



# Evaluation of Endoscopy Timing in Patients with Acute Upper Gastrointestinal Bleeding in Emergency Department

## Acil Servise Başvuran Akut Üst Gastrointestinal Kanamalı Hastalarda Endoskopi Zamanının Değerlendirilmesi

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### Abstract

**Aim:** Endoscopy is recommended in acute upper gastrointestinal bleeding (AUGIB) to detect the bleeding source and stop the bleeding. The optimal timing of endoscopy in AUGIB is controversial. We aimed to investigate the time of endoscopy and the factors affecting it.

**Material and Method:** Retrospective, single-center study. The patients were divided into four groups: endoscopy after discharge, 0-12 hours endoscopy, 12-24 hours endoscopy and 24 hours later. Age, sex, vital signs, laboratory findings were recorded. Glasgow-Blatchford Score (GBS) and Charlson comorbidity index (CCI) were calculated. The obtained data were compared between these four groups. All-cause mortality for 30 days was recorded.

**Results:** A total of 318 patients were included. In the comparison of endoscopy times, the parameters found to be statistically significant between the four groups are Hb, BUN, and INR levels, GBS and CCI. As a result of CHAID analysis, the most crucial variable affecting the timing of endoscopy was found to be the Hb value of the patients ( $\chi^2=66.528$ ; adjusted  $p=0.000$ ). Mortality occurred in 10.69% of the patients. The timing of endoscopy did not affect mortality. In binary logistic regression analysis, low systolic BP (0.967 times increase), high CCI (86,402 times increase) were found to affect mortality.

**Conclusion:** The factors affecting the timing of endoscopy are the signs of bleeding. A thorough follow-up of vital signs in patients presenting to the emergency department with acute gastrointestinal bleeding, particularly an evaluation of systolic blood pressure and detailed questioning of additional comorbid conditions, is critical to reduce mortality.

**Keywords:** endoscopy timing, emergency, upper gastrointestinal bleeding, acute gastrointestinal bleeding

### Öz

**Amaç:** Endoskopi akut üst gastrointestinal kanamada (AUGIB) kanama kaynağını tespit etmek ve kanamayı durdurmak için önerilir. Endoskopinin AUGIB'de optimal zamanlaması tartışmalıdır. Çalışmamızda endoskopi zamanını ve etkileyen faktörleri araştırmayı amaçladık.

**Gereç ve Yöntem:** Çalışma retrospektif, tek merkezlidir. Hastalar taburculuk sonrası endoskopi, 0-12 saat endoskopi, 12-24 saat endoskopi ve 24 saat sonra endoskopi olmak üzere 4 gruba ayrıldı. Yaş, cinsiyet, vital bulgular, laboratuvar bulguları kaydedildi. Glasgow-Blatchford Skoru (GBS) ve Charlson komorbidite indeksi (CCI) hesaplandı. Elde edilen veriler bu dört grup arasında karşılaştırıldı. 30 gün boyunca tüm nedenlere bağlı ölümler kaydedildi.

**Bulgular:** Toplam 318 hasta dahil edildi. Endoskopi sürelerinin karşılaştırılmasında dört grup arasında istatistiksel olarak anlamlı bulunan parametreler Hb, BUN ve INR seviyeleri, GBS ve CCI'dir. CHAID analizi sonucunda endoskopi zamanını etkileyen en önemli değişkenin hastaların Hb değeri olduğu bulundu ( $\chi^2=66,528$ ; düzeltilmiş  $p=0,000$ ). Mortalite hastaların %10.69'unda meydana geldi. Endoskopinin zamanlaması mortaliteyi etkilemedi. Binary lojistik regresyon analizinde düşük sistolik KB (0,967 kat artış), yüksek CCI (86.402 kat artış) mortaliteyi etkilediği bulundu.

**Sonuç:** Endoskopinin zamanlamasını etkileyen faktörler kanama belirtileridir. Akut gastrointestinal kanama ile acil servise başvuran hastalarda hayati bulguların tam olarak izlenmesi, özellikle sistolik kan basıncının değerlendirilmesi ve ek komorbid durumların ayrıntılı olarak sorgulanması, mortaliteyi azaltmak için kritik öneme sahiptir.

**Anahtar Kelimeler:** endoskopi zamanlaması, acil durum, üst gastrointestinal kanama; akut gastrointestinal kanama.



## INTRODUCTION

Gastrointestinal bleeding (GIB) is the most common gastrointestinal disease in the United States and requires hospitalization. There are more than half a million admissions regarding the number of patients. Approximately 80% of these patients have upper gastrointestinal bleeding (UGIB). UGIB refers to bleeding caused by the proximal part of the esophagus, stomach, or treitz ligament.<sup>[1]</sup> In acute UGIB (AUGIB), endoscopy is recommended to detect the bleeding source and stop the bleeding.<sup>[2]</sup> However, the optimal timing of endoscopy in AUGIB is controversial.<sup>[3-5]</sup> Current guidelines agree that early endoscopy (within 24 hours of admission) for AUGIB leads to better outcomes in terms of mortality and hospital stay.<sup>[2]</sup>

