Original Article

Upper Gastrointestinal Bleeding Score for Differentiating Variceal and Nonvariceal Upper Gastrointestinal Bleeding

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ABSTRACT

Background: Upper gastrointestinal bleeding (UGIB) is a common gastrointestinal emergency. In the place where urgent esophagogastroduodenoscopy (EGD) is unavailable, empirical pharmacological therapy with vasoactive drugs for variceal bleeding or proton pump inhibitors for nonvariceal bleeding is recommended. However, the values of using clinical data for predicting the types of UGIB are unclear. The aim of this study is to determine the values and efficacy of clinical and basic laboratory parameters in predicting the types of UGIB.

Methods: All patients with UGIB underwent EGD within 72 hours. Clinical and basic laboratory parameters were collected prospectively. The associations between each factors and the final diagnosis of UGIB were assessed using univariate and multivariate analysis. Model of a predicting score to predict the type of UGIB was developed.

Results: Two hundreds and sixty-one patients with UGIB were enrolled into the study. Of these, 47 (18%) were variceal and 214 (82%) were nonvariceal bleeding. Univariate analysis identified 27 distinct parameters associated with the types of UGIB. A stepwise logistic regression analysis identified 3 variables as independent factors to predict types of UGIB; previous diagnosis of cirrhosis or presence of signs of chronic liver disease (OR 22.4, 95% CI 8.3-60.4), red or bloody vomitus (OR 4.6, 95% CI 1.7-11.9), and red or bloody NG aspirate (OR 3.3, 95% CI 1.3-8.3). Variceal bleeding predicting scoring model was developed as: $Z = (3.1 \times$ *previously diagnosed cirrhosis or presence of signs of chronic liver disease)* $+ (1.4 \times$ *red or bloody vomitus)* $+ (1.2 \times$ *red or bloody NG aspirate)* $- 4.1$, while 1 and 0 are used for the presence and absence of each factor, respectively. The probability of variceal bleeding is calculated from $1/(1+e^{-Z})$ or by plotting to the exponential graph. The probabilities of variceal bleeding are >90%, >60%, <10% and <5% for the presence of 3, 2, 1 and 0 factors, respectively.

Conclusion: Three clinical parameters and variceal bleeding predicting score are useful to predict the types of UGIB and may aid clinical judgment for the initial management of UGIB before endoscopy.

Key words : UGIB, gastrointestinal bleeding

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INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a common gastrointestinal emergency which carries a mortality rate of 6-8%[1]. Causes of UGIB have been classified to variceal (e.g. esophageal and gastric varices) and non-variceal (e.g. peptic ulcer, erosive gastroduodenitis, reflux esophagitis, tumor, vascular ectatsia, etc.). Currently, esophagogastroduodenoscopy (EGD) is the standard investigation of choice for UGIB since it provides both diagnosis and treatment of the causes of UGIB. Therefore, the availability of emergency EGD within 24 hours is most desirable. However, in real life situation, emergency EGD is rarely available in most health care centers due to the insufficiency of well-trained endoscopists, teams or equipments. Thus, most patients are usually treated medically before referring for EGD at the centers with available facilities.

Most practice guideline on UGIB9[1] including Thailand Guideline 2004 recommend giving empirical treatments to patients with UGIB while waiting for EGD. If variceal bleeding is suspected, empirical treatment with vasoactive drugs (e.g. somatostatin, octreotide, terlipressin, etc.) is strongly recommended, because they can stop bleeding in up to 70-80% of cases[2] and a decreased mortality has even been shown with some drug, (i.e. terlipressin). By contrast, for suspected nonvariceal bleeding, empirical treatment with high-dose proton pump inhibitor (PPI) either in intravenous or oral double-dose forms is recommended.

In the clinical view point, to diagnose variceal bleeding precisely and promptly giving vasoactive drugs to the patients is very crucial because variceal bleeding has a very high early mortality rate up to 30% and 47-74% of then will have recurrent bleeding[2]. To predict which patient has variceal bleeding is sometimes difficult. Some authors suggest that the clinical signs of cirrhosis[3], portal hypertension, painless hematemesis and bleeding with significant change in hemodynamics may indicate variceal bleeding. However, this strategy has not been validated or confirmed. For example, one study showed that, in patients with cirrhosis and first variceal bleeding, 40% have no signs of chronic liver disease or signs of portal hypertension at all[4]. By contrast, NSAID user, the presence of dyspepsia or coffee-ground NG aspirate are in favor of nonvariceal bleeding. These suggestions also have never been confirmed. To our knowledge, there has been no study using the detailed clinical parameters and basic investigations to assess and predict the causes of UGIB as variceal or nonvariceal causes.

