Original article

Factors predicting mortality of elderly patients with acute upper gastrointestinal bleeding

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Background: Acute upper gastrointestinal bleeding (UGIB) is a common gastrointestinal disease emergency and a cause of morbidity and mortality.
Objectives: To assess the clinical outcomes and explore predictive factors for mortality of elderly patients with acute UGIB.
Methods: During the study period from January 2010 to September 2011, we prospectively enrolled 981 patients presenting with UGIB from 11 hospitals (mean age ± standard deviation (SD), 59.4 ± 14.9 years; range, 17−94 years; including 661 men). Of these 981 patients, 499 (50.9%) were elderly. Basic demographic data and clinical findings, and Rockall scores were collected and calculated.
Results: We studied 499 elderly patients. Their mean age ± SD was 71.63 ± 7.65 years. The 30-day mortality rate was 9% and rebleeding was just 1%. Regression analysis showed a pulse rate >100 beats per min at first visit, red blood in a nasogastric aspiration, comorbidity with coronary artery disease, and creatinine >1.5 mg/dL were independent predictive factors of 30-day mortality.
Conclusions: Peptic ulcer bleeding is a major cause of acute UGBI in the elderly. We recommend patients with predictive factors of mortality, pulse rate >100 beats per min at first visit, red blood in nasogastric aspiration, comorbidity with coronary artery disease, and creatinine >1.5 mg/dL be closely monitored and treated promptly. Reducing mortality from peptic ulcer bleeding should focus on preventing peptic ulcer occurrence as a result of ulcerogenic medications.

Keywords: Elderly patients, mortality, predictive factors, upper gastrointestinal bleeding

Acute upper gastrointestinal bleeding (UGIB) is a common gastrointestinal emergency and cause of hospital admission. Its prevalence ranges between 37- 172 per 100,000 adult persons and mortality ranges between 3% and 14% [1]. The incidence of UGIB has decreased significantly in the past 10 years, but

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mortality and rebleeding rates have not [2], and the mortality rate has increased in elderly patients. Initial assessment and rapid resuscitation of patients with UGIB are important from the outset. Further investigations should be conducted after stabilization. Various scoring systems have been developed to identify and stratify patients from different risk levels [3-5]. The commonly used scoring systems are the Rockall and Blatchford systems, the Baylor bleeding score, and the Cedars-Sinai Medical Center Predictive Index [5]. The challenge in caring for patients is how to identify those who are at risk of rebleeding and death. The Rockall score is the best-known risk stratification tool for patients with UGIB to predict rebleeding and mortality [3]. The Rockall score consists of patient age, hemodynamic parameters, comorbidities, and endoscopic findings. A strength of the Rockall score lies in its simplicity. It can be measured soon after presentation with UGIB as a clinical Rockall score or can be measured completely after endoscopy as a complete Rockall score [6]. The Rockall score has been validated in many countries and used to predict outcomes [7-10]. Thailand is confronted with an aging society. Although age has been considered as predictive of an adverse outcome of UGIB in several studies [3, 4, 11, 12], one study in Thailand did not find that advanced age influenced adverse outcomes [13]. Every patient, but especially elderly patients, should be stratified for risk at first presentation with UGIB. Predictive factors should be evaluated to estimate mortality in elderly patients with UGIB.

The aim of the present study was to determine the Rockall score and other factors predicting outcome of elderly patients with UGIB.

Material and methods

The study was approved by the institutional review board of each hospital involved. The hospitals included King Chulalongkorn Memorial Hospital (approval No. 480/51), Maharat Nakhonratchasima Hospital (approval No. 0027.124/443), Sawanpracharak Hospital (approval No.1/2552), Surin Hospital (approval No. 0027.102/12475), Maharaj Nakhonsithammarat Hospital (approval No. 002/2555), HRH Princess Maha Chakri Sirindhorn Medical Center (approval number 49/2552 SWUEC 5-5/2552), Chonburi Hospital (approval No. 23/2553), Bangkok Metropolitan Administration General Hospital (approval No. W68), Bangkok Hospital (approval 23/12/2552), Rajavithi

Hospital (approval No. 52116), and Thammasat University Hospital (approval No. MTU-E-1-78/ 52).Written informed consent was obtained from each patient or their nearest relative before enrollment at each center.

