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ORIGINAL ARTICLE

Acute Nonvariceal Upper Gastrointestinal Bleeding in Patients Using Anticoagulants: Does the Timing of Endoscopy Affect Outcomes?

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Abstract

Background In patients with acute nonvariceal upper gastrointestinal bleeding (NVUGIB), early (≤24 h) endoscopy is recommended following hemodynamic resuscitation. Nevertheless, scarce data exist on the optimal timing of endoscopy in patients with NVUGIB receiving anticoagulants.

Objective To analyze how the timing of endoscopy may influence outcomes in anticoagulants users admitted with NVUGIB.

Methods Retrospective cohort study which consecutively included all adult patients using anticoagulants presenting with NVUGIB between January 2011 and June 2020. Time from presentation to endoscopy was assessed and defined as early (≤24 h) and delayed (>24 h). The outcomes considered were endoscopic or surgical treatment, length of hospital stay, intermediate/intensive care unit admission, recurrent bleeding, and 30-day mortality.

Results From 636 patients presenting with NVUGIB, 138 (21.7%) were taking anticoagulants. Vitamin K antagonists were the most frequent anticoagulants used (63.8%, $n=88$). After adjusting for confounders, patients who underwent early endoscopy (59.4%, $n=82$) received endoscopic therapy more frequently (OR 2.4; 95% CI 1.1–5.4; $P=0.034$), had shorter length of hospital stay [7 (IQR 6) vs 9 (IQR 7) days, $P=0.042$] and higher rate of intermediate/intensive care unit admission (OR 2.7; 95% CI 1.3–5.9; $P=0.010$) than patients having delayed endoscopy. Surgical treatment, recurrent bleeding, and 30-day mortality did not differ significantly between groups.

Conclusion Early endoscopy (≤24 h) in anticoagulant users admitted with acute nonvariceal upper gastrointestinal bleeding is associated with higher rate of endoscopic treatment, shorter hospital stay, and higher intermediate/intensive care unit admission. The timing of endoscopy did not influence the need for surgical intervention, recurrent bleeding, and 30-day mortality.

Keywords Upper gastrointestinal bleeding · Timing of endoscopy · Anticoagulants

Introduction

Nonvariceal upper gastrointestinal bleeding (NVUGIB) is a well-known major healthcare problem with significant mortality and morbidity [1]. Nevertheless, its incidence and mortality have been decreasing in the last years, largely attributable to the widely use of proton pump inhibitors (PPI) and investigation and eradication of *Helicobacter pylori* infection, which changed the natural history of peptic ulcer disease (PUD), the most common cause of NVUGIB [2].

Anticoagulants are a well-recognized risk factor for upper gastrointestinal bleeding (UGIB), including direct oral anticoagulants (DOAC) and vitamin K antagonists (VKA) [3, 4]. The use of acid suppressants [PPI and histamine 2 receptor antagonists (H2RA)] significantly reduce the risk of UGIB

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in patients taking anticoagulants [5]. DOAC are currently the first-line option for the prevention of stroke and systemic embolism in non-valvular atrial fibrillation (AF) and for the treatment and secondary prevention of venous thromboembolism (VTE) [6, 7]. Although its use is associated with a significantly lower all-cause mortality and intracranial bleeding compared with VKA, the risk of major and clinically relevant non-major UGIB seems to be not different, irrespective of indication [8, 9].

Upper gastrointestinal endoscopy remains the modality of choice for identifying the etiology of UGIB and achieve therapeutic hemostasis. According to the recently developed European Society of Gastrointestinal Endoscopy (ESGE) guideline, following hemodynamic resuscitation, endoscopy should be performed within 24 h from the time of patient presentation because it is associated with better outcomes [10].

Patients taking anticoagulants who develop NVUGIB represent a clinical challenge since different pharmacokinetic and pharmacodynamic profiles of the anticoagulants must be considered, and this issue needs to be addressed both prior to and following endoscopy [11].

Nevertheless, few data exist specifically addressing the optimal timing of endoscopy in patients with NVUGIB receiving anticoagulants [10, 12]. Therefore, the objective of this study was to analyze if timing of endoscopy, in anticoagulants users admitted with NVUGIB, may influence outcomes, such as endoscopic or surgical treatment, length of hospital stay, intermediate/intensive care unit admission, recurrent bleeding, and 30-day mortality.

