

Original Article

Comparison of different scoring systems for non-variceal upper gastrointestinal bleeding

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Abstract: Objective: The aim of this study was to investigate the performance of various scoring systems (Glasgow-Blatchford score (GBS), Rockall score (RS), AIMS65, and Progetto Nazionale Emorragia Digestiva (PNED)) in predicting clinical outcomes for clinical intervention, re-bleeding, and mortality in patients with non-variceal upper gastrointestinal bleeding (UGIB) and to determine optimal cut-off points. Methods: A total of 233 patients with non-variceal UGIB, admitted to Affiliated Hospital of Heze Medical College, from October 2015 to December 2017, were selected for this retrospective study. Medical records of these patients were collected and analyzed. Patients were scored by the four scoring systems, GBS, RS, AIMS65, and PNED. Receiver operating characteristic (ROC) curve was plotted and area under the curve (AUC) was calculated. The predictive accuracy of these systems was evaluated and compared. Results: Of the 233 patients, 102 patients had intervention (43.7%), 15 patients had re-bleeding (6.4%), and 6 patients died (2.5%). Risk scores of patients that had intervention, re-bleeding, or that had died were all higher than those in patients that didn't (all $P < 0.05$). AUCs for predicting intervention were similar among GBS, RS, and AIMS65 (0.750 (95% CI: 0.688-0.811) vs. 0.760 (95% CI: 0.699-0.823) vs. 0.754 (95% CI: 0.692-0.815), all $P > 0.05$), whereas AUCs for predicting re-bleeding among these three systems were different (0.749 (95% CI: 0.643-0.856) vs. 0.748 (95% CI: 0.630-0.856) vs. 0.646 (95% CI: 0.545-0.747), all $P < 0.05$). In predicting mortality, AUCs calculated by GBS, RS, and AIMS65 showed no intergroup differences (0.830 (95% CI: 0.726-0.935) vs. 0.830 (95% CI: 0.753-0.908) vs. 0.826 (95% CI: 0.748-0.903), all $P > 0.05$), whereas AUC in PNED was significantly higher than the other three, indicating better predictive accuracy (0.921 (95% CI: 0.902-0.958), $P < 0.05$). Optimal cut-off points associated with the Youden index for predicting need for intervention, re-bleeding, and death were > 7 , > 8 , and > 9 in GBS, > 8 , > 8 , and > 5 in RS, and > 2 , > 2 , and > 1 in AIMS65. Optimal cut-off point for predicting death in PNED was > 3 . Conclusion: Risk scores in patients that had intervention, re-bleeding, or that had died were all higher than scores in patients that didn't. The ability to predict the need for intervention by GBS, RS, and AIMS65 was equivalent, while GBS and RS were superior to AIMS65 in predicting re-bleeding. All four scoring systems predicted mortality well. However, the performance of PNED, in this area, was greater compared to the other three. PNED is, therefore, recommended for clinical application.

Keywords: Non-variceal upper gastrointestinal bleeding, scoring system, optimal cut-off point

Introduction

Upper gastrointestinal bleeding (UGIB) is a common disease, with an incidence of 48-160 cases per 100,000 individuals and mortality rate of 5.4-10% [1, 2]. This disease can be classified into two types: variceal UGIB and non-variceal UGIB. The latter one accounts for 67% of UGIB, as most bleedings are caused by ruptured peptic ulcers [3, 4]. Despite developments in endoscopy and medications for treatment of UGIB over the decades, the mortality

rate of this disease has not declined [5]. Non-variceal UGIB is a life threatening medical emergency, incurring high medical costs. Patient prognosis can be severely affected if they are not treated in a timely manner [6]. As a result, conducting a clinical assessment of the patients as early as possible is crucial.

