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ARAŞTIRMA / RESEARCH

Mortality risk factors in patients with upper gastrointestinal bleeding in a medical intensive care unit

Bir tıbbi yoğun bakım ünitesinde üst gastrointestinal kanamalı hastalarda mortalite risk faktörleri

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Abstract

Purpose: The aim of this study was to evaluate the general clinical characteristics of acute gastrointestinal system (GIS) bleeding patients who were followed-up in the intensive care unit (ICU) and the risk factors for mortality.
Materials and Methods: The GIS bleeding patients followed up in a medical ICU between October 2016 and March 2019 were included. Patients were evaluated for demographic, clinical and laboratory data (on admission and after 24-hours) and compared according to the mortality status (surviving vs. non-surviving).
Results: A total of 64 patients (37 males and 27 females) with a median age of 73.5 (31-93) years were evaluated. All patients had upper GIS bleeding and the mortality rate was 29.7%. There was no difference between the mortality groups for gender, age and chronic co-morbid diseases except malignancy. High BUN, creatinine, INR, and lactate levels after 24 hours were significantly associated with mortality. All patients had a diagnosis of upper GIS bleeding. In the logistic regression analysis, the presence of acute respiratory insufficiency, long hospital stays before ICU, high SOFA score and high lactate levels after 24 hours were the independent predictors of ICU mortality).
Conclusion: In this study, we found that high levels of BUN, creatinine, INR, and lactate levels in the first 24 hours of follow-up, rather than the values on admission to ICU, were associated with increased mortality. Therefore, we suggest that close monitoring and rapid normalization of these values with appropriate treatments is important.
Keywords:. Gastrointestinal bleeding, intensive care unit, risk factors, mortality

Öz

Amaç: Bu çalışmada yoğun bakım ünitesinde (YBÜ) izlenen akut gastrointestinal sistem (GİS) kanamalı hastaların genel klinik özelliklerini ve mortalite için risk faktörlerini değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntem: Ekim 2016-Mart 2019 tarihleri arasında medikal YBÜ'de izlenen akut GİS kanamalı hastalar çalışmaya dahil edildi. Hastalar demografik, klinik ve laboratuvar verileri (kabul sırasında ve 24 saat sonra) açısından değerlendirildi ve mortalite durumuna (sağ kalan ve ölen) göre karşılaştırıldı.
Bulgular: Medyan yaşı 73,5 (31-93) yıl olan toplam 64 hasta (37 erkek/27 kadın) değerlendirildi. Tüm hastaların üst GİS kanaması vardı ve ölüm oranı %29,7 olarak saptandı. Sağ kalan ve ölen gruplar arasında cinsiyet, yaş ve kronik yandaş hastalıklar açısından malignite dışında fark yoktu. Takipte 24 saat sonra bakılan BUN, kreatinin, INR ve laktat düzeylerinin yüksek seviyeleri mortalite ile ilişkili bulundu. Lojistik regresyon analizinde akut solunum yetmezliği varlığı, YBÜ'den önce hastanede kalma süresinin uzun olması, yüksek SOFA skoru ve 24 saat sonra bakılan yüksek laktat seviyeleri YBÜ mortalitesinin bağımsız belirleyicileri olarak saptandı
Sonuç: Bu çalışmada hastaların YBÜ'ye yatıştaki değerlerinden ziyade 24 saat sonra bakılan ve yüksek seyreden BUN, kreatinin, INR ve laktat düzeyleri artmış mortalite ile ilişkili olduğunu saptadık. Bu nedenle bu değerlerin yakın takibi ve uygun tedaviler ile hızlıca normalleştirilmesinin önemli olduğunu düşünmekteyiz.
Anahtar kelimeler: Gastrointestinal kanama, yoğun bakım ünitesi, risk faktörleri, mortalite

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INTRODUCTION

Gastrointestinal system (GIS) bleeding is divided into two as upper and lower GIS bleeding[1]. The clinical condition of the patient varies according to the severity of bleeding, and it was shown that approximately 20% of patients admitted to hospital due to acute GIS bleeding need to be followed up in intensive care unit (ICU)[2]. Acute GIS bleeding is an important reason for ICU hospitalization and is among the important causes of morbidity and mortality[2,3]. The annual incidences of upper and lower GIS bleeding were reported as 100 and 20 per 100,000, respectively[2]. According to the co-morbid conditions and the presence of risk factors, the mortality rate in upper GIS bleeding has a wide range and varies between 1% and 48.5%[4-6].

