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Predictors of Mortality in Geriatric Patients with Upper Gastrointestinal Bleeding

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Abstract

Aim: Acute upper gastrointestinal (UGI) bleeding is a common gastrointestinal emergency and a cause of morbidity and mortality among the elderly. We aimed to evaluate the demographic and epidemiological characteristics of geriatric patients diagnosed with UGI bleeding in an emergency department (ED) to determine the predictors of 28-day mortality among them.

Materials and Methods: All patients aged ≥65 years admitted to ED and diagnosed with UGI bleeding were included in this retrospective study. Baseline demographic and clinical/endoscopic findings were evaluated. The primary outcome was 28-day mortality rate and its predictors, which among geriatric patients diagnosed with UGI bleeding in an ED.

Results: In total, 297 geriatric patients were included in the study; of them, 131 were women (44.1%). The median patient age was 79 (65-98) years. During endoscopy, the most common cause of bleeding was a gastric/duodenal ulcer (53.9% patients). A comparison of the patient characteristics in terms of in-hospital mortality (survivor/non-survivor) revealed significant differences in chronic renal failure; hemodynamic instability; hematocrit values; blood urea nitrogen, creatinine, and albumin levels; erythrocyte transfusion; rebleeding; and Rockall scores (for all variables, $p<0.05$). The regression analysis revealed that low albumin levels and hematocrit values as well as hemodynamic instability were the independent predictors of mortality.

Conclusion: Peptic ulcer bleeding is the main cause of acute UGI bleeding. Low albumin levels and hematocrit values as well as hemodynamic instability are the independent predictors of mortality. We believe that geriatric patients with UGI, particularly those with hemodynamic compromise at the time of hospital admission, should be closely monitored and promptly treated.

Keywords: Geriatric, upper gastrointestinal bleeding, mortality

Introduction

Because people in the twenty-first century are living longer worldwide, health problems that affect older population have been increasing (1). Additionally, the widespread usage of certain medications like anticoagulants and non-steroidal drugs (NSAIDs) has steeply increased the incidence of gastrointestinal (GI) bleeding among the older peoples (2,3). Acute upper gastrointestinal (UGI) bleeding in geriatric patients that occurs most frequently over 60 years of age is a life-threatening emergency that requires rapid evaluation and appropriate management (4-8). Although the use of endoscopic homeostasis and advancements in diagnostic and therapeutic modalities have improved clinical outcomes, GI bleeding remains an important clinical problem for geriatric patients because of their longer hospital stays and higher mortality and morbidity rates compared to those of younger patients (2,9). For patients suffering from GI bleeding, the mortality rate corresponds with increased age. Patients older than 70 years of age have a 20-30 times greater incidence of GI bleeding than patients younger than 30 years (9,10). Moreover, mortality rates are 12-25% for patients older than 60 years and below 10% for patients younger than 60 years (11). This increases the importance of UGI bleeding in the geriatric population.

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Identifying predictors of mortality in geriatric patients with GI bleeding may aid in the early recognition of high-risk patients. High-risk patients frequently require hospitalization, early resuscitation, close monitoring, and urgent endoscopic interventions, whereas low-risk patients may be discharged early in the course or managed on an outpatient basis, reducing emergency department (ED) costs and crowding (12,13).

In this study, we aimed to evaluate demographic and epidemiological properties to identify predictors of 28-day mortality among geriatric patients diagnosed with UGI bleeding in an ED.

Materials and Methods

Design and Setting

Our retrospective study was conducted in a tertiary care ED with approximately 250,000 patient admissions per year. Prior to implementation, our study's protocol was approved by the local ethics committee (decision no: 1792, date: 28/11/2018). As this is a retrospective study, the participants' informed consent was not required.

Study Population

All patients aged ≥65 years, admitted to the ED between January 1, 2015 and January 1, 2018, diagnosed with UGI bleeding, and investigated with endoscopic examination were enrolled in this study.

Patients' comorbidities, vital signs, hospital outcomes, laboratory results, endoscopic findings, demographic characteristics, and blood product replacements were obtained from the hospital automation system and their personal medical records. Patients with missing data were excluded.

Forrest classification was used as the endoscopic bleeding index, and Forrest 1a and 1b bleeding indicate active bleeding. Patients with a systolic blood pressure below 100 mmHg and a heart rate over 100/min at the time of ED admission were considered to have hemodynamic instability.

The primary outcome was the identification of a 28-day mortality rate and its mortality predictors, which included all causes of mortality that occurred within 28 days of hospitalization. Mortality data were obtained from the hospital automation system and the death certificate system.

