

# Predictive Factors of Mortality in Patients with Nonvariceal Upper Gastrointestinal Bleeding

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## Abstract

**Background:** Nonvariceal upper gastrointestinal bleeding (NVUGIB) is one of the most common medical emergencies and often represents a life-threatening event. The aim of this study is to find potential predictive factors associated with 30-day mortality in patients with NVUGIB.

**Methods and Results:** Our prospective study was conducted in Mother Teresa Hospital between May 2022 and December 2022. A total of 224 patients (aged >18 years) with NVUGIB were included in the study. Demographical and clinical characteristics, endoscopic findings, and laboratory tests were reviewed during a 30-day follow-up period. Logistic regression was employed to identify the independent predictors of mortality.

The mean age of the 224 patients enrolled in the study was 63.21±16.3 years and most patients (72.8%) were male. One hundred fifty (66.9%) patients had comorbidities. The most common endoscopic diagnoses underlying NVUGIB episodes were duodenal ulcers (53.1%). Recurrent bleeding was recorded in 50(22.3%) patients. Out of 224 patients included in the study, 24(10.7%) died within 30 days of admission, 20(8.9%) died during hospitalization, and 4(1.8%) died after discharge. The mean age of death was 76.42±12.59 years; 95.8% of deaths were associated with one or more major comorbidities. In the multivariate logistic regression, after the exclusion of confounding factors, low red blood cell (RBC) ( $P=0.043$ , OR=0.413, CI 95%: 0.176-0.974), warfarin ( $P=0.036$ , OR=10.547, CI 95%: 1.165-95.462), and Rockall score (RS) >5 ( $P=0.034$ , OR=4.107, CI 95%: 1.114-15.139) were found to be independent predictive factors for mortality.

**Conclusion:** The 30-day mortality rate remained high after NVUGIB, especially during hospitalization. Low RBC, warfarin, and RS>5 were independent factors of mortality in patients with NVUGIB. (International Journal of Biomedicine. 2023;13(3):110-116.)

**Keywords:** nonvariceal upper gastrointestinal bleeding • mortality • predictive factors

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## Abbreviations

**BP**, blood pressure; **BUN**, blood urea nitrogen; **GIB**, gastrointestinal bleeding; **GBS**, Glasgow-Blatchford score; **HR**, heart rate; **INR**, international normalized ratio; **NVUGIB**, nonvariceal upper gastrointestinal bleeding; **NSAIDs**, nonsteroidal anti-inflammatory drugs; **RBC**, red blood cell; **RS**, Rockall score; **WBC**, white blood cells.

## Introduction

Nonvariceal upper gastrointestinal bleeding (NVUGIB) is a common medical condition that results in significant morbidity, mortality, and cost of medical care.<sup>(1,2)</sup> Mortality rates reported for NVUGIB range from 2% to 13.2% and vary in different countries.<sup>(3)</sup> Despite advances in endoscopic treatments and the decrease in the incidence of *H. pylori*, mortality remains high, and

it might be due to increasing age, comorbidities, and health care systems, which confound the effects of therapy improvements.<sup>(3,4)</sup> Multiorgan failure, cardiopulmonary conditions, and terminal malignancies are the most common causes in these patients.<sup>(5,6)</sup> Comorbidities, hypotension, tachycardia, low hemoglobin, endoscopic findings, and administration of anticoagulants and nonsteroidal anti-inflammatory drugs are seen as risk factors for mortality in NVUGIB.<sup>(5-10)</sup>

The aim of this study is to find potential predictive factors associated with 30-day mortality in patients with NVUGIB.

## Materials and Methods

Our prospective study was conducted in Mother Teresa Hospital between May 2022 and December 2022. A total of 224 patients (aged >18 years) with NVUGIB were included in the study. Exclusion criteria were patients who did not undergo endoscopy, patients with variceal bleeding, and patients who have not been followed up to one month after hospitalization. All participants provided written informed consent.