There are many factors reported as mortality risk factors in GIS bleeding. Some of these are advanced age, hypotension, low hemoglobin level, hypoalbuminemia, high creatinine and serum aminotransferases, and concomitant diseases such as heart disease, kidney failure, cirrhosis and cancer [7-15]. The patient profiles included in these studies are quite different from each other and generally include patients with GIS bleeding who are followed in inpatient services and have a low mortality rate. However, just as the patients followed in primary, secondary and tertiary centers are different from each other, it is possible that the mortality risk factors of patients followed in the service and ICU are different from each other.

Although there are various studies[7-13] evaluating GIS bleeding in our country, the number of studies evaluating GIS bleeding patients followed up in ICU is quite limited. Because most of the cases can be successfully treated by endoscopic evaluation and high dose proton pump inhibitors (PPI) in acute GIS bleeding and do not need ICU follow-up. In our literature search, we were able to find only two studies evaluating ICU follow-up of acute GIS bleeding patients in our country in the last 10 years[2,5]. In these studies, evaluated factors and group comparisons were also differed from each other. Therefore, in our study, we aimed to evaluate the general clinical characteristics of patients who were followed up in a medical ICU with the diagnosis of acute GIS bleeding and the risk factors for mortality.

MATERIALS AND METHODS

Sample

In this study, the patients, who were at least 18 years old with complete data and followed up in our 16-bedded medical ICU of Ondokuz Mayıs University Hospital between October 2016 and March 2019, were evaluated. Patients, who were found to have hematemesis, melena, or bleeding in the upper GIS endoscopy on admission to the ICU and followed-up more than 24-h, were included in the study. Patients who had GIS bleeding during their follow-up in the ICU were excluded. The data of our patients are reliable because they are obtained from the hospital system and the progress of ICU patients is daily noted. No patient was excluded from the study due to lack of data.

This study was approved by the Institutional Ethics Committee of the Ondokuz Mayıs University (OMU-KAEK 2020/496) on 23/07/2020 and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki or comparable ethical standards.

Procedure

We examined the patients for demographic, clinical, and laboratory data including age, gender, co-morbidities, drug use affecting bleeding such as non-steroid anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (ASA), clopidogrel, anticoagulants and steroids, mortality, hospitalization periods, acute physiology and chronic health evaluation (APACHE) II score, sequential organ failure assessment (SOFA) score, Glasgow coma score (GCS), Charlson co-morbidity index (CCI), invasive procedures, imaging, endoscopy, and pathology results. Hemogram parameters (hemoglobin, hematocrit, thrombocyte), blood urea nitrogen (BUN), creatinine, international normalized ratio (INR), and blood lactate levels of the patients at the time of admission and after 24 hours were evaluated and compared according to the mortality status (surviving vs. non-surviving) of the patients. The needs for blood transfusion during ICU stay of the patients were also evaluated.

APACHE II[16] and SOFA[17] scores were calculated by using the clinical and laboratory parameters in the first 24 h for the evaluation of the acute disease severity. The baseline healths of the patients were evaluated by using the CCI scoring system, in which

the patients were scored between 0 and 33 according to their co-morbid chronic diseases[18].

The reference ranges were 6-20 mg/dl for BUN, 0.4–1.4 mg/dl for creatinine, between 12-15 g/dl for the females and 13-17 g/dl for the males for hemoglobin, 35-45% for hematocrit, 150-400 $x10^3/\mu L$ for platelet count 0.85-1.15 for INR and 0.4-1.4 mmol/L for lactate. The thrombocytopenia was graded as mild (100-150 $x10^3/\mu L$), moderate (50-100 $x10^3/\mu L$), and severe (<50 $x10^3/\mu L$) according to the lowest platelet count measured in the first 24 hours[19].

Statistical analysis

IBM SPSS for Windows version 25.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. The continuous variables were tested for a normal distribution with Shapiro-Wilk test. The results were expressed as median and interquartile range (IQR) due to non-parametric distribution of the data. The categorical variables were expressed as percentages. Groups were compared by using the Pearson chi-square test for categorical parameters and Mann-Whitney U test for continuous parameters. Logistic regression analysis (with backward elimination method) was used including variables which were significant in bivariate analysis for mortality. Backward elimination method was used, and the variables included in the first step were the presence of malignancy, acute respiratory insufficiency, sepsis, and cardiac/respiratory arrests, need for acute hemodialysis, need for vasopressors, ICU LOS, hospital LOS before ICU, APACHE II, SOFA, GCS, BUN, creatinine, INR, and lactate levels after 24 hours. The odds ratios (ORs) and their 95% confidence intervals (95% CIs) were given. A p value ≤ 0.05 was significant.

