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Optimal endoscopy timing in elderly patients presenting with acute non-variceal upper gastrointestinal bleeding

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Abstract

Background To evaluate the optimal endoscopy time in elderly patients with nonvariceal upper gastrointestinal bleeding (NVUGIB) based on clinical outcomes.

Methods Patients over 65 years of age presenting with NVUGIB are three patient groups based on endoscopy timing: very early endoscopy (< 12 h), early endoscopy (12–24 h) and late endoscopy (> 24 h). Endoscopic intervention was undertaken during the first 12 h for patients who had unstable hemodynamic settings, ongoing bleeding, or a low hematocrit despite transfusion. The clinical outcomes investigated were: The primary endpoint was 30-day mortality, with the need for endoscopic intervention, rebleeding, and length of hospital stay considered as secondary endpoints.

Results The study population was 468, 260 of whom were ≥ 65 years. Based on the timing of endoscopy, very early endoscopy (within 12 h) was performed in 180 (69.2%) patients aged > 65 years and 150 (72.1%) younger patients ($p > 0.05$). Early endoscopy (12–24 h) was performed in patients aged > 65 years and younger patients 53 (20.4%) vs. 41 (19.7%), respectively, while late endoscopy (24–48 h) was performed in 27 (10.4%) vs. 17 (8.2%) patients, respectively ($p > 0.05$, for all parameters). The clinical results of subgroups based on endoscopy time in the ≥ 65 population and comparisons between groups. When groups were compared, it was found that the very early endoscopy group had a considerably lower likelihood of need for surgical/radiological intervention than the late endoscopy group [3 (1,7) vs. (3,7), $p = 0.016$], and 30-day mortality rates by the endoscopy timing were statistically significantly different in the very early group (15.6%), early endoscopy group (7.5%), and late endoscopy group (29.6%) ($p < 0.05$, for all groups). Endoscopy time within 24–48 h (late) (OR: 3.133, 95%CI: 1.127–8.713, p: 0.029) was an independent predictor of rebleeding during the hospital stay.

Conclusions Early endoscopy may benefit the management of acute UGIB, especially in the elderly population with high comorbidities and the severity of bleeding.

Highlights

- UGIB is a significant clinical concern in older persons, who have higher rates of hospitalized adverse events and death than young patients.

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- Because mortality tends to be higher in older patients with UGIB, determining the best endoscopic time becomes even more difficult.
- Close monitoring, risk stratification, and good endoscopic and medical treatment are important approaches for decreasing poor clinical outcomes in the elderly with UGIB.
- Very early endoscopy group over the age of 65 is associated with less surgical/radiological intervention and lower 30-day mortality.
- The establishment of a health assessment strategy for older patients presenting with acute UGIB should be advantageous, considering the rise in comorbidities associated with aging concomitant medications, and various chronic diseases that have contributed to morbidity and death.
- Early endoscopy may be beneficial in the therapy of acute UGIB, particularly in the elderly with significant comorbidities and severe bleeding.

Keywords Upper gastrointestinal bleeding, Early endoscopy, Elderly patient, 30-day mortality

Introduction

Acute upper gastrointestinal bleeding (UGIB) is among the top causes of morbidity and mortality [1, 2]. Endoscopy is commonly suggested for patients with UGIB not only for diagnosis but endoscopic treatment in active bleeding lesions also [3, 4]. The European Society of Gastrointestinal Endoscopy (ESGE) recommends performing UGIB endoscopy during the first 24 h of presentation to identify the origin of the bleeding, risk-stratify patients, and suggest viable endoscopic therapies [5].

UGIB is a major clinical concern in older adults, who have higher rates of in-hospital adverse events and mortality than those who are younger, regardless of improvements in endoscopic hemostasis and diagnostic and treatment options [6, 7]. Factors including the patient's characteristics, the cause of the bleeding, and the timing of therapy all have a significant impact on the mortality and morbidity outcomes linked to UGIB. It is estimated that 35–45% of UGIB presentations include individuals over the age of 60 [8, 9]. This population is more vulnerable to UGIB complications, most likely owing to a higher proportion of concomitant diseases and the widespread use of nonsteroidal anti-inflammatory drugs (NSAIDs) or antiplatelet agents [10, 11].

Despite effective endoscopic hemostasis reduces mortality and hospital stay, early endoscopy is associated with numerous consequences (aspiration pneumonia, acute coronary syndrome, etc.) [12, 13]. Optimal endoscopy timing becomes even more complicated when taking into account the higher probability of mortality in the elderly presenting with UGIB.

The current study aimed to evaluate the optimal endoscopy time in elderly patients based on clinical outcomes.

