Clinical utility of risk scores in variceal bleeding

Sanjay CHANDNANI, Pravin RATHI, Suhas Sudhakarrao UDGIRKAR, Nikhil SONTHALIA, Qais CONTRACTOR and Samit JAIN

> Received 22/3/2019 Accepted 17/6/2019

ABSTRACT - Background - Variceal bleeding remains important cause of upper gastrointestinal bleed. Various risk scores are used in risk stratification for non-variceal bleed. Their utility in variceal bleeding patients is not clear. Objective - This study aims to compare probability of these scores in predicting various outcomes in same population. To study characteristics and validate AIMS65, Rockall, Glasgow Blatchford score(GBS), Progetto Nazionale Emorragia Digestiva (PNED) score in variceal Upper Gastrointestinal Bleed (UGIB) patients for predicting various outcomes in our population. Methods - Three hundred subjects with UGIB were screened prospectively. Of these 141 patients with variceal bleeding were assessed with clinical, blood investigations and endoscopy and risk scores were calculated and compared to non-variceal cases. All cases were followed up for 30 days for mortality, rebleeding, requirement of blood transfusion and need of radiological or surgical intervention. Results - Variceal bleeding (141) was more common than non variceal (134) and 25 had negative endoscopy. In variceal group, cirrhosis (85%) was most common etiology. Distribution of age and sex were similar in both groups. Presence of coffee coloured vomitus (P=0.002), painless bleed (P=0.001), edema (P=0.001), ascites (P=0.001), hemoglobin <7.5 gms (P<0.001), pH<7.35 (P<0.001), serum bicarbonate level <17.6 mmol/L (P<0.001), serum albumin<2.75 gms% (P<0.001), platelet count <1.2 lacs/µL (P<0.001), high INR 1.35 (P<0.001), BUN >25mmol/L (P<0.001), and ASA status (P<0.001), high lactate >2.85 mmol/L (P=0.001) were significant. However, no factor was found significant on multivariate analysis. Rockall was found to be significant in predicting mortality and rebleed. AIMS65 was also significant in predicting mortality. GBS was significant in predicting blood transfusion and need of intervention. PNED score was significant in all events except mortality. Conclusion - All four scores had lower predictive potential in predicting events in variceal bleed. However, AIMS65 & Rockall score were significant in predicting mortality, while GBS in predicting need of transfusion and intervention. PNED score was significant in all events except mortality.

HEADINGS - Upper gastrointestinal tract. Esophageal and gastric varices. Endoscopy. Predictive value of tests. Data accuracy.

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) has remained the most commonly encountered emergency in gastroenterology practice. Mortality rates have remained stagnant from 3.5%–10% despite technological advancement(1). Etiology of UGIB has remained variable in many studies. Although peptic ulcer disease has remained the predominant cause, recent reports have shown an increasing incidence of variceal cause of UGIB in India and Nepal with alcohol being the most common etiology⁽²⁻⁶⁾. However, a broad nation-wide multicenter study regarding UGIB as a whole is lacking. Various guidelines are available for management of overall populations and non-variceal bleeds^(7,8). They recommend use of risk scores for prognosticating disease severity for death, rebleeding, surgical or radiological intervention, requirement of transfusion and length of stay⁽⁷⁾. Child Turcott Pugh (CTP) scale and Model for End Stage Liver Disease (MELD) are reported to have predictive value for mortality in few studies (9,10). Data on subgroup, i.e. variceal and nonvariceal analysis, from other studies is also sparse⁽⁴⁾. Management of variceal bleeding differs from non-variceal in radical ways. Earlier endoscopy, preferably within 12 hours is shown to be beneficial in variceal bleeding management. It cuts the cost of hospitalization by classifying patients into low and high risk cases⁽¹⁰⁾. It also serves

in mortality benefit^(11,12). Hence this study was done to compare risk scores in variceal UGIB and to identify risk factors in variceal population in comparison to non variceal.

What do we already know?

- UGIB requires prompt resuscitation and endoscopic management. Management of variceal bleeding differs, so it needs to be identified early.
- Endoscopic and pre-endoscopic scores are available with mainly non-variceal bleeds. Their utility in variceal groups is not well established
- Observed cut-offs differ for variety of end points in different populations.
- Risk scores are useful for predicting high risk and low risk patients.
- Accuracy varies in clinical practice.
- Clinical application is not widespread.