RESULTS

A total of 1300 patients were hospitalized in our medical ICU between October 2016 and March 2019 and 64 (4.9%) patients were followed up for more than 24 hours with the diagnosis of acute GIS bleeding. Between 15 October 2016 and 31 March 2019, 1300 patients were hospitalized in our intensive care unit, and 64 (4.9%) patients were followed up for more than 24 hours with the diagnosis of GIS bleeding.

All these 64 patients had upper GIS bleeding. The patients were transferred to the ICU from emergency service (57.8%), inpatient services (28.1%), and an external center (14.1%).

The median age was 73.5 (31-93) and 27 (42.2%) of them were females. The The median age of the patients was 73.5 (31-93) and 27 (42.2%) of them were women.

The patients were divided into two groups according to ICU mortality (surviving vs. non-surviving) and compared in Table 1 and Table 2. There was no difference between the groups for gender and age (p=0.574, p=0.866, respectively). It was observed that 32.8% of the patients were using drugs that may cause bleeding tendency and the most common drug was acetylsalicylic acid (15.6%). All patients had a diagnosis of upper GIS bleeding.

The esophagus and fundus varices were present in 18 (28.1%) patients and in 16 (25%) of them their varicose veins were associated with upper GIS bleeding with %25 mortality rate. Bleeding due to varicose veins was not related with mortality (p= 0.636). Hypertension (46.9%), cardiovascular diseases (42.2%), and diabetes (35.9%) were the most common co-morbid diseases and tHypertension (46.9%), cardiovascular disease (42.2%) and diabetes (35.9%) were the most common accompanying diseases in the patients.

the most common comorbidities in patients with hypertension (46.9%), cardiovascular disease (42.2%) and diabetes (35.9%) were detected. There was no difference between the groups for chronic co-morbid diseases except malignancy which is more common in the non-surviving group (p=0.009). The presence of acute respiratory insufficiency, sepsis, and respiratory/cardiac arrests were found to be significantly associated with mortality (p<0.001, p=0.016, and p=0.001, respectively). The need for vasopressors, invasive mechanical ventilation, and acute hemodialysis were significantly higher in the non-surviving group (p<0.001, p<0.001, and p=0.002, respectively), (Table 1).

There was no significant effect of both presence and degree of thrombocytopenia on mortality (p=0.230 and p=0.534, respectively) (Not shown in the table). All patients required transfusion of at least one unit of blood products. While survival was higher in those who needed only erythrocyte transfusion (p=0.005), mortality was higher in those who needed erythrocyte, thrombocyte, and fresh frozen plasma transfusions (p <0.001) (Table 1).

Table 1. Clinical characteristics of the patients and comparisons according to ICU mortality.