Several scoring systems exist for predicting clinical outcomes in patients with UGIB. Calculation of scores usually requires patient clinical data, laboratory results, and endoscopic find-

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ings. Scores can be used for assessment of disease severity, prognosis, and for implementation of intervention. According to international consensus recommendations on management of patients with nonvariceal upper gastrointestinal bleeding, patients with UGIB can be categorized into either a high-risk subgroup or low-risk subgroup, based on risk assessment results, and receive different types of management and therapies accordingly [7]. The two most commonly used scoring systems are full Rockall score (RS) and Glasgow-Blatchford score (GBS) [8, 9]. RS was first proposed in 1996 and has been clinically applied since that time. This system mainly provides predictions for re-bleeding and mortality. However, RS is not suitable for patients in early stages of UGIB, as the system is quite complicated and requires an endoscopy. Since the beginning of 21st century, GBS, which requires no endoscopy, has been adopted for clinical application. Some studies have reported that the system has high sensitivity and is superior to other scoring systems for predicting mortality and the need for clinical intervention [10, 11]. Thus, the score can be employed in some healthcare settings where endoscopy is not available. In recent years, a system called AIMS65 has been introduced, clinically. This particular system requires less items and no endoscopy for score calculation, thus, it can be conducive to diagnosis and assessment of patient conditions at an early stage. However, there are still debates regarding the predictive performance of AIMS65 [10, 12-15]. Progetto Nazionale Emorragia Digestiva (PNED), another new scoring system, has recently been introduced. Some studies have argued that PNED performs better at predicting mortality than RS, but this statement requires further verification [16]. In China, AIMS65 and PNED are not as widely used as RS and GBS.

To improve patient prognosis and optimize allocation of medical resources, it was necessary to examine and compare the performances of these four scoring systems, with an aim of determining which one is more suitable for patients with UGIB and more helpful for clinical classification, prognosis assessment, and effective intervention. Therefore, this present study used these four systems to evaluate prognostic and risk factors of UGIB, desiring to obtain useful information for their clinical application.

Materials and methods

Subjects

This present study retrospectively analyzed 233 patients admitted to the Department of Gastroenterology, from October 2015 to December 2017, for treatment of non-variceal UGIB. This study was approved by Ethics Committee of the Affiliated Hospital of Heze Medical College and informed consent was obtained.

Inclusion and exclusion criteria

Inclusion criteria: 1) Patients aged 18 years and older; 2) Patients having symptoms of UGIB when admitted to the hospital; 3) Patients with non-variceal UGIB as confirmed by endoscopy [3]; 4) Patients with complete information as required by the four scoring systems, including basic information, laboratory results, and endoscopic findings; and 5) Patients that provided informed consent.

Exclusion criteria: 1) Patients aged below 18 years; 2) Patients that didn't have an endoscopy for diagnosis or patients having variceal UGIB, as confirmed by endoscopy; 3) Patients with bleeding in the mouth, nose, throat, or upper respiratory tract; 4) Patients without complete information as required by the four scoring systems; 5) Patients with bleeding caused by systemic disease, such as hematologic disease and lupus; and 6) Patients admitted to the hospital for other reasons, later developing UGIB during hospitalization.

Criteria in the four scoring systems

Scores were calculated according to the following criteria.

GBS: hemoglobin (Hb) for men: 120-129 g/L 1 point, 100-119 g/L 3 points, and < 100 g/L 6 points; Hb for women: 100-119 g/L 1 point and < 100 g/L 6 points; Blood urea nitrogen (BUN): 6.5-7.9 mmol/L 2 points, 8.0-8.9 mmol/L 3 points, 9.0-24.9 mmol/L 4 points, and ≥ 25 mmol/L 5 points; Systolic blood pressure (SBP): 100-109 mmHg (1 mmHg = 0.133 KPa) 1 point, 90-99 mmHg 2 points, and < 90 mmHg 3 points; Heart rate: ≥ 100 beats per minute 1 point; Presentation with melaena 1

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Table 1. Patient characteristics

Item	n (%)
Total number of patients	233
Male	169 (72.5%)
Female	64 (27.5%)
Age ($\bar{x} \pm sd$)	61.24 \pm 14.26
Cause of disease	
Gastric ulcer	76 (32.6%)
Duodenal ulcer	51 (21.9%)
Combined gastric and duodenal ulcers	14 (6.0%)
Digestive tract cancer	32 (13.7%)
Erosive gastritis	26 (11.2%)
Mallory-Weiss syndrome	17 (7.3%)
Esophageal ulcer	5 (2.1%)
Subtotal gastrectomy	9 (3.9%)
Other lesions	3 (1.3%)

