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Relationship of the CRP/albumin ratio and the systemic immune-inflammation index with Forrest classification in patients with gastrointestinal bleeding

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ABSTRACT

Aim: The present study aimed to investigate CRP/albumin ratio and the systemic immune-inflammation index (SII) and Forrest classification in patients who presented to the emergency department with acute upper gastrointestinal (GI) bleeding.

Materials and Method: Patients over 18 years of age who presented to the emergency department of our hospital with melena, hematemesis, and hematochezia and were diagnosed with upper GI bleeding via esophagoduodenoscopy were included in the study. Esophagoduodenoscopy results, and accordingly, the Forrest classifications, together with complete blood count, including hemoglobin, platelet, and neutrophil values, as well as demographic characteristics were recorded. SII (calculated by multiplying the platelet count with neutrophil count and dividing the value obtained by the lymphocyte count [platelet (P)×neutrophil (N)/lymphocyte (L)]) and CRP/albumin ratio was calculated.

Results: No statistically significant difference was observed among the Forrest classification groups in terms of the median SII values as well as median CRP/albumin ratios. However, a statistically significant difference in median CRP/albumin ratios was observed among the dichotomized Forrest classification groups.

Conclusion: The SII is not a reliable parameter either predicts GI bleeding or the Forrest classification in patients with upper GI bleeding. The CRP/albumin ratio might be a poor predictor of bleeding; however, it can not predict the Forrest classification.

Keywords: CRP albumin ratio, Forrest classification, systemic immune-inflammation index, upper gastrointestinal bleeding

INTRODUCTION

Patients diagnosed with upper gastrointestinal (GI) bleeding are commonly present with various etiologies and symptoms. (1) Melena or hematemesis are common symptoms of upper GI bleeding at presentation. In rare cases, the symptoms also include hematochezia. Esophagoduodenoscopy is a useful diagnostic as well as a therapeutic procedure for patients with upper GI bleeding. (2) The Forrest classification is used during esophagoduodenoscopy to determine the severity of the symptoms and to indicate the risk of re-bleeding. The Forrest classification is as follows: Forrest Ia (Active Bleeding), Ib (Oozing Bleeding), IIa (Non-bleeding visible vessel), IIb (Glutinous clot), IIc (Flat spot), and III (Flat spot, clean base) (3).

The C-reactive protein (CRP)/albumin ratio is a new generation indicator of inflammation, and its usefulness has been shown in various types of cancer and sepsis. It has also been proven that this ratio can be used in traumatic brain injury. (4) Similar to the C-reactive protein (CRP)/albumin ratio, the Systemic Immune-Inflammation Index (SII) is a valuable prognostic parameter that can be obtained through routine blood tests and provides information about the inflammatory status of the patient in a number of medical conditions, including hepatocellular, colorectal, and pancreatic cancers. (5) It was determined that the CRP value showed 30-day mortality in non-variceal GI bleeding. (6) Also, studies have also been shown that CRP/albumin ratio is a prognostic marker for gastric cancer type. (7)

In a meta-analysis investigating the relationship between gastric cancers and SII value, it showed the relationship of SII value with tumor invasion and prognosis. (8) To the best of our knowledge, our study is the first to examine the CRP/albumin ratio and the relationship between SII and GI bleeding.

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The present study aimed to investigate these inflammatory indexes and Forrest classification in patients who presented to the emergency department with acute upper GI bleeding.

MATERIALS AND METHOD

The study was initiated with the approval of the Karabük University Hospital Non-interventional Clinical Research Ethics Committee (Date: 01.10.2021, Decision No: 2021/656). All procedures were performed adhered to the ethical rules and principles of the Helsinki Declaration.

The present study was designed as a retrospective cross-sectional study. The patients over 18 years of age presented to the emergency department of our hospital between 09/01/2020 and 09/01/2021 with melena, hematemesis, and hematochezia and were diagnosed with upper GI bleeding via esophagoduodenoscopy. The study data were retrieved from the hospital information-processing system. Esophagoduodenoscopy results, and accordingly, the Forrest classifications, together with complete blood count, including hemoglobin, platelet, and neutrophil values, as well as demographic characteristics, such as age, and gender were recorded. The blood tests were performed during the first presentation to the emergency department. SII (calculated by multiplying the platelet count with neutrophil count and dividing the value obtained by the lymphocyte count [platelet (P)×neutrophil (N)/lymphocyte (L)]) and CRP/albumin ratio were calculated. Patients aged below 18 years; pregnant patients; patients with a history of hematological or autoimmune disease; those who recently underwent chemotherapy, radiotherapy, or blood transfusions; and those with lack of access to required data were excluded from the study.