Material and Methods

Study Design

This was a retrospective cohort study that consecutively included all patients admitted to the Emergency Department (ED) for UGIB and underwent endoscopy in a University-Affiliated Hospital between January 2011 and June 2020. The present study was approved by the local Ethics Committee for Health.

Patient Selection and Hospital Management Protocol

All adult patients (≥ 18 years old) with suspicion of having UGIB at presentation and submitted to endoscopy were included, namely those who presented with hematemesis, melena, hematochezia with hemodynamic instability, or detection of hematic content in a nasogastric tube. In the situation that more than one UEG was performed during the same admission, only the findings of the index endoscopy were included. In addition, patients with one or more of the following items were excluded from the study: not receiving anticoagulants; gastrointestinal variceal bleeding source; documentation of a bleeding cause in the lower or mid gastrointestinal tract; UGIB in an inpatient setting; and ED presentation due to recurrent bleeding from a previous episode of acute UGIB.

Only NVUGIB patients, including those with a definite diagnosis (namely peptic ulcer disease, mucosal erosive disease of the esophagus/stomach, malignancy, Mallory–Weiss syndrome, Dieulafoy's lesion, angiodysplasias) or without an identifiable cause in endoscopy and taking anticoagulants were considered in the final sample. Patients were then divided into two groups according to the timing of endoscopy: the early endoscopy group (≤ 24 h after presentation) and the delayed endoscopy group (> 24 h after presentation).

According to the recommendations of our department and to the emergency department protocol of our hospital, all patients started intravenous PPI as soon as UGIB was suspected. Following endoscopy, patients with high-risk endoscopic stigmata according to Forrest classification continued on intravenous infusion of PPI for 72 h [13]. Moreover, Forrest IIb stigmata was treated with clot removal followed by endoscopic hemostasis if underlying high-risk stigmata was found [13]. Otherwise, patients received oral PPI, if needed, as indicated by endoscopic findings. Immediate assessment of hemodynamic status was performed with prompt intravascular volume replacement using crystalloid fluids if hemodynamic instability existed. In hemodynamically stable patients with NVUGIB and no history of cardiovascular disease, a restrictive red blood cell transfusion strategy with a hemoglobin threshold of ≤ 7 g/dL prompted red blood cell transfusion. A post-transfusion target hemoglobin concentration of 7–9 g/dL was considered. In patients with a history of acute or chronic cardiovascular disease, a more liberal red blood cell transfusion strategy was followed with a hemoglobin threshold of ≤ 8 g/dL leading to transfusion. A post-transfusion target hemoglobin concentration of ≥ 10 g/dL was considered. Intravenous erythromycin was administered before endoscopy in patients with clinically severe or ongoing active UGIB [10]. The antithrombotic management policy was carried out in accordance with the protocol of the hematology department of our hospital, ensuring that the patient was optimized for the endoscopy without unnecessarily delaying the procedure. In patients taking low-dose aspirin as monotherapy for primary cardiovascular prophylaxis, aspirin was temporarily interrupted and restarted after careful re-evaluation of its clinical indication. For patients taking low-dose aspirin as monotherapy for secondary cardiovascular prophylaxis, aspirin was not interrupted. Patients on dual antiplatelet therapy for secondary cardiovascular prophylaxis had aspirin uninterrupted, while the second antiplatelet agent was interrupted and

restarted within 5 days. Patients taking VKA or enoxaparin had these anticoagulants withheld. In patients with hemodynamic instability, low-dose vitamin K was supplemented with intravenous prothrombin complex concentrate (PCC) or fresh frozen plasma if PCC was not available. In patients taking DOAC, the anticoagulant was withheld. For patients with severe ongoing bleeding, the use of a DOAC reversal agent or intravenous PCC was considered.

Data Collection

Several data were retrospectively collected from electronic medical records.