The study data were obtained from the anamnesis, physical examination, and clinical records of the patients. The following information was documented prospectively: *Patient data* (age, gender, date of admission); *History data* (presentation of symptoms, previous history of gastrointestinal bleeding or peptic ulcer disease); *Social history* (current smoking status, alcohol consumption); *Physical examination findings* (nasogastric lavage, rectal examination and initial hemodynamic status); *Initial laboratory data* (complete blood count, urinalysis, creatinine, platelet count and prothrombin time, transaminases, total bilirubin, electrolytes); *Comorbidities*, including hypertension, diabetes mellitus, cardiovascular diseases, cerebrovascular disease, heart failure, atrial fibrillation, liver cirrhosis (determined by clinical, laboratory and radiological data, without biopsy), malignancies; *Medications* (antiplatelet agents, vitamin K antagonists, NSAIDs, steroids, protein pump inhibitors); *Endoscopic findings*: the identification of the bleeding lesion, stigmata of recent hemorrhage at ulcer base according to the Forrest classification<sup>(7)</sup> (active bleeding, visible vessel, or adherent clots were classified as “high risk,” whereas flat spot and clean based ulcer as “low risk”).

Proton pump inhibitors were administered intravenously to all patients. Each patient’s bleeding risk was assessed by the Rockall score (RS) and Glasgow-Blatchford score (GBS) systems.

The endoscopic hemostatic technique used, as well as the presence of rebleeding, the need for surgery, and for hospital stay, were also described. Patients were followed by daily visits during hospitalization or until discharge or death. Hemodynamically unstable patients received intravenous crystalloid solutions and blood according to individual requirements. All endoscopic procedures were performed in the endoscopy unit by a gastroenterologist of the Gastroenterology Service.

### Outcomes

The outcomes evaluated were the frequency of death, rebleeding, and need for surgery. Such outcomes were monitored from the admission to the hospital or the onset of bleeding for in-hospital patients up to 30 days after the endoscopic examination. The primary outcome was mortality within 30 days of admission. Patients were advised to return for examination at 4 and 12 weeks after discharge.

i) Mortality within 30 days:

- *Intrahospital*: deaths occurring in hospital after diagnosis and treatment of bleeding.

- *After discharge*: deaths occurring after discharge from the hospital, diagnosis, and treatment of the bleeding.

ii) Recurrence of bleeding within 30 days:

- Recurrence of bleeding was defined as the onset of new hematemesis or hematochezia with hypovolemic shock or a greater than 2 g/dL drop in hemoglobin levels after a 24-hour period with stable vital signs within 30 days of admission. All bleeding episodes were confirmed by endoscopy.

iii) Unidentified cause of hemorrhage: the presence of blood in the stomach without finding a cause.

To ensure the completeness of 30-day follow-up information, patients were contacted by phone.

Statistical analysis was performed using the statistical software package SPSS version 25.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean (M) ± standard deviation (SD) for continuous variables. For data with normal distribution, inter-group comparisons were performed using Student’s t-test. Group comparisons with respect to categorical variables are performed using chi-square test. A probability value of  $P < 0.05$  was considered statistically significant. All variables were subject to univariate logistic regression, and odds ratios (ORs) were calculated between non-survived and survived groups, with a 95% confidence interval (CI). Variables were included in binary logistic regression if the corresponding  $P$ -value was less than 0.05. Binary logistic regression analysis was used to develop a multivariate model to determine the risk factors of death among critically ill patients.

## Results

Patient characteristics are reported in Table 1. The mean age of the 224 patients enrolled in the study was  $63.21 \pm 16.3$  years and most patients (72.8%) were male. On admission, the most common symptom was melena (96.5%), followed by hematemesis (47.8%) and hematochezia (1.7%). One hundred fifty (66.9%) patients had comorbidities, the most common being hypertension ( $n=122$ ), followed by atrial fibrillation ( $n=34$ ), heart failure ( $n=32$ ), and diabetes mellitus ( $n=32$ ). One hundred forty-nine (66.5%) patients were taking medications, including aspirin - 68(30.4%), NSAIDs - 21(9.3%), clopidogrel - 11(4.9%), vitamin K antagonists - 8(3.6%), and rivaroxaban (Xarelto) - 15(6.7%). A total of 26(11.6%) patients were referred for previous history of gastrointestinal bleeding, of which 7 had undergone surgical intervention. Smoking and alcohol use were observed only in men, among whom 69(30.8%) patients were smokers, and 67(29.9%) were alcohol users until the day of hospitalization. Fifty-three patients presented with tachycardia (heart rate > 100 bpm) and 41 with hypotension (systolic blood pressure < 90 mmHg) (Table 2).