Statistical Analysis

Statistical Package for the Social Sciences for Windows (IBM Corp., Armonk, NY, USA) was used for the statistical analyses of data. The normality of the distribution of continuous data was tested with the Shapiro–Wilk test and a histogram. Continuous normally distributed data were expressed in mean±standard deviation, and continuous non-normally distributed data were expressed in median (25%–75% quartile), whereas categorical data were expressed in frequency and percentage. Non-normally distributed continuous data was analyzed using the Mann–Whitney U test for paired group comparisons and Kruskal–Wallis test for multiple group comparisons. The Forrest classification was dichotomized into class 3 and others. The usefulness of the CRP/albumin ratio in predicting the dichotomized Forrest classification was analyzed using the Receiver Operating Characteristic (ROC) curve, and the criteria for the value of the CRP/albumin ratio based diagnostic test were calculated.

RESULTS

A total of 180 patients were included in the study; of these, patients who did not undergo esophagoduodenoscopy (n=29), those who underwent esophagoduodenoscopy for different purposes (such as peg insertion and foreign body removal) (n=21), and those with esophageal hemorrhages outside the Forrest classification (n=17) were excluded. 113 patients were included in the study. The median age was 64 years (45–75.5), and 82 (72.6%) of the patients were males. The basic descriptive characteristics of the study group are summarized in **Table 1**.

Table 1. Main descriptive characteristics of patients

Age (median [IQR])	64 (45–75.5)
Gender (Male) n (%)	82 (72.6)
Hemoglobin (g/dl) (mean±SD)	9.9 (2.9)
Neutrophil (10^3/uL) (median [IQR])	7 (5.5–9)
Lymphocyte (10^3/uL) (median [IQR])	1.8 (0.9–2.5)
Platelet (10^3/uL) (median [IQR])	218 (171.3–290.8)
Creatinine (mg/dl) (median [IQR])	0.9 (0.6–1.1)
INR (median [IQR])	1.12 (1.04–1.19)
CRP (mg/L) (median [IQR])	6.9 (1.8–47.6)
Albumin (g/dL) (median [IQR])	35.1 (29.2–37.7)
SII (median [IQR])	815.8 (542.4–1703)
CRP/Albumin Ratio (median [IQR])	0.21 (0.05–1.4)
Neutrophil/Lymphocyte Ratio (median [IQR])	3.7 (2.4–7.7)
Platelet/Lymphocyte Ratio (median [IQR])	126.1 (86.4–216.3)
Forrest Classification n (%)	113 (100)
Forrest 1a n (%)	1 (0.9)
Forrest 1b n (%)	13 (11.5)
Forrest 2a n (%)	4 (3.5)
Forrest 2b n (%)	9 (8)
Forrest 2c n (%)	15 (13.3)
Forrest 3 n (%)	71 (62.8)

CRP: C-reactive Protein, INR: International Normalized Ratio, SII: Systemic Immune-Inflammatory Index, SD: Standard Deviation,

No statistically significant difference was observed among the Forrest classification groups in terms of SII median values (p=0.655, Kruskal–Wallis). The Forrest classification was dichotomized into class 3 without bleeding and other classes with bleeding (**Table 2**). The difference in terms of SII median values among the groups with and without bleeding showed that there was no statistically significant difference among the groups (p=0.910, Mann–Whitney U).

Table 2*. Difference in the median Systemic Immune-Inflammatory Index (SII) values among the Forrest classification groups

	Forrest 1b	Forrest 2a	Forrest 2b	Forrest 2c	Forrest 3	p value**
SII (median (25%–75% quartile))	786.4 (478.4–2624)	813.6 (299.1–1293.4)	821.2 (714.2–2463.8)	660.8 (515.6–1235.3)	784.5 (540.3–1453)	0.655

* As there was only 1 patient in the Forrest 1a group, it could not be included in the analysis. ** Kruskal–Wallis test was used. P-values provided in boldface are statistically significant (p<0.05). SII: Systemic Immune-Inflammatory Index.

