# Scoring systems for peptic ulcer bleeding: which one to use?

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ORIGINAL ARTICLE

#### **Prospective Study**

# Scoring systems for peptic ulcer bleeding: Which one to use?

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# **Abstract**

#### AIM

To compare the Glasgow-Blatchford score (GBS), Rockall score (RS) and Baylor bleeding score (BBS) in predicting clinical outcomes and need for interventions in patients with bleeding peptic ulcers.

# **METHODS**

Between January 2008 and December 2013, 1012



consecutive patients admitted with peptic ulcer bleeding (PUB) were prospectively followed. The pre-endoscopic RS, BBS and GBS, as well as the post-endoscopic diagnostic scores (RS and BBS) were calculated for all patients according to their urgent upper endoscopy findings. Area under the receiver-operating characteristics (AUROC) curves were calculated for the prediction of lethal outcome, rebleeding, needs for blood transfusion and/or surgical intervention, and the optimal cutoff values were evaluated.

#### **RESULTS**

PUB accounted for 41.9% of all upper gastrointestinal tract bleeding, 5.2% patients died and 5.4% patients underwent surgery. By comparing the AUROC curves of the aforementioned pre-endoscopic scores, the RS best predicted lethal outcome (AUROC 0.82 vs 0.67 vs 0.63, respectively), but the GBS best predicted need for hospital-based intervention or 30-d mortality (AUROC 0.84 vs 0.57 vs 0.64), rebleeding (AUROC 0.75 vs 0.61 vs 0.53), need for blood transfusion (AUROC 0.83 vs 0.63 vs 0.58) and surgical intervention (0.82 vs 0.63 vs 0.52) The post-endoscopic RS was also better than the post-endoscopic BBS in predicting lethal outcome (AUROC 0.82 vs 0.69, respectively).

#### **CONCLUSION**

The RS is the best predictor of mortality and the GBS is the best predictor of rebleeding, need for blood transfusion and/or surgical intervention in patients with PUB. There is no one 'perfect score' and we suggest that these two tests be used concomitantly.

**Key words:** Upper gastrointestinal bleeding; Peptic ulcer bleeding; Glasgow-Blatchford score; Rockall score; Baylor bleeding score

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Core tip: Endoscopic hemostasis represents the cornerstone of upper gastrointestinal bleeding treatment, and several scores have been developed for the prediction of rebleeding. This is a first study on Croatian patients to include over 1000 participants with peptic ulcer bleeding, and the aim was to compare three scores (Glasgow Blatchford score, Rockall score and Baylor bleeding score) in the prediction of peptic ulcer bleeding treatment outcome, including need for hospital-based intervention or 30-d mortality, 30-d rebleeding rate, 30-d mortality rate, and needs for surgical intervention and blood transfusion, and to find optimal cutoff values that indicate high-risk patients.

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#### INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a common medical emergency. Incidence rates of UGIB demonstrate variations ranging from 48 to 160 cases per 100000 population[1]. The most common causes of acute UGIB are non-variceal, where 28% to 59% are caused by peptic ulcer bleeding (PUB)[1-3]. Endoscopic hemostasis represents the cornerstone of UGIB treatment, and several scores have been developed for the prediction of clinical intervention (i.e. Rockall score (RS), Glasgow-Blatchford score (GBS), Baylor bleeding score (BBS), Cedars-Sinai Medical Center predictive index, Almela score, AIMS65 score)[4-14]. The recently published American College of Gastroenterology practice guidelines on the management of patients with ulcer bleeding recommend risk assessment in all patients in order to stratify them into high or low risk categories, since it may assist in initial decisions regarding the timing of endoscopy, time of discharge, and level of care[15].

The GBS is a pre-endoscopic score and contains the following parameters: initial hemoglobin levels, urea, blood pressure, pulse, known syncope, melena, and liver or cardiac failure. Each variable has an appointed numeric value and the maximal number of points is 23 (Table 1). The GBS was designed to predict lower risk bleeds, and a GBS value of 1 or lower indicates very low risk category<sup>[8,9]</sup>. The most commonly used RS consists of a pre-endoscopic evaluation part, which includes age, signs of shock and comorbidities, along with an endoscopic part, which evaluates high-risk endoscopic characteristics as well (known as the postendoscopic RS) (Table 2). Each variable is appointed a numeric value and every value > 2 indicates a highrisk patient<sup>[7]</sup>. The maximal pre-endoscopic RS value is 7, and the maximal post-endoscopic value is 11. The post-endoscopic RS can be calculated if bleeding is diagnosed and evaluated with upper endoscopy<sup>[7,16,17]</sup>. The BBS contains a pre-endoscopic evaluation part, which includes age, severity and duration of associated diseases, along with a post-endoscopic part, which evaluates the position and type of fresh bleeding (Table 3). The maximal pre-endoscopic BBS is 15, and the maximum total (pre-endoscopic and post-endoscopic) BBS is 24<sup>[18]</sup>.

The RS was primarily developed to predict mortality and the GBS to evaluate need for clinical intervention<sup>[6-14]</sup>. Secondarily, they can be applied to asses rebleeding risk. The BBS was primarily developed to identify patients at high risk for rebleeding after endoscopic hemostasis<sup>[6,16]</sup>. In previous studies,

Table 1 Glasgow-Blatchford score			
		Assigned score	
Blood urea, mmol/L	6.5 -7.9	2	
	8.0-9.9	3	
	10.0-24.9	4	
	≥ 25	6	
Hemoglobin for men, g/dL	12 -12.9	1	
	10-11.9	3	
	< 10	6	
Hemoglobin for women, g/dL	10-11.9	1	
	< 10	6	
Systolic blood pressure, mmHg	100-109	1	
	90-99	2	
	< 90	3	
Other markers	Pulse ≥ 100	1	
	Melena	1	
	Syncope	2	
	Hepatic disease	2	
	Cardiac failure	2	

the GBS has been shown to be better than the preendoscopic and post-endoscopic RS in predicting the need for hospital-based intervention in patients with UGIB<sup>[6,13,19]</sup>. On the other hand, the RS appeared to be better at predicting mortality after rebleeding, contributing to more accurate diagnostics and shorter hospital stay<sup>[7,13,14]</sup>. Recent studies have shown that early endoscopy (within 24 h of presentation) is performed in only half of patients with UGIB, demonstrating the need for reliable and accurate preendoscopic risk assessment<sup>[6-15,20-25]</sup>.