Materials and methods

Study population and data collection

This study includes patients with nonvariceal upper gastrointestinal bleeding (NVUGIB) who were hospitalized in the emergency department of a tertiary referral center between January 2019 and April 2020. The analysis excluded patients under 18, patients with missing data, individuals who refused endoscopy, and those who could not undergo endoscopy due to poor clinical status. Based on the endoscopy timing, patients with acute UGIB are categorized into three patient groups: very early endoscopy (<12 h), early endoscopy (12–24 h), and late endoscopy (>24 h). The institutional review board approved this study (E1/22/2951).

Prospectively, information was obtained about the hemodynamic state, previous medical history, laboratory and endoscopic findings, and symptoms associated with bleeding. The hospital's electronic medical records system was used to document hospitalization, blood transfusions, endoscopic procedures, interventional radiology or surgery, rebleeding, and 30-day mortality. At admission, the AIMS65 score, the Clinical Rockall Score (CCRS), and the Glasgow Blatchford Score (GBS) were evaluated. Following endoscopy, the Complete Rockall Score (CRS) was obtained. In the first and fourth weeks, they were evaluated during an outpatient clinic scheduled when hospitalization was not required.

Patient management and clinical endpoints

All patients presenting with NVUGIB received an immediate 8 mg/h proton pump inhibitor infusion after an 80 mg bolus. The standard approach for fluid resuscitation was 3–5 ml/kg/hour infusion following a 10 ml/kg bolus saline infusion, in cases of hypotension bolus dose 20 ml/kg. Based on blood pressure and urine output, the infusion rate was titrated. The goal mean arterial pressure was >65 mmHg and urine output were >0.5 ml/kg/hour. Regarding the patient's comorbidities, aggressive fluid resuscitation was avoided in normotensive individuals to prevent volume overload. Erythrocyte suspension transfusion was administered to increase the target hemoglobin level to >9 g/dl in patients over 65 years, with chronic lung disease or coronary artery disease; in younger patients, the target hemoglobin level was 7–9 g/dl. During the first twelve hours, endoscopic intervention was performed on patients who continued bleeding, had an

unstable hemodynamic state, or had a lower hematocrit even after transfusion. Within the first 12 to 48 h, patients who were clinically stable and had not experienced severe bleeding underwent an endoscopy. Each patient's time of ES admission and the beginning of the endoscopic examination were recorded, and the gap between them was called the "time to endoscopy." In endoscopic treatment, the endoscopist applied depending on the characteristics of the lesion either thermal contact or mechanical techniques combined with adrenaline injection. Adrenaline injection alone was not evaluated as an endoscopic treatment. Once an upper gastrointestinal endoscopic examination failed to detect a lesion, a colonoscopy was performed. For individuals whose colonoscopy identified no bleeding lesions or evidence of ongoing bleeding, no further procedure was carried out. An attempt was made to identify the bleeding focus in individuals with bleeding continued or rebleeding by computed CT angiography. In patients whose bleeding focus could not be detected, angiography by interventional radiology or double balloon enteroscopy was performed. Severe bleeding that did not respond to endoscopic therapy was referred for surgical or interventional radiology. CT angiography was performed on all patients who could not be stabilized despite intense resuscitation. Interventional radiologists performed coil embolization regardless of bleeding rate when extravasation was identified. Endoscopy was performed at the ICU bedside when extravasation failed to be detected. Once endoscopic therapy and coil embolization failed, surgery was the only option. All patients were followed up outpatient clinic visits in the second week and the first month after hospitalization. Study data were obtained following hospitalization by telephone visits or by scanning the national electronic registration system for patients who missed outpatient clinic visits.

The following clinical endpoints were investigated: The primary endpoint was 30-day mortality, with the need for endoscopic intervention, rebleeding, and length of hospital stay considered as secondary endpoints. The term was determined very early endoscopy, within the first 12 h, considering that a 12-hour period would be more appropriate to ensure hemodynamic stabilization of the patient, fix the clot, and reduce the risk of aspiration before endoscopy, especially in elderly patients. Chronic lung disease refers to chronic obstructive pulmonary disease or interstitial lung disease. Coronary heart disease was defined as >70% stenosis in coronary arteries on conventional angiography or CT angiography, and congestive heart failure, New York Heart Association functional heart failure class II-III-IV. Severe bleeding was defined as hemodynamic instability (mean arterial pressure<65 mmHg and pulse rate>100 beats/min) despite adequate fluid resuscitation and evidence of ongoing bleeding (hematemesis or a decrease in hematocrit despite blood transfusion). Rebleeding was determined by a second-look endoscopy to be defined as a hemoglobin loss higher than 2.0 g/dL along with bleeding symptoms. A second-look endoscopy was performed as soon as hemodynamic stability was achieved following rebleeding. Any death that occurred within 30 days after the bleeding incidence was considered mortality.