We prospectively enrolled 981 patients with UGIB from 11 hospitals in Thailand during the study period from January 2010 to September 2011. The mean age $\pm$ SD of the patients was 59.4 $\pm$ 14.9 years (range 17 − 94 years) and they included 661 men (67%). Of 981 patients, 499 (50.9%) were elderly with UGIB. Management of UGIB was based on the Consensus for Clinical Practice Guidelines for the management of UGIB from the Thai Association for Gastrointestinal Endoscopy. All patients presenting to the emergency or outpatient departments with acute UGIB were clinically assessed initially and hemodynamically stabilized. Gastroenterologists were informed. Every patient was admitted to hospital and an esophagogastroduodenoscopy (EGD) was performed according to a standardized examination protocol. If endoscopy was not available, the patient was considered for referral. Clinical management, including medication, fluid resuscitation, and the timing of endoscopy and endoscopic therapy was decided by each individual gastroenterologist. Packed erythrocyte (PRC) transfusion was considered when hemoglobin was less than 9 g/dL. If endoscopic treatment failed, the rescue therapy was surgery or embolization. The Rockall score is the best-known of all tools for risk stratification of patients with acute UGIB. It was formulated by medical institutions in the England in 1996 and its primary negative outcome is mortality [3]. The Rockall score consists of 5 variables and is the most widely used and validated tool to predict outcome in clinical practice [6]. In the present study, we used complete Rockall scores to predict outcome in elderly patients with acute UGIB and search for other predictive factors.

Definitions and outcomes

UGIB was defined as hematemesis (including "coffee grounds" vomiting), melena, and hematochezia. All patients underwent EGD during the study period. The definition of elderly patient was "age more than 60 years".

The primary outcome was 30 day mortality and its predictor, which included all causes with mortality occurring within the 30 days of hospitalization.

High risk stigmata from endoscopic findings were characterized as adherent clots, nonbleeding, or bleeding from visible vessels and varices with a red color or a white nipple sign. Rebleeding was defined as a new episode of objective evidence of UGIB, after the initial bleeding had stopped, with a decreased hemoglobin concentration of at least 2 g/dL per day, or with the need for more than two units of PRC per day, or with circulatory instability.

Statistical analysis

IBM SPSS Statistics for Windows (version 19.0; IBM Corp, Armonk, NY, USA) was used for data analysis. Rockall score of all patients were calculated based on individual variables and summarized as complete Rockall score. Continuous variables were compared using a t test and categorical variables were compared using a chi square or Fisher exact test. Logistic regression analysis was conducted to determine independent predictors of 30-day mortality. A two-sided $P < 0.05$ was considered significant.

Results

Patient characteristics

We included 499 elderly patients (300 male, 199 female) with acute UGIB in this study. Their age range was from 60 to 94 years. Most of the patients presented with hematemesis. Comorbidities were found in 331 patients including hypertension, diabetes mellitus, cardiovascular disease, renal disease, and cirrhosis. Antiplatelet drugs (aspirin, clopidogrel), nonsteroidal anti-inflammatory drugs (NSAIDs), and warfarin were used regularly in 171 patients (**Table 1**). EGD was performed within 12-48 h of admission. The vast majority of the patients (98%) were given a proton-pump inhibitor orally, intermittently or continuously intravenously, and in cases with suspected variceal bleeding, vasoactive drugs were given. Interventions were performed in high risk lesion of peptic ulcer bleeding group with a heater probe or argon plasma coagulation in 47 cases and a hemoclip in 28 cases. Cyanoacrylate glue injections were applied in 9 cases for treatment of gastric varices and esophageal varix ligations were applied in 35 cases for esophageal variceal bleeding.

The most common cause of acute UGIB was peptic ulcer bleeding (**Table 2**). The 30 day mortality in elderly patients with UGIB was 9% and rebleeding after initial endoscopy was found in only 1% (**Table 3**). There was no significance difference in mortality between the nonelderly and elderly group (data not shown). The Rockall score was calculated based on individual data and divided into 3 risk groups (**Table 4**).