On the other hand, the definition of "too early" endoscopy is still controversial, and although the European Society for Gastrointestinal Endoscopy (ESGE) defines it as <12 hours, some authors suggest alternative timing in their study (e.g., <2 hr, < 6 hr).<sup>[6-8]</sup> Very early endoscopy is recommended for patients with a high risk of bleeding characterized by a Glasgow-Blatchford Score (GBS)  $\geq 12$ , suspected acute variceal bleeding, significant comorbidity, and contraindications for reversal of anticoagulation. However, there is no consensus on this issue yet.<sup>[9,10]</sup>

The GBS is the recommended score to be used in the guidelines for identifying risky patients and deciding on the endoscopy time.<sup>[2]</sup> GBS has the highest accuracy in predicting the need for immediate intervention and mortality.<sup>[10,11]</sup> Guidelines suggest that patients with GBS  $\leq 1$  can be treated as outpatients.<sup>[2,10,12]</sup>

It is still suggested that endoscopic hemostasis may have an advantage over medical therapy alone in reducing rebleeding. However, it does not appear to provide any benefit in terms of transfusion requirement or mortality.<sup>[13,14]</sup> Due to these conflicting data, we aimed to investigate the time of endoscopy and the factors affecting it and to determine the parameters affecting mortality in patients who presented to the emergency department with AUGIB.

## MATERIAL AND METHOD

This study was conducted as a retrospective, and carried out with the permission of İzmir Katip Celebi University Clinical Research Ethics Committee (Date: 22/05/2022, Decision No: 0234). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. According to the ICD-10 (K92.9, K29.0, K25, K28.0) code, the patients admitted to our emergency department between January 1, 2021, and March 31, 2022, who were diagnosed with AUGIB were retrospectively scanned.

**Inclusion Criteria:** Patients over 18 years who were not pregnant were included in the study.

**Exclusion Criteria:** Patients with variceal bleeding, trauma patients, and patients whose files did not have sufficient data were excluded from the study.

## Primary Outcomes

Age, sex, vital signs (systolic blood pressure, pulse), laboratory findings such as hemoglobin (Hb), blood urea nitrogen (BUN), creatinine, international normalized ratio (INR), and platelet (PLT) levels of the patients were recorded. Whether the patient had syncope in the admission complaint, liver disease diagnosed by a gastroenterologist from comorbid diseases, or heart failure diagnosed by a cardiologist were added to the data. For diagnosis liver disease, patients with cirrhosis or bilirubin  $>2$  x normal and AST/ALT/AP  $>3$ x normal were considered to have 'liver disease'.<sup>[15]</sup> Following the 2021 ESC Acute Heart Failure Guidelines, patients who had a volume excess, respiratory distress, exercise dyspnea, paroxysmal nocturnal dyspnea or orthopnea were considered heart failure patients.<sup>[16]</sup> The patients use of anticoagulant/antiaggregant drugs (acetylsalicylic acid, clopidogrel, warfarin, ticagrelor, apixaban, and rivaroxaban) was recorded. Rectal examination findings were grouped as normal stool, empty rectum, melena, and hematochezia. The GBS was calculated from the data obtained (Hb, BUN, systolic BP, sex, heart rate, melena present, recent syncope, hepatic disease history, and cardiac failure present). According to the GBS, the patients were divided into groups 0-1, 2-12, and  $\geq 12$ .<sup>[10]</sup> The patients comorbid diseases were divided into  $\leq 5$  and  $\geq 6$  according to the Charlson comorbidity index (CCI).<sup>[17]</sup> The treatments administered were recorded (medical therapy, sclerotherapy, sclerotherapy+hemoclip, band ligation, hemoclip). All-cause mortality for 30 days was recorded. Factors affecting mortality were investigated. The time from admission to the emergency department until endoscopy was calculated, and the patients were divided into four groups: endoscopy after discharge, 0-12 hours endoscopy, 12-24 hours endoscopy and 24 hours later. The obtained data were compared between these four groups.

## Statistical Method

Statistical analysis were evaluated in the IBM SPSS Statics Version 20 package program. Descriptive statistics and frequency and percentage distribution, mean, standard deviation and minimum and maximum values for continuous variables were calculated. The conformity of continuous variables to a normal distribution was evaluated with Kolmogorov-Smirnova and Shapiro-Wilk ( $p < 0.05$ ) tests, and then it was decided to use parametric or nonparametric tests. While chi-square test statistics were used to compare categorical variables between groups, Mann-Whitney U statistical analyses were used for comparisons between two groups, and Kruskal-Wallis statistical analyses were used for comparisons of more than two groups since continuous data consisted of values that did not conform to a normal distribution.

The data obtained in the study to determine the variables that may affect the mortality status of the patients admitted to the emergency department were evaluated with a binary logistic regression model. The factors affecting the endoscopy time were evaluated with CHAID analysis.