Statistical analysis

Data was evaluated by IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, New York, USA). We applied the Kolmogorov-Smirnov test to figure out the normality of the distribution of continuous variables. Continuous variables with usual distributions were given as mean ± standard deviation, while non-normally distributed variables were presented as median (interquartile range). Grouping variables were presented as occurrences and percentages. Between the two groups with constant data, the Student's t-test was used for variables with a typical distribution and the Mann-Whitney U test for abnormally distributed variables. The Chi-Square test or Fisher's Exact test was employed to compare variable categories across two-group comparisons, as applicable. For comparisons of clinical outcomes in more than two groups, the Kruskal-Wallis test or the Chi-Square test was applied. The significance level of the *P* value was set as <0,05. Considering the impact that age≥75 years has on mortality risk, with a mortality rate of 8.9% [14], taking the effect size as 0.189 of absolute difference, $\alpha = 0.05$, and power $(1-\beta) = 0.80$, the total study population was determined as 464 patients at a 95% confidence level with a G power program. Multiple variate logistic regression analysis that included clinically relevant variables were performed to identify independent predictors of secondary outcomes (endoscopic, surgical, or radiological interventions and rebleeding). Results were expressed as Odds ratio (OR), 95% confidence interval (CI), and *p*-value. For determining independent predictors for 30-day mortality, a multiple variate Cox regression analysis was done that included statistically significantly differed variables in subgroups (Aged<65 years and Aged≥65 years) comparisons. Results were given as Hazard ratio (HR), 95% CI, and *p*-value.

Results

While 208 (44.4%) of the study population was under 65 years of age, 260 (55.6%) was over 65 years of age. Male patients in the <65years population had a rate of 77.4% (161), compared to 59.2% (154) in the ≥65 years population, which was statistically significant ($p<0.001$). The most common symptom in the entire study group and subgroups was melena (68.2%), followed by hematemesis (50.9%). Hypertension (HT) (44.4%) was the most common comorbidity across all research groups and

subgroups, followed by coronary heart disease (CHD) (34.4%). Those over 65 had significantly higher rates of chronic heart failure (CHF), arrhythmia, CHD, chronic kidney failure (CKD), cerebrovascular disease (CVD), HT, and diabetes mellitus (DM) ($p<0.001$, for all parameters). The ≥65 years population had a considerably higher rate of malignancy than the <65 years population [(39 (15) vs. 17 (8,2), $p=0.024$)]. Proton pumps inhibitor (PPI) (31.9% vs. 13.9%), antiplatelet (38.8% vs. 18.8%), and anticoagulant (22.3% vs. 6.7%) use was considerably higher in the ≥65 age group ($p<0.001$, for all parameters). The ≥65 age group used fewer nonsteroidal anti-inflammatory drugs (NSAIDs) (11.2%, $n=29$ vs. 21.2%, $n=44$, $p=0.003$). Table 1 shows the characteristic features, clinical and laboratory data of the entire study group and subgroups based on age.

While hemoglobin [9,34±2,71 vs. 10,67±3] and serum albumin [35 (31–38) vs. 38,5 (34–43)] concentrations upon admission were statistically substantially lower, urea [92 (56–141) vs. 55 (36–81)] and INR [1,19 (1,08−1,36) vs. 1,09 (1,02−1,17)] values were higher in aged patients ($p<0.001$ for all parameters). GBS, AIMS65 score, CCRS, and CRS were much higher in the older than 65 population ($p<0.001$, for all parameters). The ≥65 population had a considerably higher rate of high-risk individuals ($p<0.001$, for all criteria), as assessed by scores (Table 1).

The ≥65 age group experienced considerably longer hospital stays (5 (0–11) vs. 3 (0–6), $p<0.001$). The 30-day mortality rate was substantially higher in the ≥65 age group than in the younger (15.4%, $n=40$ vs. 4.8%, $n=10$, $p<0.001$). Further clinical outcomes showed no statistically substantial variations among the groups ($p>0.05$ for all parameters) (Table 2).

The most common endoscopic finding was duodenal ulcer (34%), followed by gastric ulcer (16.5%). Duodenal ulcer was seen in 30% (78) patients in the ≥65 age group, while it was seen in 38.9% (81) patients in the <65 years population ($p=0.042$). Angioectasia was statistically significantly more common in the ≥65 years population [15 (5,8) vs. 2 (1), $p=0.006$]. Further endoscopic results revealed no considerable variations among the groups ($p>0.05$ for all parameters) (Table 3).

Among patients>65 years, 180 (69.2%) underwent endoscopy within the first 12 h, 53 (20.4%) within 12–24 h and 27 (10.4%) within 24–48 h. When analyzed between subgroups based on endoscopy timing and age the mortality rate within 30 days was higher in the ≥65 years population (15.6% vs. 5.3%, $p=0.003$) in very early endoscopy group, and (29.6% vs. 0%, $p=0.016$) (Table 4).