What this study adds to:

- Demographic characteristics of patients with variceal UGIB.
- Rising trend of variceal bleed in India
- Role of established risk scores and cut-offs for significant events in both subgroups of variceal and non-variceal bleed.

Declared conflict of interest of all authors: none Disclosure of funding: no funding received TNMC & BYL Nair Charitable Hospital, Department of Gastroenterology, Mumbai, Maharashtra, India. Corresponding author: Sanjay Chandnani. E-mail: sanjy.med@gmail.com

 Predictors of various clinical outcomes such as death, rebleed, requirement of transfusion, need of intensive monitoring, surgery or radiological intervention significant to our population in variceal sub-group.

METHODS

Study design

This was a prospective cohort study conducted at a tertiary care medical center in western India from April 2017 to March 2018. It was approved by the Institutional Ethics Committee.

Patient selection

We screened 441 consecutive patients with acute UGIB (AU-GIB) with objective evidence of hematemesis, melena or blood in Ryle's tube aspirate presenting in emergency, in wards and in ICU. Out of them, 54 did not give consent for endoscopy, 26 patients were excluded due to age <12 years, 23 patients were uncooperative for endoscopy, 19 were lost to follow up and 19 had incomplete data. After excluding these, 300 patients who had undergone EGD due to UGIB were included. (FIGURE 1).

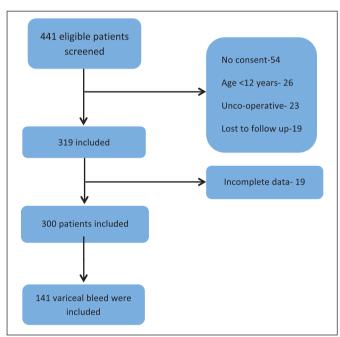


FIGURE 1. Showing patient selection protocol in our study.

Detailed history of each patient was recorded and a large bore venous access was secured. Routine blood investigations – complete blood count (CBC), renal function tests (RFT), liver function tests (LFT), Prothrombin time, International Normalized Ratio (INR), blood group and viral markers (HIV, HBsAg, Anti-HCV) were requested. Venous lactate and arterial blood gas (ABG) analysis were done. Blood was transfused to maintain Hemoglobin >7 gram% in variceal group. After resuscitative measures, patients were stabilized, informed consent was taken and upper gastrointestinal endoscopy was done at the earliest (<24 hours) after arrival in hospital. Based on endoscopy patients were classified as variceal and non-variceal groups. Baseline Glasgow Coma Scale was calculated at arrival in hospital. Necessary Imaging was done including chest

X-Ray and USG abdomen. Rockall, Glasgow Blatchford score, AIMS65, and Italian Progetto Nazionale Emorrhagia Digestiva (PNED) were compared. Patients were excluded if scores were incomplete or investigations revealed an alternative diagnosis. Pulse >100/min and systolic blood pressure <90 mmHg were considered as definition of shock. Time duration of UGIB and admission and admission to endoscopy were noted. Diagnostic and therapeutic upper GI endoscopy with Olympus GIF-150 endoscopy system was done. Classification of variceal bleed was in accordance to APASL classification, and non-variceal using Forrest classification. Patients were followed for a period of 30 days and evaluation for outcomes included requirement of blood transfusion, intensive care, rebleed, surgical intervention, and death. Information on comorbidities and length of hospitalization were noted. Following definitions were used as outcome measures:

- Death was defined as all cause mortality till follow up period.
- Rebleeding was defined by recurrent vomiting of fresh blood, melena, or both with either shock or a decrease in hemoglobin concentration of at least 2 gm % after initial successful treatment and stabilization for 48 hours and during follow up⁽⁸⁾.
- Failure of endoscopic therapy was defined by the inability to endoscopically identify or intervene during active bleeding⁽⁸⁾.
- Renal failure was defined as per definition of acute kidney injury (AKI), and chronic kidney disease (CKD).
- Cardiac failure was defined as per clinical, and echocardiographic findings.

