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Predictive value of blood urea nitrogen to serum albumin ratio in estimating in-hospital mortality in patients with upper gastrointestinal bleeding

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ABSTRACT

Introduction and aim. The aim of this study was to examine the usability of blood urea nitrogen to serum albumin ratio (BAR) as a prognostic predictor of in-hospital mortality in patients with gastrointestinal (GI) bleeding.

Material and methods. The electronic medical records of the patients who applied to the emergency department due to upper GI bleeding during the study period were reviewed. The receiver operating characteristic (ROC) curve and the area under the curve (AUC) were used to evaluate each discriminant cut-off value to estimate mortality.

Results. The study included 225 patients. The median (IQR) age of the patients was 75.0 (68.0–84.0) and 94 (41.8%) were female. AUC was determined as 0.784±0.055 (95% CI, 0.677–0.892) for BAR (p<0.001) in terms of in-hospital mortality. The cut-off value of BAR for this outcome was calculated as 16.26. In this cut-off value, sensitivity was 71.43%, specificity 82.84%, positive predictive value (PPV) 30.00% and negative predictive value (NPV) 96.57%.

Conclusion. BAR is a useful tool that can be used to predict the in-hospital mortality of patients with GI bleeding. Patients with GI bleeding with a BAR above 16.26 will require more aggressive and timely intervention.

Keywords. albumin, blood urea nitrogen, mortality, upper gastrointestinal bleeding

Introduction

Upper gastrointestinal (GI) bleeding is one of the most common causes of emergency department (ED) visits worldwide.[1–3] There are more than 800,000 ED visits in the United States each year due to the disease, and half of these are hospitalized.[4] Endoscopic and pharmacological advances have resulted in reductions in mortality from GI bleeding.[5,6] However, despite diagnostic and therapeutic advances, the mortality rate due to GI bleeding still varies between 5-10%.[7] Therefore, risk identification strategies are important in EDs.

It is aimed to predict the prognosis of the disease and to recognize critically ill patients early by using scoring systems and laboratory values in GI diseases.[8,9] There are scoring systems used to predict mortality, length of hospital stay and endoscopy requirement in GI bleeding.[10,11] However, their use in ED is difficult due to the lack of endoscopy units in every hospital and the complex structures of the scores.

Urea is formed by the liver metabolization of its nitrogen-containing products and is excreted by the kidneys. Clinicians often use blood urea nitrogen (BUN) to measure the amount of nitrogen from urea in the blood as an index of kidney function. BUN is a biomarker that provides valuable information about the clinical status of patients such as renal hypoperfusion, low cardiac out-

put, dehydration and neurohumoral activity.[12] Albumin plays an important role in many physiological mechanisms, including the regulation of osmotic pressure. It takes part in the transport of molecules such as hormones, cholesterol, calcium, iron, bilirubin, free fatty acids and drugs.[13] It has been shown by various studies that the BUN albumin ratio (BAR) increases in many diseases.[14,15]

Aim

The aim of this study was to examine predictive value of blood urea nitrogen to serum albumin ratio in estimating in-hospital mortality in patients with upper gastrointestinal bleeding who visited the ED.

Material and methods

Between June 1, 2021 and June 1, 2022, this retrospective cohort research was done in the ED of a tertiary care hospital. The institutional review board authorized the analysis and waived permission (Ethics Committee Ruling number: 2011/KAEK/50/211).

All patients over the age of 18 who visited to ED within the period determined for the study and were diagnosed with upper GI bleeding were included in the study. By scanning the hospital electronic medical records; vital parameters, comorbid diseases, medications, length of hospital stay and in-hospital mortality were recorded in a pre-created dataset. After all the data were processed by the first researcher, the second researcher controlled them. The BAR was defined as the BUN value divided by the albumin value, and this value was calculated. The definition of upper GI bleeding was based on the presence of at least one of the following three features: hematemesis, melena, or solid clinical evidence and laboratory support for acute blood loss from the upper gastrointestinal (UGI) tract. Patients with a diagnosis other than upper GI bleeding, patients with deficient BUN and/or albumin values, patients transferred from another hospital, patients who died or were discharged in the ED were excluded from the study. Death within the hospital during index admission defined as in-hospital mortality and interval between hospital admission (admissions from ED) and discharge defined as the length of hospital stay.[16] The primary study outcome was all-cause in-hospital mortality. The secondary study outcome was the relationship between BAR and length of the hospital stay.