The mean serum level of hemoglobin upon admission was 8.5g/dL. All patients underwent digital-rectal examination with patient approval, resulting in 187(83.5%) patients with melena, 7(3.1%) with hematochezia. A nasogastric tube was

performed on 90 patients, of whom 58 patients were positive. The mean number of units of packed RBCs transfused was  $2.23 \pm 1.73$ . The mean total RS was  $2.64 \pm 1.77$ , and 72(32.1%) patients had a score  $\geq 5$ , indicating a high risk of mortality. The mean GBS was  $11.75 \pm 2.06$ .

**Table 1.**

**Characteristics of the NVUGIB patients (n=224)**

Factor	Value [n (%), M $\pm$ SD]
Male sex	163 (72.8)
Age, year	63.21 $\pm$ 16.3
Hematemesis	117 (47.8)
Melena	216 (96.5)
Hematochezia	4 (1.78)
Heavy alcoholics	72 (39.1)
Current smokers	68 (37.0)
History of GIB	26 (11.6)
Comorbidities	150 (66.9)
Hypertension	122 (54.4)
Atrial fibrillation	34 (15.1)
Diabetes mellitus	32 (14.2)
Liver cirrhosis	2 (0.89)
Chronic kidney disease	13 (5.8)
Cerebrovascular disease	9 (4.0)
Heart failure	32 (14.2)
Cardiovascular disease	10(4.5)
Metastatic malignancy	8 (3.6)
Use of medication	149 (66.5)
Antiplatelet agents	79 (35.2)
NSAIDs	21 (9.3)
Vitamin K antagonist	8 (3.6)
Rivaroxaban (Xarelto)	15 (6.7)

In our study (Table 3), 142 endoscopies were performed within 12h, 45 within 12 to 24h, 22 within 24 to 48h, and 15 over 48h. The most common endoscopic diagnoses underlying NVUGIB episodes were duodenal ulcers (53.1%), followed by gastric ulcers (19.2%), erosive gastritis (7.1%), and esophageal ulcers (5.8%). Of 224 patients, 80.5% were high-risk stigmata (Forrest 1 - 38.4%, Forrest 2A - 18.3%, Forrest 2B - 23.8%) and 70(31.3%) underwent endoscopic treatment.

#### Clinical outcomes

Recurrent bleeding was recorded in 50(22.3%) patients, whereas emergency surgery was deemed necessary in only

10 cases. Forty-seven cases were in the first week. The mean hospital stay was  $7.7 \pm 3.4$  days. Of the 224 patients included in the study, 24(10.7%) died within one month of admission, whereas 20(8.9%) died during hospitalization, and 4(1.8%) died after discharge from the hospital. Among patients who died within 30 days, 17 died during the first 7 days. The mean age of death was  $76.42 \pm 12.59$  years; 95.8% of deaths were associated with one or more major comorbidities. Of all the patients, 14 underwent surgery.

**Table 2.**

**Clinical and laboratory data of the patients, at admission (n=224)**

Factor	Value [n (%), M $\pm$ SD]
Initial vital sign	
BP, mmHg	108.67 $\pm$ 16.8
Heart rate, bpm	90.02 $\pm$ 15.3
Hypotension (SBP < 90 mmHg)	41 (18.3)
Tachycardia (heart rate > 100 bpm)	53 (23.7)
Initial laboratory data	
Hemoglobin, g/dL	8.97 $\pm$ 2.95
RBC $\times 10^6/L$	3.07 $\pm$ 1.03
WBC, K/uL	11.5 $\pm$ 6.2
Platelets, K/uL	258 $\pm$ 133.9
Blood nitrogen urea, mg/dL	77.5 $\pm$ 45.2
Prothrombin time (PT), sec	76.5 $\pm$ 23.5
INR	1.71 $\pm$ 2.23
Positive nasogastric tube aspiration	58/90 (64.4)
Melena	187/224 (83.5)
Hematochezia	7/224 (3.1)
Mean transfusion requirement, no. of unit	2.23 $\pm$ 1.73
GBS	11.75 $\pm$ 2.06
RS	2.64 $\pm$ 1.77