Table 3*. Difference in median Neutrophil–Lymphocyte Ratio (NLR), Platelet–Lymphocyte Ratio (PLR), and C-reactive Protein (CRP)/Albumin ratios among the Forrest classification groups

	Forrest 1b	Forrest 2a	Forrest 2b	Forrest 2c	Forrest 3	p value**
NLR (median [IQR])	7.1 (2.1–10)	3 (1.7–5.2)	3.7 (2.9–8)	3.7 (2.3–7.4)	3.4 (2.3–6.6)	0.862
PLR (median [IQR])	115.5 (87.7–231.4)	105.7 (50.4–135.6)	116.5 (98.3–267.7)	132.3 (90–207.6)	143.6 (84.7–219.6)	0.520
CRP/Albumin (median [IQR])	0.05 (0.02–0.49)	0.84 (0.7–4.7)	0.07 (0.02–0.57)	0.05 (0.04–3.70)	0.39 (0.08–2.52)	0.147

* As there was only 1 patient in the Forrest 1a group, it could not be included in the analysis. ** Kruskal–Wallis test was used. P-values in boldface are statistically significant (p<0.05). NLR: Neutrophil–Lymphocyte Ratio, PLR: Platelet–Lymphocyte Ratio, CRP: C-reactive Protein

No statistically significant difference was found in median CRP/albumin ratios among the Forrest classification groups (p=0.147, Kruskal–Wallis) (**Table 3**). However, the difference in the median CRP/albumin ratios among the dichotomized Forrest classification groups was statistically significant (p=0.023, Mann–Whitney U) (**Table 4**). While testing the diagnostic performance of the CRP/albumin ratio in predicting the presence of bleeding via endoscopy (Forrest 1a, 1b, 2a, 2b, and 2c) using ROC analysis, the area under the curve (AUC) was determined as 0.641 (**Figure 1**). The highest sum of sensitivity and specificity, i.e., 0.06, was set as the threshold value. According to the this threshold, the sensitivity of the test was 51.4% (95% confidence interval (CI): 34%–68.6%), specificity was 81% (95% CI: 68.6%–90.1%), positive likelihood ratio was 2.71 (95% CI: 1.46–5.05), negative likelihood ratio was 0.6 (95% CI: 0.42–0.86), positive predictive value was 62.1% (95% CI: 46.8%–75.3%), negative predictive value was 73.4% (95.8%–80%), and accuracy was 69.9% (95% CI: 59.5%–79%) (**Table 5**).

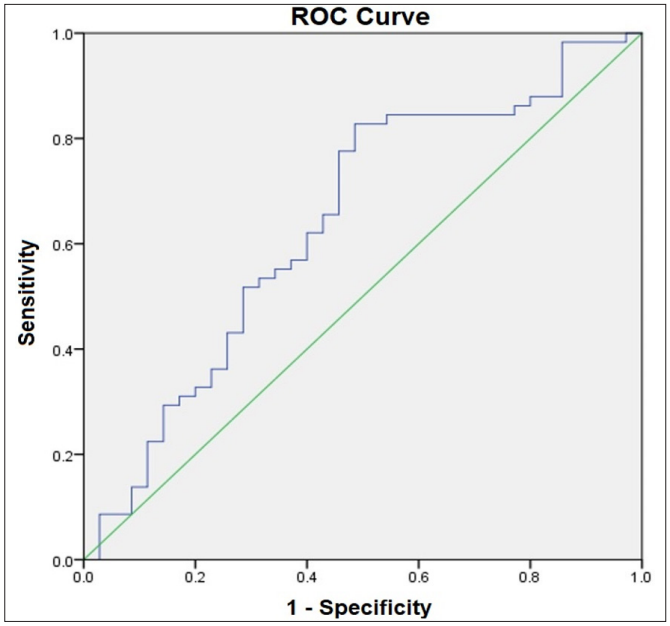

Figure 1. Receiver Operating Characteristic curve

Table 4*. Difference in median NLR, PLR, and CRP/Albumin ratios among the dichotomized Forrest classification groups

	Forrest 3	Forrest 1a, 1b, 2a, 2b, and 2c	p value**
NLR (median [IQR])	3.4 (2.3–6.6)	3.7 (2.3–8)	0.483
PLR (median [IQR])	143.6 (84.7–219.6)	116 (89.1–191.6)	0.695
CRP/Albumin (median [IQR])	0.39 (0.76–2.52)	0.05 (0.03–0.79)	0.023

* The Forrest classification was dichotomized into class 3 without bleeding and other classes with bleeding. ** Mann–Whitney U test was used. P-values provided in boldface are statistically significant (p<0,05). NLR: Neutrophil–Lymphocyte Ratio, PLR: Platelet–Lymphocyte Ratio, CRP: C-reactive Protein

Table 5. Diagnostic performance criteria of the CRP/Albumin ratio in predicting the presence of bleeding

AUC	0.641 (95% CI: 0.522–0.761)
Sensitivity	51.4% (95% CI: 34%–68.6%)
Specificity	81% (95% CI: 68.6%–90.1%)
Positive likelihood ratio	2.71 (95% CI: 1.46–5.05)
Negative likelihood ratio	0.6 (95% CI: 0.42–0.86)
Positive predictive value	62.1% (95% CI: 46.8%–75.3%)
Negative predictive value	73.4% (95% CI: 65.8%–80%)
Accuracy	69.9% (95% CI: 59.5%–79%)

AUC: Area Under the Curve, 95% CI: 95% Confidence Interval.

