiation of medical treatment without time loss, and the conduction of emergency endoscopic interventions within first 24 h. In our study, within the first week, a reduction in the finding of leukocytosis, and an increase of hemoglobin and hematocrit seen in acute bleeding are findings that we expected as an indicator of bleeding control. Furthermore, it was thought that the elevation in hemoglobin and hematocrit may be associated with erythrocyte suspension replacement during hospitalization. The reduction in platelet indices detected within the first week, however, was thought to result from loss of activation signals on bone marrow upon getting acute bleeding under control, thus resulting in platelet activation and from release of young platelets after being produced in normal shape, size, and function within the bloodstream. At the post-first month control of our patients, even though no significant difference was determined in other parameters compared to the first-week control, a significant reduction was determined in platelet indices. It was thought that this situation may be associated with the lifespan of platelets being 8–10 days, whereby active platelets remain in the bloodstream during this period.

The determination of platelet indices as being higher in the GIB group compared to the control group and reduction of platelet indices during the follow-up period in the GIB group compared to the basal levels suggest that platelet indices were associated with GIB. Reduction of GIB and its severity along with reduction in platelet indices during the follow-up indicates that platelet indices are a good index to be used in the follow-up of GIB. In the regression analysis that we performed, the prediction of risk of GIB using platelet indices, as well as low albumin levels, is strongly supports our assumptions. In the literature, independent predictors that predict GIB have been determined to be comorbid conditions [15], *H. pylori* infection, NSAID [16, 17], acetylsalicylic acid [18], alcohol use, lack of an anti-ulcer medication, signs of hypovolemia, hematemesis, and high levels of urea [19]. In our ROC curve analysis, however, the performance ranking in terms of predicting bleeding was determined to be PDW > PCT > MPV > platelet = albumin. Our study is the first study in which platelet, PCT, MPV, and PDW were determined to be independent predictors for predicting GIB.

In the literature, there are many studies intended for determining factors associated with bleeding severity in patients with GIB. The presence of chronic liver disease, presence of signs of hypovolemic shock, refluxing through nasogastric tube is active red blood, high levels of urea, leukocytosis, severe anemia [20], the presence of coagulopathy, the determination of a risky lesion during endoscopy [21], the use of NSAID, acetylsalicylic acid, and warfarin [22], the presence of massive rectal bleeding, and hypoalbuminemia [23] have all been associated with bleeding severity. In our study, Forrest classification was utilized in order to determine factors associated with bleeding severity. The patients with bleeding were classified into three groups: Forrest I (Ia and Ib), Forrest II (IIa, IIb, IIc), and Forrest III. As the bleeding severity is Forrest I > Forrest II > Forrest III, these three groups were compared by their demographical characteristics, medications, comorbidities, and lab results for predicting bleeding severity. No link between patients' age, gender, and medications, and the Forrest classification was determined. Ratio of Forrest I patients was determined to be significantly higher in patients with chronic liver disease compared to Forrest II and III. When Forrest I was compared with Forrest II, and Forrest II with Forrest III, WBC was determined to be higher, hemoglobin was determined to be lower, and platelet indices were determined to be higher. INR, however, was determined to be significantly higher in Forrest I and II compared to Forrest III. To sum up, in our study, an association was established between bleeding severity and presence of a chronic liver disease, high levels of WBC, low levels of hemoglobin, increased platelet indices, and high INR values. However, age, gender, medication, comorbidities beyond chronic liver disease, and albumin value were did not appear to be associated with bleeding severity. While our results showed parallelism with those in the literature, the number of previous studies investigating the association between platelet indices and bleeding severity were determined to be insufficient. In the study conducted Tanoğlu et al. [8], the MPV value was shown correlate with GIB

severity. However, in studies conducted by Hreinsson et al. [24] and Velayos et al. [25], no association whatsoever was determined between bleeding severity, INR, or platelet values. Given that this study is the first to investigate the association between platelet, PCT, MPV, and PDW with bleeding severity in GIB, we determined a positive association between all of the platelet indices and bleeding severity. Furthermore, our determination of platelet and PCT being independent risk factors for Forrest II and III in the regression analysis also indicates that platelet indices are closely associated with bleeding severity. In the literature, the independent risk factors predicting bleeding severity have been determined to be advancing age, the use of acetylsalicylic acid and warfarin [26], marked rectal bleeding, and low hematocrit [25, 27]. In the literature, no study citing platelet indices as being be independent predictors for predicting bleeding severity in GIB has been encountered as of yet.