### RESULTS

A total of 318 patients who met the study criteria were included. The general characteristics of the patients were as follows: The mean age of the patients was 67.01±16.96 years, 54.09% of the patients were males. A total of 52.2% of the patients were not using anticoagulant and/or antiaggregant drugs. Melena was detected on rectal examination in 66.04% of the patients. The GBS of 51.57% of the patients was 12 and above, and the CCI of 67.92% was in the range of 0-5. A total of 27.67% of the patients received endoscopy within 0-12 hours, 37.11% received endoscopy within 13-24 hours, 29.56% received endoscopy after 24 hours, and 5.66% underwent elective endoscopy after discharge.

In the comparison of endoscopy times, the parameters found to be statistically significant between the four groups are as follows. The Hb level of the patients who underwent endoscopy between 0-12 hours was found to be 7.5±2.08 mg/dl (p<0.00). The BUN level of the patients who underwent endoscopy after discharge was 26.89±14.14 mg/dl (p<0.01), and the INR level of the patients who underwent endoscopy between 13-24 hours was 1.83±3.57 (p<0.03). The rectal examination finding of 84.1% of the patients who underwent endoscopy at 0-12 hours was melena. Rectal examination was normal in 36.17% of those who had endoscopy after 25 hours. 33.3% of the patients who underwent endoscopy after discharge did not use anticoagulant/antiaggregant drugs. There was a statistically significant difference between the timing of endoscopy in terms of anticoagulant/antiaggregant drug use (p<0.00). The GBS of 72.34% of those who underwent endoscopy after 25 hours was between 2-12, and 70.5% of those who underwent endoscopy between 0-12 hours had a GBS ≥12. According to the presence of comorbid disease; The CCI of 78.72% of those

who underwent EGD at 24 hours and later was found to be between 0-5, and the CCI of 40.68% of those who underwent EGD at 12-24 hours was between 6-37 (p<0.03) (Table 1).

The factors affecting the endoscopy time were analyzed by CHAID analysis. The Hb value of the patients was found to be the most crucial variable (χ<sup>2</sup>=66,528; adjusted p=0.000). Patients with an Hb level below 6.6 mg/dl who underwent endoscopy between 0-12 and 13-24 hours constituted 80.8% of the total. Endoscopy was performed in 45.8% of patients with Hb levels between 6.6 mg/dl and 9.0 mg/dl between 13-24 hours. Endoscopy was performed in 37.5% of patients with Hb levels between 9.0 mg/dl and 10.9 mg/dl over 25 hours (Figure 1).

Mortality occurred in 10.69% of the patients. In the comparison of deceased and living patients; The mortality rate of patients with systolic blood pressure between 101.12±25.01 mmHg, liver disease, undergoing endoscopic procedure (sclerotherapy, hemoclips, band), GBS score ≥12, and CCI 6-37 was higher than surviving patients (Table 2). Binary logistic regression analysis was performed for these parameters. The Nagelkerke R<sup>2</sup> value of 0.510 was found to be 51.0% effective in explaining the response variable (mortality) of the model. The sensitivity of the model was 97.2%, the selectivity was 29.4%, and the accuracy rate was 89.9%. The probability of survival of patients with low systolic BP values is 0.967 times lower than that of patients with high systolic BP values. The probability of survival of patients with a high CCI value was 86,402 times lower than that of patients with a low CCI value. Depending on the type of treatment, the patient's survival probability increases by 2,938 times. Based on the GBS, patient survival probability varied by 0.107. The higher the GBS, the higher the death rate (Table 3).

