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Impact of duration to endoscopy in patients with non-variceal upper gastrointestinal bleeding: propensity score matching analysis of real-world data from Thailand

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Abstract

Background The findings on mortality, rebleeding rate, and hospital stay in patients who underwent early vs. late endoscopy are conflicting. We aimed to compare in-hospital outcomes and medical resource use in patients with acute non-variceal upper gastrointestinal bleeding.

Methods We retrospectively reviewed the medical records of patients with acute non-variceal upper gastrointestinal bleeding who underwent early or late endoscopy between 2016 and 2019. The primary outcome was in-hospital mortality. The secondary outcomes were the need for packed red blood cells and number of transfusions, the proportion of lesions with high-risk stigmata, endoscopic and additional hemostasis, in-hospital rebleeding, duration of stay, and admission cost. Statistical analysis was performed using Pearson's chi-squared or Fisher's exact test for categorical variables, Student's *t*-test, and Wilcoxon rank-sum test for continuous variables.

Results Early and late endoscopies were performed on 451 and 279 patients, respectively. After 1:1 propensity score matching, 278 patients from each group were included, and patients' baseline characteristics were similar in the matched groups. Compared with the late group, the early group had a significantly increased rate of endoscopic hemostasis (22.7% vs. 13.7%, $P=0.006$) and a low rate of packed red blood cell transfusion (53.6% vs. 61.9%, $P=0.048$). Duration of stay and admission costs were significantly higher in the late group than in the early group (all $P<0.05$). After adjusting for confounding factors, early endoscopy was positively associated with ulcers with high-risk stigmata (adjusted odds ratio = 1.83, $P=0.023$) and endoscopic hemostasis (adjusted odds ratio = 1.97, $P=0.004$). It was negatively associated with the need for packed red blood cell transfusion (adjusted odds ratio = 0.62, $P=0.017$) and duration of stay (adjusted coefficient=-0.10, $P<0.001$) with no impact on in-hospital mortality, rebleeding, or radiological interventions.

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Conclusions The timing of endoscopy does not affect in-hospital mortality or rebleeding rate. This study supports using early endoscopy in patients with acute non-variceal upper gastrointestinal bleeding based on the potential benefits and feasibility of medical resource use.

Keywords Early endoscopy, Time to endoscopy, Non-variceal upper gastrointestinal bleeding, Clinical outcomes, Medical resource use

Background

Upper gastrointestinal bleeding (UGIB) is a common emergency condition that can result in mortality, morbidity, and increased healthcare expenditure. Despite considerable advancements in treatment modalities, service provision, and guidelines [1, 2, 3], the mortality rate of non-variceal UGIB (NVUGIB) remains as high as 14% [4, 5]. Endoscopy is crucial for diagnosing and treating UGIB as it helps gastroenterologists identify the source of bleeding and achieve hemostasis [6].

Early endoscopy (within 24 h of admission) has been recommended as the standard treatment for NVUGIB management [2, 3]. However, current evidence does not demonstrate clearly whether the performance of endoscopy within this timeframe is clinically beneficial [7]. Previous studies have provided conflicting results regarding mortality, rebleeding rate, and hospital stay in patients who underwent early vs. late endoscopy (after 24 h) [8]. A recent meta-analysis of 13 studies did not demonstrate a clear benefit of performing endoscopy within 24 h for UGIB [8]. The increasing inconsistency among various research findings has led to concerns regarding the optimal time to perform endoscopy in patients with NVUGIB.

Notably, most existing studies on this issue are considered low-quality observational studies, which may include a high risk of selection bias and residual confounding by severity [9, 10, 11, 12, 13, 14, 15, 16]. In contrast, existing randomized controlled trials (RCTs) conducted by expert endoscopists in specialized centers with highly selective inclusion criteria have insufficient power to address this question [17]. Thus, the generalizability of these findings to community practice and unselective patient populations remains largely unknown, indicating a knowledge gap in this area. Therefore, we aimed to determine the impact of early endoscopy on clinical outcomes and medical resource use in patients with NVUGIB.

Methods

Study design and population

This retrospective, single-center cohort study was conducted between January 2016 and December 2019 using the database of Hatyai Hospital (a large community teaching hospital in southern Thailand). The inclusion criteria were patients aged > 18 years who visited the emergency room and were subsequently hospitalized due to clinical presentation with acute NVUGIB. The exclusion criteria were (a) history of confirmed UGIB within the prior 3 months, (b) prior endoscopy at another hospital, (c) intractable unstable medical conditions despite adequate resuscitation or designated as palliative, and (d) incomplete data for analysis. Based on the timing of endoscopy (from hospital presentation to the procedure), we classified patients into the "early endoscopy" group, defined as endoscopy performed within 24 h, or "late endoscopy" group, defined as endoscopy performed after 24 h. All collected data were anonymized before analysis. Our Institutional Review Board approved the study (protocol number: HYH EC 097-65-01), and the informed consent requirement was waived. This study was conducted in accordance with the principles of the Declaration of Helsinki.