Statistical analysis

The descriptive statistics were presented in median values and interquartile ranges (IQR; 25% to 75%) for the quantitative variables; and frequencies and percentages for the categorical variables. Normality tests were carried out by using one-sample Kolmogorov–Smirnov and Shapiro-Wilk tests and through histogram graphs. Patients

were divided into two groups as survivors and non-survivors and all variables were compared according to groups. The frequencies of categorical variables were compared using Pearson's chi-square and Fisher's exact test as appropriate. The median values of the quantitative variables were compared using the Mann-Whitney U test. Receiver operating characteristic (ROC) analysis was performed to evaluate the predictive power of the BAR in terms of in-hospital mortality. In the light of the ROC analysis, the optimum cut-off points were calculated for BAR according to Youden's index. The correlations of BAR, in-hospital mortality and length of hospital stay variables were evaluated using point-biserial correlation and Spearman's rho correlation. A 2-sided P-value of 0.05 was regarded as statistically significant (except correlation analyses – correlation is significant at the 0.01 level). The area under the curve (AUC) was used to evaluate each discriminant cut-off value to predict in-hospital mortality. AUC of the non-diagnostic test is 0.50. If it is a perfect test, with zero false positives and zero false negatives, the value of the field would be 1.00. If the value under the curve is 0.90–1.00, it is excellent, 0.80–0.90 is good, 0.70–0.80 is medium, 0.60–0.70 is weak, 0.50–0.60 is unsuccessful. All data analyses were performed using SPSS statistical software (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

Results

A total of 291 patients were included in the study. Because 34 patients were diagnosed other than upper GI bleeding, 8 patients had deficient BUN and/or albumin values, 17 patients were transferred from another hospital, 2 patients died in ED and 5 patients were discharged from ED; were not included in the study. The study was completed with 225 patients. The median (IQR) age of the patients was 75 (68–84) years and 94 (41.8%) were female. In the first evaluation; the Glasgow coma scale/ score (GCS) of 217 patients (96.4%) was 15, six (2.7%) of them had a GCS of 14, and two (0.9%) had a GCS of 13. The median (IQR) systolic blood pressure of the patients was 122 (115–131) mmHg and the pulse rate was 97 (87–105) bpm. The comorbidities of the patients enrolled in the study were examined, the first three were acute coronary syndrome (38.7%), diabetes mellitus (26.2%), and congestive heart failure (20.4%). Fourty-seven (20.9%) of the patients had no comorbidities, 71 (31.6%) had one, 61 (27.1%) had two, and 46 (20.4%) had three or more comorbidities. 5.8% of the patients were using steroids, 24.4% were using anticoagulants, 32.9% were using antiplatelet agents and 13.8% were using nonsteroidal anti-inflammatory drugs. While 74 (32.9%) of the patients did not use any medication, 130 (57.8%) were using one drug, 20 (8.9%) were using two drugs, and 1 (0.4%) was using three drugs. In terms of gastrointestinal (GI) bleeding symptoms melena

Table 1. Demographic, laboratory and clinical characteristics of the patients, n=225 [A]

Variables		Total (%)
Gender[a]		
	female	94 (41.8)
	male	131 (58.2)
Age[b], years		75.0 (68.0–84.0)
GCS[a]		
	13	2 (0.9)
	14	6 (2.7)
	15	217 (96.4)
SBP[b], mmHg		122 (115–131)
Pulse rate[b], bpm		97 (87–105)
Comorbidities[a]		
	Acute coronary syndrome	87 (38.7)
	Congestive heart failure	46 (20.4)
	Peripheral vascular disease	11 (4.9)
	Cerebrovascular disease	24 (10.7)
	Dementia	18 (8)
	Hemiplegia or paraplegia	1 (0.4)
	Chronic pulmonary disease	27 (12)
	Rheumatologic disease	0 (0)
	Peptic ulcer	23 (10.2)
	Diabetes mellitus	59 (26.2)
	Chronic renal failure	21 (9.3)
	Liver disease	10 (4.4)
	Malignancy	27 (12)
	Leukemia or Lymphoma	3 (1.3)
Number of comorbidities[a]		
	0	47 (20.9)
	1	71 (31.6)
	2	61 (27.1)
	2<	46 (20.4)
Drugs[a]		
	Steroids	13 (5.8)
	Anticoagulants	55 (24.4)
	Antiplatelet agents	74 (32.9)
	Nonsteroidal anti-inflammatory	31 (13.8)
Number of drugs[a]		
	0	74 (32.9)
	1	130 (57.8)
	2	20 (8.9)
	3	1 (0.4)
GI bleeding symptoms[a]		
	hematemesis	77 (34.2)
	melena	184 (81.8)
	hematochezia	6 (2.7)
Number of GI bleeding symptoms[a]		
	0	6 (2.7)
	1	172 (76.4)
	2	46 (20.4)
	3	1 (0.4)
Laboratory[b]		
	Hemoglobin, g/dL	8.7 (6.6-10.2)
	BUN, mg/dL	30.5 (18.7-50.5)
	Creatinine, mg/dL	0.99 (0.79-1.37)
	Albumin, g/dL	3.4 (2.96-3.79)
	BUN/Albumin, mg/g	8.92 (5.61-15.5)
Length of hospital stay[b], days		5 (5-7)
In-hospital mortality[a]		21 (9.3)

