Evaluation of the Relationship Between Bleeding Severity and Platelet Mass Index in Geriatric Patients with Upper Gastrointestinal Bleeding in the Emergency Department

Acil Serviste Üst Gastrointestinal Kanamalı Geriatrik Hastalarda Kanama Şiddeti İle Platelet Kitle İndeks İlişkisinin Değerlendirilmesi

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ABSTRACT

Aim: Platelet mass index (PMI) is closely correlated with platelet function in various diseases. In the present study, we aimed to evaluate the use of PMI in predicting bleeding severity and mortality in geriatric patients with acute upper gastrointestinal (GI) bleeding.

Material and Methods: This study is a retrospective study. Local ethics committee approval was obtained. It enrolled patients aged 65 years or older who presented to the emergency department (ED) with upper GI bleeding. The patients' demographic data, comorbid disorders, results of laboratory studies and endoscopic procedures, hospital outcomes, and 30-day mortality rate were evaluated. A p-value of less than 0.05 was considered statistically significant.

Results: This study included 167 patients. Among them, 40.1% were female, and their median age was 79 (IQR 25-75, 71-86) years. The median Rockall score was 4 (IQR 25-75, 2-5); and the 30-day mortality rate was 13.2 % (n=22). The most common causes of bleeding were duodenal/gastric ulcer and/or erosive gastritis. A comparison of the non-surviving and surviving patients showed that the non-survivor ones were hemodynamically more unstable, had a greater rate of heart failure, higher BUN, creatinine, and Rockall score, and lower platelet count, albumin, and PMI (p=0.026, p=0.029, p=0.048, p=0.018, p=0.013, p<0.001, p=0.025, respectively).

Conclusion: Early detection and appropriate management of high-risk elderly patients may contribute to shortening the time to stabilize these patients. Our study showed that PMI was closely associated with mortality in elderly patients who had GI bleeding. We showed that, as PMI decreased, the patients had lower survival and more severe GI bleeding.

Keywords: Geriatric, gastrointestinal bleeding, mortality, platelet mass index

ÖZ

Amaç: Trombosit kitle indeksi (PMI), çeşitli hastalıklarda trombosit fonksiyonu ile yakından ilişkili olduğu gösterilmiştir. Bu çalışmada akut üst gastrointestinal (Gİ) kanama geçiren geriatrik hastalarda trombosit kitle indekslerinin kanama şiddeti ve mortalite tahmininde kullanılabilirliğini araştırmayı amaçladık.

Gereç ve Yöntemler: Çalışma retrospektif, analitik bir çalışmadır. Lokal etik kurul izni alınmıştır. Acil Tıp Kliniğine başvuran üst Gİ kanama tanısı alan 65 yaş ve üzeri hastalar çalışmaya dahil edildi. Hastaların demografik verileri, komorbid hastalıkları, laboratuvar endoskopi sonuçları ve hastane sonlanımları ve bir aylık mortaliteleri değerlendirildi. Hastaların Rockall skorları hesaplandı. p<0.05 için sonuçlar istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışmaya 167 hasta dahil edildi. Hastaların % 40.1 kadın cinsiyette olup yaş ortancası 79 (IQR 25-75, 71-86) olarak saptandı. Rockall skorları ortancası 4 (IQR25-75, 2-5) olup 30 günlük mortalite %13.2 (n=22) bulundu. Kanamaların en sık sebebi duodenal/gastrik ülser ve/veya eroziv gastrit olduğu görüldü. Yaşayan ve ölen hastalar karşılaştırıldığında ölen hastaların hemodinamik olarak daha fazla anstabil olduğu, kalp yetmezliğinin daha fazla olduğu, ayrıca BUN, kreatinin, Rockall skorları daha yüksek, trombosit, albümin, PMI daha düşük olduğu görüldü (sırasıyla p=0.026, p=0.029, p=0.048, p=0.018, p=0.013, p<0.001, p=0.025).