In our study, increasing age, female gender, the presence of comorbidity (diabetes and hypertension), high levels of WBC, platelet, PCT, MPV and PDV, and low hemoglobin and albumin values were determined to be associated with a longer duration of hospital stay, and hence with poor prognosis. In the literature, where male subjects tend to be accompanied by poor prognosis [28], there are also studies in which no association has been be demonstrated between gender and prognosis [29]. In our study, however, poor prognostic course was determined in female subjects. In the literature, there are various studies showing use of antiaggregant and anticoagulant medications to be [21, 23, 30], as well as to not be [29, 31] associated with poor prognosis. Although there are studies showing that NSAID use increases duration of hospital stay, there are also studies showing that it reduces re-bleeding and mortality and shortens duration of hospital stay in upper GIB, and that it does not have any influence whatsoever on prognosis in lower GIB [32]. In other words, the association between medications and prognosis is not clear. In our study, no association was determined between medication and prognosis. In the literature, there are studies in which no association between endoscopic findings and bleeding severity, whereby prognosis sometimes was [21, 30, 33], and sometimes was not [29, 34, 35] determined. In our study this association was not determined. In the study conducted by Tanoğlu et al. [8], while high MPV values and bleeding severity was associated with poor prognosis, no study investigating the association between all of the platelet indices and prognosis of GIB was encountered in the literature. In our study, high platelet, PCT, MPV, and PDW values were determined to accompany longer duration of hospital stay and, hence, poor prognosis. Given that bleeding severity is one of the factors predicting the prognosis, the fact that platelet indices were found to be positively correlated with bleeding severity is a finding we expected. Furthermore, in our regression analysis, the presence of hypertension and low albumin levels, as well as platelet indices, were determined to be independent risk factors for poor prognosis. This analysis supports that platelet indices were closely associated with poor prognosis. In different studies, independent predictors that predict poor prognosis in patients with GIB were determined to be increasing age, male gender, coagulopathy, signs of hypovolemia [1], hematemesis, low hemoglobin levels and hematocrit, replacement of blood components [36], hypoalbuminemia, re-bleeding [37-39], and duration of hospital stay [38]. We have not encountered any analysis indicating prognostic importance of the platelet indices.

One of the limitations of our study is that our study was retrospective. Another limitation is that when it comes to the accurate measurement of the MPV value, examining it 60 min after the collection of the blood sample is recommended, however the availability of this condition could not be confirmed. The third limitation is the lack of approach towards certain data known to be associated with risk, severity, and prognosis of the disease (tobacco and alcohol use, presence of *H. pylori* infection, vital signs, the time to approach to endoscopy, rate of re-bleeding, need for blood component replacement, and mortality rates etc.).

In conclusion, we have determined that platelet indices are significantly higher in patients with GIB compared to the healthy control group. We also determined that there is a significant drop in platelet indices compared to the admission values at first-week and first-month controls, compared to both admission and first-week values. We moreover observed a high platelet index to be associated with bleeding severity and poor prognosis. We determined the platelet indices to be independent predictors that predict GIB severity and prognosis. In light of the results of our study, we hypothesize that platelet indices may be used for the diagnosis of GIB, as well in order to predict bleeding severity and prognosis. As our study is the first study on this issue, we think that further studies on categorical splitting of the patients regarding platelet indices to reach index levels over which the risks of GIB may be higher need to be conducted with larger patient populations in order to verify these results. I also suggest studies in the future with categorical splitting of the patients regarding platelet indices to reach index levels over which the risks of GIB may be higher.

Financial disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations of interest

None.

Acknowledgements

None.

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