The clinical results of subgroups based on endoscopy time in the ≥65 population and comparisons between groups. When groups were compared, it was found that the very early endoscopy group had a considerably lower likelihood of need for surgical/radiological intervention than the late endoscopy group [3 (1,7) vs. (3,7), $p=0.016$]. In patients>65 years old, 30-day mortality rates by the endoscopy timing were statistically significantly different in the very early group (15.6%), early endoscopy group (7.5%), and late endoscopy group (29.6%) ($p=0.035$). The remaining intergroups showed no statistically significant differences ($p>0.05$, for all parameters) (Table 5).

12–24 h endoscopy timing was an independent predictor for endoscopic, surgical, or radiological intervention (OR: 0.551, 95%Cl: 0.312–0.976, p: 0.041). Previous history of UGIB bleeding (OR: 0.227, 95%Cl: 0.105–0.489, p: <0.001), serum albumin value (OR: 0.921, 95%Cl: 0.860–0.986, p: 0.019), 24–48 h (late) endoscopy time (OR: 3.133, 95%Cl: 1.127–8.713, p: 0.029) were independent predictors for rebleeding during hospital stay. Univariate and multivariate Cox regression analysis showed that chronic renal failure (HR: 2.474, 95% Cl:1.040–5.887, p:0.041), hemoglobin level (HR: 1.327, 95% Cl:1.100-1.603, p:0.003), serum albumin level (HR: 0.870, 95% Cl:0.813–0.931, p:<0.001), and Complete Rockall score (HR: 1.520, 95% Cl:1.121–2.060, p:0.007) were found to be independent predictors for 30-day mortality. It was determined that patients over 65 had no significant impact on the 30-day mortality predictions (HR: 1.041, 95% CI: 0.355–3.055, p: 0.942) (Table 6). Clinical Rockall was not an independent risk factor for 30-day mortality, while the Complete Rockall score (HR: 1.520, 95% Cl:1.121–2.060, p:0.007) was.

Discussion

Acute UGIB poses a significant threat to older adults, with patients aged over 60 accounting for 35–45% of acute UGIB cases. UGIB remains a major clinical concern in older persons, who have higher rates of in-hospital adverse events and mortality compared to those who are younger. Designing an assessment approach for older individuals suffering from acute UGIB should be advantageous, considering the rise in comorbidities associated with age, concomitant medications, and distinct age-related illnesses that raise the risk of morbidity and mortality [15–17]. Though endoscopy should be undertaken within 24 h of presentation to the emergency room at Acute UGIB, there is no age-based recommendation. This study is the first in the literature to compare the timing of endoscopy in older and younger patients presenting with UGIB.

In this study, the clinical outcomes were compared based on endoscopy time. In the ≥65 population, the need for surgical or radiological intervention was statistically less in the very early endoscopy group than in the late endoscopy group. The 30-day mortality rate was considerably higher in the late-endoscopy group versus the early-endoscopy group. The ≥65 population

Table 1 Patient characteristics, clinical and laboratory data of the study group and subgroups by age x