[A] GCS – Glasgow coma scale, SBP – systolic blood pressure, GI – gastro-intestinal, BUN – blood urea nitrogen, [a] n (%), [b] median (IQR)

was the leading one with 81.8%. Six (2.7%) of the patients had no GI bleeding symptom (These patients were included in the study because they had decreased hemoglobin values or symptoms of GI bleeding during their observation in the ED) 172 (76.4%) had one, 46 (20.4%) had two, and 1 (0.4%) had all three (hematemesis, melena and hematochezia) symptoms. The median length of hospital stay was 5 (5–7) days and 21 patients (9.3%) died. The demographic, laboratory and clinical characteristics of the patients were shown in Table 1.

The patients were divided into two groups as survivors and non-survivors, and all variables were compared over these two groups. There was no significant difference between the groups in gender, age, GCS, SBP, pulse rate, number of comorbidities, drugs used, GI bleeding symptoms, number of symptoms and length of hospital stay variables (p>0.05 for all). Chronic renal failure was found in 23.8% of the non-survivor group and 76.2% of the survivor group (p=0.033). No significant difference was found between the groups in other comorbidities (p>0.05 for all). Laboratory tests were compared between groups; BUN, creatinine and BUN/albumin levels were significantly higher in the non-survivor group (p<0.001, p=0.008 and p<0.001; respectively); and albumin was significantly lower in non-survivors (p<0.001). There was no difference between the groups in terms of hemoglobin levels and also the length of hospital stay days (p=0.356 and 0.172, respectively). The comparisons of all these parameters were shown in Table 2.

ROC analyses were performed to evaluate the power of the BAR to predict in-hospital mortality (Figure 1).
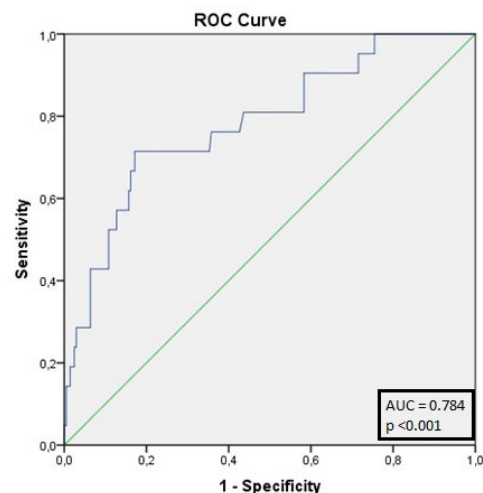

Fig. 1. ROC analysis of BUN/Albumin ratio in terms of in-hospital mortality (AUC of BUN/albumin=0.784±0.055 (95% CI=0.677–0.892), (p<0.001))

The area under the curves (AUCs) was determined as 0.784±0.055 (95% CI, 0.677–0.892) for BAR (p<0.001). According to the result of the ROC analyses, the optimum cut-off points of the BAR were determined

using Youden's index. The cut-off value of BAR for this outcome was calculated as 16.26. In this cut-off value, sensitivity was 71.43%, specificity 82.84%, PPV 30.00% and NPV 96.57% (Table 3).