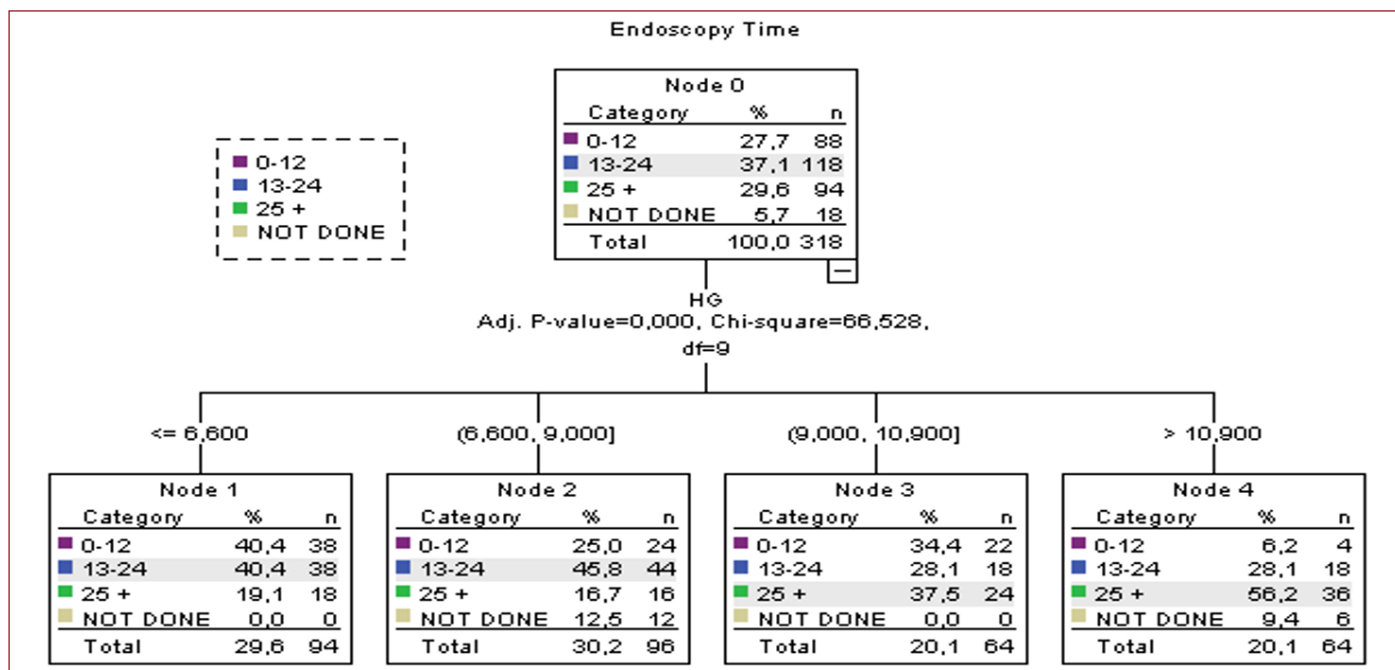


Figure 1. CHAID analysis for factors affecting endoscopy timing

**Table 1. Comparison of patients' general characteristics and study parameters between endoscopy timing groups**

Variables	All patients N=318	After discharge n=18	0- 12 hours n=88	13-24 hours n=118	25 hours and above n=94	P
	mean±std (min-max)	mean±std (min-max)	mean±std (min-max)	mean±std (min-max)	mean±std (min-max)	
Age/year	67.02±16.91 (18-95)	68.22±12.95 (51-93)	65.52±19.14 (18-95)	70.95±13.03 (21 -93)	63.26±18.75 (29-93)	0.05
Pulse/min	91.88±17.28 (12-143)	93.11±12.74 (79-121)	93.02±16.22 (61-135)	94.1±17.77 (60 -143)	87.79±17.88 (60-128)	0.13
Systolic blood pressure/mmHg	118.56±24.21 (57-190)	120.78±33.91 (80-190)	116.61±24.31 (57-190)	118.15±25.47 (75 -186)	120.47±20.26 (75-186)	0.59
Hemoglobin-gr/dl	8.49±2.75 (3-16.4)	9.34±1.77 (7.1-12.1)	7.5±2.08 (3-11.7)	8.14±2.76 (3.9 -15)	9.68±2.98 (3.0-16.4)	0.00
BUN-mg/dL	39.13±25.82 (5-151)	26.89±14.14 (12-53)	40.68±25.95 (5-151)	42.68±27.4 (6 -120)	35.57±24.51 (7-151)	0.01
INR	1.64±2.42 (0.87-28)	1.66±1.18 (0.91-4.7)	1.74±1.58 (0.9-8.29)	1.83±3.57 (0.89 -28)	1.3±1.09 (0.87-28)	0.03
PLT-mcL	251.91±104.89 (24-589)	258.89±122.27 (63-505)	256.32±104.51 (31-589)	258.97±106.42 (24 -547)	237.57±100 (24-589)	0.29
Creatinine-mg/dL	1.3±0.96 (0.5-6.92)	1.92±2.2 (0.52-6.92)	1.23±0.69 (0.5-4.63)	1.39±1.09 (0.63 -6.7)	1.12±0.39 (0.59-4.63)	0.49
	<b>Count (%)</b>	<b>Count (%)</b>	<b>Count (%)</b>	<b>Count (%)</b>	<b>Count (%)</b>	
Gender						
Male	172 (54.09)	10 (55.56)	44 (50)	68 (57.63)	50 (53.19)	0.75
Female	146 (45.91)	8 (44.44)	44 (50)	50 (42.37)	44 (46.81)	
Rectal Examination						
Melena	210 (66.04)	6 (33.33)	74 (84.1)	80 (67.8)	50 (53.19)	0.00
Normal stool	78 (24.53)	6 (33.33)	12 (13.6)	26 (22.03)	34 (36.17)	
Empty rectum	28 (8.81)	6 (33.33)	2 (2.3)	10 (8.47)	10 (10.64)	
Hematochezia	2 (0.63)	0 (0)	0 (0)	2 (1.69)	0 (0)	
Treatment						
Medical therapy	282 (88.68)	18 (100)	74 (84.1)	106 (89.83)	84 (89.36)	0.08
Sclerotherapy	8 (2.52)	0 (0)	0 (0)	4 (3.39)	4 (4.26)	
Sclerotherapy-Hemoclips	12 (3.77)	0 (0)	6 (6.8)	4 (3.39)	2 (2.13)	
Band ligation	4 (1.26)	0 (0)	4 (4.5)	0 (0)	0 (0)	
Hemoclips	12 (3.77)	0 (0)	4 (4.5)	4 (3.39)	4 (4.26)	
Anticoagulant Drug Use						
ASA	42 (13.21)	6 (33.33)	10 (11.4)	16 (13.56)	10 (10.64)	0.00
ASA + ticagrelor	8 (2.52)	0 (0)	0 (0)	6 (5.08)	2 (2.13)	
ASA + warfarin	4 (1.26)	0 (0)	2 (2.3)	2 (1.69)	0 (0)	
ASA + clopidogrel	14 (4.4)	0 (0)	0 (0)	10 (8.47)	4 (4.26)	
ASA + rivaroxaban	2 (0.63)	0 (0)	2 (2.3)	0 (0)	0 (0)	
warfarin	34 (10.69)	4 (22.22)	12 (13.6)	12 (10.17)	6 (6.38)	
apixaban	8 (2.52)	2 (11.11)	0 (0)	4 (3.39)	2 (2.13)	
clopidogrel	26 (8.18)	0 (0)	6 (6.8)	10 (8.47)	10 (10.64)	
rivaroxaban	14 (4.4)	0 (0)	2 (2.3)	10 (8.47)	2 (2.13)	
No	166 (52.2)	6 (33.33)	54 (61.4)	48 (40.68)	58 (61.7)	
Mortality						
Alive	284 (89.31)	16 (88.89)	76 (86.4)	102 (86.44)	90 (95.74)	0.12
Ex	34 (10.69)	2 (11.11)	12 (13.6)	16 (13.56)	4 (4.26)	
GBScore						
2-12	154 (48.43)	10 (55.56)	26 (29.5)	50 (42.37)	68 (72.34)	0.00
≥12	164 (51.57)	8 (44.44)	62 (70.5)	68 (57.63)	26 (27.66)	
CCI						
0-5	216 (67.92)	12 (66.67)	60 (68.2)	70 (59.32)	74 (78.72)	0.03
6-10	102 (32.08)	6 (33.33)	28 (31.8)	48 (40.68)	20 (21.28)	