Variables	All patients (n:64)	Surviving (n:45)	Non-Surviving (n:19)	P[a]
	n (%)	n (%)	n (%)	
Demographics				
Gender (Female)	27 (42.2)	20 (44.4)	7 (36.8)	0.574
Age≥ 65 years	43 (67.2)	29 (64.4)	14 (73.7)	0.472
Medical history				
Hypertension	30 (46.9)	22 (48.9)	8 (42.1)	0.619
Cardiovascular disease	27 (42.2)	20 (44.4)	7 (36.8)	0.574
Diabetes mellitus	23 (35.9)	17 (37.8)	6 (31.6)	0.637
Chronic hepatic disease	18 (28.1)	12 (26.7)	6 (31.6)	0,690
Chronic renal disease	16 (25.0)	12 (26.7)	4 (21.1)	0.636
Chronic pulmonary disease	9 (14.1)	8 (17.8)	1 (5.3)	0.188
Malignancy	19 (29.7)	9 (20.0)	10 (52.6)	0.009
Hematological	6 (9.4)	4 (8.9)	2 (10.5)	0.837
Solid tumor	13 (20.3)	5 (11.1)	8 (42.1)	0.005
Prior drug exposure	21 (32.8)	17 (37.8)	4 (21.1)	0.193
Acetylsalicylic acid	10 (15.6)	8 (17.8)	2 (10.5)	0.465
Clopidogrel	3 (4.7)	3 (6.7)	0	0.249
Anticoagulants	7 (10.9)	5 (11.1)	2 (10.5)	0.945
NSAIDs	2 (3.1)	2 (4.4)	0	-
Steroid treatment	2 (3.1)	2 (4.4)	0	-
Co-morbid diagnosis				
Acute renal failure	24 (37.5)	15 (33.3)	9 (47.4)	0.289
Acute respiratory insufficiency	14 (21.9)	3 (6.7)	11 (57.9)	<0.001
Sepsis	12 (18.8)	5 (11.1)	7 (36.8	0.016
Acute hepatic failure	7 (10.9)	3 (6.7)	4 (21.1)	0.092
Cardiac/Respiratory arrest	7 (10.9)	1 (2.2)	6 (31.6)	0.001
Invasive procedures				
Invasive mechanical ventilation	22 (34.4)	4 (8.9)	18 (94.7)	<0.001
Central venous catheter	25 (39.1)	11 (24.4)	14 (73.7)	<0.001
Hemodialysis (Acute)	9 (14.1)	2 (4.4)	7 (36.8)	
Hemodialysis (Chronic)	5 (7.8)	3 (6.7)	2 (10.5)	0.002
Varice-related bleeding	16 (25)	12 (26.7)	4 (21.1)	0.636
Thrombocytopenia	40 (62.5)	26 (57.8)	14 (73.7)	0.230
Hypotension on admission	34 (53.1)	22 (48.9)	12 (63.2)	0.296
Need for vasopressors	28 (43.8)	11 (24.4)	17 (89.5)	<0.001
Transfusion need				
Only Erythrocyte	27 (42.2)	24 (53.3)	3 (15.8)	0.005
Erythrocyte+Thrombocyte	1 (1.6)	1 (2.2)	0	-
Erythrocyte+ FFP	25 (39.1)	18 (40)	7 (36.8)	0.813
Erythrocyte+Thrombocyte+FFP	11 (17.2)	2 (4.4)	9 (47.4)	<0.001
Only medical treatment	30 (46.9)	21 (46.7)	9 (47.4)	0.959

NSAIDs; Non-steroid anti-inflammatory drugs, FFP; Fresh frozen plasma.
[a]Chi-square test was used for comparison of categorical variables.

The amount (units) of erythrocyte, thrombocyte, and fresh frozen plasma transfused to the patients were significantly higher in the non-surviving group (p=0.001, p<0.001, and p<0.001, respectively), (Table 2). There was no difference between the groups for chronic co-morbid diseases except malignancy which is more common in non-surviving group (p = 0.009). High APACHE II and SOFA and low GCS scores were significantly associated with mortality (p<0.001, for all). The ICU length of stay (LOS) and hospital LOS before ICU were significantly shorter in the surviving group (p<0.001 and p=0.019, respectively) (Table 2). In the evaluation of laboratory values on admission and after 24 hours, only BUN, creatinine, INR, and lactate levels after 24 hours were significantly higher in the non-surviving group (p=0.012, p=0.024, p<0.001, and p<0.001, respectively) (Table 3).

Table 2. Comparison of clinical characteristics and the factors related with illness severity of the patients according to ICU mortality.

Variables Median (IQR)	**All patients (n:64)**	**Surviving (n:45)**	**Non-Surviving (n:19)**	**P[b]**
Age (years)	73.5 (26)	73 (29)	75 (16)	0.866
ICU LOS **(days)**	5 (6)	4 (3)	10 (6)	<0.001
Hospital LOS before ICU **(days)**	1 (4)	1 (2)	4 (15)	0.019
APACHE II Score	17 (13)	15 (8)	29 (16)	<0.001
SOFA Score	6 (6)	5 (5)	10 (6)	<0.001
Glasgow Coma Score	13 (5)	14 (3)	9 (12)	<0.001
CCI Score	4 (3)	4 (3)	4 (4)	0.422
Transfusion need				
Erythrocyte (units)	5 (3)	4 (1)	9 (12)	0.001
Thrombocyte (units)	0 (0)	0 (0)	0 (16)	<0.001
Fresh frozen plasma (units)	2 (4)	0 (2)	4 (8)	<0.001

ICU; Intensive care unit, LOS; Length of Stay, SOFA; Sequential Organ Failure Assessment, APACHE II; Acute Physiology and Chronic Health Evaluation II, CCI; Charlson Comorbidity Index. The data was given as median (interquartile range-IQR) due to non-parametric distribution and Mann-Whitney U test[b] was used for the comparison of two groups.