The aim of this study is to assess the clinical and basic laboratory parameters that can help differentiating variceal and nonvariceal causes of UGIB before EGD. If they are identified, a model of scoring system will be developed based on these parameters and the accuracy of the model to predict cause of UGIB will be analyzed.

PATIENTS AND METHODS

All patients who presented with acute UGIB at Siriraj Hospital during June 2006 to December 2006 were prospectively enrolled into the study.

Inclusion criteria were: 1. UGIB defined by the presence of hematemesis, melena or hematochezia, and a positive NG tube aspiration for a coffee ground, black or bloody content. 2. Underwent EGD within 72 hours after admission to the hospitals. 3. Age ≥15 years old. Exclusion criteria were patients who refused performing EGD and if definite cause of UGIB is undetermined.

Data collection

Data were collected by gastroenterology fellows at the time of patients' presentation. Patients' history includes age, sex, appearance of vomitus, (red bloody, coffee-ground, clear), appearance of stool (red or maroon stool, melena, brown or yellow stool), presence of dyspepsia or abdominal pain, underlying cirrhosis, history of previous variceal or non-variceal bleeding within 1 year), other comorbid diseases (e.g. acute or chronic kidney diseases, diabetes, hypertension, cardiac diseases, chronic lung diseases, and cerebrovascular diseases, etc), history of medications used within 4 weeks (i.e. nonsteroidal anti-inflammatory drugs (NSAIDs) aspirin, anticoagulant, corticosteroid and alcohol)

Physical examinations include blood pressure (presence of shock or BP <90/60 mmHg), heart rate (presence of tachycardia, HR >100 beats/min), degree of pallor (marked, mild, moderate, none), findings on nasogastric (NG) tube aspiration (red blood, coffee ground, clear), findings on rectal examination (red or maroon stool, melena, brownish to yellowish stool), Presence signs of chronic liver disease (palmar erythema, spider nevi, parotid gland enlargement, gynecomastia, testicular atrophy, etc), epigastric tenderness, ascites, splenomegaly, and hepatic encephalopathy.

Laboratory data includes hemoglobin, hematocrit, white blood cells count, platelet count, BUN, creatinine, prothrombin time, and panel of liver chemistry tests.

Esophagogastroduodenoscopy

EGD was performed within 72 hours after admission in all cases. Causes of bleedings were classified to variceal (esophageal or gastric varices) and nonvariceal (others causes).

Statistical analysis

Statistical analysis was done by using SPSS version 13.0. Univariate analysis of the correlation between clinical parameters and causes of UGIB used Chi-square test or Fisher-exact test for categorical variables and student t-test for continuous variable data. Statistical significance was considered when $p < 0.05$. Logistic regression analysis to identify independent parameters in predicting causes of UGIB was performed and presented with odds ratio. Scoring system will be developed based on these parameters.

RESULTS

There were 261 patients enrolled into the study. Of these, 214 patients (82%) had nonvariceal and 47 (18%) had variceal bleedings. The causes of nonvariceal bleeding were gastric ulcer (39%), duodenal ulcer (22%), both gastric and duodenal ulcer (9%), erosive gastroduodenitis (12%), malignancies (5%), Mallory-Weiss syndrome (3%), severe portal hypertensive gastropathy (3%), reflux esophagitis (2%) and miscellaneous (5%). Causes of variceal bleeding were esophageal varices (89%) and gastric varices (11%). Clinical characteristics and laboratory data of the 2 groups and univariate analysis of the associations between these factors and the cause of UGIB are shown in Table 1 and 2.

Clinical characteristics

Variceal UGIB significantly occurred in younger age (mean 52.7 vs. 60.8 years), more frequently had red bloody vomitus or NG aspirate (59% vs. 18% for both) and more commonly had previous diagnosis of cirrhosis (36% vs. 19%), presence of signs of chronic liver disease (64% vs. 15%), splenomegaly (32% vs. 6%) and hepatic encephalopathy (15% vs. 5%). Patients with non-variceal UGIB more commonly had comorbid diseases (62% vs. 28%), history of ulcerogenic drugs use (53% vs. 21%) and dyspeptic symptoms (21% vs. 6%) compared to variceal patients. Hemodynamic changes (hypotension or tachycardia) at presentation were not different between variceal and nonvariceal UGIB.