This is the first prospective study in Croatia to include over 1000 patients with PUB, and the aim was to compare the GBS, pre-endoscopic RS and pre-endoscopic BBS, as well as the post-endoscopic RS and post-endoscopic BBS, in the prediction of PUB treatment outcome, need for hospital-based intervention (endoscopic treatment, transfusion, surgery intervention) or 30-d mortality, including 30-d rebleeding rate, 30-d mortality rate, and needs for surgical intervention and blood transfusion, and to find optimal cutoff values that indicate high-risk patients.

# **MATERIALS AND METHODS**

This prospective study was conducted in the University Hospital Center "Sestre Milosrdnice" that covers a population of approximately 300000 in the City of Zagreb, Croatia. All patients presenting to the Emergency Unit between January 2008 and December 2013 with hematemesis, melena, hematochezia, or blood admixture upon nasogastric insertion were considered for study enrolment. If initial work-up indicated the need for hospitalization, patients were admitted to the Interventional Gastroenterology Unit.

Upper gastrointestinal endoscopy was performed in all patients within 24 h of admission. Only patients with gastric and/or duodenal ulcers, or an ulcer at the site of gastro-enteric anastomosis found during

emergency endoscopy, without any other possible cause of bleeding were included in the study. All patients with high-risk ulcer stigmata and patients selected depending on clinical judgment received high-dose acid suppression therapy (pantoprazole or esomeprazole 80 mg as an intravenous bolus, followed by 40 mg intravenously 2 times daily or 200 mg daily in the form of continuous infusion for at least 48 h followed by 40 mg daily by mouth). The institution's ethics committee approved the study. Data was prospectively entered into a database, with patient details stored in a depersonalized manner to protect patient confidentiality.

#### Data collection

The following data were collected for each patient: demographic data, history of ulcer or liver disease, coexisting and past illnesses, medication use, clinical characteristics of the bleeding episode, laboratory results, endoscopic diagnosis including stigmata of ongoing or recent hemorrhage, endoscopic intervention, medical treatment, rebleeding, surgical therapy, duration of hospitalization and cause of death. The grading of overall health and co-morbidity was performed according to the American Society of Anesthesiology (ASA) classification (grade 1, normal healthy patients; grade 2, mild systemic illness; grade 3, severe but incapacitating systemic illness; grade 4, life-threatening illness). Stigmata of hemorrhage were defined according to the Forrest classification (Forrest Ia, spurting bleeding; Forrest Ib, oozing bleeding; Forrest II a, non-bleeding visible vessel; Forrest II b, adherent clot; Forrest II c, hematin on ulcer base; Forrest III, clean ulcer base).

Shock was defined as syncope or signs of shock at physical examination, including systolic blood pressure less than 100 mmHg and pulse rate more than 100 beats/min.

Post-hemorrhagic anemia was corrected with red blood cell transfusion (2 units, approximately 500 mL) at a hemoglobin threshold of 70-80 g/L.

All patients diagnosed with PUB and high-risk stigmata underwent initial hemostasis (injection of dilute epinephrine into and around the bleeding point, positioning of clips or thermal coagulation, or both, but never epinephrine alone). Two biopsy specimens were obtained from the gastric antrum and body in all patients and the presence of *Helicobacter pylori* (*H. pylori*) infection was assessed by histopathological examination of the specimens using hematoxylin-eosin (HE) stain.

All patients with negative histology for *H. pylori* at index endoscopy had a control endoscopy with repeating biopsy samples, or urea breath test (UBT), performed 2 wk after proton-pump inhibitor treatment was discontinued. Patients in whom the described protocol was not followed were excluded from the study about *H. pylori* infection.

Table	2 Roc	ckall sc	ore

			Points		
	Variable	0	1	2	3
Pre-endoscopic score	Age, yr	< 60	60-79	≥ 80	
	Shock	Systolic blood pressure $\geqslant$	Systolic blood	Systolic blood pressure < 100	
		100	$pressure \geqslant 100$		
			mmHg Pulse ≥ 100/min		
		Pulse < 100/min			
	Comorbidity	No major comorbidity		Cardiac failure, ischemic heart	Renal failure, liver failure,
				disease, any major comorbidity	disseminated malignancy
Post-endoscopic score	Diagnosis	Mallory-Weiss tear, no	All other diagnosis	Malignancy of upper	
		lesion identified and no		gastrointestinal tract	
		signs of recent hemorrhage			
	Major signs	None or dark spot only		Blood in upper gastrointestinal	
	of recent			tract, adherent clot, visible or	
	hemorrhage			spurting vessel	

Table 3 Baylor bleed	ling score				
Assigned score	Age, yr	No. of parallel illnesses	Severity of illnesses	Site of bleeding	Stigmata of bleeding
0	< 30	0			
1	30-49	1 or 2			Clot
2	50-59				
3	60-69				Visible vessel
4		3 or 4	Chronic	Posterior wall bulb	
5	≥ 70	≥ 5	Acute		Active bleeding
Score		Pre-endoscopic		Post-en	doscopic

Rebleeding was defined as one or more signs of recurrent bleeding, including fresh hematemesis or melena, hematochezia, aspiration of fresh blood *via* nasogastric tube, instability of vital signs, and reduction of hemoglobin levels by 2 g/dL or more, occurring 24-h after the primary bleeding was stopped.

