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Alternative Predictors of Severity for Gastrointestinal Bleeding (Abdullah T, *et al.*)
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R E S E A R C H   A R T I C L E

Modified Glasgow-Blatchford Bleeding Score as an Alternative Predictors of Severity for Non-Variceal Upper Gastrointestinal Bleeding

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Abstract

BACKGROUND: Upper gastrointestinal bleeding (UGIB) is a frequent cause of emergency hospital admissions. Despite the dependency of most risk scoring systems for this disorder, the Glasgow-Blatchford bleeding score (GBS) is based on simple variables. This research intended for investigate the accuracy of a modified GBS (mGBS) to predict the severity of non-variceal UGIB.

METHODS: Study conducted in Emergency Department of Dr. Saiful Anwar Hospital, Malang, from November 2012 to April 2013. Endoscopy performed between 12-24 hours after the patient stabilized. Sixty patients diagnosed were included. The accuracy of the mGBS in predicting the severity of non-variceal UGIB was compared with the full GBS using receiver operating characteristic (ROC) curve. The severity based on high risk in mGBS score compared by Forrest classification.

RESULTS: For prediction of the severity of non-variceal UGIB, the GBS (AUC 0.947, 95% CI 0.87-1.03) had a slightly had a slightly higher accuracy than the mGBS (AUC 0.943, 95% CI 0.86-1.02, $p<0.01$). Compared to the GBS, the mGBS was more specific (63% and 97%, respectively) but less sensitive (96% and 84%, respectively).

CONCLUSION: The mGBS is an alternative diagnostic tool in predicting the severity of non-variceal UGIB.

KEYWORDS: non variceal-UGIB, GBS, modified GBS

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Introduction

Upper gastrointestinal bleeding (UGIB) is the emergency case commonly found either in the hospital or in the center of primary health care. The case fatality rate is estimated at 10% and has not changed significantly since 1960s. Therefore, diagnostic modalities should take precedence over the therapeutic techniques. UGIB is often easily identified in the patient presenting with vomiting blood (hematemesis) or passing black, tarry stools (melena). Such complaints are usually accompanied by signs and symptoms of hypovolemia such as dizziness, weakness, or syncope.(1)

In the United States, approximately 350,000 patients are hospitalized due to UGIB each year, and 35-45% of them are over 60 years old. The incidence of UGIB ranges between 50 and 150 per 100,000 of the population per year. About 60% of women aged 60 years or older are estimated to have experienced this case. Meanwhile, according to study conducted in the United Kingdom, UGIB mortality rate is approximately 14% of the total population, and only 0.6% for those younger than 60 years without the presence of malignancy or organ failure. Almost all reported cases of death in the older people are due to a serious illness that accompanies.(1,2,3)

In Indonesia, according to the medical records of patients admitted to the Internal Medicine Department of

Hasan Sadikin Hospital, Bandung, in 1996-1998, there were 2.5-3.5 % patients treated for UGIB of all patients. In Saiful Anwar hospital, Malang, in January-June 2013, there were 124 cases patients UGIB undergoing endoscopic, 60% patients with non-variceal. Data in 2008, there are only 733 patients (2%) come to emergency departement Saiful Anwar hospital with complain hematemesis, melena, or both. From endoscopic results, we found gastritis erosive (40%), gastritis erythematous (11%), ulcus duodenum (5%), ulcus gaster (18%), varices esofagus (13%), and the others (13%). The overall mortality of UGIB is high at around 25%, and mortality in patients with rupture of varices can reach 60%. The most common cause of death in patients with UGIB is not because of the bleeding itself, but because of other diseases.(4-7)

It is still difficult to predict a severity for the patients presenting with variceal bleeding. Some literatures stated that the clinical signs of cirrhosis, portal hypertension, and spontaneous hematemesis accompanied by hemodynamic changes may indicate the possibility of variceal bleeding. However, this statement is still difficult to be confirmed or validated. Studies suggested that in patients with cirrhosis and first time variceal bleeding, about 40% did not reveal any signs of chronic liver disease and portal hypertension.(5,8)