Table 2. Clinical outcomes

Clinical outcome	Case	Percentage (%)
Improved	212	91.0
Intervention	102 [#]	43.8
RBC transfusion	88	37.8
Endoscopic treatment	19	8.2
Interventional therapy	14	6.0
Surgical treatment	7	3.0
Re-bleeding	15	6.5
Death	6	2.5
Gastrointestinal cancer	3	1.3
Recurrent gastric ulcer bleeding	1	0.4
Recurrent duodenal ulcer bleeding	1	0.4
Subtotal gastrectomy	1	0.4

Note: RBC: red blood cell; [#]some patients received two or more interventions.

point; Presentation with syncope 2 points; Liver disease 2 points; Cardiac failure 2 points [9].

RS: age: < 60 0 point, 60-79 1 point, and \geq 80 2 points; Shock: no shock 0 points, heart rate \geq 100 beats per minute 1 point, and SBP \leq 100 mmHg 2 points; Co-morbidity: none 0 points, cardiac failure, ischemic heart disease, or other major co-morbidity 2 points and renal failure, liver failure, or metastatic cancer 3 points; Endoscopic diagnosis: no lesions or Mallory-Weiss syndrome 0 points, ulcer or other lesions 1 point, and malignancy of upper gastrointestinal (GI) tract 2 points; Evidence of bleeding examined by endoscopy: none 0 points, blood

in upper GI tract, adherent clots, and visible or spurting vessels 2 points [8].

AIMS65: Plasma albumin level < 30 g/L 1 point, international normalized ratio > 1.5 1 point, Glasgow coma scale score < 14 1 point, SBP < 90 mmHg 1 point, and age > 65 1 point [12].

PNED: American society of anesthesiology (ASA) 3 1 point, ASA4 3 points, admission time < 8 h 1 point, age \geq 80 2 points, kidney failure 2 points, re-bleeding 3 points, neoplasia 3 points, cirrhosis of the liver 3 points, and failure in endoscopic treatment 4 points [16].

GBS, RS, and AIMS65 scoring systems were utilized for predicting re-bleeding, need for intervention, and mortality. PNED is specifically designed to predict mortality, thus, it could not be used for predicting the other two outcomes.

Outcome measures

Apart from the abovementioned variables covered for these four scoring systems, re-bleeding, clinical intervention, and death during hospitalization were also taken as main outcome measures. They were recorded and compared.

Signs and symptoms of re-bleeding included: 1) Increased occurrence of hematemesis or melena, presence of red colored vomit, or hematochezia; 2) Hb concentration decreasing to 20 g/L or lower during hospitalization; some patients even developed peripheral circulatory failure; 3) Large amounts of fresh blood observed from gastric tube; and 4) Urgent intervention or surgical treatment was required for bleeding control [8]. Clinical intervention included red blood cell (RBC) transfusions, endoscopic treatment, interventional therapy, and surgical treatment during patient hospital stay [11]. Mortality refers to death occurring during hospitalization.

Statistical analysis

Statistical software SPSS 17.0 was applied for data analysis. Measurement data are present-

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Table 3. GBS, Rockall, and AIMS65 scores regarding need for clinical intervention

Score	Patients who had intervention	Patients who didn't have intervention	t value	P value
GBS	6.75 ± 3.28	8.72 ± 2.91	-4.812	0.001
RS	3.51 ± 1.72	4.57 ± 1.72	-2.785	0.015
AIMS65	0.42 ± 0.64	1.07 ± 0.82	-2.223	0.045

Note: GBS: Glasgow-Blatchford score; RS: Rockall score.

positive likelihood ratio (LR), and negative LR were examined. AUCs in the two groups were compared by Z test. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

Of the 233 patients with non-variceal UGIB, there were 169 males and 64 females (male: 72.5%, female: 27.5%, male to female ratio: 2.64:1, 61.24 ± 14.26 years). Causes of disease included gastric ulcer (76, 32.6%), duodenal ulcer (51, 21.9%), combined gastric and duodenal ulcers (14, 6%), digestive tract cancer (32, 13.7%), erosive gastritis (26, 11.2%), Mallory-Weiss syndrome (17, 7.3%), esophageal ulcer (5, 2.1%), subtotal gastrectomy (9, 3.9%), and other lesions (3, 1.3%) as shown in **Table 1**.