BUN: Blood Urea Nitrogen, INR: International Normalized Ratio, PLT: Platelet, ASA: Acetylsalicylic acid, GBS: Glasgow-blatchford score, CCI: Charlson Comorbidity Index

**Table 3. Evaluation of Risk Factors Associated with Mortality in Binary Logistic Regression Model**

Variables in the Equation		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1a	Systolic Blood Pressure	-.033	.012	8.243	1	.004	.967	.946	.989
	CCI	4.459	.953	21.878	1	.000	86.402	13.337	559.734
	Hepatic Disease	.903	.574	2.475	1	.116	2.467	.801	7.600
	Applied Treatment	1.078	.355	9.214	1	.002	2.938	1.465	5.893
	GBS Score	-2.236	1.131	3.910	1	.048	.107	.012	.980
	Constant	-3.198	2.886	1.228	1	.268	.041		

a. Variable(s) entered on step 1: Systolic, Comorbit, Hepatic, Treatment, GBS, Blood Transfusion. GBS: Glasgow-blatchford score, CCI: Charlson Comorbidity Index

**Table 2. Comparison of the parameters considered in the study between deceased and living patients**

Variables	Alive n=284	Ex n=34	p
	mean±std (min-max)	mean±std (min-max)	
Age/year	66.7±16.99 (18-95)	69.71±16.27 (25-90)	0.27
Pulse/min	91.84±17.44 (12-143)	92.24±16.16 (64-121)	0.98
Systolic blood pressure/mmHg	120.65±23.3 (80-190)	101.12±25.01 (57-158)	0.00
Hemoglobin gr/dl	8.57±2.77 (3-16.4)	7.82±2.51 (3.1-13)	0.22
BUN mg/dL	38.78±25.93 (5-151)	42.06±25.06 (6-87)	0.27
INR	1.69±2.56 (0.87-28)	1.25±0.33 (1-2.26)	0.38
PLT-mcL	255.49±100.06 (26-589)	222±137.07 (24-538)	0.08
Creatinine-mg/dL	1.31±0.99 (0.58-6.92)	1.22±0.59 (0.5-2.47)	0.92
	Count (%)	Count (%)	
Gender			
Male	156 (54.93)	16 (47.06)	0.38
Female	128 (45.07)	18 (52.94)	
Rectal Examination			
Melena	190 (66.9)	20 (58.82)	0.44
Normal stool	66 (23.24)	12 (35.29)	
Empty rectum	26 (9.15)	2 (5.88)	
Hematochezia	2 (0.7)	0 (0)	
Syncope			
No	246 (86.62)	32 (94.12)	0.21
Yes	38 (13.38)	2 (5.88)	
Hepatic Disease			
No	264 (92.96)	24 (70.59)	0.00
Yes	20 (7.04)	10 (29.41)	
Cardiac Failure			
No	228 (80.28)	24 (70.59)	0.19
Yes	56 (19.72)	10 (29.41)	
Applied Treatment			
Medical therapy	256 (90.14)	26 (76.47)	0.04
Sclerotherapy	6 (2.11)	2 (5.88)	
Sclerotherapy-Hemoclips	10 (3.52)	2 (5.88)	
Band ligation	2 (0.7)	2 (5.88)	
Hemoclips	10 (3.52)	2 (5.88)	
Anticoagulant Drug Use			
ASA	40 (14.08)	2 (5.88)	0.26
ASA + ticagrelor	8 (2.82)	0 (0)	
ASA + warfarin	4 (1.41)	0 (0)	
ASA + clopidogrel	12 (4.23)	2 (5.88)	
ASA + rivaroxaban	2 (0.7)	0 (0)	
warfarin	32 (11.27)	2 (5.88)	
apixaban	8 (2.82)	0 (0)	
clopidogrel	24 (8.45)	2 (5.88)	
rivaroxaban	10 (3.52)	4 (11.76)	
No	144 (50.7)	22 (64.71)	
GBS Score			
0-1	0 (0)	0 (0)	0.02
2-12	146 (51.41)	8 (23.53)	
≥13	138 (48.59)	26 (76.47)	
CCI			
0-5	214 (75.35)	2 (5.88)	0.00
6-10	70 (24.65)	32 (94.12)	
Endoscopy Time			
After discharge	16 (5.63)	2 (5.88)	0.18
0-12 hours	76 (26.76)	12 (35.29)	
13-24 hours	102 (35.92)	16 (47.06)	
≥25 hours	90 (31.69)	4 (11.76)	