The non-variceal UGIB is commonly caused by peptic ulcer, erosive gastroduodenitis, reflux esophagitis, tumor, and others.(5,6) Sometimes coffee-ground color is also found in the nasogastric (NG) tube of patients with a history of non-steroidal anti-inflammatory drug (NSAID) intake. However, this fact is still difficult to be proven. Peptic ulcer disease is the hardest and most frequent case of non-variceal UGIB, which is about 60% of cases, but approximately 80% of the ulcer bleeding may stop spontaneously without any intervention. *Helicobacter pylori* (*H. pylori*) is also commonly attributed as the cause of chronic gastritis, peptic ulcers, and gastric cancer. In certain condition, such as gastric mucosal damage caused by NSAIDs, *H. pylori* is able to invade the gastric mucosa causing inflammation resulting in acute non-erosive gastritis, then this can quickly progress to peptic ulcer (15-25%).(9,10) However, the prevalence of gastritis due to *H. pylori* in Indonesia is not yet known exactly.

There are many clinical scoring systems have been developed to direct appropriate patient management. These systems using a combination of many variables to produce a score that predicts the risk of haemorrhage, for clinical intervention or suitability for discharge. Although these systems are very accurate, they are limited by the availability of endoscopy within 24 hours, especially in our country. Factors commonly associated with poor outcome from UGIB may be related to the patient's presentation and morbidities, or the ulcer. Risk stratification using nonendoscopic parameters has the advantage that it can be performed readily on initial presentation in the emergency department, and appropriate initial risk assessment is still possible, even if early endoscopy, which requires skilled staff and resources, is not always available.(2,4,8,11)

As before, the Glasgow-Blatchford bleeding score (GBS) was derived from logistic regression analysis of clinical and laboratory values used to predict need for hospital intervention or death. For prediction of need for intervention or death, the GBS was superior to both admission and full Rockall scores.(4,12) In which this study, we investigate the accuracy the GBS compared with new modified score. We add the new parameter in that GBS, includes history of hematemesis, renal disease, and NSAIDs or herbal medicine intake, as well as laboratory tests of hemostasis and *H. pylori* IgG antibody, to predict the severity of non-variceal UGIB.

Methods

Study Design and Population

The study design is a diagnostic test. Based on ethical clearance No. 368/KEPK/XI/2012, this study conducted in Emergency Department and Endoscopy Unit of Dr. Saiful Anwar Hospital, Malang, from November 2012 to April 2013. All patients presenting with non-variceal UGIB were evaluated. Endoscopy performed between 12-24 hours after the patient stabilized. Patients who refused endoscopic examination or without consents were excluded. This study had been approved by the institutional ethics committee of Dr. Saiful Anwar Hospital, Malang, and informed consents were obtained from all enrolled patients.

Survey Content and Administration

The diagnosis of non-variceal UGIB was based on patients' presentation, including hematemesis, coffee-ground emesis, and melena. Variables including age, sex, chief complaints, presenting vital signs, presence of comorbid medical conditions (heart disease, liver disease, and kidney disease), history of medication with NSAIDs or herbs, laboratory data (hemoglobin/Hb, blood urea nitrogen/BUN, hemostasis, and *H. pylori* IgG antibody), and the findings of endoscopy were recorded. The high-risk patient was defined as patient needing blood transfusion, therapeutic endoscopy to control bleeding, or surgical intervention to control bleeding.

Data Analysis

Diagnostic tests were used to assess the relationship between the modified GBS (mGBS) and endoscopic (Forrest) score. High risk if we found there were active bleeding or adherent clots (Ia-IIb). High risk in mGBS if we calculate the score more than 11. The severity based on high risk score from both of them. The Chi-square tests and independent t-tests were first performed to assess the statistically significant differences between each of the parameters be used in the mGBS. Only probability values of $p<0.05$ were considered statistically significant. Diagnostic tests were performed to assess the sensitivity, specificity, positive predictive value, negative predictive value, and receiver operating characteristic (ROC) curves with 95% confidence interval (CI). Statistical analysis were performed using the software SPSS17.0 for Windows.