Statistical Analysis

Data analysis was performed using SPSS for Windows 16. The normality of the distribution of the discrete and continuous variables was checked using the Kolmogorov-Smirnov test. Descriptive statistics included numbers and percentages for qualitative variables and medians (minimum-maximum) for discrete and continuous variables. Categoric variables were compared using the chi-square test, and continuous variables with the Mann-Whitney U test. Predictors of in-hospital mortality were determined using univariate tests, and statistically significant ($p<0.2$) variables were tested with a multivariate logistic regression model. The fitness of this model was tested with the Hosmer-Lemeshow test. A p value <0.05 was considered to be statistically significant.

Results

We enrolled 319 patients during the study period. Of these 319 patients, 22 patients were excluded due to missing data. In total, 297 patients were included in the final statistical analysis. The median age of the patients was 79 years (65-98), and 131 patients were women (44.1%).

The most common comorbidity was hypertension (n=147, 49.5%). The 28-day mortality rate was 14.1% (n=42).The most common causes of death were multiorgan failure (n=12, 28.5%), sepsis (n=9, 21.5%)., and acute renal failure (n=9, 21.5%).The mean time from admission to death was 11 days (0 day-28 days). Patient demographics and laboratory results are shown in Table 1.

The endoscopic findings, Forest classifications, and endoscopic interventions are summarized in Table 2. The most common bleeding etiologies were gastric and duodenal ulcers (n=160, 53.9%). Active bleeding was present in 20.5% of patients (n=61), and 56 of these patients (18.8%) underwent sclerotherapy. Five patients (1.7%) could not receive sclerotherapy because they could not tolerate the procedure and/or had their vital signs deteriorate during endoscopy. One patient underwent subtotal gastrectomy. The Rockall scores of the patients were calculated and divided into three risk groups (Table 3). 21.5% of the patients (n=64) were in the mild group, while 48.8% (n=145) were in the high-risk group. Re-bleeding was detected in seven patients (2.4%). Four patients were treated with sclerotherapy, and three patients could not tolerate the procedure of endoscopy and sclerotherapy.

A comparison of the in-hospital mortality factors for the patients (survivors/non-survivors) revealed significant differences related to chronic renal failure, hemodynamic instability, hematocrit, blood urea nitrogen (BUN), creatinine, albumin, erythrocyte suspension transfusion, re-bleeding, and Rockall score ($p=0.007$, $p<0.001$, $p<0.001$, $p<0.001$, $p=0.005$, $p<0.001$, $p=0.014$, $p<0.001$, $p<0.001$, respectively; Table 4).

Univariate regression analysis was performed to investigate the mortality variables (Table 5). Next, a multivariate logistic

Table 1. Demographic data of patients	
All patients, n (%)	297 (%)
Female, n (%)	131 (44.1%)
Age, years, median (minimum-maximum)	79 (65-98)
***Comorbidity, n (%)**	
Hypertension	147 (49.5%)
Diabetes mellitus	80 (26.9%)
Coronary heart disease	75 (25.3%)
Chronic heart failure	32 (10.8%)
Chronic renal failure	39 (13.1%)
Liver disease	25 (8.4%)
Other	32 (10.8%)
NSAID drugs use n (%)	103 (34.7%)
Oral anticoagulant drugs use n (%)	70 (23.6 %)
Presenting symptoms, n (%)	
Hematemesis	160 (53.9%)
Melena	100 (33.7%)
Syncope	9 (3%)
Others	28 (9.4%)
Hemodynamic status (%)	
Unstable	109 (36.7%)
Stable	188 (63.3%)
Rockall score, median (minimum-maximum)	4 (1-10)
Laboratory results, median (minimum-maximum)	
Hematocrit %	31 (10-57)
Platelet x10^3/µL	253.75 (32-910)
BUN mg/dL	32 (6-324)
Creatinine mg/dL	1.1 (0.5-9,6)
AST U/L	18.5 (16-363)
ALT U/L	13 (12-264)
Albumin g/dL	3.4 (1.38-6.30)
Replacement of blood products, n (%)	
Erythrocyte suspension	132 (44.4%)
Unit, median (minimum-maximum)	2 (1-11)
Re-bleeding, n (%)	7 (2.4%)
Hospital stay duration median (minimum-maximum)	4 (2-32)
28-day mortality n (%)	42 (14.1%)
Causes of death, n (%)	
Multiorgan failure	12 (28.5%)
Sepsis	9 (21.5%)
Acute renal failure	9 (21.5%)
Acute coronary syndromes	8 (19%)
Others	4 (9.5%)