Table 3. Comparison of laboratory values of the patients on admission and after 24 hours according to ICU mortality.

Variables Median (IQR)	**Reference ranges**	**All patients (n:64)**	**Surviving (n:45)**	**Non-Surviving (n:19)**	**P[b]**
On admission					
BUN (mg/dL)	6-20	44.4 (39)	40.0 (38)	50.0 (36.1)	0.136
Creatinine (mg/dL)	0.4–1.4	1.34 (1.62)	1.12 (1.13)	1.67 (2.19)	0.134
Hemoglobin (g/dL)	F: 12-15 M: 13-17	7.0 (2.1)	7.0 (1.9)	6.50 (2.6)	0.889
Hematocrit (%)	35-45	21.4 (6)	21.4 (5.6)	18.7 (7.5)	0.889
Platelet (x10^3/μL)	150-400	151 (150)	176 (178)	108 (161)	0.106
INR	0.85-1.15	1.35 (0.4)	1.32 (0.33)	1.45 (0.76)	0.132
Lactate (mmol/L)	0.4-1.4	1.6 (1.6)	1.5 (1.2)	2.2 (2.2)	0.446
After 24-hours					
BUN (mg/dL)		40.0 (37.5)	31.0 (31.5)	50.0 (47.0)	0.012
Creatinine (mg/dL)		1.29 (1.57)	1.1 (1.2)	2.0 (1.7)	0.024
Hemoglobin (g/dL)		8.9 (2)	9.2 (1.8)	8.3 (3.1)	0.257
Hematocrit (%)		27.1 (5.6)	27.5 (4.9)	24.8 (9.2)	0.374
Platelet (x10^3/μL)		116 (144)	124 (149)	112 (116)	0.184
INR		1.3 (0.39)	1.2 (0.31)	1.45 (0.48)	<0.001
Lactate (mmol/L)		1.39 (0.83)	1.3 (0.61)	2.49 (1.47)	**<0.001**

BUN; Blood urea nitrogen, INR; International normalized ratio. The data was given as median (interquartile range-IQR) due to non-parametric distribution and Mann-Whitney U test[b] was used for the comparison of two groups.

Table 4. Endoscopy findings of the patients

Endoscopy findings	Patients with endoscopy n=57 (%)
Gastritis and erosions	21 (36.8)
Gastric ulcer	10 (17.5)
Duodenal ulcer	12 (21.1)
Esophagus and fundus varices	18 (31.6)
Esophagitis/Esophageal ulcer	8 (14)
Gastric cancer	5 (8.8)
Mallory-Weiss tear	3 (5.3)
Angiodysplasia	3 (5.3)
Anastomotic ulcers	3 (5.3)
Normal endoscopic findings	2 (3.5)

In the endoscopic evaluation, the most common lesions were duodenal and gastric ulcers (38.6%), gastritis and erosions (36.8%), and esophagus and fundus varices (31.6%). Seven of 64 patients (10.9%) could not undergo endoscopy due to their poor general condition and three of them were died during follow-up (Table 4). We found there was no effect of endoscopy on mortality (p=0.419) (Not shown in the table).

The treatment approaches in patients were also evaluated. A proton pump inhibitor (PPI) was given to all patients. While 46.9% of the patients received only PPI treatment, sclerotherapy (28.1%), somatostatin infusion (25%), varicose band ligation (18.8%), argon plasma coagulation (12.5%), and hemoclips (7.8%) were among other treatments.

The independent risk factors for mortality were evaluated with binary logistic regression analysis in Table 5. Significant parameters related to transfusion products were not included in the logistic regression analysis because they were considered to be the result of the primary causes of death (heavy bleeding, thrombocytopenia and high INR) rather than the primary cause of death. The significant primary causes were included in the analysis. The results for variables retained in the final multivariable model were presented in Table 5 (Nagelkerke R2=0.808, p<0.001). Accordingly, acute respiratory insufficiency, hospital LOS before ICU, SOFA score, and lactate levels after 24 hours were found as independent predictors of ICU mortality (p=0.009, p=0.012, p=0.041, and p=0.021, respectively).