Results

A total of 60 patients were enrolled in this study consisted of 34 men (56%) and 26 women (44%). Subjects aged under 60 years (63%), between 60-69 years (27%), and over 69 years (10%). Based on the chief complaints, 29 subjects (48%) present with melena, 21 subjects (35%) with hematemesis, and 16 subjects (27%) with hematemesis and melena. Based on the hemodynamic conditions, 54 subjects (90%) had a systolic blood pressure (SBP) of more than 99 mmHg, 36 subjects (60%) had a normal pulse between 80-100/min, and only 1 subject (1.7%) had a history of syncope. Based on morbidity, only 10 subjects had history of heart disease (17%), 8 subjects (13.3%) had liver disease, and 7 subjects (11.7%) had kidney disease. Based on the history, there were 41 subjects (68.3%) had a history of taking NSAIDs/herbal medicine and only 1 subject (1.7%) had a history of *H. pylori* infection. Meanwhile, according to laboratory data, 31 subjects (51.7%) had Hb <10 g/dL, 29 subjects (48.3%) had Hb >10g/dL, 28 subjects (47%) had abnormal blood urea nitrogen (BUN) values, while 32 subjects (53%) had normal BUN values, and only 1 subject (1.7%) had abnormal hemostatic value. The characteristic data are shown in Table 1.

The patients were categorized as high-risk and low-risk. The independent t-tests (Table 1) showed that the SBP and pulse were not significantly different, but hemoglobin and BUN were significantly ($p<0.05$) different between the 2 groups. The Chi-Square tests (Table 1) indicated not significant differences in syncope, history of heart or liver disease, intake of NSAID's or herbal medicine, hemostasis

Table 1. The comparison of characteristics in high- and low-risk patients stratified by occupation.

Characteristics	The mGBS		*p*
	High Risk n (%)	Low Risk n (%)	
SBP: mean±SD	122.00±32.44	114.6±17.81	0.332
Pulse: mean±SD	103.64±18.28	96.24±19.05	0.147
HEMATEMESIS			
Negative	10 (45.45)	29 (76.32)	0.016
Positive	12 (54.55)	9 (23.68)	
MELENA			
Negative	5 (22.73)	26 (68.42)	0.001
Positive	17 (77.27)	12 (31.58)	
SYNCOPE			
Negative	21 (95.45)	38 (100)	0.185
Positive	1 (4.55)	0 (0)	
HEART DISEASE			
Negative	18 (81.82)	32 (84.21)	0.811
Positive	4 (18.18)	6 (15.79)	
LIVER DISEASE			
Negative	17 (77.27)	35 (92.11)	0.103
Positive	5 (22.73)	3 (7.89)	
KIDNEY DISEASE			
Negative	16 (72.73)	37 (97.37)	0.004
Positive	6 (27.27)	1 (2.63)	
***NSAIDs/HERBSUSE**			
Negative	4 (18.18)	15 (39.47)	0.088
Positive	18 (81.82)	23 (60.53)	
Hb: mean ± SD	6.70±2.52	11.03±1.88	0.000
BUN: mean ± SD	48.62±43.54	19.0114.45	0.005
HEMOSTASIS TEST VALUE			
Abnormal	21 (95.45)	38 (100)	0.185
Normal	1 (4.55)	0 (0)	
***H. pylori* IgG ANTIBODY**			
Negative	22 (100)	37 (97.37)	0.443
Positive	0 (0)	1 (2.63)	
ENDOSCOPY			
High Risk	21 (84)	4 (16)	0.000
Low Risk	1 (2.9)	34 (7.1)	

*NSAIDs indicates nonsteroidal anti-inflammatory drug

test value, and *H. pylori* IgG antibody between the 2 groups. Whereas, there were significant ($p<0.05$) differences in hematemesis, melena, and kidney disease between the 2 groups.