For all patients with gastric ulcer in whom recurrent bleeding was not observed, control endoscopy was performed 4-5 d after initial hemostasis and biopsy specimens were obtained from the margins and base of gastric ulcers to exclude malignancy. Control endoscopy with histology had been planned to be performed in all patients with gastric ulcer.

Documented clinical outcomes were: need for hospital-based intervention or 30-d mortality, 30-d rebleeding, 30-d mortality and interventions (transfer to the Department of Surgery and the need for blood transfusion).

The collected data was used to calculate the GBS score, as well as the pre-endoscopic RS and pre-endoscopic BBS for each patient presenting with UGIB. The post-endoscopic RS and BBS were calculated if bleeding from gastric, duodenal or gastro-enteric ulcers was endoscopically diagnosed. Methods for calculating the GBS, RS and BBS were as previously described. Pre-endoscopic and post-endoscopic scores were separately evaluated.

#### Statistical analysis

The Mann-Whitney *U*-test and Kruskal-Wallis analysis

of variance test were used to analyze differences in quantitative data. The discriminative ability of the scoring systems to predict outcomes was evaluated by receiver operating characteristics curves (ROC) with 95%CI. The areas under ROC (AUROC) curves were compared using the method of Delong et al<sup>[26]</sup> (1988) for the calculation of the standard error of the Area Under the Curve (AUC) and of the difference between two AUCs. The optimal thresholds of the GBS, RS and BBS for the prediction of rebleeding, death, and needs for blood transfusion and/or surgical intervention were identified as the threshold associated with the highest Youden index[27]. A two-tailed significance level of 5% was used in all comparisons. All analyses were performed using a statistical package MedCalc for Windows, version 15.8 (MedCalc Software, Ostend, Belgium).

# **RESULTS**

The analysis included 2643 patients with UGIB, of that 2326 (88%) patients had non-variceal bleeding, 225 (8.5%) had variceal bleeding, and 92 (3.5%) had an unidentified cause of bleeding.

From 2418 patients with non-variceal bleeding, 41.9% (1012) had PUB; specifically, the cause of bleeding in 49% (496) was gastric ulcer, in 47% (476) duodenal ulcer, in 2.4% (24) both gastric and duodenal ulcer, and in 1.6% (16) gastro-enteric anastomosis ulcer. Endoscopic treatment was required in 58% of