According to our center's protocol, patients with UGIB were admitted and underwent endoscopy during hospitalization. For unstable patients, resuscitation was performed to achieve hemodynamic stability, defined as shock resolution with or without the use of low-dose inotropic support. The attending physician decided on the pre-endoscopic management (including intravenous fluid replacement, coagulopathy correction, medication, and time of endoscopy) based on the patient's condition and bleeding severity. Patients were prescribed intravenous proton pump inhibitors (PPIs) immediately after establishing a provisional UGIB diagnosis. Blood transfusion was considered in cases of shock or when hemoglobin level was ≤ 8 g/dL, or in the presence of inadequate oxygen delivery symptoms [3, 18]. Our hospital provides 24 h endoscopy services, although the decision to perform endoscopy at night or on holidays depends on the availability of the on-call gastroenterologist and clinical urgency of each case. Therefore, although the service is always technically available, practical factors such as endoscopist availability and competing clinical emergencies may delay the procedure. Endoscopic hemostasis was indicated in cases with high-risk stigmata (HRS); however, the need for endoscopic hemostasis was determined by the endoscopist based on the patient's endoscopic findings and clinical status. According to our institution's endoscopic practice, high-risk lesions with visible vessels or ongoing bleeding were treated with dual-modality therapy, including injection therapy with diluted

adrenaline and mechanical clips or coagulation (using a heater probe or argon plasma). If hemostasis was not achieved after the dual-modality therapy, a third endoscopic treatment modality was used. Monotherapy with adrenaline injection is not commonly used in our center. For lesions with adherent clots, diluted adrenaline was injected around the culprit lesion, followed by adhered blood clot removal using water irrigation and ulcer-based treatments [3]. After endoscopy, patients with HRS or those who underwent endoscopic hemostasis were maintained on intravenous infusion of PPIs for 72 h. In other cases, patients received oral PPIs, if needed, based on endoscopic findings [3]. If bleeding could not be controlled or rebleeding occurred despite two adequate endoscopic hemostasis attempts, a multidisciplinary team consultation was performed with an interventional radiologist and general surgeons to determine a rescue therapy [3].

Data collection

The following data were manually retrieved directly from patients or their medical records: age, sex, medical history, clinical presentation, pre-admission medication within 4 weeks, vital signs, symptoms, laboratory results upon admission, and final diagnosis. UGIB severity before endoscopy was assessed using the Glasgow–Blatchford score (GBS) and albumin, international normalized ratio, mental status, systolic blood pressure, and age > 65 years score based on parameters obtained on admission [19]. In addition, the study outcomes were assessed.

Outcomes and definitions

The primary outcome was in-hospital mortality, defined as death of any cause occurring during the hospitalization period. The secondary outcomes were the need for packed red blood cells (PRBC) and number of PRBC transfusions, proportion of lesions with HRS, endoscopic and additional hemostasis (including angioembolization and surgery), in-hospital rebleeding, duration of stay (DOS), and admission cost.

Lesions with HRS were determined based on the presence of active bleeding, visible vessels, or adherent clots on endoscopic examination. Rebleeding was defined as a new episode of objective evidence of UGIB after the initial endoscopy that was associated with hemodynamic instability or a decrease in the hemoglobin level by > 2 g/dL after achieving a stable hemoglobin level. Shock was defined as a heart rate of > 100 beats/min with a calculated mean arterial pressure of < 65 mmHg or inotrope use. *Helicobacter pylori* infection was tested by histology and rapid urease test. Admission costs were determined based on the total cost of the universal health coverage invoice.

Propensity score matching

Due to the non-randomized nature of this study, 1:1 propensity score nearest neighbor matching was applied to minimize bias in patient selection between the two groups. The probability of allocation into the study groups was assessed using multivariate analysis, including factors that might affect the timing of endoscopy (sex, age, presence of comorbidities, presence of shock at initial assessment, and GBS) and imbalanced baseline characteristics between the two groups (*H. pylori* infection and hemoglobin level before endoscopy). The propensity scores for each patient were generated using the multivariate model. We set the caliper distance used for the propensity score matching at 0.2 of the standard deviation of the logit of the propensity score.

Statistical analyses

For bivariate two-sided comparisons between the two groups, we used Pearson's chi-squared test or Fisher's exact test for categorical variables and Student's *t*-test and Wilcoxon rank-sum test for continuous variables. We tested for normality using the Shapiro-Wilk test. Parametric variables are presented as the mean and standard deviation, and non-parametric variables as the median and interquartile range (IQR). Time to in-hospital rebleeding was estimated using the non-parametric Kaplan–Meier method, and group differences were evaluated using the log-rank test. Logistic and linear regression, as well as Cox proportional hazard models adjusted for demographic factors, were used to examine the association between outcomes and timing of endoscopy. Statistical analyses were performed using STATA, version 15.1 (StataCorp LLC, College Station, TX, USA). Statistical significance was set at $P < 0.05$.