NSAID: Non-steroidal anti-inflammatory drug, ALT: Alanine amino transferase, AST: Aspartate transaminase, BUN: Blood urea nitrogen, n: Number
*Some patients had multiple comorbid diseases

Table 2. The endoscopic findings, Forest classification and endoscopic interventions	
Endoscopic diagnoses	**n (%)**
Gastric/duodenal ulcer	160 (53.9%)
Gastric erosion/gastritis	131 (44.1%)
Cancer stomach	32 (10.8%)
Esophageal varices	18 (6.1%)
Dieulafoy's lesion	5 (1.7%)
Mallory-Weiss tear	5 (1.7%)
Forrest classification for gastric/duodenal ulcer	
1a	3 (1.8%)
1b	29 (18.1%)
2a	12 (7.5%)
2b	34 (21.3%)
2c	32 (20%)
3	50 (31.3%)
Active bleeding	61 (20.5%)
Endoscopic intervention	
Sclerotherapy	44 (14.8%)
Hemoclip + sclerotherapy	6 (2%)
Endoscopic band ligation	6 (2%)

n: Number
Some patients presented with more than 1 endoscopic finding

Table 3. Rockall score stratification into three groups with percentage of re-bleeding and mortality of patients			
Group		**Re-bleeding (%)**	**Mortality (%)**
Low risk	64 (21.5%)	0 (0%)	0 (0%)
Moderate risk	88 (29.6%)	0 (0%)	8 (9.1%)
High risk	145 (48.8%)	7 (4.8%)	34 (23.4%)

regression analysis was conducted. Because BUN and creatinine levels correlate with albumin, Rockall score correlates with hypotension, and ES replacement correlates with hematocrit levels, these properties were not included in the model. The multivariate model included chronic renal failure, syncope, hemodynamic instability, hematocrit, albumin, rebleeding, age, and sex (Table 5), which had a p value <0.2. The model was found to be fit using the Hosmer-Lemeshow test. Low albumin and hematocrit levels as well as hemodynamic instability at the time of admission were found to have adverse effects on mortality (Table 6).

Discussion

The present study which we investigated the characteristics of geriatric patients with UGI bleeding and the factors that affected their 28-day mortality provided two important results. First,

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Table 4. A comparison of the patient characteristics regarding in 28-day mortality (survivor/nonsurvivor)

	Survivor (n= 255)	Dead (n=42)	p
Age	79 (65-98)	79.4 (67-96)	0.581
Gender, n (%)			
Female	111 (66.3%)	20 (47.6%)	0.621
Male	144 (56.5%)	22 (52.4%)	
Comorbidity			
Hypertension	124 (48.6%)	23 (54.8%)	0.461
Diabetes mellitus	67 (26.3%)	13 (31%)	0.527
Coronary heart disease	67 (26.3%)	8 (19%)	0.318
Chronic renal failure	28 (11%)	4 (26.2%)	0.007
Liver disease	21 (8.2%)	4 (9.5%)	0.765
Drugs, n (%)			
NSAID	90 (35.3%)	13 (31%)	0.584
Oral anticoagulant	61 (23.9%)	9 (21.4%)	0.724
Hemodynamic Instability, n (%)	72 (28.2%)	37 (88.1%)	<0.001
Rockall score, median (minimum-maximum)	4 (1-10)	6 (3-10)	<0.001
Presenting symptoms, n (%)			
Hematemesis	137 (53.7%)	23 (54.8%)	0.901
Melena	88 (34.5%)	12 (28.6%)	0.450
Syncope	6 (2.4%)	3 (7.1%)	0.093
Endoscopic diagnosis, n (%)			
Gastric/duodenal ulcer	139 (54.5%)	21 (50%)	>0.05
Gastric erosion/ gastritis	111 (43.5%)	20 (47.6%)	
Esophageal varices	14 (5.5%)	4 (9.5%)	
Dieulafoy's lesion	5 (2%)	0 (0%)	
Mallory-Weiss tear	5 (2%)	0 (0%)	
Laboratory results, median (minimum-maximum)			
Hematocrit %	32 (10-57)	26.75 (15.7-42)	<0.001
Platelet x10^3/µL	245 (32-910)	250 (55-507)	0.562
BUN mg/dL	30 (6-324)	44 (13-125)	<0.001
Creatinine mg/dL	1.03 (0.5-9.6)	1.42 (0.5-6.5)	0.005
AST U/L	18 (6-363)	19.5 (10-154)	0.507
ALT U/L	13 (3-264)	13 (6-217)	0.954
Albumin g/dL	3.45 (1.38-6.30)	3 (1.8-4)	<0.001
Active bleeding in endoscopy, n (%)	50 (19.6%)	11 (26.2%)	0.328
Endoscopic intervention	45 (15%)	11 (26.2%)	0.679
Re-bleeding	1 (0.4%)	6 (14.3%)	<0.001
Replacement of blood products, n (%) Erythrocyte suspension	106 (41.6%)	26 (61.9%)	0.014
Unit, median (minimum-maximum)	2 (1-11)	2 (1-9)	0.361