BUN: Blood Urea Nitrogen, INR: International Normalized Ratio, PLT: Platelet, ASA: Acetylsalicylic acid, GBS: Glasgow-blatchford score, CCI: Charlson Comorbidity Index

## DISCUSSION

The 2021 ESGE recommends endoscopy within 24 hours of hospital admission for AUGIB patients to identify the bleeding source and provide endoscopic treatments.<sup>[2]</sup> Few clinical data exist on the optimal 24-hour endoscopy timing.<sup>[7,12,18]</sup> BUN, Hb, GBS score, melena, anticoagulant use, and CCI values were statistically significant in four patient groups based on EGD timing. Our results showed that low CCI patients had endoscopy late and high CCI patients within 12-24 hours. A CCI is calculated by evaluating 19 factors. The scoring process weighs diseases.<sup>[18]</sup> Thus, a high CCI indicates worse comorbidities. In our study, UGIB increased the comorbidity burden in high CCI patients. Thus, early endoscopy is appropriate for high CCI patients.

The GBS, which was statistically significant between patient groups, is the best risk assessment score for identifying low-risk patients who can avoid hospitalization and should be treated outpatiently. The American College of Gastroenterology (ACG) and the UK National Institute for Health and Care Excellence (NICE) recommend outpatient evaluation of GBS = 0 patients.<sup>[19]</sup> The 2015 ESGE guidelines and 2018 Asia-Pacific consensus group guidelines recommend using GBS ≤ 1 to identify low-risk patients, reflecting recent evidence and publications.<sup>[18,19]</sup> No endoscopy timing is recommended based on GB score. A randomized controlled study by Wong et al. found that emergency endoscopy was not beneficial for high-risk patients with GBS ≥ 12, either within 6 hours or 24 hours of admission.<sup>[20]</sup> In our study, 70.5% of patients with endoscopy at 0-12 hours had GBS ≥ 12. In patients with high GBS, early EGD may be due to changes in the parameters that make up this score, not the calculated GBS score. Melena, low Hb, and high BUN indicate active bleeding when the statistically significant GBS parameters are evaluated separately. Thus, early endoscopy was likely performed on the patients. Sasaki et al. found that endoscopic intervention is needed at 22.4 BUN.<sup>[21]</sup> Lin et al. classified patients by nasogastric tube aspirations.<sup>[22]</sup> Patients with blood aspirates had endoscopy within 12 hours. Early endoscopy helps actively bleeding patients. Our study found melena on rectal examination in 85% of endoscopy patients at 0-12 hours. We think bleeding findings in UGIB patients help decide on early endoscopy. Hb level was the most effective factor on endoscopy time, according to CHAID analysis. Endoscopy was performed within 24 hours in 80.8% of Hb-low patients. Low Hb levels in bleeding patients indicate acute blood loss and should be treated with endoscopy immediately. Thus, the bleeding focus can be found and hemostasis achieved. Cooper et al. recommended early endoscopy for endoscopic hemostasis patients because it reduced rebleeding and surgery.<sup>[24]</sup>