Results

Patient population

Of the 836 patients admitted for confirmed NVUGIB, 106 were excluded. The two groups showed significant differences in terms of hemoglobin levels before esophagogastroduodenoscopy (EGD) and the proportion of *H. Pylori* infection (Table 1). We matched 278 pairs (556 patients) using propensity scores (Fig. 1). After matching, the differences between the groups were balanced (Table 1).

Endoscopic diagnosis and outcome

Table 2 summarizes the comparison of clinical outcomes and medical resource use between the groups. The early endoscopy group had a higher tendency to have lesions with HRS (16.9% vs. 11.2%, $P = 0.051$) and required a significantly greater amount of endoscopic hemostasis (22.7% vs. 13.7%, $P = 0.006$) compared with the late endoscopy group. The early endoscopy group showed

Table 1 Baseline patient characteristics

Baseline characteristic	Original participants (*n* = 730)			Propensity score matching (*n* = 556)		
	Early endoscopy (*n* = 451)	Late endoscopy (*n* = 279)	*P*-value	Early endoscopy (*n* = 278)	Late endoscopy (*n* = 278)	*P*-value
Age (years), mean ± SD	60.36 ± 17.60	60.36 ± 17.28	0.674	60.36 ± 17.55	60.36 ± 17.31	0.720
Male sex, *n* (%)	344 (76.3)	221 (79.2)	0.357	215 (77.3)	220 (79.1)	0.607
Body weight (kg), mean ± SD	60.9 ± 12.7	60.4 ± 12.1	0.772	62.7 ± 13.5	60.4 ± 12.1	0.226
Body mass index (kg/m^2), mean ± SD	23.08 ± 4.81	23.04 ± 4.49	0.794	23.90 ± 4.91	23.04 ± 4.48	0.223
Previous upper gastrointestinal bleeding, *n* (%)	61 (13.5)	37 (13.3)	0.919	43 (15.5)	37 (13.3)	0.468
Underlying disease	229 (50.8)	151 (54.1)	0.379	149 (53.6)	151 (54.3)	0.865
Hypertension, *n* (%)	150 (33.3)	108 (38.7)	0.134	90 (32.4)	108 (38.8)	0.111
Diabetes mellitus, *n* (%)	91 (20.2)	50 (17.9)	0.607	50 (18.0)	62 (22.3)	0.420
Cirrhosis, *n* (%)	39 (8.6)	30 (10.8)	0.337	30 (10.8)	30 (10.8)	0.988
Chronic kidney disease, *n* (%)	42 (9.3)	25 (9.0)	0.873	30 (10.8)	25 (9.0)	0.478
Cerebrovascular disease, *n* (%)	35 (7.8)	18 (6.5)	0.508	20 (7.2)	18 (6.5)	0.737
Ischemic heart disease, *n* (%)	21 (4.7)	9 (3.2)	0.344	11 (4.0)	9 (3.2)	0.649
Presence of shock at initial assessment, *n* (%)	43 (9.5)	17 (6.1)	0.100	16 (6.2)	17 (6.6)	0.857
Medication						
Antiplatelet, *n* (%)	44 (9.8)	31 (11.1)	1.00	23 (8.3)	31 (11.2)	0.252
Anticoagulant, *n* (%)	16 (3.5)	9 (3.2)	0.941	9 (3.5)	9 (3.5)	0.990
Nonsteroidal anti-inflammatory drugs, *n* (%)	106 (23.5)	71 (25.4)	0.551	67 (24.1)	71 (25.5)	0.695
Laboratory value at admission						
Hemoglobin (g/dL), mean ± SD	8.98 ± 3.42	8.96 ± 3.39	0.941	9.41 ± 3.51	8.96 ± 3.40	0.128
Platelet count (×10^3/μL): median (P_{25}–P_{75})	227 (157–295)	219 (162–283)	0.542	227 (157–295)	219 (162–283)	0.553
Serum creatinine (mg/dL), median (P_{25}–P_{75})	1.02 (0.83–1.41)	1.04 (0.81–1.39)	0.820	1.03 (0.83–1.40)	1.04 (0.81–1.39)	0.867
Serum albumin (mg/dL), median (P_{25}–P_{75})	3.30 ± 0.72	3.35 ± 0.74	0.318	3.30 ± 0.72	3.35 ± 0.74	0.318
International normalized ratio, median (P_{25}–P_{75})	1.14 (1.05–1.28)	1.12 (1.05–1.27)	0.124	1.14 (1.05–1.28)	1.12 (1.05–1.27)	0.196
Glasgow–Blatchford score, median (P_{25}–P_{75})	10 (6–12)	10 (6–12)	0.457	10 (6–12)	10 (6–12)	0.890
AIMS65 score, median (P_{25}–P_{75})	1 (0–2)	1 (0–1)	0.605	1 (0–2)	1 (0–1)	0.605
Hemoglobin level before endoscopy (g/dL), mean ± SD	9.10 ± 2.88	9.53 ± 2.24	0.032	9.66 ± 2.93	9.53 ± 2.25	0.543
Helicobacter pylori infection, n (%)	147 (32.6)	70 (25.1)	0.031	80 (28.8)	70 (25.2)	0.339