Clinical outcomes

Among all participants, 212 patients (91.0%) experienced improvement after treatment. A total of 102 patients (43.7%) needed at least one intervention (RBC transfusion: 88, 37.8%, endoscopic treatment: 79, 8.2%, interventional therapy: 14, 6.0%, surgical treatment: 7, 3.0%). A total of 15 patients (6.5%) experienced re-bleeding while 6 patients (2.5%) with the following conditions died: digestive tract cancer (3, 1.4%), recurrent gastric ulcer bleeding (1, 0.4%), recurrent duodenal ulcer bleeding (1, 0.4%), and bleeding after subtotal gastrectomy (1, 0.4%) as shown in **Table 2**.

Comparison of the four scoring systems in prediction of clinical outcomes

Prediction of need for clinical intervention by GBS, RS, and AIMS65: A total of 102 patients had at least one intervention while 131 patients didn't need any intervention. GBS, RS, and AIMS65 scores in patients having intervention were 8.72 ± 2.91 , 4.57 ± 1.72 , and 1.07 ± 0.82 , respectively, all higher than patients not needing intervention (6.75 ± 3.28 , 3.51 ± 1.72 , 0.42 ± 0.64 , all $P < 0.05$) as shown in **Table 3**.

AUCs calculated in the three scoring systems (GBS, RS, and AIMS65) predicting need for

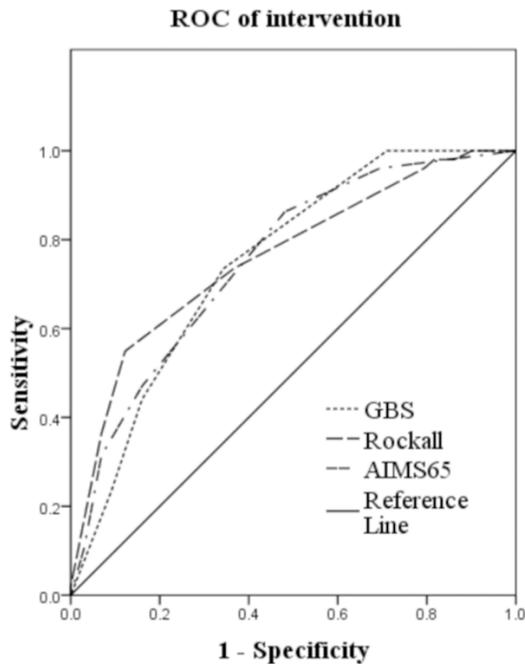


Figure 1. ROC curves of GBS, RS, and AIMS65 in prediction of need for intervention.

ed as mean \pm standard deviation. Homogeneity of variance test was performed for independent sample. If variances in the two groups were equal and data were normally distributed, groups were compared by t test. Otherwise, they were compared by Mann-Whitney test. Count data are presented as rate or percentage and comparisons between groups were carried out by Pearson's χ^2 test, Yates' correction, or Fisher's exact test, with a significance level of 0.05. ROC curve was plotted and AUC was calculated with 95% confidence interval (CI). An AUC of over 0.9 indicated excellent discrimination. AUC of 0.7-0.9 indicated acceptable discrimination and an AUC of 0.5-0.7 suggested poor discrimination. Calculation of the optimal cut-off point was associated with maximum Youden index and sensitivity, specificity,

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Table 4. GBS, Rockall, and AIMS65 scores regarding re-bleeding

Score	Patients who had no re-bleeding	Patients who had re-bleeding	t value	P value
GBS	7.48 ± 3.27	9.79 ± 2.35	-4.784	0.001
RS	3.69 ± 1.71	5.12 ± 1.98	-4.352	0.002
AIMS65	0.61 ± 0.69	1.12 ± 1.15	-3.254	0.025

Note: GBS: Glasgow-Blatchford score; RS: Rockall score.