On presentation, demographic data (age and sex), clinical presentation (hematemesis, melena, hematochezia), Glasgow Coma Scale (GCS) score, history of syncope, vital signs [heart rate (HR), systolic and diastolic blood pressure (SBP and DBP, respectively)], laboratory values [i.e., hemoglobin, platelets, creatinine, urea, albumin, and international normalized ratio (INR)], as well as comorbidities (namely, chronic liver disease (CLD), congestive heart failure (CHF), chronic kidney disease (CKD) and disseminated neoplasia] were retrieved. Data were also obtained regarding the use of certain drugs that could be related to bleeding, such as acetylsalicylic acid (ASA) and other antiplatelet agents, nonsteroidal anti-inflammatory drugs (NSAID), anticoagulants (including DOAC, VKA and enoxaparin), steroids, and selective serotonin reuptake inhibitors (SSRI), as well as could drugs that could decrease the probability of bleeding (PPI or H2RA). Date and time of presentation and endoscopy, endoscopic findings, namely etiology of bleeding and stigmata of recent bleeding (for PUD, Forrest classification), and length of hospital stay (days) were recorded [13]. Forrest Ia, Ib, and IIa were considered high-risk stigmata according to Forrest Classification [10].

Different clinical outcomes were analyzed, namely the need for endoscopic or surgical treatment, length of hospital stay, intermediate/intensive care unit admission, recurrent bleeding, and 30-day mortality. Surgery was performed in patients with persistent bleeding refractory to all modalities of endoscopic hemostasis.

Based on these data, many clinical and endoscopic-based scores were calculated for each patient, namely the pre- and the post-endoscopic Rockall score (RS), the Glasgow-Blatchford (GBS) score, and the AIMS65 [14].

Definition of Variables, Comorbidities, and Other Covariates

Timing of endoscopy was defined as the time elapsed between presentation in the ED and beginning of endoscopy. In patients with PUD as the source of NVUGIB, Forrest classification was assessed [13].

CLD was considered in patients with a known history, or clinical, laboratory, and imaging evidence of liver disease [15], while CHF was defined as a known history or clinical evidence and echocardiography of CHF [16]. CKD was defined in patients with an estimated glomerular filtration rate < 60 mL/min/1.73 m^2 for ≥ 3 months calculated using the Modification of Diet in Renal Disease Study equation [17]. Disseminated neoplasm was considered in patients with a malignant tumor in whom metastasis was identified. Therapeutic endoscopic intervention included one or more of the following hemostatic strategies: use of hemoclips, endoscopic elastic ligation, argon plasma coagulation, bipolar electrocoagulation, sclerotherapy, with or without a previous injection of adrenaline. Mortality was defined as death for any cause (overall mortality) occurring within 30 days of hospital admission. The need for surgery was defined as the necessity of undergoing laparotomy/laparoscopic intervention if persistent bleeding occurred, defined as ongoing active bleeding (spurting, arterial pulsatile bleeding, or oozing) that was present at the end of index endoscopy and refractory to standard hemostasis modalities [10]. Recurrent bleeding was defined as the observation of an overt bleeding event (hematemesis or melena) or a decrease of at least 2 g/dL in hemoglobin levels after initial treatment and stabilization [18]. Pre- and post-endoscopic RS, GBS, and AIMS65 scores were calculated according to their description in the original articles [14, 19, 20].

Statistical Analysis

Statistical Package for Social Sciences program version 26 (IBM Corporation, Armonk, NY) was used. A univariable analysis was performed to assess differences between the two groups (early and delayed endoscopy). Categorical variables were described using absolute frequencies and percentages. χ^2 Test or Fisher's exact test was used to compare categorical variables. Depending on the normality tests, continuous variables were expressed as mean $\pm$ standard deviation (SD) or median and interquartile range (IQR). Means were compared between the distinct groups using independent samples *t*-test. When applicable, non-parametric tests were performed. In addition, multivariable analysis using a logistic or linear regression analysis was performed to assess if timing of endoscopy had any influence on the outcomes that in univariable analysis were significantly different between early and delayed groups. Statistical significance was defined as $P < 0.05$.

Results

From a total of 759 patients admitted for UGIB and submitted to endoscopy, 123 had UGIB secondary to bleeding varices and 636 patients had NVUGIB. Among patients with

NVUGIB, 138 (21.7%) were taking anticoagulants. Vitamin K antagonists ($n=88$, 63.8%) were the most frequently used anticoagulants, followed by enoxaparin ($n=27$, 19.6%) and DOAC ($n=23$, 16.7%).