#### Table 4 Patient characteristics and clinical outcomes

Age         Median, yr         65.3 (20-100)           Sex         Male/Female         638 (63)/374 (37)           Findings at endoscopy         496 (49)           Gastric ulcers         496 (49)           Duodenal ulcers         24 (24)           Ulcer on gastro-enteric anastomosis High-risk ulcers (Forrest I a- II b)         526 (52)           Forrest I b         111 (11)           Forrest II a         212 (21)           Forrest II b         112 (14)           Low-risk ulcers (Forrest II c- III)         486 (48)           Forrest II c         172 (17)           Forrest III d         314 (31)           Hemodynamic shock         111 (11)           Comorbidity         Ischemic and valvular heart disease         172 (17)           Renal failure         111 (11)           Any malignancy         131 (12-9)           Comorbidity (ASA class)         ASA I           ASA II         283 (28)           ASA II         283 (28)           ASA II         283 (28)           ASA II         283 (28)           ASA II         284 (24-6)           Drugs         Without previous therapy         433 (42.8)           NSAIDs         284 (28.1) <td< th=""><th></th><th></th></td<>		
Male/Female   638 (63)/374 (37)	Age	
Male/Female   638 (63)/374 (37)	Median, yr	65.3 (20-100)
Findings at endoscopy   Gastric ulcers   496 (49)   Duodenal ulcers   476 (47)   Gastric and duodenal ulcers   24 (2.4)   Ulcer on gastro-enteric anastomosis   16 (1.6)   High-risk ulcers (Forrest I a — II b)   526 (52)   Forrest I a   61 (6)   Forrest I b   111 (11)   Forrest II a   212 (21)   Forrest II b   142 (14)   Low-risk ulcers (Forrest II c-III)   486 (48)   Forrest II c   172 (17)   Forrest III   314 (31)   Hemodynamic shock   111 (11)   Comorbidity   Ischemic and valvular heart disease   172 (17)   Renal failure   111 (11)   Any malignancy   131 (12.9)   Comorbidity (ASA class)   ASA II   283 (28)   ASA III   283 (29)   Antiplatelet therapy   433 (42.6)   Drugs   Without previous therapy   433 (42.8)   NSAIDs   284 (28.1)   Acetylsalicylic acid   203 (20)   Antiplatelet therapy   31 (3.1)   Anticoagulant therapy   41 (4)   NOAC   20 (2)   Treatment   Endoscopic therapy   587 (58)   Epinephrine   213 (36.3)   Hemoclips + epinephrine   180 (30.7)   Thermocoagulation + epinephrine   180 (30.7)   Thermocoagulation required   496 (49)   Red blood cell   406 (40.1)   Median (range), unit   2.5 (1-16)   Fresh frozen plasma   81 (8)   Median (range), unit   6 (4-8)   Median	Sex	
Gastric ulcers	Male/Female	638 (63)/374 (37)
Duodenal ulcers	Findings at endoscopy	
Gastric and duodenal ulcers   24 (2.4)     Ulcer on gastro-enteric anastomosis   16 (1.6)     High-risk ulcers (Forrest I a — II b)   526 (52)     Forrest I a   61 (6)     Forrest I b   111 (11)     Forrest II a   212 (21)     Forrest II b   142 (14)     Low-risk ulcers (Forrest II c-III)   486 (48)     Forrest II c   172 (17)     Forrest III   314 (31)     Hemodynamic shock   111 (11)     Comorbidity   Ischemic and valvular heart disease   172 (17)     Renal failure   111 (11)     Any malignancy   131 (12.9)     Comorbidity (ASA class)     ASA II   283 (28)     ASA II   283 (28)     ASA III   283 (28)     ASA III   283 (28)     ASA III   283 (28)     ASA III   324 (42.6)     Drugs   Without previous therapy   433 (42.8)     NSAIDs   284 (28.1)     Acetylsalicylic acid   203 (20)     Antiplatelet therapy   31 (3.1)     Anticoagulant therapy   41 (4)     NOAC   20 (2)     Treatment     Endoscopic therapy   587 (58)     Epinephrine   213 (36.3)     Hemoclips   156 (26.6)     Hemoclips   213 (36.3)     Hemoclips   156 (26.6)     Hem	Gastric ulcers	496 (49)
Ulcer on gastro-enteric anastomosis High-risk ulcers (Forrest I a - II b) Forrest I a Forrest I b Forrest II b Low- risk ulcers (Forrest II c- III) Forrest II c Forrest II c Forrest II c Forrest II d Forrest II c Forrest II d	Duodenal ulcers	476 (47)
High-risk ulcers (Forrest I a - II b)   526 (52)     Forrest I a   61 (6)     Forrest I b   111 (11)     Forrest II a   212 (21)     Forrest II b   142 (14)     Low-risk ulcers (Forrest II c - III)   486 (48)     Forrest II c   172 (17)     Forrest III   314 (31)     Hemodynamic shock   111 (11)     Comorbidity   Ischemic and valvular heart disease   172 (17)     Renal failure   111 (11)     Any malignancy   131 (12-9)     Comorbidity (ASA class)     ASA I   42 (14)     ASA II   283 (28)     ASA II   283 (28)     ASA II   283 (28)     ASA II   424 (42-6)     H. pylori   760 (75-1)     H. pylori-positive   324 (42-6)     Drugs   Without previous therapy   433 (42-8)     NSAIDs   284 (28-1)     Acetylsalicylic acid   203 (20)     Antiplatelet therapy   31 (3.1)     Anticoagulant therapy   41 (4)     NOAC   20 (2)     Treatment     Endoscopic therapy   587 (58)     Epinephrine   213 (36-3)     Hemoclips + epinephrine   180 (30.7)     Thermocoagulation + epinephrine   12 (2)     Repeated endoscopic therapy   71 (7)     Blood transfusion required   496 (49)     Red blood cell   406 (40.1)     Median (range), unit   2.5 (1-16)     Fresh frozen plasma   81 (8)     Median (range), unit   2.5 (1-16)     Fresh frozen plasma   81 (8)     Median (range), unit   2.5 (1-16)     Fresh frozen plasma   81 (8)     Median (range), unit   6 (4-8)     Whole blood   0 (0)     Surgery   55 (5.4)     Outcome     Rebleeding   95 (9.4)     Rebleeding (anticoag, and NOAC)   9 (14.8)     30-d mortality   53 (5.2)	Gastric and duodenal ulcers	24 (2.4)
Forrest I a 61 (6) Forrest I b 111 (11) Forrest II a 212 (21) Forrest II b 142 (14) Low-risk ulcers (Forrest II c-III) 486 (48) Forrest II C 172 (17) Forrest III 314 (31) Hemodynamic shock 111 (11) Comorbidity Ischemic and valvular heart disease 172 (17) Renal failure 111 (11) Any malignancy 131 (12-9) Comorbidity (ASA class) ASA I 283 (28) ASA II 283 (28) ASA II 283 (28) ASA II 142 (14) ASA II 283 (28) ASA III 324 (42.6) Drugs Without previous therapy 433 (42.8) NSAIDs 284 (28.1) Acetylsalicylic acid 203 (20) Antiplatelet therapy 31 (3.1) Anticoagulant therapy 41 (4) NOAC 20 (2) Treatment Endoscopic therapy 587 (58) Epinephrine 1213 (36.3) Hemoclips + epinephrine 180 (30.7) Thermocoagulation + epinephrine 180 (30.7) Thermocoagulation required 496 (49) Red blood cell 406 (40.1) Median (range), unit 2.5 (1-16) Fresh frozen plasma 81 (8) Median (range), unit 2.5 (1-16) Fresh frozen plasma 81 (8) Median (range), unit 9 (0.9) Median (range), unit 9 (0.9) Median (range), unit 9 (0.9) Median (range), unit 9 (4.8) Whole blood 0 (0) Surgery 55 (5.4) Outcome Rebleeding (anticoag, and NOAC) 9 (14.8) 30-d mortality 53 (5.2)	Ulcer on gastro-enteric anastomosis	16 (1.6)
Forrest I b	High-risk ulcers (Forrest I a- II b)	526 (52)
Forrest I b Forrest II a Forrest II a Forrest II a Forrest II b Forrest II b Forrest II c For	Forrest I a	61 (6)
Forrest     a   212 (21)   Forrest     b   142 (14)   Low-risk ulcers (Forrest     c-	Forrest I b	
Forrest II b Low-risk ulcers (Forrest II c-III) Low-risk ulcers (Forrest II c-III) Forrest III Forrest	Forrest ∐a	
Low-risk ulcers (Forrest II c-III)	Forrest ∐b	
Forrest II c	Low-risk ulcers (Forrest II c-III)	
Forrest III 314 (31) Hemodynamic shock 111 (11) Comorbidity Ischemic and valvular heart disease 172 (17) Renal failure 111 (11) Any malignancy 131 (12.9) Comorbidity (ASA class) ASA I 12(14) ASA II 283 (28) ASA III-IV 587 (58) H. pylori Tested 760 (75.1) H. pylori-positive 324 (42.6) Drugs Without previous therapy 433 (42.8) NSAIDs 284 (28.1) Acetylsalicylic acid 203 (20) Antiplatelet therapy 31 (3.1) Anticoagulant therapy 41 (4) NOAC 20 (2) Treatment Endoscopic therapy 587 (58) Epinephrine 213 (36.3) Hemoclips + epinephrine 180 (30.7) Thermocoagulation + epinephrine 12 (2) Repeated endoscopic therapy 71 (7) Blood transfusion required 496 (49) Red blood cell 406 (40.1) Median (range), unit 6 (4-8) Whole blood 0 (0) Surgery 55 (5.4) Outcome Rebleeding (anticoag. and NOAC) 9 (14.8) 30-d mortality 53 (5.2)		1 1