Data are expressed as the number (%) unless otherwise specified

SD, standard deviation; AIMS65, albumin, international normalized ratio, mental status, systolic blood pressure, age > 65 years

a trend toward a higher frequency of surgical intervention compared to the late endoscopy group (2.5% vs. 0.4%, $P = 0.068$). During admission, the proportion of patients who required PRBC transfusions was higher in the late endoscopy group than in the early endoscopy group (53.6% vs. 61.9%, $P = 0.048$). However, the number of PRBC units transfused during admission did not differ significantly between the groups. Based on the time of endoscopy, no significant differences were observed in in-hospital clinical outcomes, including mortality, rebleeding, and additional hemostasis requirement (including angioembolization and surgery) between the groups. According to the Kaplan–Meier analyses, the timing of endoscopy did not significantly correlate with the risk of death and rebleeding during admission (all log-rank $P > 0.05$; Fig. 2). Furthermore, the DOS (median [IQR], 3 [3–5], d for early endoscopy vs. 5 [4–6], d for late endoscopy) and admission costs (median [IQR], $526 [391–577] for early endoscopy vs. $577 [412–828] for late endoscopy) were significantly lower in the early endoscopy group than in the late endoscopy group (all $P < 0.05$).

Association of early endoscopy with outcomes

After adjusting for confounding factors, early endoscopy was positively associated with the presence of lesions with HRS (adjusted OR, 1.83; 95% confidence interval [CI], 1.09–3.08, $P = 0.023$) and the requirement for endoscopic hemostasis (adjusted OR, 1.97; 95% CI, 1.24–3.14, $P = 0.004$) but was negatively associated with the need for PRBC transfusion (adjusted OR, 0.62; 95% CI, 0.41–0.92, $P = 0.017$) and DOS (adjusted coefficient of natural log-transformed days, -0.10; 95% CI, -0.14 to -0.06; $P < 0.001$). Early endoscopy was marginally positively associated with in-hospital rebleeding (adjusted OR, 2.81; 95% CI, 0.99–7.96, $P = 0.052$) and time to rebleeding (adjusted hazards ratio, 2.53; 95% CI, 0.99–6.47, $P = 0.053$). However, the timing of endoscopy was not associated with in-hospital mortality, time to