Sonuç: Yüksek riskli yaşlı hastaların erken tespiti ve uygun yönetimi, bu hastaların stabilizasyon süresinin kısaltılmasına katkıda bulunabilir. Çalışmamız, GI kanaması olan yaşlı hastalarda PMI'nin mortalite ile yakından ilişkili olduğunu gösterdi. PMI azaldıkça hastaların sağ kalımlarının daha düşük olduğunu ve daha şiddetli GI kanaması yaşadıklarını gösterdik.

Anahtar Kelimeler: Geriatri, gastrointestinal kanama, mortalite, trombosit kitle indeksi

Introduction

Rising life expectancy in the twenty-first century has led to the emergence of an older society. Acute upper gastrointestinal (GI) bleeding is an important cause of emergency department (ED) admissions (1). People over the age of 60 constitute 35-45% of the ones with acute upper GI bleeding (2). Additionally, the widespread use of medications like nonsteroidal anti-inflammatory drugs (NSAID) and anticoagulants has led to a dramatic rise in GI bleeding rates among the elderly (2, 3). Advanced age and co-morbidities cause an increase in the morbidity and mortality rates among elderly patients (4). Despite an improvement in clinical outcomes with ongoing progress in diagnosis and treatment, as well as hemostasis achieved by endoscopic means, GI bleeding poses a constant challenge as an important clinical problem in geriatric patients compared with the younger ones due to prolonged hospital stay and higher morbidity, mortality rates (5, 6). Acute upper GI bleeding episodes do not tend to be self-limiting even though they originate from a superficial focus; they may also progress to hemorrhagic shock. This constitutes an important clinical issue owing to lengthy hospital admissions and rising morbidity and mortality rates particularly in geriatric patients; thus, there is an unmet need for cost-effective, easy-to-access, and noninvasive methods to be employed for early treatment guidance and prediction of prognosis, hospitalization, and need for intensive care in this population.

Platelet mass index (PMI) is calculated by multiplying platelet count with mean platelet volume (MPV); PMI has been shown to be closely correlated to platelet function in various disorders (7-9). Platelet mass index is known to correlate with too many inflammatory, ischemic, and thrombotic events (7-9). It has been shown that patients with gastrointestinal system disorders including ulcerative colitis and Crohn's disease have a high platelet count and a low MPV, and lower MPV levels are associated with disease severity and poor prognosis (10). It is also recognized that aging affects platelet count and function. A reduced platelet count and function with aging have also been shown (11, 12). Although a review of the literature has found a number of studies on platelet indexes among adult patients with upper GI bleeding, there is an insufficient body of information concerning the geriatric age group (9, 13).

Herein we aimed to determine PMI, a low-cost, readily available parameter derived from complete blood count, among geriatric patients with acute upper GI bleeding and to use for the severity of bleeding and mortality prediction.

Material and Methods:

Study type and design

This is a retrospective, analytic study. It was approved by the local ethics committee. This study was approved by Kecioren Training and Research Hospital Ethics Committee on 08.01.2020 with the protocol code of 2012-KAEK-15/2022. As this is a retrospective study, the participants' informed consent was not required. It included patients aged 65 years or older, who were admitted to ED and diagnosed with upper GI bleeding between 01.01.2015-01.11.2019. The demographic information, comorbid disorders, vital signs, laboratory and endoscopy results, and hospital outcomes of the patients were evaluated. The Rockall scores of the patients were calculated by looking at the patient files. Patients with a Rockall score of 4 or lower were considered to have a mild risk and those with a Rockall score of 5 or higher were considered to fall in a moderate-to-high risk group. The severity of the patients' endoscopic images was rated according to the Forrest classification, where Forrest 1a and 1b were considered active bleeding. Systolic blood pressure below 90 mmHg and a pulse rate above 100 bpm at the time of ED admission were considered signs of hemodynamic instability. The mortality status of patients was determined using the hospital automation system. Patients with missing data and those who did not undergo an endoscopic study were excluded.