NSAID: Non-steroidal anti-inflammatory drug, ALT: Alanine amino transferase, AST: Aspartate transaminase, BUN: Blood urea nitrogen, n: Number

Table 5. Univariate analysis of factors associated with 28-day mortality

	p value	Odds ratio	(95% CIs)
Age	0.574	1.01	0.9-1.05
Gender	0.621	0.84	0.4-1.6
Chronic renal failure	0.009	2.87	1.3-6.3
Syncope	0.111	3.19	0.7-13.2
Hemodynamic instability	<0.001	18.8	7.1-49.7
Albumin	<0.001	0.24	0.12-0.4
Hematocrit	<0.001	0.92	0.8-0.9
Rockall scores	<0.001	1.55	1.3-1.85
Erythrocyte suspension	0.016	2.28	1.1-4.4
Re-bleeding	<0.001	42.32	4.9-361.8

CI: Confidence interval

Table 6. Multivariate regression model to predict in 28-day mortality

	p value	Odds ratio	(95% CIs)
Age	0.82	0.99	0.9-1.06
Gender	0.092	0.42	0.1-1.1
Chronic renal failure	0.297	1.84	0.5-5.7
Syncope	0.139	4.97	0.5-41.8
Hemodynamic instability	<0.001	26.2	6.1-111.4
Albumin	0.003	0.26	0.1-0.6
Hematocrit	0.015	1.11	1.02-1.2
Re-bleeding	0.088	12.47	0.68-225.6

CI: Confidence interval

we determined that the most common cause of GI bleeding was peptic ulcer, which had a 28-day mortality rate of 14%. We revealed that the deceased patients were more hemodynamically unstable, had lower hematocrit and albumin levels, had higher BUN and creatinine levels, and had greater needs for blood product transfusions. Second, we demonstrated that the most important predictors of in-hospital mortality for geriatric patients with GI bleeding were hemodynamic instability at the time of ED admission and low albumin and hematocrit levels.

The increased incidence of UGI bleeding in the older population has been linked to various causes, such as increased NSAIDs usage, *Helicobacter* pylori incidence, and gastroesophageal reflux disease (14,15). Kawaguchi et al. (3) evaluated nonvariceal UGI bleeding in the geriatric patients. They found that 41% of their patients were using NSAIDs and 34% were using anticoagulants, and they determined that these rates were higher in geriatric patients than in patients under 65 years of age. According to our results, 34.7% of the patients were using NSAIDs and 23.6%

were using anticoagulants. A systematic review indicated that the relative risk of GI bleeding was 2.7-33.9 for NSAIDs users (16). Notably, NSAIDs use in the geriatric patients is often overlooked. In addition to a greater prevalence of rheumatologic disorders in the geriatric population, many patients from developing countries, where medication regulation is inadequate, use these drugs without prescriptions or adequate oversight. NSAIDs users also frequently take one or more antiplatelet agents to combat cardiac or cerebrovascular comorbidities. A meta-analysis reported that taking low-dose aspirin increases the risk of UGI bleeding (17). This risk is even more pronounced among patients with a history of GI bleeding, extended aspirin usage, or simultaneous clopidogrel or anticoagulant usage (17). In the older patients, the risk of developing ulcers is increased due to their frequent NSAID and anticoagulant usage. The most common etiology of UGI bleeding in the geriatric population is peptic ulcer disease (4). In the geriatric patients, hospital admissions due to peptic ulcer disease, along with esophagitis and gastritis, comprise of 70-91% of all admissions due to UGI bleeding (18). In previous studies, the prevalence of UGI bleeding ranges from 5-43% for stomach/duodenum ulcers, 6-42% for gastritis, and 1-20% for esophageal varices (16,17,19). Similar to literature, our endoscopic findings also revealed gastric or duodenal ulcer at a rate of 53.9%. Our rate for esophageal variceal bleeding was 6.1%. The rate of UGI bleeding episodes due to esophageal varices is around 10% in the previous studies (12). Chronic liver diseases and their associated GI complications are less common in Turkey than in other countries, and this may have contributed to the low rate of esophageal varices in our study.