#### Predictive factors for 30-day mortality in NVUGIB

In the univariate analysis, significant risk factors for 30-day mortality were age ( $P=0.000$ ), tachycardia ( $P=0.002$ ), hypertension ( $P=0.039$ ), chronic kidney disease ( $P=0.025$ ), heart failure ( $P=0.037$ ), diabetes mellitus ( $P=0.033$ ), malignancies ( $P=0.004$ ), low RBC ( $P=0.040$ ), leukocytosis ( $P=0.021$ ), increased urea ( $P=0.001$ ), aspirin ( $P=0.031$ ), warfarin ( $P=0.015$ ), hospital stay ( $P=0.000$ ),  $RS \geq 5$  ( $P=0.000$ ), and  $GBS > 12$  ( $P=0.010$ ) (Table 4).

Low RBC ( $P=0.043$  OR=0.413, CI 95%: 0.176-0.974), warfarin ( $P=0.036$ , OR= 10.547, CI 95%: 1.165-95.462), and  $RS > 5$  ( $P=0.034$ , OR=4.107, CI 95%: 1.114-15.139) were found to be independent predictive factors for mortality in the multivariate logistic regression (Table 5).

**Table 3.**  
**Endoscopic features and clinical outcomes of patients with NVUGIB (n = 224)**

Factor	Value [n (%)]
Urgent endoscopy(<12h)	142 (63.4)
Endoscopy findings	
Duodenal ulcer	119 (53.1)
Gastric ulcer	43 (19.2)
Erosive gastritis	16 (7.1)
Esophageal ulcer	13 (5.8)
Neoplasia	16 (7.1)
Mallory-Weiss syndrome	5 (2.2)
Angiodysplasia	1 (0.4)
Dieulafoy's lesion	2 (0.8)
No evidence of upper GIB	3 (1.3)

**Table 3 (continued).**  
**Endoscopic features and clinical outcomes of patients with NVUGIB (n = 224)**

Factor	Value [n (%)]
Forrest classification	
I	63/164 (38.4)
IIa	30/164 (18.3)
IIb	39/164 (23.8)
IIc	19/164 (11.5)
III	13/164 (8.0)
Outcomes	
Rebleeding	50 (22.3)
Death	24 (10.7)
During hospitalization	20 (8.9)
Hospital stay, day	7.7±3.4