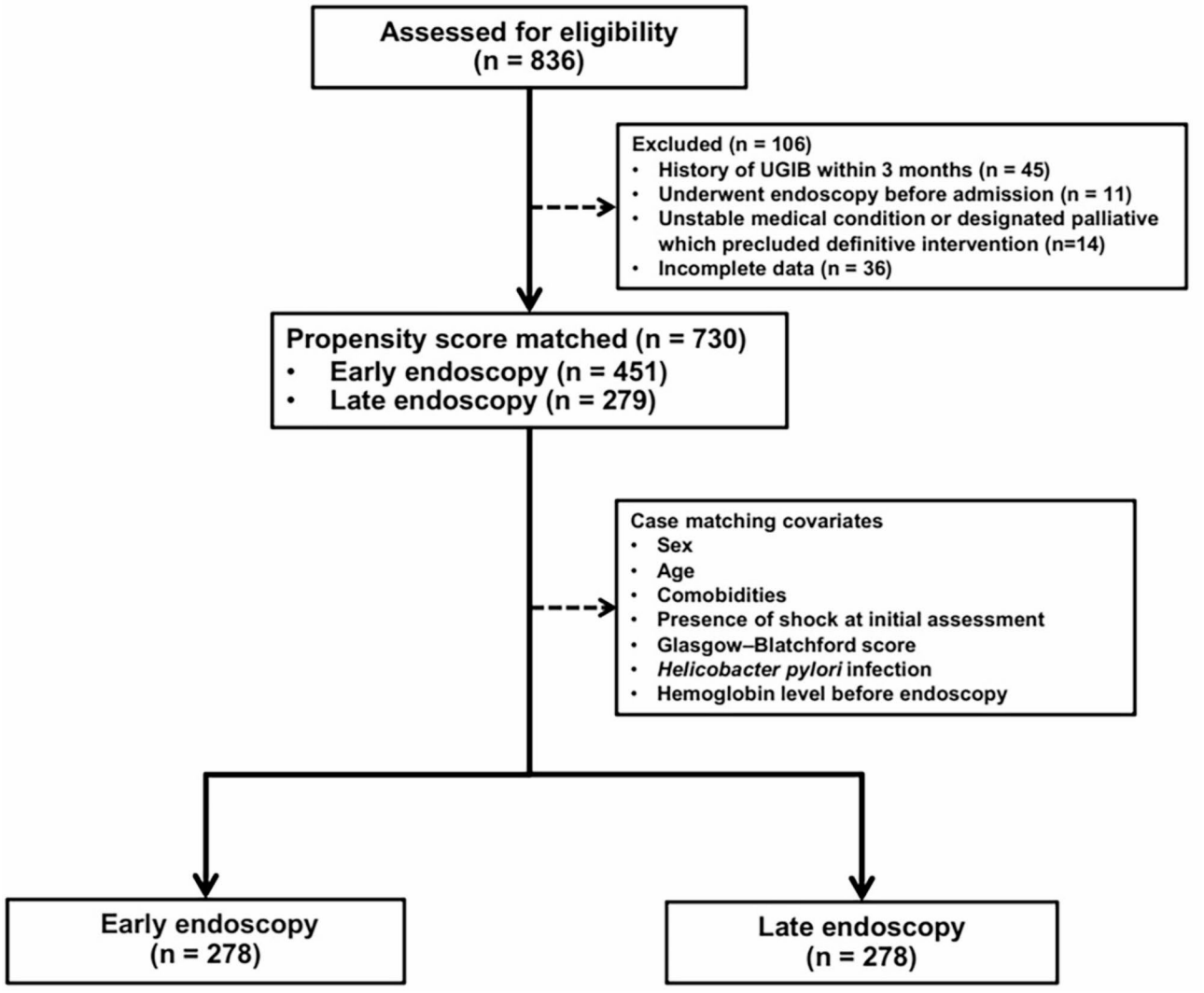

Fig. 1 Flow chart of participant selection in the study

Table 2 Comparisons of in-hospital clinical course and medical resource usage between early and late endoscopy

Outcomes	Original patients (*n* = 730)			Propensity score matching (*n* = 516)		
	Early endoscopy (*n* = 451)	Late endoscopy (*n* = 279)	*P*-value	Early endoscopy (*n* = 278)	Late endoscopy (*n* = 278)	*P*-value
Ulcer with high-risk stigmata of recent bleeding, *n* (%)	93 (20.6)	31 (11.1)	0.001	47 (16.9)	31 (11.2)	0.051
Endoscopic hemostasis, *n* (%)	123 (27.3)	39 (14.0)	< 0.001	63 (22.7)	38 (13.7)	0.006
Additional intervention						
Radiologic intervention, *n* (%)	3 (0.7)	3 (1.1)	0.680	3 (1.1)	3 (1.1)	1.000
Surgical intervention, *n* (%)	12 (2.7)	1 (0.4)	0.022	7 (2.5)	1 (0.4)	0.068
Need for red blood cell transfusion, *n* (%)	401 (64.0)	246 (66.7)	0.386	149 (53.6)	172 (61.9)	0.048
Total red blood cell transfusion (units), median (P_{25}–P_{75})	1 (0–3)	1 (0–3)	0.488	1 (0–3)	1 (0–3)	0.132
In-hospital rebleeding, *n* (%)	21 (4.7)	7 (2.5)	0.141	14 (5.1)	7 (2.5)	0.117
In-hospital mortality, *n* (%)	20 (4.4)	11 (3.9)	0.749	11 (4.0)	11 (4.0)	1.000
Duration of stay (days), median (P_{25}–P_{75})	3 (3–5)	5 (4–6)	< 0.001	3 (3–5)	5 (4–6)	< 0.001
Admission cost (US dollar), median (P_{25}–P_{75})	549 (398–847)	577 (412–828)	0.023	526 (391–577)	577 (412–828)	0.002