Table 3. Optimum cut-off points* of BUN/albumin ratio in terms of in-hospital mortality [A]

Cut-off point	Sens (%)	Spec (%)	PPV (%)	NPV (%)	AUC	Youden's Index
16.15	71.43	81.86	28.85	96.53	0.784	0.533
16.18	71.43	82.35	29.41	96.55	0.784	0.538
16.26	71.43	82.84	30.00	96.57	0.784	0.543

[A] BUN – blood urea nitrogen, Sens – sensitivity, Spec – specificity, PPV – positive predictive value, NPV – negative predictive value AUC – area under the curve, *Cut-off points with the three highest Youden's index value were shown

Correlation analysis was performed to evaluate the relationships between BAR, in-hospital mortality and length of hospital stay parameters (Table 4). There was a fair positive correlation between BAR and in-hospital mortality (R=0.366, p<0.001), and there was also a poor positive correlation between BAR and lenght of the hospital stay (R=0.244, p<0.001).

Table 4. Correlation matrix of BUN/albumin, in-hospital mortality and length of hospital stay [A]

Correlations	BUN/albümin	In-hospital mortality	Length of hospital stay
BUN/albumin	-		
In-hospital mortality	R=0.366 p<0.001*	-	
Length of hospital stay	R=0.244 p<0.001**	R=0.103 p=0.125*	-

[A] BUN – blood urea nitrogen, *Point-biserial correlation, correlation is significant at the 0.01 level (2-tailed), **Spearman's rho correlation, correlation is significant at the 0.01 level (2-tailed)

Discussion

This study examined the relationship between BAR and in-hospital mortality and length of the hospital stay in patients with GI bleeding who visited the ER. It was concluded that BAR can be used as a good predictor in patients with GI bleeding.

GI bleeding is a disease condition that is frequently seen in EDs and can be seen in clinical presentations with high mortality. Although there are some clinical scoring systems used to determine the severity of GI bleeding; these scoring systems are not always useful in emergency practice. For this reason, laboratory parameters that can be viewed quickly in the ED can guide physicians in patient management.

There are studies in the literature in which albumin and BUN values are used as prognostic tools in patients

Table 2. The comparison of parameters between survivors and non-survivors [A]

Variables	Survivors, n=204 (%)	Non-survivors, n=21 (%)	p value
Gender[a]			0.719*
female	86 (91.5)	8 (8.5)	
male	118 (90.1)	13 (9.9)	
Age[b], years	75.0 (68.0-83.0)	81.0 (75.0-85.0)	0.061**
GCS[a]			0.165***
<15	6 (66.7)	2 (33.3)	
15	198 (91.2)	19 (8.8)	
SBP[b], mmHg	122 (115-132)	121 (102-124)	0.103**
Pulse rate[b], bpm	97 (87-105)	104 (93-109)	0.058**
Comorbidities[a]			
Acute coronary syndrome	77 (37.7)	10 (47.6)	0.376*
Congestive heart failure	40 (19.6)	6 (28.6)	0.392***
Peripheral vascular disease	9 (4.4)	2 (9.5)	0.274***
Cerebrovascular disease	23 (11.3)	1 (4.8)	0.708***
Dementia	16 (7.8)	2 (9.5)	0.678***
Hemiplegia or paraplegia	1 (0.5)	0 (0.0)	1.000***
Chronic pulmonary disease	25 (12.3)	2 (9.5)	1.000***
Rheumatologic disease	0 (0.0)	0 (0.0)	-
Peptic ulcer	20 (9.8)	3 (14.3)	0.458***
Diabetes mellitus	52 (25.5)	7 (33.3)	0.437*
Chronic renal failure	16 (7.8)	5 (23.8)	0.033***
Liver disease	9 (4.4)	1 (4.8)	1.000***
Malignancy	25 (12.3)	2 (9.5)	1.000***
Leukemia or Lymphoma	3 (1.5)	0 (0.0)	1.000***
Number of comorbidities[a]			0.199***
0	45 (22.1)	2 (9.5)	
1	65 (31.9)	6 (28.6)	
2	56 (27.5)	5 (23.8)	
2<	38 (18.6)	8 (38.1)	
Drugs[a]			
Steroids	11 (5.4)	2 (9.5)	0.347***
Anticoagulants	47 (23.0)	8 (38.1)	0.126*
Antiplatelet agents	66 (32.4)	8 (38.1)	0.594*
Nonsteroidal anti-inflammatory	26 (12.7)	5 (23.8)	0.181***
Number of drugs[a]			0.036***
0	71 (34.8)	3 (14.3)	
1	117 (57.4)	13 (61.9)	
2	15 (7.4)	5 (23.8)	
3	1 (0.5)	0 (0.0)	
GI bleeding symptoms[a]			
hematemesis	70 (34.3)	7 (33.3)	0.928*
melena	166 (81.4)	18 (85.7)	0.773***
hematochezia	5 (2.5)	1 (4.8)	0.448***
Number of GI bleeding symptoms[a]			0.890***
0	6 (2.9)	0 (0.0)	
1	156 (76.5)	16 (76.2)	
2	41 (20.1)	5 (23.8)	
3	1 (0.5)	0 (0.0)	
Laboratory[b]			
Hemoglobin, g/dL	8.8 (6.7-10.3)	8.4 (5.7-10.0)	0.356**
BUN, mg/dL	29.2 (18.2-46.3)	57.9 (37.9-73.8)	<0.001**
Creatinine, mg/dL	0.96 (0.78-1.28)	1.21 (0.96-2.91)	0.008**
Albumin, g/dL	3.42 (3.01-3.84)	2.96 (2.42-3.36)	0.001**
BUN/Albumin, mg/g	8.5 (5.3-15.1)	20.6 (11.5-31.6)	<0.001**
Length of hospital stay[b], days	5 (5-7)	6 (5-10)	0.172**