Table 5. Binary logistic regression analyses of independent predictors of ICU mortality.

Variables	Odds Ratio	95% CI	P[c]
Acute respiratory insufficiency (presence) (categoric data)	60.771	2.763-1336.489	0.009
Hospital LOS before ICU (day), per point	1.284	1.057-1.560	0.012
SOFA Score, per point	1.577	1.018-2.444	0.041
Lactate after 24-hours (mmol/L)	31.743	1.692-595.464	0.021

OR; Odds Ratio, CI; Confidence Interval, ICU; Intensive care unit, LOS; Length of Stay, SOFA; Sequential Organ Failure Assessment, APACHE II; Acute Physiology and Chronic Health Evaluation II, BUN; Blood urea nitrogen, INR; International normalized ratio.
[c]Logistic regression analysis backward elimination method was used, and the variables included in the first step were the presence of malignancy, acute respiratory insufficiency, sepsis and cardiac/respiratory arrest, need for acute hemodialysis, need for vasopressors, ICU LOS, hospital LOS before ICU, APACHE II score, SOFA score, Glasgow Coma score, BUN, creatinine, INR and lactate levels after 24 hours. Only results for variables retained in the final multivariable model were presented (Nagelkerke R^2=0.808, p <0.001).

DISCUSSION

Approximately 85% of GIS bleedings originate from the upper GIS[20]. There are few studies about ICU follow-up of GIS bleeding patients. Most of the studies included the patients with new onset GIS bleeding in the ICU follow-up. In our study, all patients had upper GIS bleeding on admission to ICU. Upper GIS bleedings in ICU patients were reported with percentages between 0.06% and 14% in the world[5,21,22] and 4%-5% in our country[2,5]. In our study, the rate of upper GIS bleeding was 0.49 per

1000 ICU admissions in accordance with the literature.

GIS bleeding is generally more common in men[7-13] and over 60 years of age[7-9,13], and this also appears to be correct for patients requiring ICU follow-up[2,5]. Our results also support these findings with a higher median age (73.5 years) than previously reported and a male predominance (57.8%). There are studies reported that whether the age is associated with increased mortality[11,23] or not[5]. In our study, there was no difference between the groups in terms of gender and age for mortality.

The average mortality rate for upper GIS bleeding is ranging from 1 to 20%[6,14,24] mostly but there are few studies reported mortality rates higher than 30%[6,25]. As expected, mortality rates of upper GIS bleeding are higher for ICU patients[2-5,26]. ICU mortality was reported as %45.8 (APACHE II score: 22.9) by Cook et al.[3], %52.3 (APACHE II score: 30) by Kuşçu et al.[5], and %20 (APACHE II score: 17) by Turkoğlu et al.[2]. The median APACHE II score was 17 (4-43) and the The median age of the patients was 73.5 (31-93) and 27 (42.2%) of them were women.

ICU mortality rate was 29.7% in our study. The ICU LOS, hospital LOS before ICU, APACHE II, and SOFA scores were significantly higher and GCS was lower in the non-surviving group in accordance with the literature3,5,15. Hypotension was present in 53.1% of the patients at the time of admission and the need for vasopressors, invasive mechanical ventilation and acute hemodialysis were significantly higher in the non-surviving group. Jimenez-Rosales et al.[14] also found systolic blood pressures were lower in the non-surviving group.

It is a known fact that the presence of co-morbidities in ICU patients is important for the prognosis. As in many studies[7,8,10], hypertension (46.9%), cardiovascular diseases (42.2%) and diabetes (35.9%) were the most common co-morbid diseases in our study. Previous studies showed that mortality increases in patients with co-morbid diseases such as coagulopathy[21,22,27], liver and kidney failure[6,27], heart disease[14], and malignancy[6,14]. In our study, the presence of malignancy, acute respiratory insufficiency, sepsis, and respiratory/cardiac arrests were found as important risk factors for mortality.