Data are expressed as the number (%) unless otherwise specified

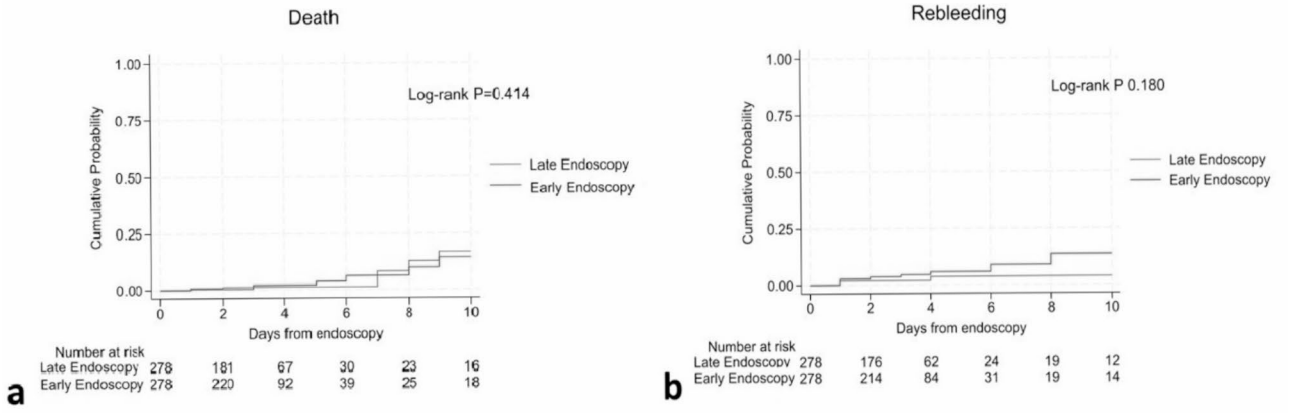

Fig. 2 Kaplan–Meier plots of cumulative estimate of the outcomes of **(a)** in-hospital death and **(b)** in-hospital rebleeding after endoscopy among patients with non-variceal upper gastrointestinal bleeding. Comparison between early endoscopy (within 24 h) and late endoscopy (after 24 h)

Table 3 Unadjusted and adjusted outcomes of patients with NVUGIB who received early versus late EGD

Outcomes	Crude effect size* (95% CI)	*P*-value	Adjusted effect size*† (95% CI)	*P*-value
Lesion with high-risk stigmata	1.62 (0.99–2.64)	0.052	1.83 (1.09–3.08)	0.023
Endoscopic hemostasis	1.85 (1.19–2.88)	0.006	1.97 (1.24–3.14)	0.004
Radiologic intervention	1.00 (0.20–5.00)	1.000	1.17 (0.21–6.36)	0.859
Surgical intervention	7.16 (0.87–58.54)	0.067	7.31 (0.78–68.70)	0.082
Need for red blood cell transfusion	0.71 (0.51–0.99)	0.049	0.62 (0.41–0.92)	0.017
Units of red blood cell transfusion±	-0.11 (-0.23–0.01)	0.085	-0.09 (-0.20–0.01)	0.075
In-hospital rebleeding	2.06 (0.82–5.19)	0.125	2.81 (0.99–7.96)	0.052
Time to rebleeding+	2.02 (0.81–5.000)	0.129	2.53 (0.99–6.47)	0.053
In-hospital mortality	1.00 (0.43–2.35)	1.000	1.13 (0.44–2.89)	0.798
Time to death+	0.73 (0.29–1.81)	0.492	0.863 (0.33–2.23)	0.760
Total duration of stay±	-0.11 (-0.15 to -0.07)	< 0.001	-0.10 (-0.14 to -0.06)	< 0.001
Admission cost±	-0.03 (-0.08 to 0.02)	0.202	-0.03 (-0.07 to 0.02)	0.249

*Presented as odds ratio or hazard ratio or coefficient, as appropriate

† Adjusted for sex, age, use of nonsteroidal anti-inflammatory drugs, presence of shock at initial assessment, serum albumin, serum creatinine, and international normalized ratio

± Natural log-transformed variables

+ Cox proportional hazards model

CI, confidence interval; EGD, esophagogastroduodenoscopy; NVUGIB, non-variceal upper gastrointestinal bleeding

in-hospital death, additional hemostasis, units of PRBC transfusion required during admission, or hospital costs (all $P > 0.05$; Table 3).

Discussion

This retrospective cohort study was based on data from a large community teaching center and reflected "real-world" outcome data from urban areas in a middle-income country. This current study revealed the following key results. First, the timing of endoscopy was not statistically associated with in-hospital mortality. Second, after adjusting for possible confounding factors, early endoscopy was associated with an increased risk of developing lesions with HRS and endoscopic hemostasis requirements, but was not significantly associated with other adverse outcomes of UGIB. Finally, early endoscopy was associated with a significantly reduced need for blood transfusion and hospital stay.