Table 1. Characteristics of 499 elderly patients presenting with acute upper gastrointestinal bleeding

Variable [number (%) or mean ± SD]	Total (n = 499)
Age (year)	71.6 ± 7.65
Male: n (%)	300 (60.1%)
Presenting symptom: n (%)	
Hematemesis	250 (50.1%)
Melena	221 (44.3%)
Hematochezia	28 (5.6%)
Clinical findings: n (%)	
Pulse rate >100 beats/min	26 (5.2%)
Systolic blood pressure <100 mmHg	26 (5.2%)
Presence of hemodynamic instability (pulse >100 bpm and systolic blood pressure <100 mmHg)	71 (14.2%)
Nasogastric lavage findings: n (%)	
Red blood on nasogastric lavage	60 (12%)
"Coffee grounds"	181 (36.3%)
Normal content	144 (28.8%)
No nasogastric lavage	114 (22.8%)
Concomitant illness	
Diabetes mellitus	125 (25%)
Hypertension	220 (44%)
Cardiovascular disease	44 (8.8%)
Chronic renal failure	37 (7.4%)
Cirrhosis	56 (11.2%)

Table 1. Characteristics of 499 elderly patients presenting with acute upper gastrointestinal bleeding (Con)

Variable [number (%) or mean ± SD]	Total (n = 499)
Alcohol drinking: n (%)	73 (14.6%)
Smoking: n (%)	80 (16%)
Previous use of medication: n (%)	
Low-dose aspirin	86 (17.2%)
Non-steroidal anti-inflammatory drugs	77 (15.4%)
Warfarin	9 (1.8%)
Clopidogrel	13 (2.6%)
Laboratory features at presentation	
Hemoglobin (g/dL)	8.70 ± 3.3
White blood count ($10^3/\mu$L)	11.6 ± 12.9
Platelets ($10^3/\mu$L)	218.7 ± 115.5
International normalized ratio of prothrombin time	1.2 ± 0.8
Blood urea nitrogen (mg/dL)	32.8 ± 23.1
Creatinine (mg/dL)	1.7 ± 1.5
Blood transfusion	
Pack red cell: n (%)	354 (70.9%)
Fresh frozen plasma: n (%)	58 (11.6%)
Platelets: n (%)	35 (7%)
Proton pump inhibitor: n (%)	
Oral route	25 (5%)
Intravenous bolus	392 (78.5%)
Intravenous continuous drip	72 (14.4%)

Table 2. Endoscopic findings in 499 elderly patients presenting with acute upper gastrointestinal bleeding

Variable	Total (n = 499)
Peptic ulcer as source of bleeding: n (%)	
Clean base	263 (52.7%)
Pigment spot	37 (7.4%)
Adherent clot	8 (1.6%)
Nonbleeding visible vessel	51 (10.2%)
Bleeding visible vessel	36 (7.2%)
Variceal bleeding as source of bleeding: n (%)	
Esophageal varices (EV)	41 (8.2%)
Gastric varices (GV)	2 (0.4%)
EV and GV	16 (3.2%)
Portal hypertensive gastropathy	46 (9.2%)
Other Endoscopic findings (%)	
Mallory–Weiss tear	8 (1.6%)
Esophagitis	19 (3.8%)
Ulcerative mass	5 (1%)
Gastroduodenitis	136 (27.2%)
Angiectasia	3 (0.6%)
No lesion identified	3 (0.6%)

Some patients presented with more than 1 endoscopic finding.