Blood Sample Analysis

Complete blood count parameters were analyzed using an Abbott CellDyn 3700 (USA) automatic blood cell counter and biochemistry tests were studied on Beckman Coulter AU 5800 USA. Platelet mass index was calculated with the formula (platelet counts x MPV/10^3 fL/nL).

Statistical Analysis

All study data obtained and recorded on specific study forms during the study period were analyzed using IBM SPSS 20.0 (Chicago, IL, USA) statistical software. The normality of discrete and continuous numeric variables was tested with the Kolmogorov Smirnov test. The descriptive statistics included median (interquartile range 25-75) for discrete and continuous numeric variables and a number of cases and percentage (%) for categoric variables. Categoric variables were compared with the Chi-square test and continuous variables with the Mann-Whitney-U test. A receiver-operating characteristic (ROC) analysis was performed, and the area under the curve (AUC) was calculated to find out the cutoff level for PMI level for the distinction between the surviving and non-survivor patients. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 188 patients were enrolled. Twenty-one patients with missing data were excluded, and the remaining 167 patients were included in the final analysis. Of the patients, 40.1% were female, and the median age was 79 (IQR 25-75, 71-86) years. Their most common comorbidity was hypertension. The median Rockall score was 4 (IQR25-75, 2-5); the 30-day mortality rate was 13.2% (n=22). The demographic information of the study population was shown in Table 1.

An analysis of the endoscopy results showed that the most common cause of bleeding was duodenal/gastric ulcer and/or erosive gastritis (Table 2). Non-survivor groups were more hemodynamically unstable, had a greater rate of heart failure, higher BUN, creatinine, Rockall scores, and lower platelet count, albumin, and PMI (p=0.026, p=0.029, p=0.048, p=0.018, p=0.013, p<0.001, p=0.025, respectively) (Table 3).

A receiver-operating characteristic (ROC) analysis was performed and the area under the curve (AUC) was

Female n (%)	67 (40.1%)
Age, years, *median (IQR 25-75)*	79 (71-86)
Co-morbidity n (%)	
Hypertension	134 (80.2%)
Diabetes Mellitus	71 (42.5%)
Coronary heart disease	89 (53.3%)
Chronic heart failure	44 (26.3%)
Chronic renal failure	20 (12%)
Liver disease	18 (10.8%)
Others	25 (15%)
Drugs n (%)	
NSAID	36 (21.6%)
Oral anticoagulant	104 (62.3%)
Presenting symptoms n (%)	
Hematemesis	137 (82%)
Melena	123 (73.7%)
Syncope	18 (10.8%)
Hemodynamic status (%)	
Unstable	36 (21.6%)
Rockall score *median (IQR 25-75)*	4 (2-5)
Laboratory *median (IQR 25-75)*	
Hematocrit %	28.9 (22.9-34.6)
Platelet x10^3 /μL	246 (189-300)
BUN mg/dL	39 (25-58)
Creatinine mg/dL	1.14 (0.84-1.7)
AST U/L	19 (13-27)
ALT U/L	13 (8-19)
Albumin g/dL	3.4 (3-3.7)
MPV	8.1 (7.1-9.8)
PMI	1962.8 (1625-2651)
Replacement of blood products n (%)	
Erythrocyte suspension	87 (52.1%)
ES Unit *median (IQR 25-75)*	1 (0-2)
FFP	20 (12%)
FFP Unit *median (IQR 25-75)*	0 (0-1)
Hospital stay duration *median (IQR 25-75)*	6 (4-8)
30-day mortality n (%)	22 (13.2%)

ALT: Alanine Amino Transferase AST: Aspartate Transaminase BUN: Blood urea nitrogen FFP: Fresh frozen plasma IQR: Interquartile range MPV: Mean platelet volume NSAID: Non-steroidal anti-inflammatory drug PMI: Platelet mass index