In patients on anticoagulants, the overall mean time to endoscopy was 23.8 ± 19.3 h. Eighty-two (59.4%) patients were submitted to early endoscopy (median time to endoscopy: 9.0 [IQR 11] h) and 56 patients (40.6%) to delayed endoscopy (median time to endoscopy: 44.0 [IQR 27] h).

Table 1 presents the demographic and clinical characteristics of both study groups.

Outcomes

Table 2 displays the outcome variables according to the time from presentation to endoscopy. Of the outcomes considered, only endoscopic treatment [31 (37.8%) vs. 11 (19.6%), $P=0.025$] and intermediate/intensive care unit admission [42 (51.2%) vs. 15 (26.7%), $P=0.005$] were significantly different between early and delayed groups, respectively.

After adjusting for confounders, on multivariable analysis, the timing of endoscopy (early/delayed) was still identified as an independent predictive factor for endoscopic treatment, length of hospital stay, and intermediate/intensive care unit admission. Patients who underwent early endoscopy received endoscopic therapy more frequently (OR 2.4; 95% CI 1.1–5.4; $P=0.034$), had shorter length of hospital stay [7 (IQR 6) vs. 9 (IQR 7) days, $P=0.042$] and higher rate of intermediate/intensive care unit admission (OR 2.7; 95% CI 1.3–5.9; $P=0.01$] than patients having delayed endoscopy (Tables 3, 4, 5). In addition, the GCS at admission was found to be an independent predictive factor for intermediate/intensive care unit admission. Patients with lower GCS score at presentation were more likely to be admitted to the intermediate/intensive care unit (OR 0.6; 95% CI 0.37–0.96; $P=0.032$).

Discussion

To the best of our knowledge, this is the first study to specifically investigate the relationship between the timing of endoscopy in patients with NVUGIB receiving anticoagulants and critical clinical outcomes. We found that patients on anticoagulants who underwent early (≤ 24 h) endoscopy, had a higher rate of endoscopic treatment, shorter length of hospital stay, and higher intermediate/intensive care unit admission. However, other outcomes, such as the need for surgical intervention, recurrent bleeding, and 30-day mortality, did not significantly differ between the two groups.

The optimal timing to perform endoscopy in patients with NVUGIB has been a subject of intense debate and the focus of many studies. In 2021, the ESGE guideline addressing the management of NVUGIB patients recommended that, following hemodynamic resuscitation, early (≤ 24 h from the time of patient presentation) endoscopy should be performed (strong recommendation, high-quality evidence), being associated with lower in-hospital mortality, shorter length of stay, and lower total hospital costs. In addition, performing urgent endoscopy (≤ 12 h) is not recommended because, when compared to early endoscopy, patient outcomes are not consistently improved [10]. While some studies concluded that urgent endoscopy was an independent predictor of lower mortality in high-risk patients [21, 22], others have shown that urgent endoscopy was a predictor of worse patient outcomes [23, 24], or that clinical outcomes were not significantly different between urgent and early endoscopy [25, 26]. On the other hand, the American College of Gastroenterology guideline, also published in 2021, is more conservative in their recommendations, only "suggesting" that patients admitted in hospital for NVUGIB should undergo endoscopy within 24 h of presentation, being stated as a conditional recommendation supported with very low-quality evidence [27].

Unfortunately, this controversy becomes more evident regarding the optimal timing of endoscopy in anticoagulant users admitted with NVUGIB [10, 12].

No systematic reviews, randomized trials, or observational studies specifically addressing the impact of the timing of endoscopy on clinically relevant outcomes in patients receiving anticoagulants have been published [10, 12]. This is particularly relevant because, although the overall incidence of NVUGIB has decreased in recent years and is stabilizing globally, some risk factors for gastrointestinal bleeding are becoming more common. These factors include the aging of the population, resulting in an increasing prevalence of cardiovascular diseases, and the progressive broadening of indications for anticoagulants use in the clinical practice [11, 28]. In addition, it is known that the use of anticoagulants in patients for NVUGIB is associated with increased admitted second-look endoscopy and recurrent bleeding rates compared to patients who were not using anticoagulants [29]. Therefore, optimizing the management of these patients is of paramount importance.