Hemodynamic shock   111 (11)		
Comorbidity   Ischemic and valvular heart disease   Liver di		
Liver disease	-	111 (11)
Liver disease 172 (17)  Renal failure 111 (11)  Any malignancy 131 (12.9)  Comorbidity (ASA class)  ASA I 12 142 (14)  ASA II 283 (28)  ASA II 283 (28)  ASA III 283 (28)  ASA IIII 283 (28)  ASA IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	•	012 (01 E)
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Comorbidity (ASA class)  ASA I  ASA II  ASA III  BASA III  ASA III  BASA (58)  BAST (58)  BUILDING  AFOOD (75.1)  BAST (42.6)  BAST (42.6)  BAST (42.6)  BAST (42.6)  BAST (42.8)  B		` '
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H. pylori-positive   324 (42.6)	H. pylori	
Drugs         Without previous therapy         433 (42.8)           NSAIDs         284 (28.1)           Acetylsalicylic acid         203 (20)           Antiplatelet therapy         31 (3.1)           Anticoagulant therapy         41 (4)           NOAC         20 (2)           Treatment         Endoscopic therapy           Epinephrine         213 (36.3)           Hemoclips         156 (26.6)           Hemoclips + epinephrine         180 (30.7)           Thermocoagulation         26 (4.4)           Thermocoagulation + epinephrine         12 (2)           Repeated endoscopic therapy         71 (7)           Blood transfusion required         496 (49)           Red blood cell         406 (40.1)           Median (range), unit         2.5 (1-16)           Fresh frozen plasma         81 (8)           Median (range), unit         2 (1-6)           Platelet         9 (0.9)           Median (range), unit         6 (4-8)           Whole blood         0 (0)           Surgery         55 (5.4)           Outcome         Rebleeding (anticoag. and NOAC)         9 (14.8)           30-d mortality         53 (5.2)	Tested	760 (75.1)
Without previous therapy       433 (42.8)         NSAIDs       284 (28.1)         Acetylsalicylic acid       203 (20)         Antiplatelet therapy       31 (3.1)         Anticoagulant therapy       41 (4)         NOAC       20 (2)         Treatment       Endoscopic therapy         Endoscopic therapy       587 (58)         Epinephrine       213 (36.3)         Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	H. pylori-positive	324 (42.6)
NSAIDs       284 (28.1)         Acetylsalicylic acid       203 (20)         Antiplatelet therapy       31 (3.1)         Anticoagulant therapy       41 (4)         NOAC       20 (2)         Treatment       Endoscopic therapy         Epinephrine       213 (36.3)         Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	Drugs	
Acetylsalicylic acid Antiplatelet therapy Anticoagulant Endoscopic therapy Epinephrine Endoscopic therapy Anticoagulation Anticoagulatio	Without previous therapy	433 (42.8)
Antiplatelet therapy 31 (3.1) Anticoagulant therapy 41 (4) NOAC 20 (2)  Treatment  Endoscopic therapy 587 (58)  Epinephrine 213 (36.3) Hemoclips 156 (26.6) Hemoclips + epinephrine 180 (30.7) Thermocoagulation 26 (4.4) Thermocoagulation + epinephrine 12 (2) Repeated endoscopic therapy 71 (7) Blood transfusion required 496 (49) Red blood cell 406 (40.1) Median (range), unit 2.5 (1-16) Fresh frozen plasma 81 (8) Median (range), unit 2 (1-6) Platelet 9 (0.9) Median (range), unit 6 (4-8) Whole blood 0 (0) Surgery 55 (5.4) Outcome Rebleeding 95 (9.4) Rebleeding (anticoag. and NOAC) 9 (14.8) 30-d mortality 53 (5.2)	NSAIDs	284 (28.1)
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NOAC       20 (2)         Treatment       587 (58)         Epinephrine       213 (36.3)         Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	Antiplatelet therapy	31 (3.1)
NOAC       20 (2)         Treatment       587 (58)         Epinephrine       213 (36.3)         Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	Anticoagulant therapy	41 (4)
Treatment         Endoscopic therapy         587 (58)           Epinephrine         213 (36.3)           Hemoclips         156 (26.6)           Hemoclips + epinephrine         180 (30.7)           Thermocoagulation         26 (4.4)           Thermocoagulation + epinephrine         12 (2)           Repeated endoscopic therapy         71 (7)           Blood transfusion required         496 (49)           Red blood cell         406 (40.1)           Median (range), unit         2.5 (1-16)           Fresh frozen plasma         81 (8)           Median (range), unit         2 (1-6)           Platelet         9 (0.9)           Median (range), unit         6 (4-8)           Whole blood         0 (0)           Surgery         55 (5.4)           Outcome         Rebleeding         95 (9.4)           Rebleeding (anticoag. and NOAC)         9 (14.8)           30-d mortality         53 (5.2)		
Epinephrine       213 (36.3)         Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       8ebleeding         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	Treatment	· /
Epinephrine       213 (36.3)         Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       8ebleeding         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	Endoscopic therapy	587 (58)
Hemoclips       156 (26.6)         Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       8         Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)		
Hemoclips + epinephrine       180 (30.7)         Thermocoagulation       26 (4.4)         Thermocoagulation + epinephrine       12 (2)         Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       8         Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)		
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Repeated endoscopic therapy       71 (7)         Blood transfusion required       496 (49)         Red blood cell       406 (40.1)         Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       75 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)		
Blood transfusion required 496 (49)  Red blood cell 406 (40.1)  Median (range), unit 2.5 (1-16)  Fresh frozen plasma 81 (8)  Median (range), unit 2 (1-6)  Platelet 9 (0.9)  Median (range), unit 6 (4-8)  Whole blood 0 (0)  Surgery 55 (5.4)  Outcome  Rebleeding 95 (9.4)  Rebleeding (anticoag. and NOAC) 9 (14.8)  30-d mortality 53 (5.2)	0 1 1	
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Median (range), unit       2.5 (1-16)         Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       8         Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	-	
Fresh frozen plasma       81 (8)         Median (range), unit       2 (1-6)         Platelet       9 (0.9)         Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome       8         Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)		
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Platelet 9 (0.9)  Median (range), unit 6 (4-8)  Whole blood 0 (0)  Surgery 55 (5.4)  Outcome  Rebleeding 95 (9.4)  Rebleeding (anticoag. and NOAC) 9 (14.8)  30-d mortality 53 (5.2)	-	
Median (range), unit       6 (4-8)         Whole blood       0 (0)         Surgery       55 (5.4)         Outcome         Rebleeding       95 (9.4)         Rebleeding (anticoag. and NOAC)       9 (14.8)         30-d mortality       53 (5.2)	, 0,	
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Rebleeding 95 (9.4) Rebleeding (anticoag. and NOAC) 9 (14.8) 30-d mortality 53 (5.2)	Surgery	55 (5.4)
Rebleeding (anticoag. and NOAC) 9 (14.8) 30-d mortality 53 (5.2)	Outcome	
30-d mortality 53 (5.2)	Rebleeding	95 (9.4)
30-d mortality 53 (5.2)	Rebleeding (anticoag. and NOAC)	9 (14.8)
` '		
	•	6 (0-45)