Rockall scoring considers age, comorbid diseases, presence of shock, and endoscopic findings, and it is the most widely used GI bleeding scoring system (7,13). In our study, 21.5% of the patients were in the mild group, while 48.8% were in the high-risk group. The Rockall scores were lower for the survivors than the non-survivors, and this difference was statistically significant.

Previous studies have reported in-hospital mortality rates ranging from 8.7-11.2% for geriatric patients (4,20). Mortality rates are affected by the cause of the bleeding and the presence of comorbidities. Our mortality rate was 14.3%. Our relatively high mortality rate may be related to our greater comorbidity rate and the extreme age of our study population. Similar to previous studies, we found low re-bleeding rates. Although these prior studies on geriatric patients with GI bleeding have linked increased mortality with the coexistence of coronary artery disease, we could not detect any significant differences (10). Chronic renal disorders were more common among deceased patients. Hence, we identified higher BUN and creatinine levels in our deceased patients. In addition, our deceased patients had lower hematocrit levels at the time of ED admission and needed more blood product transfusions.

Recent studies on GI bleeding in the older people report heterogeneous findings on the predictors of in-hospital mortality. A study reported that high age, being hypotensive at admission, failure to achieve endoscopic hemostasis, and the presence of comorbidities, particularly liver cirrhosis associated with other comorbidities, were independent predictors of mortality (18). However, we did not find any difference in liver disease status between survivors and non-survivors. Cirrhosis is associated with many potential complications, notably the development of portal hypertension. Portal hypertension with the production of ascites, hepatic and gastric varices bleeding in the upper part of the GI tract is associated with a considerably worse prognosis and an increased risk of mortality (21). This risk may be reduced by using modern pharmacotherapeutic agents and therapeutic endoscopic methods (e.g., esophageal stents and transjugular intrahepatic portosystemic shunt) to treat acute bleeding in cirrhosis patients who have experienced GIS bleeding.

Thongbai et al. (13) associated hemodynamic instability, bright red bleeding upon nasogastric aspiration, creatinine <1.5 mg/dL, and, crucially, coexisting coronary artery disease with mortality (10). In contrast, our study found that admission hemodynamic instability and low albumin and hematocrit levels negatively affected our patients' survival rates. Among patients with UGI bleeding, admission hemoglobin and hematocrit levels are critical for determining prognosis and managing treatment (22). A low admission hematocrit should inform an emergency specialist about the severity of the bleeding and the presence of active bleeding. Prior studies have reported that the serum albumin level has an important role in the prognosis of patients with GI bleeding (23,24). González-González et al. (25) recently argued that the albumin level was the sole independent predictor of mortality. They showed that it had a negative predictive value as high as 97% for geriatric patients with a serum albumin level below 2.35 g/dL, and they reported that it was quite effective for discriminating between survivors and non-survivors (25). We assert that being hypotensive at the time of ED admission is a strong predictor of mortality. The hemodynamic status of geriatric patients who are initially hypotensive may suddenly deteriorate and require aggressive therapy. Therefore, care should be taken to rapidly stabilize their hemodynamic status, begin pharmacological treatment, and schedule endoscopy.

Study Limitations

Our study has some limitations. As a single-center study, its findings cannot be generalized to other centers. Notably, since our study was retrospective and some patients were referred,

patient information such as smoking status, alcohol and drug usage, and treatment management could not be obtained. Moreover, there were five patients who could not undergo endoscopic treatment due to various reasons and we could not include to regression analysis. This situation may have affected the mortality of patients.

Conclusion

As conclusion, in the present study, hemodynamic instability, low hematocrit levels, and low albumin levels were independent predictors of mortality. It is possible to stabilize geriatric patients and prevent mortality by diagnosing high-risk patients and applying appropriate therapies. To improve outcomes, such patients should be closely monitored, resuscitative procedures should be rapidly initiated, and endoscopic interventions should be performed as soon as possible.

Ethics

Ethics Committee Approval: Prior to implementation, this study's protocol was approved by Ankara Keçiören Training and Research Hospital Ethics Committee (decision no: 1792, date: 28/11/2018).

Informed Consent: As this is a retrospective study, the participants' informed consent was not required.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.E., S.D., S.K.Ç., Design: E.E., S.D., Y.Ç., Data Collection or Processing: E.E., H.U., M.U., R.H.K., Analysis or Interpretation: E.E., S.K.Ç., Y.Ç., Literature Search: H.U., M.U., R.H.K., Writing: E.E., S.D.

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