[A] GCS – Glasgow coma scale, SBP – systolic blood pressure, GI – gGastro-intestinal, BUN – blood urea nitrogen, [a] n (%), [b] median (IQR), *Pearson Chi-Square test, ** Mann-Whitney U test, ***Fischer's Exact test

with GI bleeding. Albumin level decreases in chronic diseases. It also gives information about the nutritional and dehydration status of patients.[17] The serum BUN level increases in cases of severe hemorrhage and dehydration. For these reasons, these two laboratory parameters are used as variables of GI bleeding risk scores. BUN is a variant of the Glasgow Blatchford score, while albumin is a variant of the AIMS65 score.[11]

BAR increases in various critical diseases. In a retrospective study conducted by Huang et al. in 1370 patients diagnosed with COVID-19 in 2021, it was concluded that BAR is an independent predictor for the risk of critical illness in COVID-19 patients, with superior performance than CURB-65.[15] In the retrospective study of Zhao et al. in 1827 patients diagnosed with acute myocardial infarction in 2022; they concluded that BAR was calculated as 11.06 (7–18.59) (p<0.001) in the mortality group and 10.42 (7–16.71) in the four-year mortality group, and that a higher BAR value could be used as an independent predictor for four-year mortality.[18] In a study by Lee et al. in patients with lower GI bleeding in 2021, BUN ≥ 30 mg/dL and albumin ≤ 3.0 g/dL were associated with all-cause mortality.[19] In the study of Bae et al., the data of 596 geriatric patients with GI bleeding were analyzed and BAR and AIMS65 scores were compared. The study concluded that BAR was as successful as AIMS65 in estimating in-hospital mortality with an AUC of 0.770.[20] In our study, BAR was found to be successful in estimating in-hospital mortality with an AUC of 0.784. At a cut-off value of 16.26, its sensitivity was calculated as 71.43%, specificity 82.84%, PPV 30.00% and NPV 96.57%. In the light of this information, our study was found to be compatible with the studies in the literature.

The main limitations of our study are that it is single-center and retrospective. The lack of data in the medical records, the fact that the tests we used in our study were not requested, and the prognosis information could not be obtained by being transferred to another hospital caused many patients to be excluded from the study.

Conclusion
Simple, inexpensive, rapid and noninvasive tests should be used to diagnose, treat, and predict prognosis in patients with GI bleeding in EDs. BAR is a useful tool that can be used to predict the outcome of patients with GI bleeding. Patients with GI bleeding with a BAR above 16.26 will require more aggressive and timely intervention.

Declarations
Funding

Author contributions
Conceptualization, E.K. and S.Z.E.K.; Methodology, E.K.; Software, E.K.; Validation, E.K. and S.Z.E.K.; Formal Analysis, S.Z.E.K.; Investigation, E.K.; Resources, S.Z.E.K.; Data Curation, E.K.; Writing – Original Draft Preparation, E.K..; Writing – Review & Editing, E.K. and S.Z.E.K.; Visualization, S.Z.E.K.; Supervision, E.K.; Project Administration, E.K.; Funding Acquisition, S.Z.E.K.

Conflicts of interest
Authors declare that they have no conflicts of interest.

Data availability
The authors agree to the conditions of publication including the availability of data and materials in our manuscript.

Ethics approval
This study was approved by the local ethics committee (2011/KAEK/50/211).

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