In upper GIS bleeding, most frequently reported etiologies are peptic ulcer and gastric or esophageal varices, while gastric erosions, esophagitis, Mallory-Weiss tears, and neoplasms are the other causes of bleeding[7,8,12,13,28]. In our endoscopic findings, the most common lesions were duodenal and gastric ulcers (38.6%), gastritis and erosions (36.8%), and esophagus and fundus varices (31.6%). In our study, the rates of gastric and duodenal ulcers were lower than the rates reported (50%) in the literature[12,13]. The rate of any drug use that may cause bleeding tendency was 32.8% in our patients and the rate of NSAIDs use (3.1%) was well below the reported rate (≥30%) in the literature[8,29,30]. The presence of high rates of hematological or solid malignancies (29.7%), chronic hepatic disease (28.1%) and thrombocytopenia (62.5%) may be associated with the low rate of NSAIDs use in our patients. In fact, we suggest that the low rates of NSAIDs and ASA usage also explain the low rates of peptic ulcer in our patient population. The higher rates of gastritis and erosive lesions as a cause of bleeding, compared to the literature, may be due to clinical characteristics of our patients who are older and prone to bleed with multiple co-morbid diseases, including malignancy and thrombocytopenia. In addition, the difference in inclusion criteria between the studies may be another factor.

In our study, the number of blood transfusions was higher in the non-surviving group as expected in accordance with the literature[5,20]. All patients required transfusion of at least one unit of blood products. In addition to the findings of previous studies, we found that there was no significant effect of both presence and degree of thrombocytopenia on mortality, but the survival was higher in those who needed only erythrocyte transfusion than in those who needed erythrocyte, thrombocyte, and fresh frozen plasma transfusions.

In laboratory tests, we evaluated BUN, creatinine, hemoglobin, hematocrit, platelet, INR, and lactate levels. While the previous studies mostly evaluated the laboratory values on admission, we evaluated laboratory values both on admission and after 24 hours. Moledina et al.[6] found that BUN, creatinine, and INR values on admission were higher in the non-surviving group, but there was no difference for hemoglobin and platelet values. Jimenez-Rosales et al.[14] found that the non-surviving group had lower hemoglobin and platelet values and higher BUN and creatinine values on admission. Shah et al.[31] reported that hematocrit levels were not associated with mortality. Unlike other studies, we found that there was no significant difference between the surviving and non-surviving groups for laboratory values on

admission, while BUN, creatinine, INR, and lactate levels after 24 hours were significantly higher in the non-surviving group.

In the binary logistic regression analysis, the presence of acute respiratory insufficiency, long hospital LOS before ICU, high SOFA scores, and increased lactate levels after 24 hours were the independent predictors of ICU mortality. Lactate is a marker of hypoperfusion and anaerobic metabolism and is an easily accessible test. It is a good indicator of mortality risk in various shock conditions, including trauma and sepsis[20,31-33]. There are few studies[20,31,34] about the relationship between lactate levels and mortality in patients with GIS bleeding. It was reported that lactate levels were significantly higher in GIS bleeding patients requiring ICU follow-up[20] and this high lactate levels were associated with increased mortality[31,34]. The presence of acute respiratory failure increases the probability of possible perfusion disorder in a patient and a high SOFA score is a marker showing that the patient's general condition and perfusion are poor. In the previous studies, it was also found that a longer hospital stay was associated with increased mortality[5,15]. We suggest that if the hemodynamics cannot be stabilized in the first 24 hours, BUN, creatinine, INR, and lactate levels will be increased due to impaired organ and tissue perfusion. So, high levels of these laboratory values are also indicators of increased mortality.

The most important limitations of our study are that it is retrospective and a single-center study with limited number of patients. We think that our study is valuable because it contributes to the epidemiological data on GIS bleeding patients followed in the ICU in Turkey.

Gastrointestinal bleeding is an important cause of morbidity and mortality in ICUs. With this study, we defined the patient profile and mortality risk factors in patients with GIS bleeding who need ICU follow-up. Accordingly, the presence of co-morbid diseases such as malignancy and acute conditions such as acute respiratory insufficiency, sepsis, and respiratory/cardiac arrests were found to be associated with increased mortality. In addition, high levels of BUN, creatinine, INR, and lactate levels in the first 24 hours of follow-up, rather than the values on admission to ICU, were associated with increased mortality. Therefore, close monitoring and rapid normalization of these values with appropriate treatments are important. These findings can be used to identify patients who may benefit from more intensive management.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SK, EA, İG; Veri toplama: SK; Veri analizi ve yorumlama: SK; Yazı taslağı: SK; İçeriğin eleştirel incelenmesi: SK, EA, İG; Son onay ve sorumluluk: SK, EA, İG; Teknik ve malzeme desteği: SK, EA, İG; Süpervizyon: SK, EA, İG; Fon sağlama (mevcut ise): yok.
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