The appropriate timing for endoscopy is arbitrary and has been debated in the literature. A recent RCT revealed no benefit in urgent endoscopy (within 6 h) compared to early endoscopy (6–24 h) [20]. In this study, we chose the threshold of 24 h because it aligns with current practice guidelines and allows for a clear comparison between patients receiving early intervention and those for whom endoscopy was delayed beyond 24 h. Although guidelines recommend performing endoscopy within 24 h [2, 3], the rate of early endoscopy varies widely, from 40 to 80% [11, 12, 13]. Nationwide studies from the UK and US show that < 50% of patients with UGIB receive endoscopy within this timeframe [12, 13]. In our study, 60% of patients underwent early endoscopy, highlighting

real-world challenges, especially in middle-income settings, where infrastructural limitations and selective use of early endoscopy by physicians may hinder adherence to guidelines [21, 22]. Notably, several observational studies that form the basis for these recommendations may also be confounded by patient condition and bleeding severity [17, 23, 24]. In addition, some logistical and clinical factors (such as the availability of the on-call endoscopist, prioritization of other emergencies, and patients requiring longer stabilization periods) might contribute to the delay in performing endoscopy within 24 h in some cases. Thus, the timing of endoscopy was decided by the treating physicians, and patients with more severe bleeding could have been prioritized for early endoscopy, introducing selection bias [11, 12, 25]. To address this, we performed propensity score matching to control for confounders. We used logistic and linear regression models to further adjust for potential biases, assessing the effect of early endoscopy on treatment outcomes and resource use.

Consistent with the findings of prior studies [26, 27, 28], the rate of endoscopic hemostasis exceeded the rate of ulcers with HRS. This discrepancy reflects the endoscopist's clinical judgment, incorporating both endoscopic findings and the patient's overall condition. In certain cases, lesions with low-risk stigmata were treated prophylactically to prevent rebleeding, particularly in critically ill patients, which likely contributed to the higher rate of endoscopic hemostasis. After adjusting for possible confounders, early endoscopy was found to be associated with increased HRS findings and the need for endoscopic hemostasis. This suggests that lesions with HRS had become less severe by the time the endoscopy was performed. A longer period until endoscopy and a longer duration of acid suppression could enhance the healing of previously bleeding lesions to commence healing and may downstage the culprit lesion from one that required endoscopic hemostasis to a low-risk lesion that could be managed with pharmacological therapy [29]. An RCT demonstrated that acid suppression before endoscopy accelerates the resolution of signs of bleeding in ulcers and reduces the need for endoscopic hemostasis [30]. Our findings support this hypothesis. However, more frequent lesions with HRS or endoscopic treatment did not translate into any difference in rebleeding. Similarly, the major risk factor for recurrent bleeding is the presence of HRS during endoscopy [7]. However, the effect of early endoscopy on rebleeding remains controversial. Previous studies demonstrate no difference in rebleeding according to the timing of endoscopy [24, 29, 31]. Our study demonstrated that early endoscopy was marginally positively associated with in-hospital rebleeding and time to in-hospital rebleeding. However, a previous large retrospective study found that early endoscopy was associated with a decreased risk of recurrent bleeding in high-risk patients with UGIB [32]. Further investigation should be carried out in future studies.

In our study, in-hospital mortality was not affected by the timing of endoscopy. Our results are consistent with those of a previously reported meta-analysis [7, 8]. Besides endoscopic management, patient variables are important factors that may affect mortality. Approximately 80% of mortalities were not bleeding-associated, but due to coexisting medical illness [33]. Laursen et al. postulated a U-shaped correlation between endoscopy timing and mortality in patients with peptic ulcer disease [34]. This phenomenon highlights that basic resuscitation plays an important role in the early stages of treatment before endoscopy. Late endoscopy may increase the risk of ongoing bleeding and reduce the effect of endoscopic hemostasis. However, early endoscopy may lead to suboptimal resuscitation, destabilization of comorbidities, and interference with the quality of endoscopic examination (due to poor preparation), which may result in worse outcomes [29, 35]. Thus, an "appropriate timing of endoscopy" is more important than "early endoscopy," and endoscopy should be performed within the "therapeutic window" period, which allows sufficient time for pre-endoscopic optimization but does not substantially delay the performance of necessary endoscopy [36, 37]. The efficient triage protocols for identifying the appropriate patients who are at a heightened risk of mortality or unfavorable outcomes and performing the necessary early endoscopy are key aspects in improving patients' clinical courses [22], and this remains an area for future research.

Finally, our results are consistent with those of previous studies that showed that early endoscopy was significantly associated with decreased DOS and lower requirements for blood transfusion [7, 23]. Early EGD can potentially lead to a reduction in hospital stay [6, 10, 32]. A large retrospective multicenter study involving 909 patients from 13 hospitals revealed that early endoscopy was associated with a significant decrease in DOS [32]. Similarly, a nationwide study of 2592 patients found decreased hospital stay in patients receiving endoscopy within 1 d of admission [10]. The restrictive transfusion strategy has also yielded clinical outcomes superior to those of the liberal strategy in most patients with UGIB [18], highlighting the need for PRBC transfusion-relevant outcomes that should be observed in patients with UGIB. The use of early endoscopy helps physicians stratify low-risk patients who can be discharged early and offers a procedure to control hemorrhage in high-risk patients. The shorter duration between presentation and endoscopic hemostasis should result in reduced blood loss, which could explain the reduced requirement for blood transfusion in our study [23]. Collectively, our study's

results suggest that routine early endoscopy may be a potentially beneficial strategy in patients with UGIB.