	Study group (*n* = 468)	Aged < 65 years (*n* = 208)	Aged ≥ 65 years (*n* = 260)	*P*
Age, years	67 (51–78,75)	49 (38–58)	77 (70,25–84)	**< 0,001**
Gender, male, n (%)	315 (67,3)	161 (77,4)	154 (59,2)	**< 0,001**
Presenting symptoms, n (%)	238 (50,9)	112 (53,8)	126 (48,5)	0,247
Hematemesis	319 (68,2)	139 (66,8)	180 (69,2)	0,579
Melena	39 (8,3)	17 (8,2)	22 (8,5)	0,911
Hematochezia	41 (8,8)	17 (8,2)	24 (9,2)	0,688
Syncope				
Comorbidities, n (%)	53 (11,3)	6 (2,9)	47 (18,1)	**< 0,001**
CHF	84 (17,9)	11 (5,3)	73 (28,1)	**< 0,001**
Arrhythmia	161 (34,4)	28 (13,5)	133 (51,2)	**< 0,001**
CHD	51 (10,9)	10 (4,8)	41 (15,8)	**< 0,001**
CRF	38 (8,1)	10 (4,8)	28 (10,8)	**< 0,001**
CVD	10 (2,1)	6 (2,9)	4 (1,5)	0,351
CLD	208 (44,4)	48 (23,1)	160 (61,5)	**< 0,001**
HT	98 (20,9)	27 (13)	71 (27,3)	**< 0,001**
DM	56 (12)	17 (8,2)	39 (15)	**0,024**
Malignancy				
PPI usage, n (%)	112 (23,9)	29 (13,9)	83 (31,9)	**< 0,001**
Previous history of UGIB, n (%)	99 (21,2)	42 (20,2)	57 (21,9)	0,649
Previous history of GIS surgery, n (%)	16 (3,4)	11 (5,3)	5 (1,9)	**0,046**
Medication, n (%)	73 (15,6)	44 (21,2)	29 (11,2)	**0,003**
NSAIDs	138 (29,5)	37 (17,8)	101 (38,8)	**< 0,001**
Antiaggregants	125 (26,7)	32 (15,4)	93 (35,8)	**< 0,001**
ASA	13 (2,8)	5 (2,4)	8 (3,1)	0,660
DAPT	72 (15,4)	14 (6,7)	58 (22,3)	**< 0,001**
Anticoagulants	41 (8,8)	14 (6,7)	27 (10,4)	0,165
Warfarin	31 (6,6)	-	31 (11,9)	**< 0,001**
DOACs				
Pulse, > 100 beats/min, n (%)	198 (43,2)	82 (39,4)	116 (44,6)	0,259
Systolic blood pressure, < 90 mmHg, n (%)	34 (7,3)	10 (4,8)	24 (9,2)	0,067
Hgb level on admission (g/dL)	9,93 ± 2,92	10,67 ± 3	9,34 ± 2,71	**< 0,001**
Urea level on admission (mg/dL)	71 (47–113)	55 (36–81)	92 (56–141)	**< 0,001**
INR on admission	1,13 (1,05 – 1,27)	1,09 (1,02 – 1,17)	1,19 (1,08 – 1,36)	**< 0,001**
Serum albumin level on admission (g/L)	36 (32–40)	38,5 (34–43)	35 (31–38)	**< 0,001**
Serum platelet level on admission (10^9/L)	253,5 (201,25–332,75)	246 (204,25–315,5)	263,5 (196–349,5)	0,226
Endoscopy time, n (%)	330 (70,5)	150 (72,1)	180 (69,2)	0,683
< 12 h	94 (20,1)	41 (19,7)	53 (20,4)	0,496
12–24 h	44 (9,4)	17 (8,2)	27 (10,4)	0,857
24–48 h				0,415
GBS	9 (6–12)	7 (5–10)	11 (8–13)	**< 0,001**
≤ 1*, n (%)	26 (5,6)	21 (10,1)	5 (1,9)	**< 0,001**
≥ 7**, n (%)	336 (71,8)	124 (59,6)	212 (81,5)	**< 0,001**
AIMS65 score	1 (0–2)	0 (0–0)	1 (1–2)	**< 0,001**
= 0*, n (%)	181 (38,7)	175 (84,1)	6 (2,3)	**< 0,001**
≥ 2**, n (%)	136 (29,1)	12 (5,8)	124 (47,7)	**< 0,001**
CCRS	3 (1–4)	1 (0–3)	4 (3–5)	**< 0,001**
= 0*, n (%)	83 (17,7)	83 (39,9)	-	**< 0,001**
≥ 3**, n (%)	292 (62,4)	60 (28,8)	232 (89,2)	**< 0,001**
CRS	5 (3–6)	3 (1–5)	6 (4–7)	**< 0,001**
≤ 2*, n (%)	83 (17,7)	75 (36,1)	8 (3,1)	**< 0,001**
≥ 8**, n (%)	50 (10,7)	4 (1,9)	46 (17,7)	**< 0,001**

[x] Results are expressed as: mean ± standard deviation, median (interquartile range), or frequency (%)

*: Patients classified as low risk

**: Patients classified as high risk

Significant *P* values are in bold

CHF: Congestive heart failure, CHD: Coronary heart disease, CRF: Chronic renal failure, CVD: Cerebrovascular disease, CLD: Chronic liver disease, HT: Hypertension, DM: Diabetes mellitus, PPI: Proton pump inhibitors, UGIB: Upper gastrointestinal bleeding, GIS: Gastrointestinal system, NSAIDs: Non-steroidal anti-inflammatory drugs, ASA: Acetylsalicylic acid, DAPT: Dual antiplatelet therapy, DOACs: Direct oral anticoagulants, Hgb: Hemoglobin, INR: International normalized ratio, GBS: Glasgow-Blatchford score, CCRS: Clinical Rockall score, CRS: Complete Rockall score