Fifty-eight patients were known cases of cirrhosis. 30 pateint (52%) were bleed from varices and another 28 (48%) had nonvariceal UGIB.

Laboratory findings

Patients with variceal bleeding had lower platelet counts, and lower albumin level, but more commonly had reverse albumin/globulin ratio (81% vs. 45%), higher mean AST and ALT levels (133 vs. 62 U/L and 62 vs. 36 U/L, respectively). Prolonged prothrombin time was found in 94% of variceal bleeding compared to 29% of nonvariceal bleeding.

Multivariate analysis

Multivariate analysis was performed using a stepwise logistic regression analysis. Three factors were found to be independent factors associated with variceal bleeding; previously diagnosed cirrhosis or signs of chronic liver disease, red or bloody vomitus, and red or bloody NG aspirate.

In subgroup analysis in patient who were known of cirrhosis or presence of sign chronic liver disease, variceal type had Child Pugh A 5%, B 52.5%, and C 42.5% and nonvariceal type had Child Pugh A 12%, B 55% and C 33 %, respectively. Multivariate analysis were perform and found the independent factors that differentiated type of UGI bleeding in cirrhotic patient are the character of vomitus and the content of NG aspiration, If there was red or bloody content, it favored to variceal type bleeding.

Variceal bleeding predicting score

Using the 3 independent factors above, computer-generating model for predicting variceal cause of UGIB was constructed and the predicting score is:

$Z = (3.1 \times$ previous diagnosis of cirrhosis or presence signs of chronic liver disease$) + (1.5 \times$ character of vomitus$) + (1.2 \times$ character of NG aspirate$) - 4.1$

Previous diagnosis of cirrhosis or Presence of any sign of chronic liver disease is counted as 1 if present and 0 if absent. Character of vomitus is 1 for red or bloody vomitus and 0 for coffee-ground, clear or no

Table 1 Univariate analysis of clinical parameters of patients with variceal and non-variceal UGIB

Clinical parameters	Causes of UGIB		P value
	Variceal (n = 47)	Non-variceal (n = 214)	
Age (mean ± S.D)	53 ± 15	61 ± 15	0.001
Sex n (%)			
Male	41 (87)	151 (71)	0.030
Female	6 (13)	63 (29)	
Character of vomitus n (%)			
Red	28 (60)	39 (18)	<0.001
Coffee-ground or clear	19 (40)	175 (82)	
Stool appearance n (%)			
Red or maroon	6 (13)	14 (6)	0.220
Melena, brown or yellow	41 (87)	200 (93)	
Dyspepsia or abdominal pain n (%)	3 (6)	45 (21)	0.032
NSAID, ASA, anticoagulant use n (%)	10 (21)	114 (53)	<0.001
Previously diagnosed cirrhosis n (%)	30 (64)	28 (13)	<0.001
History of variceal UGIB n (%)	13 (28)	8 (4)	<0.001
History of non-variceal UGIB n (%)	0 (0)	21 (10)	0.018
Comorbid illness n (%)	13 (28)	132 (62)	<0.001
Alcohol drinking n (%)	14 (30)	43 (20)	0.207
Hypotension (BP <90/60 mmHg) n (%)	13 (28)	39 (18)	0.206
Tachycardia (HR >100/min) n (%)	26 (55)	93 (44)	0.188
Epigastric tenderness n (%)	2 (4)	25 (12)	0.212
Signs of chronic liver disease n (%)	30 (64)	32 (15)	<0.001
Previously diagnosed cirrhosis or			
presence of signs of chronic liver disease n (%)	40 (85)	42 (19)	<0.001
Child Pugh A	2 (5)	5 (12)	
Child Pugh B	21 (52.5)	23 (55)	0.235
Child Pugh C	17 (42.5)	14 (33)	
Splenomegaly n (%)	15 (32)	14 (6)	<0.001
Ascites n (%)	20 (4)	20 (9)	<0.001
Hepatic encephalopathy n (%)	7 (15)	10 (5)	0.018
Character of NG aspirate n (%)			
Red or bloody	28 (60)	38 (18)	<0.001
Coffee-ground or clear	19 (40)	176 (82)	

vomiting. Similarly, character of NG content is 1 for red or bloody and 0 for coffee-ground or clear. Z score is calculated from this model and the probability of variceal bleeding is calculated by: Probability = $1/(1+e^{-Z})$ or by plotting the Z score to the exponential graph in Figure 1.