This study has several limitations. First, this is a retrospective cohort study and not an RCT. RCTs remain the gold standard for hypothesis testing; however, conducting one in this context is challenging due to ethical concerns and logistical barriers. We used propensity score matching to minimize selection bias and applied regression models to adjust for confounding variables, but the possibility of unmeasured or missing confounders cannot be entirely excluded. For example, patients in the late endoscopy group are more likely to require transfusions before intervention due to prolonged bleeding. Second, even if an assessment for bleeding severity was performed with the GBS, unrecognized factors would have influenced clinical outcomes. These might include the adequacy of pre-endoscopic resuscitation and subtle differences in patients' care that were not captured in the medical records. Third, this study was conducted at a single center in Thailand, which limits the generalizability of our findings to other healthcare settings. Different patient demographics, resource availability, and clinical practices might have different results in other regions or healthcare systems. Fourth, patients who did not undergo endoscopy were excluded. This group, which was composed of very stable patients (for whom endoscopy might not alter management) or critically ill patients (where risks of the procedure outweighed potential benefits) limited the comprehensiveness of our findings. Fifth, the relatively small sample size would have limited the statistical power to detect differences in rare outcomes, such as in-hospital mortality or rebleeding. Power calculations indicated that at least 588 patients per group would be necessary to detect a 3% mortality rate difference with 80% power, which we were unable to achieve. Sixth, data were extracted from medical charts. Therefore, it might have provided misclassification or missing information. Key variables, such as smoking status, nasogastric aspirate characteristics, and stool findings, were unavailable and would have affected the analysis. In addition, documentation of pre-endoscopic resuscitation was inconsistent. Seventh, outcomes were only evaluated during admission, whereas most patients stayed in hospital for fewer than 7 d. This limited timeframe might not completely capture longer-term outcomes, such as 30-day mortality or rebleeding rates, which are commonly evaluated as endpoints in upper gastrointestinal bleeding research. Eight, the timing of endoscopy was influenced by logistical factors, such as endoscopist availability, competing clinical emergencies, and patient stabilization requirements. These real-world constraints may have introduced variability in timing and outcomes. Finally, the unmatched cohort had significant differences in baseline characteristics, such as more cases of shock and lower hemoglobin levels in the late endoscopy group. Although propensity score matching addressed these imbalances, it reduced the sample size and limited applicability to patients with severe bleeding. Despite these limitations, our study offers valuable insights into the real-world impact of delayed endoscopy, including increased transfusion requirements and longer hospital stays. Addressing these limitations in future studies with multicenter designs, larger sample sizes, and longer follow-up periods could further refine clinical guidelines on the optimal timing of endoscopy in non-variceal UGIB.

Conclusions

In this cohort study of patients with acute NVUGIB using propensity score matching analysis, we found that the timing of endoscopy has no effect on in-hospital mortality. Using early endoscopy in patients with NVUGIB was associated with an increased risk of lesions with HRS and endoscopic hemostasis requirements but was not significantly associated with other adverse outcomes. Early endoscopy was also associated with a significant reduction in the need for blood transfusion and a shorter duration of hospital stay. Considering the potential benefit of medical resource use, this study supports the routine use of early endoscopy within 24 h in patients with acute NVUGIB unless specific contraindications exist.

Abbreviations

UGIB	Upper Gastrointestinal Bleeding
NVUGIB	Non-Variceal Upper Gastrointestinal Bleeding
RCT	Randomized Controlled Trial
PPI	Proton Pump Inhibitor
HRS	High-Risk Stigmata
GBS	Glasgow–Blatchford Score
PRBC	Packed Red Blood Cell
DOS	Duration of Stay
IQR	Interquartile Range
EGD	Esophagogastroduodenoscopy

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None.

Author contributions

AC designed and conceptualized the study; acquired, analyzed, and interpreted the data, and drafted the manuscript. NS designed and conceptualized the study and acquired, analyzed, and interpreted the data. NP, KC, KA, and AR acquired, analyzed, and interpreted the data. SS, MR, and BO critically revised the manuscript for important intellectual content. VP designed and conceptualized the study, interpreted the data, and critically revised the manuscript for important intellectual content. All authors have reviewed and approved the final version of the manuscript.

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Data availability

The dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The Institutional Review Board of Hatyai Hospital approved the study (protocol number: HYH EC 097-65-01). This study was conducted in accordance with the principles of the Declaration of Helsinki. Our Institutional Review Board deemed that no additional informed consent was required apart from the standard consent for endoscopy.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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