The tests of normality with Kolmogorov-Smirnov tests showed that the data of GBS and the mGBS had normal distributions ($p>0.05$). The t-tests indicated a significant ($p<0.01$) difference between GBS and the mGBS. Moreover, the mGBS (8.87±4.20) had higher average score than GBS (7.80±3.85) (Table 2).

The ROC curve was performed to determine the accuracy of the mGBS in predicting the severity of non-

variceal UGIB compare to GBS. The GBS (AUC 0.947, 95% CI 0.87-1.03) had a slightly higher accuracy than the mGBS (AUC 0.943, 95% CI 0.86-1.02, $p<0.01$) (Figure 1). This suggested that GBS is superior than mGBS to assess severity of non-variceal UGIB.

This study also indicated that the limit of scores in determining the severity of non-variceal UGIB was not much different between GBS and the mGBS, where a score of 10 is the minimum score considered high risk in patients with non-variceal UGIB (GBS of 10, sensitivity 88%, specificity 100%; the mGBS of 10, sensitivity 92%, specificity 85%) (Figure 2).

Diagnostic tests indicated that the GBS in diagnosing the severity of non-variceal UGIB had a higher sensitivity than the mGBS (96% and 84%, respectively), but a lower specificity than the mGBS (63% and 97%, respectively). The accuracy of GBS in predicting positive value was lower than the mGBS (PPV, 65% and 95%, respectively), but higher in predicting negative value (NPV, 96% and 89%, respectively) (Table 3).

Discussion

The results showed that only hemoglobin, BUN, hematemesis, melena, and kidney disease were significant in the mGBS. Whereas, SBP, pulse, syncope, heart disease, liver disease, hemostasis, *H. pylori* IgG antibody, and intake of NSAIDs/herbal medicine were not significant in the mGBS. Hematemesis and melena, according to the previous study, were proved as an early manifestation of UGIB, both variceal and non-variceal, where approximately 30% of patients with bleeding ulcers begins with hematemesis, 20% with melena, and 50% both.(5,13)

Patients with a history of UGIB is usually followed by a significant decrease in hemoglobin. This study indicated a significant difference between the increase in the mGBS and the decline in hemoglobin in patients with UGIB. It is also supported by the data of patients presenting UGIB; approximately 51.7% of patients is characterized by decreased hemoglobin. Besides hemoglobin, hematocrit is also a useful test. Hematocrit value can determine the presence of anemia or polycythemia. Significant changes in hematocrit indicated blood loss. Infusion of normal saline can accelerate the equilibration of hematocrit, but a rapid infusion of crystalloid in non-bleeding patients can lower the hematocrit value due to hemodilution. Optimal hematocrit value in regulating the oxygen carrying capacity and viscosity in critically ill patients reaches 33%. In general,

Table 2. Independent t-tests of each parameter of GBS and the mGBS.

Variable	Mean±SD	t-statistic	p
Total Blatchford score	7.80±3.85	-9.824	0.000
Total modified Blatchford score	8.87±4.20		

Table 3. Diagnostic tests of GBS and the mGBS.

|	GBS		mGBS	
	High risk	Low risk	High risk	Low risk
Endoscopy: high risk	24	13	21	1
Endoscopy: low risk	1	22	4	34
Sensitivity	96%		84%	
Specificity	63%		97%	
Positive predictive value	65%		95%	
Negative predictive value	96%		89%	

acute bleeding patients with hemoglobin of 8g/dL or less (hematocrit less than 25%) need blood transfusion. After transfusion, and certainty no blood loss again, hematocrit is expected to increase by 3% in any given unit of blood (hemoglobin increased by 1g/dL).(1)