No statistically significant difference was observed among the Forrest classification groups in terms of the median neutrophil-lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) (p=0.862, p=0.520, Kruskal–Wallis, respectively). Moreover, there was no statistically significant difference among the dichotomized Forrest groups in terms of median NLR and median PLR (p=0.483, p=0.695, respectively, Mann–Whitney U). These results are summarized in **Tables 3** and **4**.

DISCUSSION

The SII is a new marker that is calculated using a complete blood count test and was shown to have been associated with adverse outcomes of cancer types.(9) It was first developed in 2014. (5) The SII reflects the balance between inflammatory status at the systemic

level. This index was comprehensively studied in recent years as it is inexpensive, easy to calculate, and easy to obtain. (9) The SII was reported to be a powerful predictor of poor prognosis and mortality in cardiovascular diseases, including endocarditis and pulmonary embolism, as well as a predictor of prognosis in patients with, for instance, kidney, lung, and prostate cancers. The SII was also used as a prognostic marker in patients with contrast-induced nephropathy, ischemic stroke, Bell's palsy, sinus vein thrombosis, intracerebral hemorrhage, glioma, and subarachnoid hemorrhage. (9-12) In a study conducted in patients with the acute coronary syndrome, they investigated the comorbidities of the patients using the Elixhauser Comorbidity Index and it was found that the SII value was higher in patients with comorbidity.(13) To the best of our knowledge, the usefulness of the SII was evaluated for the first time for upper GI bleeding in the present study; however, it was not a useful parameter in predicting the Forrest classification as well as in determining the likelihood of bleeding present during esophagoduednoendoscopy.

Several blood-related parameters, including CRP and albumin, are reported as prognostic markers for various diseases. (14-16) However, a single blood parameter is not to be reliable because such parameters are inevitably susceptible to a series of other diseases. (16) An elevated CRP alone often suggests an infective or inflammatory condition. (17) Elevated CRP was shown in relation to increased severity in various diseases, including ischemic heart disease, and chronic liver disease. (18,19) Higher serum CRP levels are associated with poor prognosis and increased mortality in patients with upper GI bleeding, (18-21) whereas low albumin levels are often associated with chronic diseases due to nutritional deficiencies. These parameters are easily accessible and often obtained automatically as a part of the application profile. (17) The CRP/albumin ratio is both a nutritional and inflammation-based index similar to the SII; thus, the same may increase in many diseases. (16) This ratio is less affected by age, despite the fact that prognosis in many diseases is affected by age. (17) The present study found that the CRP/albumin ratio might serve as a useful parameter in detecting upper GI bleeding upon dichotomization by the presence or absence of bleeding, but CRP/albumin ratio could not predict the Forrest classification. Based on the threshold value of 0.06, i.e., the highest sum of sensitivity and specificity, the sensitivity and the specificity of the test were 51.4% and 81%, respectively. Although it is not an ideal test in the given circumstances, its low cost and frequent request may favor its use.

NLR and PLR markers can be obtained and were shown to have been associated with negative outcomes in various types of cancers as well as inflammatory diseases and coronary artery-related diseases. (9) In the present study, it proved to be inadequate to predict either the Forrest classification or the presence of bleeding.

The median age of the 113 patients included in our study was 64 years; this is similar to the findings of many studies in the literature. (22-26) Diseases with a higher prevalence in older individuals and increased drug use associated with such diseases may account for the increased upper GI bleeding observed in older individuals. However, such data were not collected in the present study. A total of 72.6% of the patients in the present study were males. Except for a study by Okutur et al. (27), different rates in terms of sex were found in other studies. (22,23)

Limitations

It was a single-center study. There was no data regarding the prognosis of the patients, this study did not include the mortality and morbidity rates of the patients. Further prospective studies with larger numbers of patients are needed.

CONCLUSION

The SII is not a reliable parameter either predicts GI bleeding or the Forrest classification in patients with upper GI bleeding. The CRP/albumin ratio might be a poor predictor of bleeding; however, it can not predict the Forrest classification.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Karabük University Hospital Non-interventional Clinical Research Ethics Committee (Date: 01.10.2021, Decision No: 2021/656).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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