From this predicting score, the presence of 3 factors is required to have a probability of variceal bleeding of more than 90%. In the presence of 2 factors (previously diagnosed cirrhosis or presence of signs of chronic liver diease and had Red or bloody vomitus or Red or bloody NG tube aspiration), the probability of variceal bleeding is more than 60%. On the other hand, the presence of only 1 factor (except the previously diagnosed cirrhosis or presence of signs of chronic liver disease 10-50%) has less than 10% chance of variceal bleeding and in the absence of all 3 factors, the chance of variceal bleeding is less than 5%. Table

Table 2 Univariate analysis of laboratory findings of patients with variceal and non-variceal UGIB

Laboratory findings	Causes of UGIB		P value
	Variceal (n = 47)	Non-variceal (n = 214)	
Hemoglobin (g/dl)	8.6 ± 2.2	8.5 ± 2.6	0.731
Hematocrit (%)	25.8 ± 6.3	25.9 ± 7.3	0.965
WBC ($\times 10^3$ / mm^3)	12.2 ± 8.7	14.3 ± 13.5	0.319
Platelets ($\times 10^3$ / mm^3)	165.0 ± 115.8	248.6 ± 129.9	<0.001
Platelets <100 $\times 10^3$ / mm^3 n (%)	16 (34)	23 (11)	<0.001
BUN (mg/dl)	31 ± 18	44 ± 29	0.003
Creatinine (mg/dl)	1.3 ± 0.7	1.6 ± 1.8	0.190
Albumin (g/L)	2.8 ± 0.7	3.2 ± 0.7	0.001
Globulin (g/L)	3.7 ± 0.9	3.2 ± 0.8	<0.001
A/G ratio <1 n (%)	38 (81)	83 (45)	<0.001
Total bilirubin (mg/dl)	4.1 ± 5.8	2.3 ± 5.5	0.054
SGOT (U/L)	133 ± 187	62 ± 107	0.001
SGOT > 2 × UNL n (%)	25 (53)	36 (20)	<0.001
SGPT (U/L)	62 ± 76	36 ± 50	0.003
SGPT > 2 × UNL n (%)	8 (21)	21 (12)	0.359
SGOT/SGPT >1 n (%)	43 (92)	132 (75)	0.025
Alkaline phosphatase (U/L)	158 ± 112	115 ± 105	0.015
Prothrombin time (second)	21 ± 11	16 ± 8	0.002
>12.5 second n (%)	44 (94)	58 (29)	<0.001
APRI >1.2 (AST/Platelet $\times 10^3$) n (%)	10 (21)	18 (10)	0.041

Table 3 Multivariate analysis indicates independent factors associating with variceal UGIB

Clinical parameters	Odds ratio	95% CI	P value
Previously diagnosed cirrhosis or presence of signs of chronic liver disease	22.4	8.3-60.4	<0.001
Red or bloody NG aspirate	3.3	1.3-8.3	0.011
Red or bloody vomitus	4.6	1.8-11.9	0.020

4 shows the probabilities of variceal bleeding according to the number of the factor present.

DISCUSSION

The present study is the first study that extensively assesses the values of clinical parameters and basic laboratory findings to predict the types of UGIB as variceal or nonvariceal bleeding before endoscopy. Our study differs considerably from other published studies on the use of clinical predictors in patients with UGIB. Most of them aim to assess and predict patients at high-risk for the worse outcomes from UGIB in order to triage patients for appropriate cares. Most demonstrated that clinical parameters (e.g. hemodynamics[5-7], NG aspirate[8] and comorbid illnesses) and endoscopic findings (stigmata of recent hemorrhage and the presence of varices) strongly associated with worse outcomes. Multiple scoring systems, e.g. Rockall Score[6], Baylor bleeding score[7], Blatchford score[5] were also developed for this purpose. By contrast, our present study aims to determine clinical parameters and scoring system that predict the types of UGIB. Results of the present study may help phy-