218 patients did not. Patients with re-bleeding had higher GBS, RS, and AIMS65 scores than patients that didn't (9.79 ± 2.35 vs. 7.48 ± 3.27 , 5.12 ± 1.98 vs. 3.69 ± 1.71 , and 1.12 ± 1.15 vs. 0.61 ± 0.69 , all $P < 0.05$) as shown in **Table 4**.

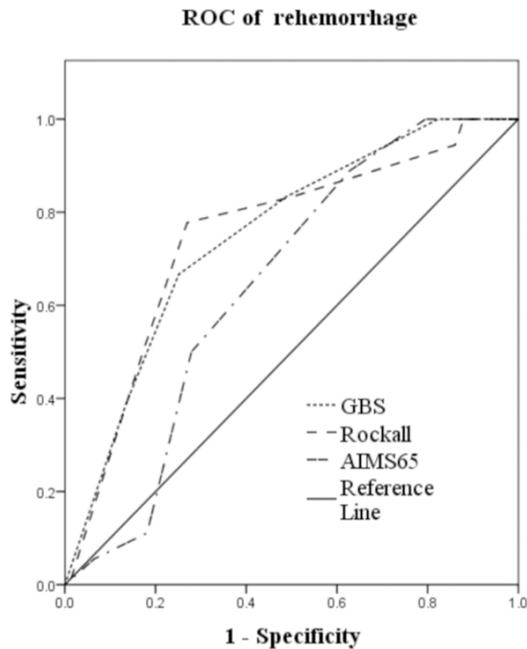


Figure 2. ROC curves of GBS, RS, and AIMS65 in prediction of re-bleeding.

intervention were 0.750 (95% CI: 0.688-0.811), 0.760 (95% CI: 0.699-0.823), and 0.754 (95% CI: 0.692-0.815). The scores showed no inter-group differences (all $P > 0.05$), indicating similar performances in this area. Calculation of optimal cut-off points was associated with maximum Youden index. Optimal thresholds of GBS, RS, and AIMS65 were > 7 (Youden index 39.1%, sensitivity 73.0%, specificity 65.6%, positive LR 2.13, negative LR 0.4), > 8 (Youden index 42.7%, sensitivity 54.9%, specificity 87.8%, positive LR 4.50, negative LR 0.51), and > 2 (Youden index 38.2%, sensitivity 86.3%, specificity 51.9%, positive LR 1.69, negative LR 0.26), respectively as shown in **Figure 1**.

Prediction of re-bleeding by GBS, RS, and AIMS65: Fifteen patients had re-bleeding while

AUCs calculated by the three scoring systems (GBS, RS, and AIMS65) predicting re-bleeding were different from each other (0.749 (95% CI: 0.643-0.856) vs. 0.748 (95% CI: 0.630-0.856) vs. 0.646 (95% CI: 0.545-0.747), all $P < 0.05$). It was found that both GBS and RS were better at predicting re-bleeding than AIMS65. Optimal thresholds of GBS, RS and AIMS65 were > 8 (Youden index 41.6%, sensitivity 66.7%, specificity 74.9%, positive LR 2.65, negative LR 0.44), > 8 (Youden index 50.8%, sensitivity 77.8%, specificity 73.0%, positive LR 2.88, negative LR 0.30), and > 2 (Youden index 26.1%, sensitivity 88.9%, specificity 37.2%, positive LR 1.41, negative LR 0.29), respectively as shown in **Figure 2**.

Prediction of modalities by GBS, RS, AIMS65, and PNEC: In total, six patients died while 227 patients survived. GBS, RS, AIMS65, and PNEC scores in patients that survived were 7.59 ± 3.22 , 3.91 ± 1.72 , 0.55 ± 0.75 , and 1.95 ± 2.41 , all lower than the scores of patients that died (11.11 ± 2.39 , 5.91 ± 1.65 , 1.74 ± 1.09 , 7.65 ± 3.36 , all $P < 0.05$) as shown in **Table 5**.