In our study, we found that a significant proportion (21.7%) of the patients admitted for UGIB and submitted to endoscopy were taking anticoagulants. Interestingly, Vitamin K antagonists were the most commonly used anticoagulants (63.8%), followed by enoxaparin (19.6%), and DOAC (16.7%). Although DOACs have been increasingly prescribed worldwide in recent years, they were not the most used anticoagulants in our sample. This might be due to a substantial proportion of the patients experiencing the bleeding event in the first half of the 2010s, reflecting the clinical practice at that time.

Table 1 Baseline demographic, clinical, laboratory, and endoscopic findings according to the time from presentation to endoscopy in patients with nonvariceal upper gastrointestinal bleeding that were taking anticoagulants

Baseline characteristics of the patients included*			
Variables	Early endoscopy ($n=82$)	Delayed endoscopy ($n=56$)	*P* value
Age (years)	77 (12)	80 (11)	0.672
Male sex	49 (59.8)	34 (60.7)	1.000
Clinical presentation			0.116
Hematemesis	22 (26.8)	12 (21.4)	0.549
Melena	56 (68.3)	35 (62.5)	0.584
Hematochezia	1 (1.2)	5 (8.9)	0.050
Hematemesis and melena	3 (3.7)	4 (7.1)	0.441
HR (beats/min)	83 (28)	83 (16)	0.527
SBP (mmHg)	115 (33)	118 (21)	0.949
DPB (mmHg)	64 ± 15	65 ± 14	0.576
Syncope	5 (6.1)	2 (3.6)	0.701
Glasgow Coma Scale	15 (0)	15 (0)	0.112
Laboratorial parameters			
Hemoglobin (g/dL)	8.8 ± 2.8	8.7 ± 2.5	0.906
Platelet count ($\times 10^3$ µL)	212 (129)	221 (84)	0.855
Creatinine (mg/dL)	1.17 (0.86)	1.10 (0.96)	0.833
Urea (mg/dL)	92.3 (79)	88 (68)	0.859
Albumin[†] (g/dL)	2.8 ± 0.64	2.8 ± 0.73	0.909
INR	1.9 (2.0)	2.8 (2.4)	0.069
Comorbidities			
Chronic liver disease	5 (6.1)	3 (5.4)	1.000
Congestive heart failure	32 (39.0)	27 (48.2)	0.299
Chronic kidney disease	11 (13.4)	7 (12.5)	1.000
Disseminated neoplasm	2 (2.4)	2 (3.6)	1.000
Relevant medication			
Anticoagulants			0.162
DOAC	16 (19.5)	7 (12.5)	0.355
VKA	47 (57.3)	41 (73.2)	0.072
Enoxaparin	19 (23.2)	8 (14.3)	0.275
Antiplatelets	27 (32.9)	23 (41.1)	0.370
Acetylsalicylic acid	20 (24.4)	18 (32.1)	0.337
Others[a]	7 (8.5)	5 (8.9)	1.000
Additional medication			
NSAIDs	7 (8.5)	6 (10.7)	0.769
Steroids	7 (8.5)	2 (3.6)	0.311
SSRI	11 (13.4)	7 (12.5)	1.000
PPI	28 (34.1)	18 (32.1)	0.856
Endoscopy risk stratification scores			
Rockall score[¶]			
Pre-endoscopic	4 (2)	4 (2)	0.386
Post-endoscopic	5 ± 2	5 ± 2	0.381
Blatchford score[¶]	12 ± 3	12 ± 3	0.849
Blatchford ≥ 12	58 (70.7)	36 (64.3)	0.460
AIMS65 score[¶]	2 (1)	3 (1)	0.680
Endoscopic management			
Timing of endoscopy (h)	9.0 (11)	44.0 (27)	< 0.001
Endoscopic findings			0.133
PUD	23 (28.0)	18 (32.1)	0.705
Forrest			0.363

Table 1 (continued)

Baseline characteristics of the patients included*			
Variables	Early endoscopy ($n=82$)	Delayed endoscopy ($n=56$)	*P* value
Ia	0	0	–
Ib	0	1 (5.6)	0.406
IIa	9 (39.1)	3 (16.7)	0.360
IIb	2 (8.7)	2 (11.1)	1.000
IIc	2 (8.7)	4 (22.2)	0.223
III	10 (43.5)	8 (44.4)	0.799
Mallory–Weiss	10 (12.2)	2 (3.6)	0.122
Erosive Gastritis	1 (1.2)	4 (7.1)	0.303
Erosive esophagitis	2 (2.4)	3 (5.4)	0.395
Dieulafoy	4 (4.9)	0	0.146
Neoplasia	3 (3.7)	6 (10.7)	0.158
Angiodysplasia	10 (12.2)	4 (7.1)	0.401
No endoscopic findings	29 (35.4)	19 (33.9)	1.000