Table 1. Demographic data of patients

calculated to find out the cut-off level for PMI level between the surviving and non-surviving patients. Accordingly, the AUC value was found to be 0.709 (0.596-0.823) for mortality (p=0.002) (Figure-1). Accordingly, when a cut-off value of 2125.5 was taken, the sensitivity was found 48.2% and specificity 86.3% for 30-day mortality. The patients were grouped into two by the cut-off PMI level, with 56.8% of them having a low PMI and 43.1% a high PMI. The group with a lower PMI had a significantly higher mortality rate and Rockall score (Table 4) (p=0.003, p=0.021, respectively).

Discussion

Upper GI bleeding in the geriatric population is an emergency that is more frequent and fatal than the younger population. In the present study where we investigated the role of PMI for the prediction of 30-day mortality among patients with upper GI bleeding, we reached two important conclusions. Firstly, we determined a 30-day mortality rate of 13.2%. We showed that the non-survivor patients were hemodynamically more unstable, had a greater rate of heart failure, lower platelet count, albumin, and PMI levels but higher Rockall score, BUN, and creatinine levels compared to

Endoscopic diagnoses	n (%)
Gastric erosion/gastritis	133 (79.6%)
Gastric /Duodenal ulcer	97 (58.1%)
Cancer stomach	11 (6.6%)
Esophageal varices	12 (7.2%)
Dieulafoy's lesion	4 (2.4%)
Polyp	4 (2.4%)
Angiodysplasia	4 (2.4%)
Mallory–Weiss tear	1 (0.6%)
Forrest classification for Gastric /Duodenal ulcer	
1a	5 (5.2%)
1b	23 (23.7%)
2a	13 (13.4%)
2b	19 (19.6%)
2c	11 (11.3%)
3	26 (26.8%)
Active bleeding	29 (17.4%)
Endoscopic intervention	
Scleroterapy	55 (32.9%)
Hemoclip + Scleroterapy	11 (6.6%)
Endoscopic band ligation	10 (6%)

Some patients presented with more than 1 endoscopic finding.

Table 2. The endoscopic findings, Forest classification and endoscopic interventions

the survivors. Secondly, when we dichotomized our patients base on the cut-off level yielded by the ROC analysis, we showed that patients with a higher PMI level were more likely to survive and to have a lower Rockall score. In the geriatric population upper GI bleeding episodes are common and more severe due mainly to a greater prevalence of use of NSAIDs and anticoagulant/antiplatelet agents and a greater prevalence of systemic and gastrointestinal comorbidities (2, 3).

Platelets play an important role in hematological and inflammatory system functions. In the literature there is a limited number of studies examining the relationship between platelet functions and mortality and bleeding severity among patients suffering GI bleeding; moreover, no study to date has scrutinized such a relationship in the geriatric population (9, 13). MPV is a good indicator of platelet activation (14). In vitro studies have shown that large-volume platelets possess bigger granules and show a greater level of membrane protein activation and aggregation (15, 16). Various clinical studies that investigated the relationship between hemostasis and platelet volume have found MPV to be an independent risk factor for thrombosis and that large-volume platelets are selectively consumed more (15-18). A study by Nalbant on adult GI bleeding found no significant relationship between the MPV and the number of transfusions, endoscopic findings, and prognosis after three months of follow-up (13). We, similarly, found no difference between the non-survivor and survivor patients with respect to MPV. This may be due to many factors including timing of MPV measurement, measurement technique, timing of blood sampling, and use of anticoagulants (18, 19). Platelet mass index, a parameter calculated by multiplying MPV and platelet count, which has recently been popularized and allegedly reflects platelet functions better, has been suggested to be a more significant indicator of platelet count in various conditions (8,9,20). For a PMI cut-off level of 2125.5, we found a sensitivity of 48.2% and a specificity of 86.3%. Rockall score is currently the most

widely used GI bleeding scoring system. As the score increases, the likelihood of death and re-bleeding also