AUCs in these four scoring systems (GBS, RS, AIMS65, and PNEC) predicting mortality were 0.830 (95% CI: 0.726-0.935), 0.830 (95% CI: 0.753-0.908), 0.826 (95% CI: 0.748-0.903), and 0.921 (95% CI: 0.902-0.958), respectively. The results displayed no differences among GBS, RS, and AIMS65 (all $P > 0.05$), while showing that PNEC was superior to the other three in predicting mortality (all $P < 0.05$). Optimal thresholds of GBS, RS, AIMS65, and PNEC were: > 9 (Youden index 61.2%, sensitivity 86.2%, specificity 73.8%, positive LR 3.79, negative LR 0.18), > 5 (Youden index 51.1%, sensitivity 69.1%, specificity 82.9%, positive LR 4.08, negative LR 0.37), > 1 (Youden index 48.2%, sensitivity 93.2%, specificity 54.1%, positive LR

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Table 5. GBS, Rockall, AIMS65, and PNED scores regarding mortality

Score	Patients who survived	Patients who died	t value	P value
GBS	7.59 ± 3.22	11.11 ± 2.39	-5.257	0.001
RS	3.91 ± 1.72	5.91 ± 1.65	-3.544	0.025
AIMS65	0.55 ± 0.75	1.74 ± 1.09	-3.698	0.018
PNED	1.95 ± 2.41	7.65 ± 3.36	-5.957	0.001

Note: GBS: Glasgow-Blatchford Score; RS: Rockall score; PNED: Progetto Nazionale Emorragia Digestiva.

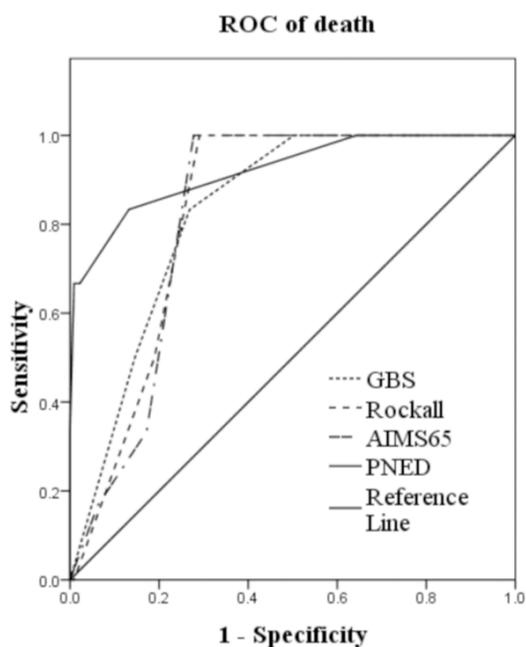


Figure 3. ROC curves of the four scoring systems in prediction of mortality.

1.98, negative LR 0.13), and > 3 (Youden index 73.7%, sensitivity 92.6%, specificity 81.2%, positive LR 4.83, negative LR 0.07), respectively as shown in **Figure 3**.

Discussion

Non-variceal UGIB is a major type of UGIB. This disease usually has a sudden onset, often leaving patients in critical condition. Therefore, making predictions regarding clinical outcomes using risk scoring systems would be helpful in guiding treatment. In this present study, male to female ratio was 2.6:1 while peptic ulcers were the main cause of disease, consistent with previous studies. Men have higher incidence of UGIB, as they are more likely to indulge

in bad habits, such as smoking and drinking [17]. The incidence of re-bleeding and death were lower, in this present study, compared with those in other reports (6.4% and 2.6%, vs. (10.0-30.0)% and (6.0-8.0)%) [18, 19]. This might be associated with the fact that 30-day follow up visits were not conducted among patients discharged from the hospital and deaths occurring in that period were not counted. RBC transfusion is the most common method for intervention. However, due to advances in medical technology, endoscopic treatment is currently widely applied. Although this treatment can provide rapid hemostasis, 5-10% patients will experience re-bleeding after endoscopic intervention [20].