Table 3. Clinical outcomes of elderly patients presenting with acute upper gastrointestinal bleeding

Variable	N = 499
Endoscopic therapy for bleeding peptic ulcer: n	
Epinephrine injection	89
Coaptive thermocoagulation	47
Hemoclip	28
Combined therapy	70
Endoscopic therapy for variceal bleeding: n	
Endoscopic band ligation	35
Cyanoacrylate injection	9
Hospital stay: days	13.9
Rebleeding within 30 days: n (%)	5 (1%)
In hospital mortality: n (%)	17 (3.4%)
30-day mortality: n (%)	45 (9%)
Surgery or intervention: n (%)	6 (1.2%)

Table 4. Rockall score stratification into 3 groups with percentage of rebleeding and mortality of elderly patients presenting with acute upper gastrointestinal bleeding

Group	Score	Cases (%)	Rebleeding (%)	Mortality (%)
Low-risk	<3	244 (48.9%)	1 (0.2%)	21 (8.6%)
Moderate-risk	3-4	199 (39.9%)	3 (0.60%)	18 (9.0%)
High-risk	>4	56 (11.2%)	1 (0.2%)	6 (11%)

Subgroup analysis of patients with or without survival outcome

In hospital mortality and 1 month mortality were 3.4% and 9%, respectively. The common causes of death were sepsis and multiorgan failure. Mean age, hemoglobin, blood urea nitrogen, and creatinine levels were significantly higher in patients in the nonsurvival group than in the survival group (**Table 5**). The following variables had significant influence on predicting mortality of elderly patients by univariate analysis: comorbidities with coronary artery disease (CAD), chronic kidney disease, hemodynamic instability, pulse >100 beats per min, red blood in nasogastric lavage, fresh-frozen plasma transfusion, endoscopic finding of esophageal and gastric varices, and glue injection (**Table 6**). Multivariate analysis showed that mortality was significantly associated with hemodynamic instability at presentation (pulse rate >100 beats per min), comorbidity with CAD, red blood in nasogastric lavage, and creatinine more than 1.5 mg/dL (**Table 7**).

Table 5. Predictor of 30-day mortality by univariate analysis (continuous variables) of 499 elderly patients presenting with UGIB

Predictors	Death (n = 45)	Survival group (n = 454)	P
Mean age (± SD) in years	74.1 ± 7.3	71.4 ± 7.7	0.01
Hemoglobin (g/dL)	9.7 ± 5.5	8.6 ± 3	0.02
Platelet count	213.9 ± 134.1	219.2 ± 113.6	0.38
International normalized ratio of prothrombin time	1.4 ± 1.3	1.2 ± 0.8	0.06
Blood urea nitrogen	40.7 ± 23.6	32 ± 22.9	0.008
Creatinine (mg/dL)	2.5 ± 2.1	1.6 ± 1.5	0.004
Rockall score	2.9 ± 1.7	2.7 ± 1.5	0.4

Table 6. Predictors of 30 day mortality of 499 elderly patients presenting with acute upper gastrointestinal bleeding on univariate analysis (categorical variables)

Predictors	No. of deaths/ No. of patients with predictors	No. of deaths/ No. of patients without predictors	P	Odds Ratio (95% CI)
Coronary artery disease	8/44 (18%)	37/455 (8%)	0.048	2.49 (1.1–5.7)
Chronic kidney disease	7/37 (19%)	38/462 (8%)	0.03	2.58 (1.1–6.3)
Presence of hemodynamic instability (pulse >100 bpm and SBP <100 mmHg)	12/62 (19%)	33/437 (8%)	0.003	2.9 (1.4–5.9)
Pulse rate >100 bpm	8/26 (31%)	37/473 (8%)	0.001	5.19 (2.1–12.7)
Red blood in NGT	18/60 (30%)	27/43 (6%)	<0.001	6.48 (3.3–12.7)
FFP transfusion	11/58 (19%)	34/441 (8%)	0.006	2.73 (1.3–5.7)
EV and GV finding	4/16 (25%)	41/433 (10%)	0.048	3.56 (1.1–11.5)
Cyanoacrylate glue injection	4/9 (44%)	41/490 (8%)	0.005	8.68 (2.2–33.6)

CI, confidence interval; SBP, systolic blood pressure; NGT, nasogastric tube; FFP, fresh-frozen plasma; EV, esophageal varices; GV, gastric varices

Table 7. Independent predictors of 30 day mortality (logistic regression analysis)