	Survivor (n= 145)	Dead (n=22)	p value
Age	79 (71-85.5)	79.5 (73-88)	0.293
Gender n (%)			
Female	57 (39.3%)	10 (45.5%)	0.584
Co-morbidity			
Hypertension	119 (82.1%)	15 (68.2%)	0.151
Diabetes Mellitus	63 (43.4%)	8 (36.4%)	0.531
Coronary heart disease	80 (55.2%)	9 (40.9%)	0.211
Chronic heart failure	34 (23.4)	10 (45.5)	0.029
Chronic renal failure	15 (10.3%)	5 (22.7%)	0.149
Liver disease	15 (10.3%)	3 (13.6%)	0.710
Drugs n (%)			
NSAID	33 (22.8%)	3 (13.6%)	0.415
Oral anticoagulant	93 (64.1%)	11 (50%)	0.202
Hemodynamic Instability n (%)	27 (18.6%)	9 (40.9%)	0.026
Rockall score *median (IQR 25-75)*	4 (2-5)	5 (3-7)	0.043
Rockal grup			
Low-risk	99 (68.3%)	10 (45.5%)	0.036
Moderate/High-risk	46 (31.7%)	12 (54.5%)	
Laboratory results *median (IQR25-75)*			
Hematocrit %			
BUN mg/dL	30 (22.8-35.2)	27 (22.9-31.9)	0.337
Creatinine mg/dL	38 (24-57.5)	45 (34.5-77)	0.048
Albumin g/dL	1.07 (0.84-1.57)	1.62 (0.97-2.51)	0.018
Platelet x10^3 /µL	3.4 (3-3.8)	3 (2.4-3.2)	<0.001
MPV	255 (200-305)	178 (121-258)	0.001
PMI	8.1 (7-9.7)	8.7 (7-10.7)	0.292
	2093 (1662-2738)	1745 (1088-2022)	0.002
Active bleeding in endoscopy n (%)	24 (16.6%)	5 (22.7%)	0.545
Replacement of blood products n (%)			
Erythrocyte suspension			
Unit *median (IQR 25-75)*	76 (52.4%)	11 (50%)	0.833
FFP	1 (0-2)	0.5 (0-2)	0.760
FFP *median ((IQR 25-75)*	17 (11.7%)	3 (13.6%)	0.731
	0 (0-1)	0 (0-1)	0.804

BUN: Blood urea nitrogen FFP: Fresh frozen plasma MPV: Mean platelet volume NSAID: Non-steroidal anti-inflammatory drug PMI: Platelet mass index

Table 3. Comparisons of the patient characteristics regarding in 30-day mortality

increases (1). We detected a higher Rockall score among patients with a lower PMI. We also demonstrated that as PMI decreased, the patients' survival rate is parallelly reduced and the severity of GI bleeding worsened. There are clear age-related changes in platelet count and function, driven by changes in hematopoietic tissue, the composition of the blood and vascular health. It is recognized that a reduction in platelet functions occur with aging (11).