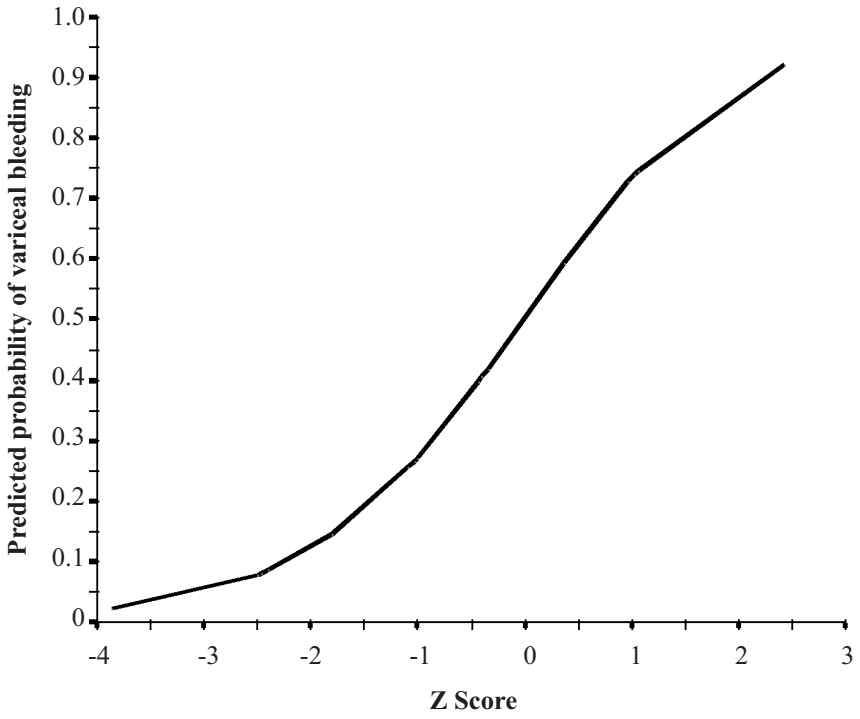

Figure 1 Exponential graph of the probability of variceal UGIB from the calculated Z score

Table 4 Probabilities of variceal bleeding according to the number of the factor present

Number of factors present	Probability of variceal bleeding
3 factors	>90%
2 factors (previously diagnosed cirrhosis or presence of sign of chronic liver disease and another factor)	60-70%
2 factors or previously diagnosed cirrhosis or presence of signs of chronic liver disease	20-30%
1 factor (Red or bloody vomitus or Red or bloody NG tube aspiration)	<10%
None	<5%

sicians, particularly in general practice where emergency EGD is usually unavailable, decide the type of empirical treatments more precisely, i.e. the use of pharmacological treatments and in some situation, the use of balloon tamponade in case of highly-suspected severe variceal bleeding.

In the present study, we found variceal bleeding in 18% and nonvariceal bleeding in 82% of all 261 UGIB patients. This proportion is comparable to most studies on UGIB in the literatures. Although the present study demonstrated that variceal and nonvariceal bleeding have many significant distinct features. Only 4 most important independent factors were identified that may help predicting the variceal bleeding; previous diagnosis of cirrhosis or presence, signs of chronic liver disease, character of vomitus, and findings on NG aspirate with OR from 3.3 to 22.4 (Table 3). Although these factors are not new findings, our study clearly strengthened and demonstrated the powers of these factors. Furthermore, some previously believed predictors, e.g. signs of portal hypertension (for variceal bleeding) or the presence of dyspepsia (for nonvariceal bleeding) were found to be less useful due to the uncommonness or weak associations of them. Some factors, particularly the severity of hemodynamic changes at presentation were also found to be indistinguishable in this study.

Although among the 3 factors, 2 factors seem to

relate to the another, i.e. characters of vomitus and NG aspirate but these are independent factors based on the multivariate analysis. We believe they are somehow different and will confirm each others and using more factors would increase the accuracy and delineate more details in the prediction.

For the developed variceal bleeding predicting score in this study, we demonstrated the values of using different cutoff numbers of factors to predict the chance of variceal bleeding accordingly. Choosing the appropriate cutoff depends on the aims in using the score, for example, if we need only >50% probability of variceal bleeding for deciding to initiate vasoactive drugs, the presence of 2 factors (one is previously diagnosed cirrhosis or presence of sign of chronic liver disease) is required. For deciding to use balloon tamponade which carries a significant risk, we may need a >90% probability of variceal bleeding. Thus, the presence of all 3 factors is needed. On the other hand, if only 0-1 factor is present, the chance of variceal bleeding would be lower than 5-10%, thus empirical treatment as nonvariceal bleeding would be appropriate. However, before we can apply this score to routine practice with confidence, we need to validate this score prospectively on different population. The validation study is now on the way.

In conclusion, 3 clinical parameters were found to be helpful in predicting variceal causes of UGIB. Variceal bleeding predicting score which was developed from these 3 factors may be helpful in predicting the chance of variceal bleeding more precisely. Prospective study to validate this score is on the way.

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