Table 2 Results and comparisons of clinical outcomesx

	Study group (*n* = 468)	Aged < 65 years (*n* = 208)	Aged ≥ 65 years (*n* = 260)	*P*
Length of hospital stay, days	4 (0–8)	3 (0–6)	5 (0–11)	**< 0,001**
Need for endoscopic hemostasis, n (%)	137 (29,3)	58 (27,9)	79 (30,4)	0,555
Need for surgical/radiological intervention, n (%)	2 (0,4)	1 (0,5)	1 (0,4)	0,082
Radiological intervention	6 (1,3)	-	6 (2,3)	1
Surgical intervention				**0,036**
Rebleeding, during hospital stay, n (%)	36 (7,7)	11 (5,3)	25 (9,6)	0,081
30-day mortality, n (%)	50 (10,7)	10 (4,8)	40 (15,4)	**< 0,001**

[x] Results are expressed as: median (interquartile range), or frequency (%)

Significant *P* values are in bold

Table 3 Results and comparisons of endoscopic findingsx

	Study group (*n* = 468)	Aged < 65 years (*n* = 208)	Aged ≥ 65 years (*n* = 260)	*P*
Lesion not visualized, n (%)	20 (4,3)	9 (4,3)	11(4,2)	0,959
Gastric ulcer, n (%)	77 (16,5)	27 (13)	50 (19,2)	0,070
Duodenal ulcer, n (%)	159 (34)	81 (38,9)	78 (30)	**0,042**
Upper GIS malignancy, n (%)	42 (9)	19 (9,1)	23 (8,8)	0,914
Mallory-Weiss syndrome, n (%)	16 (3,4)	7 (3,4)	9 (3,5)	0,955
Erosive gastritis, n (%)	53 (11,3)	21 (10,1)	32 (12,3)	0,453
Erosive duodenitis, n (%)	20 (4,3)	7 (3,4)	13 (5)	0,385
Erosive esophagitis, n (%)	17 (3,6)	8 (3,8)	9 (3,5)	0,825
Esophageal ulcer, n (%)	28 (6)	14 (6,7)	14 (5,4)	0,542
Angioectasia, n (%)	17 (3,6)	2 (1)	15 (5,8)	**0,006**
Cameroon lesion, n (%)	5 (1,1)	4 (1,9)	1 (0,4)	0,176
Dieulafoy lesion, n (%)	5 (1,1)	3 (1,4)	2 (0,8)	0,660
Anastomotic ulcer, n (%)	9 (1,9)	6 (2,9)	3 (1,2)	0,195

[x] Results are expressed as: frequency (%)

Significant *P* values are in bold

GIS: Gastrointestinal system

Table 4 Comparisons of clinical outcomes based on endoscopy timex

	Very early (< 12 h)			Early (12–24 h)			Late (> 24 h)		
	< 65 years (*n* = 150)	≥ 65 years (*n* = 180)	*P*	< 65 years (*n* = 41)	≥ 65 years (*n* = 53)	*P*	< 65 years (*n* = 17)	≥ 65 years (*n* = 27)	*P*
Length of hospital stay, days	6 (3–9)	10 (4–20,7)	**0,001**	3 (0–7)	6 (3–12)	**0,031**	7 (3,5–9)	6 (3–13)	0,680
30-day mortality, n (%)	8 (5,3)	28 (15,6)	**0,003**	2 (4,9)	4 (7,5)	0,693	-	8 (29,6)	**0,016**

[x] Results are expressed as: median (interquartile range) or frequency (%)

Significant *P* values are in bold

Table 5 Comparisons of clinical outcomes based on endoscopy time in patients aged ≥ 65 yearsx

	Very early (< 12 h) (*n* = 180)	Early (12–24 h) (*n* = 53)	Late (> 24 h) (*n* = 27)	*P*
Length of hospital stay, days	10 (4–20,7)	6 (3–12)	6 (3–13)	0,197
Need for endoscopic hemostasis, n (%)	61 (33,9)	13 (24,5)	5 (18,5)	0,157
Need for surgical /radiological intervention, n (%)	3 (1,7) *	3 (5,7)	1 (3,7) *	**0,016**
Rebleeding, during hospital stay, n (%)	15 (8,3)	4 (7,5)	6 (22,2)	0,063
30-day mortality, n (%)	28 (15,6)	4 (7,5) *	8 (29,6) *	**0,035**

[x] Results are expressed as: median (interquartile range) or frequency (%)

[*] Groups that significantly differed in subgroup analysis

Significant *P* values are in bold

Table 6 Multiple variate Cox regression analysis of predictors for 30-day mortality