DPB diastolic blood pressure, *DOAC* direct oral anticoagulants, *HR* heart rate, *INR* international normalized ratio, *NSAID* nonsteroidal anti-inflammatory drugs, *PPI* proton pump inhibitors, *PUD* peptic ulcer disease, *SBP* systolic blood pressure, *SSRI* selective serotonin reuptake inhibitors, *VKA* vitamin K antagonists

*Plus–minus values are means ± standard deviation. Alternatively, in cases of skewed distributions, data are median (interquartile range). Nominal or ordinal variables are described as total number (percentage). *P* values are derived from Student's *t*-test for data normally distributed or, in cases of skewed distributions, from a Mann–Whitney *U* test. χ^2 Test or Fisher's exact test was used to compare categorical variables

[†]Data on albumin were missing in 22 and 13 patients in the early endoscopy and delayed group, respectively

[¶]Scores were calculated according to their description in the original articles [14, 19, 20]

[a]Including clopidogrel, ticagrelor, and ticlopidine

Table 2 Outcome variables according to the time from presentation to endoscopy in patients with nonvariceal upper gastrointestinal bleeding and taking anticoagulants

Variables*	Early endoscopy ($n=82$)	Delayed endoscopy ($n=56$)	*P* value
Endoscopic treatment	31 (37.8)	11 (19.6)	0.025
Bipolar electrocoagulation	10 (32.3)	6 (54.5)	0.281
Through the scope clips	12 (38.7)	1 (9.1)	0.127
Argon plasma coagulation	9 (29.0)	4 (36.4)	0.713
Length of hospital stay (days)	7 (6)	9 (7)	0.042
Surgical treatment	1 (1.2)	1 (1.8)	1.000
Intermediate/intensive care unit admission	42 (51.2)	15 (26.7)	0.005
Recurrent bleeding	12 (14.6)	6 (10.7)	0.611
30-day mortality	4 (4.9)	5 (8.9)	0.485

*Nominal or ordinal variables are described as total number (percentage). Plus–minus values are means ± standard deviation. Alternatively, in cases of skewed distributions, continuous data are median (interquartile range)

Endoscopy was performed within 24 h after presentation in most patients (59.4%). We believe that endoscopy was not performed within 24 h of presentation in a substantial proportion of the patients (40.6%) because, in our unit, endoscopy is only available between 8 AM and 8 PM on working days which is the Gastroenterology Department's schedule. Therefore, it is probable that some patients admitted with UGIB during the weekend and who were clinically stabilized after initial management in the ER might not have been transferred to another center. Consequently, they were submitted to endoscopy only in the morning of the following working day, possibly explaining this delay.

Regarding clinical outcomes, only endoscopic treatment, duration of hospital stay, and intermediate/intensive care unit admission were significantly different between the early and delayed groups. In fact, even after adjusting for confounders, the timing of endoscopy (early/delayed) was still identified as an independent predictive factor for all outcomes. Although studies that evaluated the influence of timing of endoscopy in NVUGIB on clinical outcomes did not specifically address the impact of anticoagulants use, their results are in line with our findings, showing higher rates of endoscopic treatment and shorter hospital stay in the early endoscopy group [30, 31]. On the other hand, Freitas et al.

Table 3 Predictive factors for endoscopic treatment in patients with nonvariceal upper gastrointestinal bleeding and taking anticoagulants, according to univariable and multivariable analyses

Variables	Univariable analysis*			Multivariable analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Timing of endoscopy (early vs. delayed)	2.487	1.122–5.513	0.025	2.400	1.067–5.400	0.034

CI confidence interval, *OR* odds ratio

*Only significant (P < 0.05) variables displayed

Table 4 Results of a multiple regression analysis with length of hospital stay as the outcome variable

Variables*	Regression coefficient	SE	Standardized regression coefficient	*P* value
Timing of endoscopy (early vs. delayed)	4.49	2.03	0.204	0.029
Albumin	−5.4	1.5	−0.34	< 0.001

SE standard deviation

*Only significant (*P* < 0.05) variables displayed

[32] found that performing endoscopy within 24 h of presentation was associated with a higher need of endoscopic treatment only in low-risk (GBS < 12) patients but not in high-risk patients (GBS ≥ 12). While we observed higher rates of endoscopic treatment in the early endoscopy group, this did not significantly influence the potential benefits in terms of need of subsequent surgical treatment, intermediate/intensive care unit admission, recurrent bleeding and 30-day mortality, compared to patients who underwent early endoscopy and did not receive endoscopic therapy.