BUN increased in patients with UGIB because of blood absorption in the gastrointestinal tract and hypovolemia that can lead to renal failure. This study showed that nearly half of non-variceal UGIB patients (47%) had abnormal BUN value. This suggested that patients with abnormal BUN value may cause UGIB symptoms. Ratio of BUN and serum creatinine can also be used to estimate the origin of bleeding. The peak ratio is between 24-48 hours from the onset of bleeding, and the ratio of 20 is considered normal. The ratio of more than 35 indicates that the bleeding source may be from UGIB. After 24 hours, hypovolemia predominantly leads to azotemia if there is recurrent bleeding.(1,7,14)

The history of kidney disease significantly aggravates UGIB due to the uremia or too much ammonia accumulating in the patient's body, thus causing either of gastritis, peptic ulcer disease, and gastric mucosal ulceration at various levels. Some studies suggested that uremia may affect the aggregation of platelets (coagulation), so it can prolong bleeding in renal failure patients with UGIB.(15,16) The upper gastrointestinal tract lesions in patients with renal failure is still unclear. Some mechanism of studies indicated that hypergastrinemia plays a role in increasing the acid secretion resulting in the gastrointestinal lesions, but another study showed that hypergastrinemia actually causes hypochloridia. Other studies also suggested that *H. pylori* played an important role in increasing the

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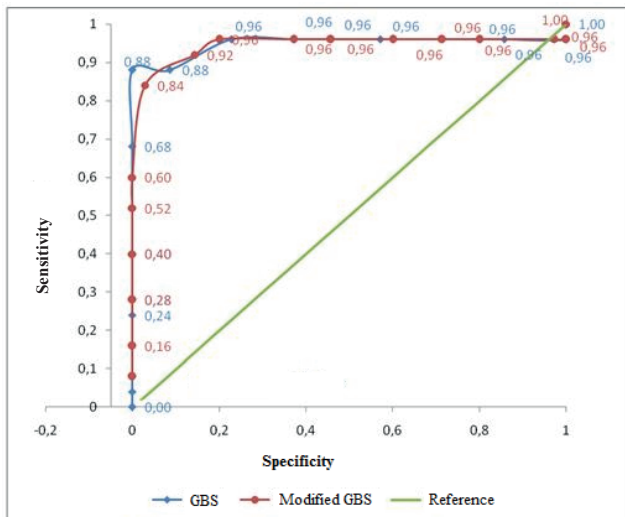
Figure 1. Comparison of GBS and the mGBS with AUC figures. (GBS, AUC 0.947, 95% CI 0.87-1.03; the mGBS, AUC 0.943, 95% CI 0.86-1.02).
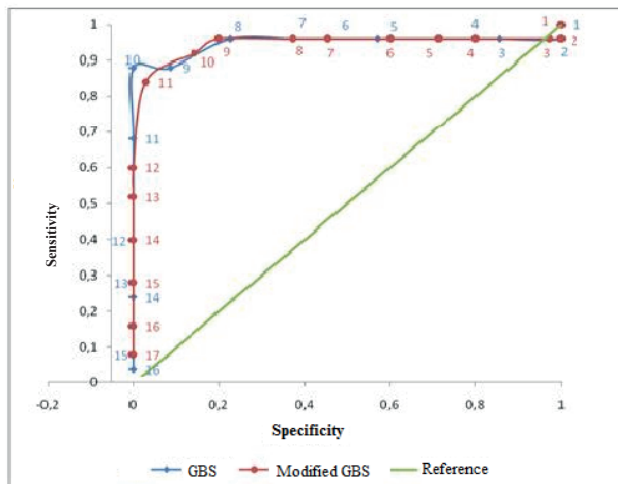
Figure 2. Comparison of GBS and the mGBS in determining the severity of non-variceal UGIB. (GBS score of 10, sensitivity 88%, specificity 100%; the modified GBS score of 10, sensitivity 92%, specificity 85%).

prevalence of gastrointestinal lesion in patients with renal failure. Although it is still controversial whether the risk of *H. pylori* infection is greater in patients with renal failure compared to normal people, previous study indicated that the prevalence of *H.pylori* infection is about 49-66% in patients with renal failure, and about 35-75% in the normal.(15)