Data are presented as n (%) or mean (range). ASA: American society of anesthesiology; NOAC: New(er) oral anticoagulant; NSAIDs: Non-steroidal anti-inflammatory drugs.

patients with ulcer bleeding, and in 57.3% hemostasis was achieved with hemoclips or with combination

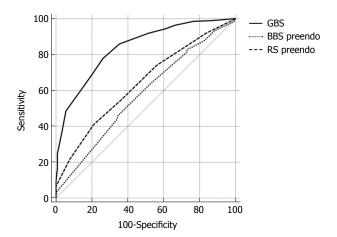


Figure 1 Comparison of Glasgow-Blatchford score, pre-endoscopic Rockall score and pre-endoscopic Baylor bleeding score in predicting need for hospital-based intervention or 30-d mortality. AUROC [0.83 (95%CI: 0.81-0.86)] vs [0.63 (95%CI: 0.59-0.68)] vs [0.57 (95%CI: 0.53-0.61)]. GBS: Glasgow-Blatchford score; BBS: Baylor bleeding score; RS: Rockall score.

hemoclips/diluted epinephrine. The rate of rebleeding was 9.4%, and in patients that were on anticoagulant therapy the rebleeding rate was 14.8% (P = 0.245), which was not statistically significant. In total, 5.4% of the patients were transferred to the Department of Surgery. The 30-d mortality was 5.2% and the median length of hospitalization was 6 d. Transfusion of red blood cells was performed in 49% of patients. Patients were predominantly men (median age 65.3). In 52% of patients, high-risk ulcers were verified (Forrest Ia-II b), 11% of the patients presented with shock, and moderate to severe comorbidity was found in 58%. Furthermore, 28.1% patients with peptic ulcer had been taking nonsteroidal anti-inflammatory drugs, 20% acetylsalicylic acid, 3.1% antiplatelet medication and 6% anticoagulant therapy.

*H. pylori* testing was performed in 760 (75.1%) patients, of which 324 (42.6%) tested positive. Table 4 shows the patient characteristics and clinical outcomes.

Using ROC curve analysis we found that the GBS was clearly superior to pre-endoscopic RS and pre-endoscopic BBS, in predicting need for hospital-based intervention or 30-d mortality (AUROC 0.84 *vs* 0.57 *vs* 0.64 respectively) (Figure 1).

The cutoff value that maximized the sum of the sensitivity and specificity for predicting 30-d mortality for the pre-endoscopic RS was 4 (sensitivity 0.63, specificity 0.85, total 1.48), and 5 for the post-endoscopic RS (sensitivity 0.83, specificity 0.68, total 1.51).

Based on ROC analysis of sensitivity and specificity, the optimal cutoff value of the pre-endoscopic BBS for 30-d mortality was 8 (0.63 sensitivity, 0.58 specificity, total 1.21), and the optimal cutoff post-endoscopic BBS value for 30-d mortality was 9 (0.88 sensitivity, 0.40 specificity, total 1.28).