However, patients without active bleeding should not undergo early endoscopy. Schacher et al. found that emergency department endoscopy within 3 hours did not improve patient outcomes.<sup>[25]</sup> In their study, Lau et al. compared urgent (<6 hours) and early (<24 hours) endoscopy patients.<sup>[7]</sup> The two groups had similar mortality and rebleeding rates. He reported

that more urgent endoscopy patients received endoscopic hemostatic treatment than early endoscopy patients. because urgent endoscopy found more ulcers that were actively bleeding and had major stigmas. Because early endoscopy patients received medical treatment, the number of ulcers with possibly bleeding stigmas decreased. Stabilization with medical treatment was advised over early endoscopy.<sup>[7]</sup> Our study found similar treatment modalities to Schacher et al. and Lau et al.<sup>[7,25]</sup> Our survivors received medical treatment 90.14% of the time. The regression analysis showed that the treatment method increased survival by 2.908 times. We found that endoscopic patients had higher mortality. Early endoscopic treatment also involves medically controlled bleeding foci, which may not be necessary for low-risk patients. Using graphs, Laursen et al. examined the relationship between endoscopy timing and mortality.<sup>[8]</sup> The distribution charts showed lower mortality in patients who had endoscopy between 6-24 hours. Lee et al. and Schacher et al. found no significant mortality difference between early ( $\leq 3$  hours) and late endoscopy ( $\geq 48$  hours) groups.<sup>[12,25]</sup> Lau et al. and Guo et al. found no mortality difference between early and urgent endoscopy (<6 hours) patients.<sup>[7,23]</sup> These studies also show that endoscopy within 3-6 hours of admission does not improve clinical outcomes. Our findings match these studies. The timing of endoscopy does not affect patient mortality.

Systolic BP affects mortality. Systolic BP values of deceased patients were  $101 \pm 12.25.01$ /mmHg, while surviving patients had  $120 \pm 65.23.3$ /mmHg. Low-BP patients are 0.967-fold less likely to survive than high-BP patients. A drop in systolic BP indicates class 3 hemorrhagic shock with a 40% volume loss.<sup>[26]</sup> Systolic hypotension in UGIB patients causes hemorrhagic shock and death from rapid blood loss. A decrease in blood oxygen-carrying capacity causes hypoxia and ischemia in all organs and tissues as blood loss increases. GBS parameters include systolic BP. GBS also affected mortality in our study. The 2000 GBS risk assessment tool predicts hospital-based treatment like blood transfusion, endoscopic treatment, or surgery.<sup>[10]</sup> Guidelines recommend assessing GBS $\geq 12$  patients as high-risk.<sup>[2,10]</sup> In accordance with recommendations, 76.47% of deceased patients had GBS $\geq 12$ . According to regression analysis, patient survival probabilities ranged from 0.107. The mortality rate increased with score.

The most influential mortality factor was CCI. Our regression analysis showed that patients with a CCI of 6-37 were 86,402 times more likely to die than those with a CCI of 0-5. CCI, which we used to assess comorbid diseases, increases with age, severity, and number of diseases.<sup>[17]</sup> Siddique et al. found that GIB patients with comorbital disease are at risk for complications, hospitalization, and death.<sup>[27]</sup> In a similar study by Siebenhüner et al., 61% of patients took additional antithrombotic drugs.<sup>[28]</sup> UGIB risk factors include nongastrointestinal comorbidities, according to Crooks et al.<sup>[29]</sup> Comorbid diseases may be the leading cause of patient death. A high CCI indicates a higher death risk and more severe comorbidities.<sup>[29]</sup> Carlson et al. found that the higher the CCI

for any disease state, including UGIB, the higher the mortality.<sup>[17]</sup> Insufficient compensating mechanisms against bleeding owing to concomitant disorders in UGIB patients with high CCI may potentially lead to high mortality.

## CONCLUSION

In conclusion, we can say that the factors affecting the timing of endoscopy in patients admitted to the emergency department due to UGIB are the signs of bleeding. We found that patients with low Hb, high BUN values, GBS $\geq 12$ , and melena on rectal examination underwent endoscopy early in 0-12 hours. However, we found that the timing of endoscopy did not affect mortality. The main factors affecting mortality are systolic BP, CCI, treatment modality, and GBS. Specifically, CCI was found to be the most important determinant of mortality. A thorough follow-up of vital signs in patients presenting to the emergency department with UGIB, particularly an evaluation of systolic blood pressure and detailed questioning of additional comorbid conditions, is critical to reduce mortality.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of İzmir Katip Celebi University Clinical Research Ethics Committee (Date: 22/05/2022, Decision No: 0234).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

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

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

## REFERENCES

1. Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. *Am J Gastroenterol.* 2021;116(5):899-917.
2. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy.* 2021;53(3):300-32.
3. Lim LG, Ho KY, Chan YH, et al. Urgent endoscopy is associated with lower mortality in high-risk but not low-risk nonvariceal upper gastrointestinal bleeding. *Endoscopy.* 2011;43(4):300-6.
4. Laursen SB, Leontiadis GI, Stanley AJ, Møller MH, Hansen JM, Schaffalitzky de Muckadell OB. Relationship between timing of endoscopy and mortality in patients with peptic ulcer bleeding: a nationwide cohort study. *Gastrointest Endosc.* 2017;85(5):936-44.e3.
5. Cho SH, Lee YS, Kim YJ, et al. Outcomes and Role of Urgent Endoscopy in High-Risk Patients With Acute Nonvariceal Gastrointestinal Bleeding. *Clin Gastroenterol Hepatol.* 2018;16(3):370-7.
6. Bjorkman DJ, Zaman A, Fennerty MB, Lieberman D, Disario JA, Guest-Warnick G. Urgent vs. elective endoscopy for acute non-variceal upper-GI bleeding: an effectiveness study. *Gastrointest Endosc.* 2004;60(1):1-8.