There were no significant differences in SBP, pulse, and syncope to the risk of UGIB. This may occur because of bleeding in patients with non-variceal UGIB is not as much as in variceal UGIB. This study showed that patients categorized as high risk in GBS had SBP over 122 mmHg and pulse above 103 x/min, while syncope occurred in

only one patient. This suggested that non-variceal UGIB patients arriving at the hospital generally did not have significant hemodynamic disturbances. Acute hemorrhage in the amount exceeding 20% of the intravascular volume will result in an unstable hemodynamic conditions, such as hypotension (blood preassure/BP less than 90/60 mmHg or mean arterial pressure/MAP less than 70 mmHg), pulse over 100x/min, diastolic blood pressure fall more than 10 mmHg or systolic blood pressure fall more than 20 mmHg, cold acral, decreased consciousness, syncope, and even anuria or oliguria (urine output less than 30 mL/hour). In addition, acute bleeding can also be characterized by hematemesis, hematochezia, and fresh blood on the NG that was not immediately clear with lavage, persistent hypotension, and the need of blood transfusion exceeding 800-1000 mL within 24 hours.(5)

Although this study suggested that a history of heart disease was not significant in patients with non-variceal UGIB, but patients with heart disease can aggravate the risk of UGIB with age due to unstable hemodynamic conditions. Decreased cardiac output can cause gastric mucosa ischemia, increased risk of ulceration, and potentially bleeding. The constant use of drugs such as aspirin in patients with a history of coronary heart disease may also play a role in increasing the risk of UGIB.(5,17)

This study also showed that there was no significant history of liver disease in patients with non-variceal UGIB. The effects of liver disease or cirrhosis is more apparent in patients with variceal UGIB. Complications of cirrhosis can lead to the bleeding of esophageal varices, splenomegaly, ascites, portal hypertension, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome, and liver cancer.(7,13,15,18,19) In cirrhotic patients, disorders of coagulopathy and hemostasis manifested as profuse gastrointestinal tract bleeding. On the other hand, there were no significant changes in hemostasis in non-variceal UGIB. Thus, it was probable that the bleeding occurred have not yet induced coagulation disorders and the liver function of patients was good.

The role of *H. pylori* infection and NSAIDs/herbal medicine as etiology of non-variceal UGIB remains unclear. In white population, studies showed that UGIB was mostly caused by *H. pylori* infection.(3,7,9,10,14,18) *H. pylori* infection occurs in approximately 95% of patients with duodenal ulcers and about 70% of patients with gastric ulcers. However, in this study the result of *H. pylori* IgG antibody test and the history of NSAIDs/herbal medicine use were not significant. There was a possibility that the results of *H. pylori* tests were not significant because of the

false negative results due to the samples were obtained from blood, instead of gastric mucosal biopsy (histopathology) which is more accurate. The history of taking NSAIDs or herbal medicine, although not significant, still served as the etiology of non-variceal UGIB in Indonesia, particularly in Saiful Anwar Hospital, Malang.

Diagnostic test results indicated that GBS has a slightly superior sensitivity but lower specificity compared to the modified GBS. This proved that the modified GBS can be used as an alternative to endoscopy which is still be a gold standard in diagnosing the severity of patients presenting non-variceal UGIB. These results were also supported by the high PPV and NPV in the mGBS compared to GBS. The data confirmed that the mGBS can be used as an initial screening to determine the severity of patients presenting with non-variceal UGIB.

Conclusion

The mGBS can be used as an alternative tools in determining the severity of patients presenting with non-variceal UGIB. Certainly, the use of the mGBS is only as far early detection (early screening), particularly in the community health service centers and hospitals in Indonesia, where is endoscopy equipment not available. More parameter that we add in mGBS make this predictor more specific to predict the severity patients with non variceal UGIB. Finally, due to the scientific development and the use of the mGBS as an early predictor of the severity of patients presenting with non-variceal UGIB, further research is needed with a larger sample and longer time of research.

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