**Table 4.**  
**Univariate analysis of clinical variables for mortality in patients with NVUGIB.**

Factor	Univariate analysis			
	30-Day death (+) (n = 24)	30-Day death (-) (n = 200)	P-value	OR (95% CI)
Age, yrs.	76.42±12.59	61.63±16.09	<b>0.000</b>	1.093 (1.046 -1.142)
Hematemesis	13 (54.2)	94 (47.0)	0.508	1.333 (0.570-3.117)
Melena	23 (95.8)	193 (96.5)	0.868	0.834 (0.098-7.086)
Alcohol	5 (20.8)	62 (31.0)	0.309	0.586 (0.209-1.640)
Current smoker	10 (41.7)	59 (29.5)	0.226	1.707 (0.718-4.060)
History of GIB	1 (4.1)	25 (12.5)	0.081	0.164 (0.021-1.246)
Comorbidities				
Hypertension	18 (75.0)	104 (52.0)	<b>0.039</b>	2.769 (1.055-7.266)
Atrial fibrillation	6 (25.0)	28 (14.0)	0.163	2.048 (0.748-5.603)
Diabetes mellitus	7 (29.2)	25 (12.5)	<b>0.033</b>	2.882 (1.087-7.641)
Chronic kidney disease	4 (16.7)	3 (1.5)	<b>0.025</b>	4.244 (1.198-15.033)
Cerebrovascular disease	3 (12.5)	6 (3.0)	0.318	1.593 (0.639-3.975)
Heart failure	7 (29.1)	25 (12.5)	<b>0.037</b>	2.076 (1.053-7.432)
Cardiovascular disease	2 (8.3)	8 (4.0)	0.099	1.468 (0.930-2.317)
Metastatic malignancy	4 (16.7)	4 (2.0)	<b>0.004</b>	2.355 (1.320-4.202)
Aspirin	12 (5.0)	56 (28.0)	<b>0.031</b>	2.571 (1.091-6.062)
Warfarin	3 (12.5)	4 (2.0)	<b>0.015</b>	7.000 (1.466-33.416)
Hypotension (SBP < 90 mmHg)	7 (29.2)	34 (17.0)	0.152	2.010 (0.774-5.221)
Tachycardia (HR >100 bpm)	12 (50.0)	41 (20.5)	<b>0.002</b>	3.878 (1.624-9.263)
Hemoglobin, g/dL	7.66 ±2.39	8.65±2.81	0.102	0.868 (0.733-1.028)
RBC × 10 <sup>6</sup> /L	2.67± 0.84	3.12±1.05	<b>0.040</b>	0.599 (0.368-0.978)
WBC, K/uL	11.7±6.8	10.4±5.8	<b>0.021</b>	1.065 (1.009-1.123)
Platelets, K/uL	279.0±115.47	255.47±136.0	0.417	1.001 (0.998-1.004)
BNU, mg/dL	108.88±58.43	73.75±42.05	<b>0.001</b>	1.014 (1.006-1.022)
Prothrombin time (PT), sec	61.35±29.40	78.11±22.27	<b>0.004</b>	0.977 (0.961-0.992)
Positive nasogastric tube	9 (37.5)	81 (4.1)	0.387	2.059 (0.401-10.560)
Positive rectal examination	21 (91.7)	166 (86.0)	0.124	0.479 (0.188-1.223)
Transfusion requirement, no. of unit	2.29±2.18	2.22±1.68	0.848	1.024 (0.804-1.304)

Table 4 (continued).

Univariate analysis of clinical variables for mortality in patients with NVUGIB.

Factor	Univariate analysis			
	30-Day death (+) (n = 24)	30-Day death (-) (n = 200)	P-value	OR (95% CI)
GBS >12	17 (70.8)	84 (42.0)	<b>0.010</b>	3.354 (1.331-8.448)
RS >5	18 (75.0)	54 (27.0)	<b>0.000</b>	8.111 (3.059-21.509)
Urgent endoscopy(<12h)	15 (62.5)	127 (63.5)	0.893	0.895 (0.178-4.507)
Endoscopy findings				
Peptic ulcer disease	18 (75.0)	144 (72)	0.853	1.103 (0.390-3.120)
Non-Peptic ulcer disease	5 (21.0)	41 (20.5)	0.830	1.133 (0.362-3.549)
Neoplasia	1 (4.1)	15 (7.5)	0.555	0.536 (0.068-4.250)
Forrest classification				
I	8 (33.3)	55 (27.5)	0.440	1.487 (0.543-4.067)
IIA	2 (8.3)	28 (14.0)	0.369	0.497 (0.108-2.283)
IIB	5 (20.8)	34 (17.0)	0.870	1.104 (0.338-3.605)
Rebleeding	7 (29.2)	43 (21.5)	0.397	1.503 (0.586-3.859)
Hospital stay, day	7.04	6.76	<b>0.000</b>	0.704 (0.579-0.856)

Table 5.

Logistic Regression Model to determine the predictors of mortality.

Factor	P-value	OR	95% CI	
			Lower	Upper
Age	0.066	1.053	0.997	1.113
RBC × 10 <sup>6</sup> /uL	<b>0.043</b>	0.413	0.176	0.974
WBC, K/uL	0.635	1.017	0.948	1.092
BUN, mg/dL	0.686	1.003	0.990	1.015
Heart rate > 100 bpm	0.223	2.134	0.631	7.220
Hypertension	0.472	0.591	0.141	2.479
Heart failure	0.798	0.831	0.201	3.438
Aspirin	0.066	3.519	0.920	13.467
Warfarin	<b>0.036</b>	10.547	1.165	95.462
GBS >12	0.592	0.655	0.139	3.079
RS>5	<b>0.034</b>	4.107	1.114	15.139
Hospital stay, day	0.056	0.700	0.566	0.864