When assessing scores for the prediction of lethal outcome in patients with PUB, the pre-endoscopic

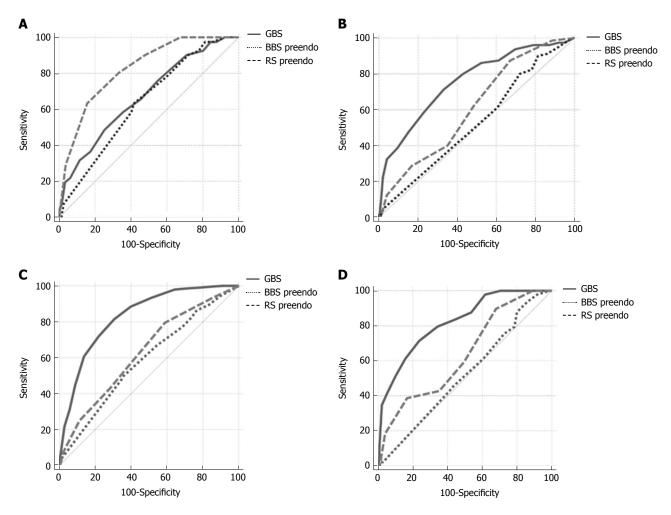


Figure 2 Comparison of the Glasgow-Blatchford score, pre-endoscopic Rockall score and pre-endoscopic Baylor bleeding score for the prediction of death, recurrent bleeding, transfusion or surgical intervention. A: AUROC [0.67 (95%CI: 0.64-0.70)] vs [0.82 (95%CI: 0.79-0.84)] vs [0.63 (95%CI: 0.60-0.66)]; B: AUROC [0.75 (95%CI: 0.72-0.78)] vs [0.61 (95%CI: 0.57-0.64)] vs [0.52 (95%CI: 0.49-0.56)]; C: AUROC [0.83 (95%CI: 0.80-0.85)] vs [0.63 (95%CI: 0.59-0.66)] vs [0.58 (95%CI: 0.55-0.62)]; D: AUROC [0.82 (95%CI: 0.79-0.84)] vs [0.63 (95%CI: 0.60-0.66)] vs [0.52 (95%CI: 0.48-0.55)]. GBS: Glasgow-Blatchford score; BBS: Baylor bleeding score; RS: Rockall score.

RS was superior compared to the GBS and the preendoscopic BBS (AUROC 0.82 *vs* 0.67 *vs* 0.63, respectively) (Figure 2A).

Based on the ROC analysis of sensitivity and specificity, the optimal cutoff GBS value for 30-d mortality was 12 (0.49 sensitivity, 0.75 specificity, total 1.24), for rebleeding 11 (0.71 sensitivity, 0.67 specificity, total 1.38), for blood transfusion 9 (0.71 sensitivity, 0.67 specificity, total 1.38) and for surgery 12 (0.71 sensitivity, 0.76 specificity, total 1.47).

The GBS score was superior to the pre-endoscopic RS and BBS in the prediction of rebleeding (AUROC 0.75 vs 0.61 vs 0.52) (Figure 2B).

The GBS score was superior to the pre-endoscopic RS and BBS in predicting the need for blood transfusion (AUROC  $0.83\ vs\ 0.63\ vs\ 0.59$ , respectively) (Figure 2C) and transfer to the Department of Surgery (AUROC  $0.82\ vs\ 0.63\ vs\ 0.52$ , respectively) (Figure 2D). Also, the post-endoscopic RS was superior to the post-endoscopic BBS (AUROC  $0.82\ vs\ 0.69$ ) in the prediction of lethal outcome (Figure 3A).

There was no significant difference between the

post-endoscopic RS and BBS in the prediction of rebleeding (AUROC 0.70 vs 0.73) (Figure 3B).

The rebleeding cutoff point that maximized the sum of the sensitivity and specificity for the pre-endoscopic BBS was 3 (sensitivity 0.90, specificity 0.19, total 1.09), and 11 for the post-endoscopic BBS (sensitivity 0.66, specificity 0.76, total 1.42).

There was no significant difference between the post-endoscopic RS and BBS in predicting the need for blood transfusion (AUROC 0.68 vs 0.71) (Figure 3C) and transfer to the Department of Surgery (AUROC 0.68 vs 0.74) (Figure 3D).

#### DISCUSSION

UGIB is the most important cause of emergency gastroenterological admissions and the most frequent condition requiring emergency endoscopy<sup>[1]</sup>. The most common causes of acute UGIB are non-variceal, of which 30% to 60% are attributed to PUB<sup>[28]</sup>. In our study, 42% of all non-variceal bleeding was caused by PUB. In order to assess the adequate timing of



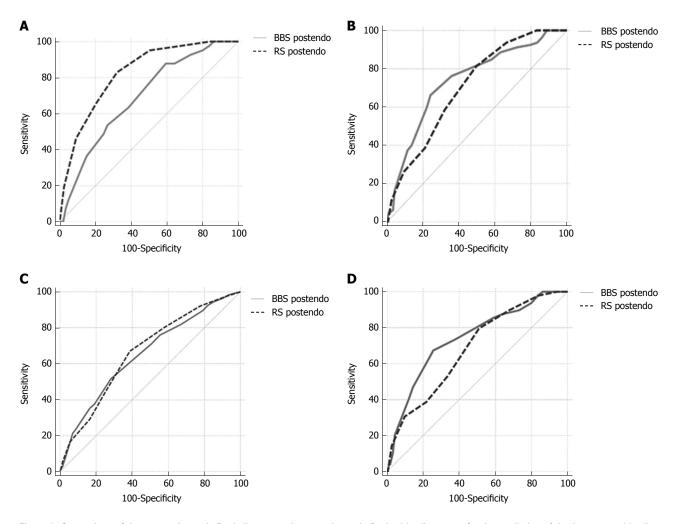


Figure 3 Comparison of the post-endoscopic Rockall score and post-endoscopic Baylor bleeding score for the prediction of death recurrent bleeding, transfusion or surgical intervention. AUROC: [0.82 (95%CI: 0.79-0.84)] vs [0.69 (95%CI: 0.65-0.72)]; B: AUROC [0.70 (95%CI: 0.67-0.73)] vs [0.73 (95%CI: 0.70-0.76)]; C: AUROC [0.66 (95%CI: 0.62-0.70)] vs [0.65 (95%CI: 0.61-0.69)]; D: AUROC [0.68 (95%CI: 0.65-0.71)] vs [0.74 (95%CI: 0.71-0.77)]. BBS: Baylor bleeding score; RS: Rockall score.

endoscopy and selection of patients for hospital admission, several scoring systems for risk estimation have been developed. With the array of available scoring systems, it is often difficult to select the ideal scoring system for a particular patient or clinical outcome of interest. Therefore, in this study, we compared the performance of these scoring systems in the risk assessment of various clinical outcomes.