Predictors	P	Odds Ratio	95% CI
Pulse rate >100 beats/min	0.019	3.91	1.2–12.2
Red blood in nasogastric tube	<0.001	5.44	2.3–12.6
Creatinine more than 1.5	0.002	3.13	1.5–6.5
Coronary artery disease	0.028	3.27	1.1–9.4

Discussion

The main findings of the present study were factors predictive for mortality of elderly patients with acute UGIB. The elderly are a special population who are prone to have more complications from any illness because of their physiological instability, and from comorbidities and medications. In this study, we focused on elderly patients with acute UGIB, in terms of mortality and factors predictive of mortality. The cause of UGIB was peptic ulcer bleeding in 84.8% of patients, which is consistent with previous studies [13-16]. The cause of peptic ulcer bleeding might be from ulcerogenic medications (including aspirin, clopidogrel, NSAIDs, and warfarin). Rebleeding in this study was found to be around 1%; very low compared with a previous study [13]. Mortality was found to be 9% as consistent with previous studies [12-13], but lower than in some studies that found high mortality in the elderly ranging from 12% to 25% [17-19]. An extremely elderly population had mortality rates higher than a moderately elderly group (13.6% and 8.1% respectively), with no significant difference between them (P = 0.1). The low mortality found in the present study may be explained by new devices used to stop bleeding, and the skill of the physicians as exemplified by the low rate of surgical rescue and invasive radiological interventions (1.6%) reported. The leading causes of death were sepsis and multiorgan failure.

In the present study, there were no differences in mortality among elderly patients with UGIB and low, moderate, or high Rockall scores, which differs from earlier research that found the Rockall score to be clinically useful and accurate in predicting rebleeding, rescue surgery, and mortality in elderly patients [12], and patients in all age groups [20-23]. However, if we look at individual factors in the Rockall score, the results are different in univariate analysis. The present study found pulse rate >100 beats per min, comorbidities with CAD or chronic kidney disease, and endoscopic findings of gastric varices were significantly associated with mortality.

Factors predictive of mortality are clinically important in the management of disease because patients with such factors should be evaluated first and repeatedly. We found that independent factors

predictive of mortality were a pulse rate of >100 beats per min, red blood in the nasogastric tube, comorbidity with coronary artery disease, and creatinine more than 1.5 mg/dL. This information is important in clinical practice because these factors in patients should alert doctors to perform prompt resuscitation, urgent endoscopic diagnosis, and treatment to reduce mortality. Previous studies found early predictors of adverse prognosis in acute UGIB in the elderly, were shock, severe comorbidities, red blood emesis, variceal bleeding, gastric ulcer larger than 2 cm, and units of blood transfused [11, 24-28]. Rapid clinical triage decisions in emergency acute UGIB is crucial. The most common cause of acute UGIB was peptic ulcer bleeding (gastric or duodenal ulcer), which is not surprising considering *Helicobacter pylori* infection is found in 48.2% of the Thai population [29]. Explanations for the cause of peptic ulcer bleeding are common concomitant use of aspirin, clopidogrel for prevention of atherosclerosis, and excessive use of NSAIDs for musculoskeletal pain.

The strength of this study is the use of sample data from multiple centers in four regions of Thailand, which reflect authentic life clinical situations and practices. There are some limitations in this study. First, the decision regarding the endoscopic therapy and blood transfusion is subjective, and there may be variability between gastroenterologists among the 11 centers. Second, emergency endoscopies were not available in several of the study centers. Third, patients with UGIB managed as outpatients were not enrolled in this study.

Conclusion

The 30 day mortality in elderly patients with UGIB was found to be 9%. The most common cause was peptic ulcer bleeding. Factors predictive of mortality were found to be a pulse rate of more than 100 beats per min on first visit, red blood cells in nasogastric aspiration, and comorbidities, such as having CAD or a creatinine level of more than 1.5 mg/dL. These factors should be taken into consideration when triaging high risk patients for immediate attention, resuscitation, close monitoring, and early treatment.

Acknowledgment

Conflict of interest statement

The authors declare that there is no conflict of interest in this research.

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