## Discussion

NVUGIB is one of the most common medical emergencies and often represents a life-threatening event. The results of this study have differences from and similarities to other studies. Acute NVUGIB remains a common medical problem associated with high morbidity, 30-day mortality, and healthcare costs.<sup>(1)</sup> The incidence of acute upper gastrointestinal bleeding in the Western world is 103 per 100,000 adults annually, with a mortality of about 2%-10%.<sup>(4)</sup>

Our study enrolled 224 patients with a mean age of 63.21±16.3 years. Our patients were younger than those in Greek (66±15),<sup>(11)</sup> Italian (68±16),<sup>(12)</sup> and Canadian (66±17)<sup>(13)</sup>

studies and older than in the Turkish study (57.75±18.85).<sup>(13)</sup> Male patients accounted for 72.8% of participants—the same model as in Western studies.

In our study, 66.9% of patients had comorbidities, the most common of which were hypertension (122[54.4%]), followed by atrial fibrillation (34[15.1%]), diabetes mellitus (32[14.2%]), and heart failure (32[14.2%]). The same results have been seen in different studies.

As for the use of medications, in our study, the prevalence of aspirin use was 30.3%, 9.8% for vitamin K antagonists, 9.3% for NSAIDs, 6.6% for rivaroxaban (Xarelto), and 4.9% for clopidogrel. Compared to other studies,<sup>(12-14)</sup> it turned out that we had a higher use of aspirin and lower of NSAIDs.

At admission, the most frequent clinical presentation was melena (96.5%), 47.8% with hematemesis, and 1.7% with hematochezia. In our study, there was no significant correlation with mortality, while in the Turkish study,<sup>(14)</sup> hematemesis was one of the predictors of patient management and clinical outcomes of NVUGIB.

The most frequent source of bleeding was peptic ulcers, among which duodenal ulcers (53.1%) prevailed, followed by gastric ulcers (19.2%) and erosive gastritis (7.1%). The frequency was similar to that of previous studies conducted at the Gastrohepatology Department in Mother Teresa Hospital in 2015<sup>(15)</sup> and 2019.<sup>(16)</sup> Compared to Western studies<sup>(13,17)</sup> we had a higher percentage of peptic ulcers, similar to the Turkish study.<sup>(14)</sup> This result is due to the lack of investigation and the failure to eradicate *H. pylori*, knowing that its eradication has been associated with a decrease of peptic ulcers.

Also, there was a high percentage of high-risk stigmata lesions (Forrest 1 - 38.4%, Forrest 2A - 18.3%, Forrest 2B - 23.8%, and Forrest 3 - 8.0%), unlike in Western studies.<sup>(12-14)</sup> This may be for several reasons, including low socio-economic conditions and patient negligence. Also, the study

was conducted in a tertiary center, and the referral of active bleeding and severe cases is higher even from the regional hospitals.

Regarding the endoscopy time in our study, 63.4% were done within 12 hours, and 20.0% within 12-24 hours. This result was similar to the Korean study (65.8%) of Lee et al.<sup>(18)</sup> In other studies, most endoscopies are performed within 24 hours.<sup>(12,13)</sup> In many studies and gastroenterology societies, endoscopy is not recommended within 12 hours because no change in the outcomes has been observed.<sup>(19-21)</sup> And in our study, no significant correlation was found between the time of endoscopy and mortality.

The recurrence of bleeding in our study was 22.3%, which was higher than in the Italian, Canadian, and Turkish studies (3.2%, 14.1%, and 9.0%, respectively).<sup>(12-14)</sup> All the episodes were during the hospitalization and mostly within 24 hours. The high percentage is due to the limited endoscopic treatment procedures and the high rate of high-risk stigmata ulcerative lesions. Also, no significant correlation was found between rebleeding and mortality. In some other studies, rebleeding was considered an independent predictive factor for mortality.<sup>(11,22)</sup> The number of surgical interventions (10) was higher than in the Italian and Turkish studies (1.3% and 2.6%, respectively).<sup>(12,14)</sup> This is due to the limited endoscopic procedures.

Out of 224 patients included in the study, 24(10.7%) died within 30 days of admission, 20(8.9%) died during hospitalization, and 4(1.8%) died after discharge.