In regard to the rate of intermediate/intensive care unit admission, contrary to our results, most studies did not find a different rate of intermediate/intensive care unit admission between early and delayed endoscopy groups, even when considering high and low-risk GBS groups and different cut-off values of timing of endoscopy from presentation [22, 23, 25, 31–33]. We speculated that this finding could be potentially explained by the longer time to medical optimization that patients in the delayed group had when compared with the early group. In line with our findings, Guo et al. [34] observed that urgent (< 6 h from presentation) vs. early (6–24 h from presentation) endoscopy was associated with higher ICU admission rates. Finally, we found that GCS was an independent predictive factor for intermediate/intensive care unit admission. Therefore, patients with lower GCS score at presentation were more likely to be admitted in intermediate/intensive care unit. This is not surprising as altered mental status is one of the variables used in the AIMS65 score, a simple risk stratification score for upper gastrointestinal bleeding capable of predicting in-hospital mortality and the need for ICU admission [35].

Our study presents some limitations. This was a single-center study, with retrospective design with its possible inherent bias. Although we relied on medical records to measure the data and outcomes of interest, missing data were minimal. Even though we chose to use the time from presentation to endoscopy, we did not record the time from presentation-to-endoscopy referral, nor the time from endoscopy referral to endoscopy, both of which could have influenced the overall presentation-to-endoscopy time. Despite these limitations, we believe our study is relevant because we considered potential confounders in the analysis, and it includes a nonnegligible sample of patients.

Despite current guidelines recommending performing endoscopy within the first 24 h after initial stabilization and not using anticoagulants as a determinant of the timing of endoscopy in patients with acute UGIB, the literature regarding this topic in this specific population is scarce. According to our results, outcomes such as need for surgery, recurrent bleeding, and 30-day mortality did not differ between anticoagulated patients submitted to early or

Table 5 Predictive factors for intermediate/intensive care unit admission in patients with nonvariceal upper gastrointestinal bleeding and taking anticoagulants, according to univariable and multivariable analyses

Variables	Univariable analysis*			Multivariable analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Timing of endoscopy (early vs. delayed)	2.870	1.379–5.973	0.005	2.749	1.272–5.942	0.010
GCS	0.546	0.336–0.888	0.015	0.594	0.369–0.956	0.032
SBP (mmHg)	0.982	0.966–0.999	0.036	0.983	0.965–1.001	0.059

SBP systolic blood pressure, *GCS* Glasgow Coma Scale, *CI* confidence interval, *OR* odds ratio

*Only significant (*P* < 0.05) variables displayed

delayed endoscopy. However, as those submitted to early endoscopy had shorter length of hospital stay, performing early endoscopy might be considered the mainstay strategy in patients with acute UGIB taking anticoagulants. However, further data are needed to clarify the impact and the optimal timing of endoscopy in patients with NVUGIB using anticoagulants, in different-risk patients, as evidence remains scarce.

Author's contribution TLC: Involved in design of the study; collection, statistical analysis, and interpretation of the data; drafting of the article and in the final approval of the article. VMS: Involved in conception of the study and final approval of the article. MF: Involved in conception of the study and final approval of the article. TCG: Involved in conception of the study and final approval of the article. JC: Involved in conception of the study and in the final approval of the article.

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Declarations

Conflict of interest All authors report no conflict of interest or funding source to declare. The authors declare that they have no competing interests.

Ethical approval Ethical approval was waived by the "Senhora da Oliveira Hospital's Ethics Committee" in view of the retrospective nature of the study. All methods were carried out in accordance with relevant guidelines and regulations and were approved by the "Senhora da Oliveira Hospital's Ethics Committee."

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