Our study showed that the GBS is superior to the pre-endoscopic RS and BBS in predicting need for hospital-based intervention or 30-d mortality. This is in concordance with the results from a study by Laursen<sup>[22]</sup> and a study by Bryant *et al*<sup>[19]</sup>. Our study also showed that the GBS is superior to the pre-endoscopic RS and BBS in predicting peptic ulcer re-bleeding. An explanation for why the GBS best predicts peptic ulcer rebleeding is that it incorporates hemoglobin and serum urea values. Serum urea is a good biochemical marker for UGIB because it rises rapidly when there is catabolism of isoleucine-poor hemoglobin<sup>[8,29]</sup>. The maximal level of hemoglobin and urea account for half of the maximal sum of points in

the GBS score.

Our study showed that there is no significant difference between the post-endoscopic BBS and post-endoscopic RS in predicting peptic ulcer rebleeding. This is in concordance with the results from a study by Laursen  $et\ a^{[6]}$ . Similar data was published by Italian and Dutch researchers, who also found low values under the ROC curve [(0.59-0.68) and 0.61] and concluded that the RS is not appropriate for prediction of rebleeding<sup>[16,30]</sup>.

Our study showed that the GBS is superior to the pre-endoscopic RS and pre-endoscopic BBS in predicting the needs for blood transfusion and/or transfer to the Department of Surgery. The ROC curve for GBS rebleeding was similar to the GBS ROC curve for blood transfusion requirement and transfer to the Department of Surgery because peptic ulcer rebleeding is the main cause of blood transfusion requirement and need for surgical intervention. Bryant *et al*<sup>[19]</sup> published similar data.

Our study showed that the pre-endoscopic RS was superior to the GBS and pre-endoscopic BBS

in predicting mortality. The RS best predicted fatal outcome because it incorporated the majority of risk factors (age, shock, moderate to severe co-morbidities and high-risk endoscopic signs for rebleeding), which was valuable in a multivariate analysis of risk for fatal outcome<sup>[7,13,30,31]</sup>. Our study showed that the postendoscopic RS is superior to the post-endoscopic BBS in predicting lethal outcome in patients with PUB. Laursen<sup>[22]</sup> did not find any significant difference in AUROC among post-endoscopic BBS and post-endoscopic RS.

According to studies by Hyett  $et\ al^{[14]}$  and Bryant  $et\ al^{[19]}$ , the GBS cutoff points for high-risk of lethal outcome and rebleeding were  $\ge 10$  and  $\ge 12$ , respectively. In a recent retrospective study, Lim  $et\ al^{[32]}$  suggested urgent endoscopy in the first 13 h after clinical presentation in high-risk patients with GBS > 12, in the first 24 h in patients with GBS > 7 and for patients with GBS values between 4 and 7 urgent endoscopy in the first 24 h is recommended, but not necessary.

Our cutoff points for high-risk of rebleeding and lethal outcome in PUB patients are significantly different in comparison with original research papers (GBS  $\geq$  2, pre-endoscopic BBS > 5, post-endoscopic BBS  $\geq$  10, post-endoscopic RS  $\geq$  4), which all refer to UGIB<sup>[6-9,13,14]</sup>. An explanation for this could be that the original series included an unselected group of patients with UGIB, with a significant proportion of patients with a low-risk of death, recurrent bleeding, and needs for blood transfusion and/or surgical intervention. These were patients that presented with low-risk bleeding ulcers (Forrest II c and Forrest III), Mallory-Weiss syndrome, ulcerative esophagitis, angiodysplasia and portal hypertensive gastropathy.

When considering possible limitations of our study, there is always a certain level of subjectivity in the endoscopic classification of ulcers and variation in endoscopic treatment. Furthermore, our study had a relatively short follow-up period of 30 d.

By comparing the ROC curves of the aforementioned pre-endoscopic scores, the RS proved to be the best score for predicting lethal outcome. The post-endoscopic RS was also better than the post-endoscopic BBS in predicting lethal outcome in patients with PUB. On the other hand, among the three pre-endoscopic scores, the GBS best predicted need for hospital-based intervention or 30-d mortality, rebleeding, and needs for blood transfusion and/or surgical intervention.

# **COMMENTS**

#### **Background**

This paper delivers a prospective single-center study, with a sample size of more than 1000 patients, that compared the scoring systems of the Glasgow-Blatchford score, Rockall score and Baylor bleeding score in predicting clinical outcomes and need for interventions in patients with bleeding peptic ulcers.

#### Research frontiers

Endoscopic hemostasis represents the cornerstone of upper gastrointestinal bleeding treatment, and several scores have been developed for the prediction of rebleeding.

### Innovations and breakthroughs

The authors concluded that although there is no 'perfect score', the Rockall score is the best predictor of mortality and the Glasgow-Blatchford score is the best predictor of need for hospital-based intervention or 30-d mortality, rebleeding, and needs for blood transfusion and/or surgical intervention in patients with peptic ulcer bleeding.

#### Peer-review

A detailed description is provided to allow other investigators to reproduce or validate the results. The statistical methods used are appropriate. The results provide sufficient experimental evidence to draw firm scientific conclusions. The discussion is well organized and provides systematic theoretical analysis and valuable conclusions.

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