	95% CI			
	HR	**Lower**	**Upper**	***P***
Age, ≥ 65 years	1.041	0.355	3.055	0.942
Gender, male	1.686	0.858	3.314	0.130
CHF, yes	0.915	0.361	2.318	0.852
Arrhythmia, yes	0.886	0.340	2.310	0.805
CHD, yes	1.142	0.555	2.347	0.719
CRF, yes	2.474	1.040	5.887	**0.041**
CVD, yes	0.834	0.285	2.436	0.740
HT, yes	0.953	0.455	1.995	0.898
Malignancy, yes	2.186	0.978	4.886	0.057
PPI usage, yes	1.397	0.692	2.821	0.350
Previous history of UGIB, yes	1.537	0.291	8.118	0.613
NSAIDs usage, yes	0.891	0.335	2.370	0.818
ASA usage, yes	1.632	0.724	3.681	0.238
DOACs usage, yes	0.554	0.162	1.889	0.345
Hgb level	1.327	1.100	1.603	**0.003**
Urea level	0.996	0.989	1.002	0.176
INR	0.903	0.717	1.138	0.387
Serum Albumin level	0.870	0.813	0.931	**< 0.001**
GBS	1.165	0.998	1.359	0.053
AIMS65 score	1.396	0.897	2.170	0.139
CCRS	0.648	0.426	0.985	**0.042**
CRS	1.520	1.121	2.060	**0.007**

Significant *P* values are in bold

HR: Hazard ratio, CI: Confidence interval, CHF: Congestive heart failure, CHD: Coronary heart disease, CRF: Chronic renal failure, CVD: Cerebrovascular disease, HT: Hypertension, DM: Diabetes mellitus, PPI: Proton pump inhibitors, UGIS: Upper Gastrointestinal system, NSAIDs: Non-steroidal anti-inflammatory drugs, ASA: Acetylsalicylic acid, DOACs: Direct oral anticoagulants, Hgb: Hemoglobin, INR: International normalized ratio, GBS: Glasgow-Blatchford score, CCRS: Clinical Rockall score, CRS: Complete Rockall score

had considerably higher rates of comorbidity, PPI, and antithrombotic usage compared with other groups. At admission, hemoglobin and serum albumin values were statistically significantly lower, and urea and INR values were higher in elderly patients. Furthermore, risk scoring systems involving GBS, AIMS65, CCRS, and CRS were statistically substantially higher in the ≥65 population ($p<0.001$, for each parameter). Based on the thresholds used in each risk score system, high-risk patients were statistically more likely to be elderly. Those over 65 had significantly longer hospitalizations and a higher 30-day mortality. GBS is widely used to predict the need for endoscopy in patients presenting with UGIB. GBS is recommended by the European Society of Gastrointestinal Endoscopy [5], especially for identifying low-risk patients. When the score is ≤1, the need for endoscopy is quite low and outpatient follow-up can be recommended. In the current study, only 26 (5.6%) patients had a GBS score of 0 or 1, statistically less in the elderly. GBS≥7 is used as a basis for predicting high-risk patients. In the current analysis, the number of patients with high scores in the elderly was statistically higher than in the younger.

The incidence of UGIB was reported to be significantly higher at 425.2 per 100,000 in the population over 75 compared with 31.7 per 100,000≤65 years of age [18]. UGIB, whose incidence and mortality increases as people get older, is an issue of concern and difficulty for physicians. Previous studies have reported NVUGIB mortality as 5% in all age groups while the mortality rate in patients aged≥75 years increased to 15% [7, 14, 19]. In the present study, the 30-day mortality rate was 4.8% in patients under 65 to 15.4%, and as high as 15.4% in older than 65 years. In the current study, multivariate analysis showed that age over 65 was not an independent predictor of 30-day mortality (HR: 1.041, 95% CI: 0.355–3.055, p: 0.942). The fact that patients over 65 have a mortality rate that is significantly higher than younger patients may seem paradoxical, however, independent risk factors including comorbidities and decreased serum albumin and hemoglobin level in patients over 65 years may have contributed to a high mortality rate. Comprehensive surveillance, risk assessment, and successful endoscopic and medical treatment are important measures for decreasing bad clinical outcomes in older individuals who suffer from UGIB [10, 20].

Considering the increased acute UGIB mortality rates in the elderly patient group, the optimal endoscopy time is even more important in this patient group. Previous studies suggest the benefits of early endoscopy [21, 22]. Cooper et al. [23] carried out early endoscopy (endoscopy within 24 h) in the majority of 909 patients. Endoscopy within 24 h was linked to lower rebleeding, surgery, and hospitalization rates. Brennan Spiegel more clearly claimed that it was time for 24-hour endoscopy to become universal [24]. In line with the studies above, in studies based in Denmark and Korea, when endoscopy performed within 24 h was compared with endoscopy performed between 24 and 48 h, the early endoscopy group was associated with reduced mortality [25, 26]. Contrary to the very early endoscopy advocated above, many studies have revealed questionable results [13, 27–29]. Very early endoscopy correlates with a higher length of stay, and need for surgical/radiological interventions, especially in the high-risk patient group. Elderly individuals with acute UGIB may be classified as high-risk, and early endoscopy in this population might be linked with unfavorable clinical outcomes. In the current study, in the ≥65 age group, late endoscopy was associated with increased mortality, and was linked to an increased need for surgical/radiological intervention. Although there was no statistical difference, when the very early endoscopy and early endoscopy groups were compared, the mortality rates were higher in the very early group. Endoscopy during the first 12 h provided no advantage