7. Lau JYW, Yu Y, Tang RSY, et al. Timing of Endoscopy for Acute Upper Gastrointestinal Bleeding. *N Engl J Med*. 2020;382(14):1299-308.
8. Lee JG, Turnipseed S, Romano PS, et al. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. *Gastrointest Endosc*. 1999;50(6):755-61.
9. Chaudhary S, Stanley AJ. Optimal timing of endoscopy in patients with acute upper gastrointestinal bleeding. *Best Pract Res Clin Gastroenterol*. 2019;42-43:101618.
10. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet*. 2000 Oct 14;356(9238):1318-21.
11. Stanley AJ, Laine L, Dalton HR, et al. Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. *BMJ*. 2017;356:i6432.
12. Barkun AN, Almadi M, Kuipers EJ, et al. Management of Nonvariceal Upper Gastrointestinal Bleeding: Guideline Recommendations From the International Consensus Group. *Ann Intern Med*. 2019;171(11):805-22.
13. Jensen DM, Kovacs TO, Jutabha R, et al. Randomized trial of medical or endoscopic therapy to prevent recurrent ulcer hemorrhage in patients with adherent clots. *Gastroenterology*. 2002;123(2):407-13.
14. Bleau BL, Gostout CJ, Sherman KE, et al. Recurrent bleeding from peptic ulcer associated with adherent clot: a randomized study comparing endoscopic treatment with medical therapy. *Gastrointest Endosc*. 2002;56(1):1-6
15. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010;138(5):1093-100.
16. Bauersachs J, Soltani S. Herzinsuffizienzleitlinien 2021 der ESC [Guidelines of the ESC 2021 on heart failure] *Herz*. 2022;47(1):12-8.
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-83.
18. Sung JJ, Chiu PW, Chan FKL, et al. Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018. *Gut*. 2018;67(10):1757-68.
19. Acute upper gastrointestinal bleeding in over 16s: management. London: National Institute for Health and Care Excellence (NICE); 2016 Aug. (NICE Clinical Guidelines, No. 141.) Available from: <https://www.ncbi.nlm.nih.gov/books/NBK554919/>
20. Gralnek IM, Dumonceau JM, Kuipers EJ, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2015;47(10):a1-46.
21. Wong JC, Lau JY, Tang RS, Au KW, Chan FK, Sung JJ. Urgent versus early endoscopy for upper gastrointestinal bleeding with Glasgow-Blatchford score  $\geq$  12. *Gastroenterology*. 2015;148(4):S-154.
22. Sasaki Y, Abe T, Kawamura N, et al. Prediction of the need for emergency endoscopic treatment for upper gastrointestinal bleeding and new score model: a retrospective study. *BMC Gastroenterol*. 2022;22(1):337.
23. Lin HJ, Wang K, Perng CL, et al. Early or delayed endoscopy for patients with peptic ulcer bleeding. A prospective randomized study. *J Clin Gastroenterol*. 1996;22(4):267-71.
24. Guo CLT, Wong SH, Lau LHS, et al. Timing of endoscopy for acute upper gastrointestinal bleeding: a territory-wide cohort study. *Gut*. 2022;71(8):1544-50.
25. Cooper GS, Chak A, Way LE, Hammar PJ, Harper DL, Rosenthal GE. Early endoscopy in upper gastrointestinal hemorrhage: associations with recurrent bleeding, surgery, and length of hospital stay. *Gastrointest Endosc*. 1999;49(2):145-52.
26. Schacher GM, Lesbros-Pantoflickova D, Ortner MA, Wasserfallen JB, Blum AL, Dorta G. Is early endoscopy in the emergency room beneficial in patients with bleeding peptic ulcer? A "fortuitously controlled" study. *Endoscopy*. 2005;37(4):324-8.
27. Hooper N, Armstrong TJ. Hemorrhagic Shock. [Updated 2022 Sep 26] In: StatPearls [Internet] Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470382/>
28. Siddique SM, Mehta SJ. Bundled Payments for Hospitalized Patients With Gastrointestinal Disease: Current Opportunities and Challenges for Gastroenterology Practices. *Clin Gastroenterol Hepatol*. 2021;19(2):215-8.
29. Siebenhüner K, Blaser J, Nowak A, et al. Comorbidities Associated with Worse Outcomes Among Inpatients Admitted for Acute Gastrointestinal Bleeding. *Dig Dis Sci*. 2022;67(8):3938-47.
30. Crooks CJ, West J, Card TR. Comorbidities affect risk of nonvariceal upper gastrointestinal bleeding. *Gastroenterology*. 2013;144(7):1384-93.