	Low PMI (n= 95)	High PMI (n=72)	
Age *median ((IQR 25-75)*	79 (71-86)	79 (71-86)	0.815
Gender n (%)			
Female	37 (38.9%)	30 (41.7%)	0.723
Co-morbidity			
Hypertension	75 (78.9.1%)	59 (81.9.2%)	0.630
Diabetes Mellitus	44 (46.3%)	27 (37.5%)	0.254
Coronary heart disease	44 (46.3%)	45(62.5%)	0.038
KKY	24 (25.3%)	20 (27.8%)	0.715
Chronic renal failure	13 (13.7%)	7 (9.7%)	0.435
Liver disease	17 (17.9%)	1 (1.4%)	0.001
Hemodynamic Instability n (%)	24 (25.3%)	12 (16.7%)	0.181
Rockall score *median ((IQR 25-75)*	4 (2-5)	4 (3-4.75)	0.533
Rockall grup			
Low-risk	55(57.9%)	54 (75%)	0.021
Moderate /High -risk	40 (42.1%)	18 (25%)	
Laboratory *median (IQR 25-75)*			
Hematocrit %	28.7 (22.9-35.5)	29.2 (22.9-34.5)	0.659
BUN mg/dL	39 (25-59)	40.5 (25-57)	0.660
Creatinine mg/dL	1.18 (0.85-1.7)	1.1 (0.84-1.70)	0.806
Albumin g/dL	3.4 (2.9-3.7)	3.3 (3-3.8)	0.364
Active bleeding in endoscopy n (%)	16 (16.8%)	13 (18.1%)	0.838
Replacement of blood products n (%)			
Erythrocyte suspension			
Unit *median ((IQR 25-75)*	44 (46.3%)	43 (59.7%)	0.086
FFP	0 (0-2)	1 (0-2)	0.232
FFP *median ((IQR 25-75)*	9 (9.5%)	11 (15.3%)	0.253
	0 (0-1)	0 (0-1)	0.198

| Mortality n (%) | 19 (20%) | 3 (4.2%) | 0.003 |

BUN: Blood urea nitrogen FFP: Fresh frozen plasma NSAID: Non-steroidal anti-inflammatory drug PMI: Platelet mass index

Table 4 Characteristics of patients below and above the receiver operating curve based cut-off value for platelet mass index (PMI)
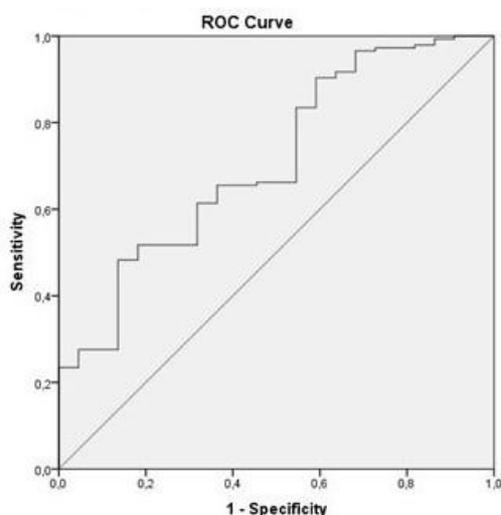
Figure 1. Receiver-operating characteristic (ROC) analysis for platelet mass index between the survivor and no-survivor groups

These changes affect both bleeding and thrombosis and are particularly pertinent given that thrombotic disease and use of anti-platelet drugs is much more prevalent in the elderly population (12). Such a change in platelet function in the geriatric population may have caused GI bleeding episodes to be more severe in the elderly compared to the younger age group.

Limitations

Our study has some limitations. First of all, it is a single-center study and thus its results are not generalizable to all centers. Secondly, missing or inaccurate data stemming from the retrospective nature of the study may have affected its results. Another limitation is the lack of optimization of the measurement time for MPV value.

Conclusion

Early detection and appropriate management of high-risk elderly patients may shorten the time to stabilization in these patients. We showed that PMI was closely correlated to mortality among elderly patients suffering GI bleeding. As PMI is reduced, patients suffer more severe GI and have a worse prognosis.

Conflict of Interest: The authors declare no conflict of interest regarding this study.

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Authors' Contribution: Concept – HU, SKC, YC; Supervision – EE, MY, SD; Materials -EE, SD; Data Collection and Processing -HU, SKC; Analysis and Interpretation -SKC; Writing – HU, SKC.

Ethical Statement: This study was approved by Kecioren Training and Research Hospital Ethics Committee on 08.01.2020 with the protocol code of 2012-KAEK-15/2022. All authors declared that they follow the rules of Research and Publication Ethics.

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