over endoscopy performed between 12 and 24 h. In the very early endoscopy group, 6 patients experienced hypotension, 4 patients had hypoxia due to aspiration, and one patient had cardiac arrest during the procedure, while just 1 patient experienced hypoxia due to aspiration in the early endoscopy group. The 30-day mortality between very early and early endoscopy groups was [28 (15.6%) and 4 (7.5%), respectively, $p=0.035$]. This may be due to adverse events developing during the procedure. No statistically significant difference was found between subgroups regarding rebleeding in patients > 65 years and younger and also based on endoscopy timing in patients > 65 years. This may be due to an endoscopy nurse, two gastroenterologists (one senior), and an anesthetist being on duty out of working hours.

Although acute UGIB decreases in the elderly population, it is mostly self-limiting. Immediately starting high-dose PPI infusion (can stabilize clots and accelerate ulcer healing), saline infusion, and blood transfusion when necessary (can allow time to optimize patients' medical conditions) allow endoscopy to be performed under safer conditions [30, 31]. It was previously claimed to compare endoscopy < 12 h to endoscopy < 24 h. The rationale is to allow sufficient time for resuscitation and stabilization of medical conditions in of further hemorrhage and death. The optimal time may be endoscopy between 6 and 12 h [32]. For the above reasons, when determining the timing of endoscopy, we determined it as within 12 h after admission, 12–24 h, and afterward 24 h rather than the first 6 h. The first 12 h may be a safe time limit for hemodynamic stabilization, acid suppression, and reduction of endoscopic procedure-related complications (such as aspiration pneumonia and acute coronary syndrome). It may benefit the management of acute UGIB, especially in the elderly population with high comorbidities and the severity of bleeding.

The study's limitations comprise a single-center retrospective methodology and a possible tendency to a higher acceptance of patients at high risk, which could have altered the outcomes. In addition, Helicobacter Pylori (HP) status was not analyzed in all patients. Though the prevalence of drug-related hemorrhage rises with getting older, HP-associated peptic ulcer is still essential [33, 34]. Although we started PPI and fluid infusion as standard in all patients, we could not define the optimal fluid and blood transfusion protocol. The fact that the patients had different hemodynamics made it difficult to determine the standard optimal transfusion strategy patients with bleeding secondary to malignant lesions were also enrolled in this study which can affect the evaluation of the role of urgent endoscopy on the clinical outcomes since its high mortality rates. However, there was no difference in endoscopic findings between the groups. Patients presenting with severe bleeding, patients had endoscopies within the first 12 h. Endoscopy was scheduled as soon as possible after 12 h for patients whose hemodynamically were stable. As a result, there could be discrepancies in the results if the group that had an endoscopy within the first 12 h had worse outcomes. The study's strengths were a comparative design, skilled endoscopists performing endoscopy on all patients, and data collection by gastroenterologists.

Conclusion

An assessment approach based on age in acute UGIB may be advantageous given the increased risk of poor outcomes. Unlike very early or late endoscopic timing, early endoscopy (12–24 h) may benefit the management of acute UGIB, especially in the elderly with high comorbidities and bleeding severity.

Abbreviations

UGIB	Upper gastrointestinal bleeding
ESGE	European society of gastrointestinal endoscopy
NSAIDs	Nonsteroidal anti-inflammatory drugs
NVUGIB	Nonvariceal upper gastrointestinal bleeding
CCRS	Clinical rockall score
GBS	Glasgow blatchford score
CRS	Complete rockall score
ES	Erythrocyte suspension
OR	Odds ratio
CI	Confidence interval
HT	Hypertension
CHD	Coronary heart disease
CHF	Chronic heart failure
CKD	Chronic kidney failure
CVD	Cerebrovascular disease
DM	Diabetes mellitus
PPI	Proton pumps inhibitor
DOAC	Direct oral anticoagulant
HP	Helicobacter pylori

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Author contributions

YC: Investigation, data collection, writing-original draft preparation, reviewing and editing, visualization. MBD: Writing-original draft preparation, statistics, reviewing and editing. IY: Conceptualization, Methodology, Investigation, Supervision, writing- reviewing and editing.

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Data availability

Data is available from corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the ethical guidelines of the institutional research committee, the 1964 Declaration of Helsinki, and its subsequent amendments, or comparable ethical standards. The Ankara Bilkent City Hospital Scientific Research and Ethics Committee accepted the project with approval No: E1/22/2951. Informed consent statement was waived by the committee due to the retrospective design of the study.

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

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