The mortality rate was higher than that in Western countries such as the USA and most of Europe, and similar to mortality in Denmark (10.5%-11%).<sup>(3)</sup> This may be because the study was done in a tertiary hospital center, where the patients' conditions may be more severe and contribute to poor clinical outcomes and higher mortality rates. The higher mortality rate occurred in the first week (70.8%), and 29.2% had a recurrence of bleeding. These findings were similar to the findings of studies conducted in Italy.<sup>(12)</sup> The mean age of death was  $76.42 \pm 12.59$ , the same as studies in Italy ( $76.6 \pm 14.0$ )<sup>(12)</sup> and Canada ( $72 \pm 12.6$ ),<sup>(13)</sup> in which advanced age was also an independent predictive factor for mortality.

Studies in the literature refer to comorbidities as independent risk factors not only for gastrointestinal bleeding but also for mortality.<sup>(23)</sup> They are also important factors in scoring systems for patient risk assessment.<sup>(24)</sup>

In our study, 95.8% of deaths were associated with one or more major comorbidities. The most frequent comorbidities were hypertension, atrial fibrillation, heart failure, chronic kidney disease, and malignancies.

Also, many studies have identified many risk factors for mortality in NVUGIB, such as hypotension, tachycardia, advanced age, comorbidities, coagulopathy, low hemoglobin, anticoagulants, and antiplatelets.<sup>(23,25)</sup> Some of these risk factors have also been identified in our study. In the univariate analysis, significant risk factors for 30-day mortality were age ( $P=0.000$ ), tachycardia ( $P=0.002$ ), hypertension ( $P=0.039$ ), chronic kidney disease ( $P=0.025$ ), heart failure ( $P=0.037$ ), diabetes mellitus ( $P=0.033$ ), malignancies ( $P=0.004$ ), low RBC ( $P=0.040$ ), leukocytosis ( $P=0.021$ ), increased urea

( $P=0.001$ ), aspirin ( $P=0.031$ ), warfarin ( $P=0.015$ ), hospital stay ( $P=0.000$ ),  $RS \geq 5$  ( $P=0.000$ ), and  $GBS > 12$  ( $P=0.010$ ).

In many studies, leukocytosis has been associated with a poor prognosis and mortality. It has been hypothesized that the reason leukocytosis could lead to mortality could be an infectious or inflammatory condition.<sup>(26)</sup> Regarding medications, aspirin and warfarin were found to be risk factors for mortality. Aspirin is thought to increase mortality due to the increased severity of ulcer and hemorrhagic lesions and antiplatelet effects.<sup>(8)</sup> Warfarin is known as a risk factor for mortality,<sup>(27)</sup> which we also found in our study; and it is thought that it may be due to its anticoagulant effects and irregular monitoring of PT and INR. In the Multivariate logistic regression, after the exclusion of confounding factors, low RBC ( $P=0.043$ , OR=0.413, CI 95%: 0.176-0.974), warfarin ( $P=0.036$ , OR=10.547, CI 95%: 1.165-95.462), and  $RS > 5$  ( $P=0.034$ , OR=4.107, CI95%: 1.114-15.139) were found to be independent predictive factors for mortality. Similar results were observed in different studies.<sup>(12, 17,22)</sup>

In our study, both RS and GBS scores were calculated for all the patients on the basis of clinical and endoscopic variables.<sup>(28)</sup> Thirty-day mortality rates tended to be higher in patients with a high  $RS > 5$  and  $GBS > 12$  in univariate analysis. Also, RS was identified as an independent predictor of mortality. It is important to identify these factors because they can be used before endoscopy to identify high-risk patients, for whom a high level of care is needed to prevent adverse outcomes.

Our study has some limitations: First, our study was realized in a short period and had a small sample size. This could lead to bias. Second, although *H. pylori* is the main cause of peptic ulcers and its eradication reduces the possibility of rebleeding, the patients were not tested.<sup>(29,30)</sup>

**In conclusion**, our study shows that the 30-day mortality rate remained high after NVUGIB, especially during hospitalization. Low RBC, warfarin, and  $RS > 5$  were independent factors of mortality in patients with NVUGIB. These findings show that high-risk patients should be carefully monitored to prevent adverse outcomes.

## Competing Interests

The authors declare that they have no competing interests.

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