PNED was not adopted to predict need for intervention and re-bleeding in this present study, as this system is designed specifically for predicting mortality and variables such as re-bleeding. Also, failure of intervention is required by PNED for score calculation. In predicting need for intervention, GBS, RS, and AIMS65 scores in patients having interventions were all higher than those that didn't (all $P < 0.05$). AUCs calculated in the three systems were similar (GBS: 0.750 (95% CI: 0.688-0.811), RS: 0.760 (95% CI: 0.699-0.823), and AIMS65: 0.754 (95% CI: 0.692-0.815), all $P > 0.05$). Some studies have reported that GBS is superior to RS in predicting need for intervention and superior to AIMS65 in predicting need for blood transfusions [15, 21, 22]. However, this present study found that the predictive accuracy of GBS regarding intervention was similar to the other two systems. The inconsistency may be associated with differences in patient race and ethnicity, location of bleeding, and medical facilities.

For prediction of re-bleeding, GBS, RS, and AIMS65 scores in patients that had re-bleeding were all higher than scores in those that didn't (all $P < 0.05$). In addition, AUCs calculated in the three scoring systems (GBS, RS, and AIMS65) were different (0.749 (95% CI: 0.643-0.856) vs. 0.748 (95% CI: 0.630-0.856) vs. 0.646 (95% CI: 0.545-0.747), all $P < 0.05$). Both GBS and RS were better at predicting re-bleeding than AIMS65, consistent with previous studies [10]. Currently, there are still some controversies regarding AIMS65's predictive accuracy. One study claimed that the perfor-

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mance of AIMS65 was poor when used in patients with peptic ulcers, suggesting that AIMS65 may not be suitable for this condition [23]. As peptic ulcers accounted for 54.5% in the current study, the performance of AIMS65 may have been affected. However, some researchers have argued that AIMS65 has similar abilities as GBS regarding prediction of re-bleeding [24].

In predicting mortality, scores of the four scoring systems in patients that died were all higher than scores in patients that survived. AUCs calculated in GBS, RS, and AIMS65 were similar (0.830 (95% CI: 0.726-0.935) vs. 0.830 (95% CI: 0.753-0.908) vs. 0.826 (95% CI: 0.748-0.903), all $P > 0.05$), while PNED was superior to these three (0.921 (95% CI: 0.902-0.958), all $P < 0.05$), indicating a better performance in predicting mortality. These results are consistent with other studies [25]. At present, the PNED scoring system is not widely applied. However, due to good predictive accuracy regarding death, this method should be recommended for wide clinical application.

Optimal cut-off points associated with Youden index in predicting need for intervention, re-bleeding, and death were > 7 , > 8 , and > 9 in GBS (sensitivity 73.5%, 66.7%, and 86.3%, specificity 65.6%, 74.9%, and 73.8%), > 8 , > 8 , and > 5 in RS (sensitivity 54.9%, 77.8%, and 69.1%, specificity 87.8%, 73%, and 82.9%), and > 2 , > 2 , and > 1 in AIMS65 (sensitivity 86.3%, 88.9%, and 93.2%, specificity 51.9%, 37.2%, and 54.1%). The optimal cut-off point for predicting death in PNED was > 3 (Youden index 73.7%, sensitivity 92.6%, specificity 81.2%). According to Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding, the GBS threshold regarding no need for intervention in patients with low-risk UGIB can be 0 [26]. However, some researchers have reported that this value could be increased to 1 without affecting accuracy [27, 28]. In terms of predicting intervention, some studies have documented thresholds of > 2 , > 5 , > 5 , and > 4 for AIMS65, GBS, Full RS, and PNED, respectively [29]. Additionally, there have been some studies claiming that optimal cut-off values for death and re-bleeding in GBS were both 10, while in AIMS65 they were 3 and 2. Optimal cut-off values for clinical intervention without a blood transfusion in GBS, RS, and AIMS65

were 10, 2, and 1 [13, 21]. Since inconsistencies remain among different studies concerning these cut-off points, more research is necessary for further verification.

In conclusion, scores calculated by the four risk scoring systems in patients having intervention, re-bleeding, or having died were higher than scores in patients that didn't. GBS, RS, and AIMS65 had similar performances in predicting need for intervention, while GBS and RS were superior to AIMS65 in predicting re-bleeding. All four scoring systems predicted mortality well, however, PNED appears to have better accuracy in this area and should be recommended for clinical application.

Disclosure of conflict of interest

None.

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