Statistical analysis

Clinical data including demographic and endoscopic findings of variceal and non-variceal groups were first analyzed by chi square test and Students *t* test. Risk scores were calculated by summing up all points as per variables. The score was 0 when patient had none of the variables with mentioned cut-offs. Final scores were compared using AUROC curves based on the method by Delong et al. for prediction of outcomes of death, rebleed, surgical or radiological intervention, requirement of blood transfusion. Sensitivity, specificity, positive and negative predictive values were calculated for various cut-offs for each score pertaining to the above outcomes. All statistical analyses were performed using the Medcalc software version 17.1 system. A *P* value <0.05 was considered significant.

RESULTS

Of three hundred cases, demographic characteristics of 141 cases of variceal bleed were compared with 134 non-variceal and followed up for 30 days. In 25 cases etiology of UGIB could not be found on endoscopy. Mean age and sex distribution were found similar in both the groups. Clinically presence of painless bleed (P value <0.001), coffee colored vomitus (P value <0.001), presence of ascites (P value <0.001) and edema (P value <0.001) favored presence of variceal bleed. Platelet counts <1.2 lacs/ μ L (P value <0.001), INR >1.35 (P value <0.001), serum albumin <2.75 (P value <0.001), pH <7.35 (P value <0.001), bicarbonate <17.6 meq/L (P value <0.001), venous lactate >2.85 mmol/L (P value <0.001), were found significant in the variceal group. (refer TABLE 1).

Chronic liver disease was the most common etiology (43.33%). Ten cases of chronic liver disease had non-variceal bleed. Extra hepatic portal vein obstruction (EHPVO) and Non Cirrhotic Portal fibrosis (NCPF) were present in 11 (3.66%). History of significant alcohol intake was associated with 92 (65.24%) cases of variceal

TABLE 1. Comparison of parameters between variceal and non-variceal group.

	Non-variceal (%)	Variceal (%)	Test statistic (P value)		
N	134	141			
Hematemesis	(92.68) 124/134	(93.61) 132/141	0.514		
Melena	(60.01) 80/134	(20.56) 29/141	< 0.0012		
Hospital bleeding	(77.86) 103/134	(84.68) 118/141	0.085^{2}		
Painful	(58.95) 79/134	(20.56) 29/141	< 0.0012		
Clots	(68.65) 92/134	(51.77) 73/141	0.002^2		
Coffee colored	(57.46) 77/134	(74.46) 105/141	0.002^{2}		
Ascites	2.98 (3/134)	17.73 (25/141)	< 0.0012		
Age(years) (IQR & SD)	27/43/58 (42±19)	35/45/55 (45±15)	0.294^{1}		
Sex	(31.34) 42/134	(28.36) 40/141	0.586^{2}		
First episode	(86.57) 116/134	(65.24) 92/141	< 0.0012		
Bleeding P/R	(89.55) 120/134	(94.32)133/141	0.043^{2}		
SBP<90 mmHg	(20.14) 20/134	(21.98) 31/141	0.703^{2}		
Icterus	(8.95) 12/134	(14.89) 21/141	0.124^{2}		
Edema	(5.97) 8/134	(22.69) 32/141	< 0.0012		
WBC (IQR & SD)	5967/9300/13400 (10763±6386)	4617/7500/11700 (8564±4998)	0.001^{1}		
Platelet (IQR & SD)	95667/154000/210000 (159130±87506)	80000/98000/141000 (126475±99835)	< 0.0011		
INR (IQR & SD)	$1.00/1.00/1.21 (1.17 \pm 0.49)$	$1.00/1.30/1.49 (1.35 \pm 0.40)$	< 0.0011		
Serum Albumin (IQR & SD)	2.90/3.10/3.30 (3.10±0.48)	$2.60/2.80/2.90 (2.75 \pm 0.39)$	< 0.0011		
HBsAg	(0.74) 1/134	(13.47)19/141	< 0.0012		
Anti HCV	(0.74) 1/134	(8.51) 12/141	0.001^{2}		
Admission to endoscopy (duration)	(01, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1	(3.2 -)	0.270^{2}		
<12 hours	(81.34) 109/134	(84.89) 119/141	V.=, V		
12-24 hours	(14.17) 19/134	(7.81) 11/141			
24-72 hours	(3.73) 5/134	(6.41) 9/141			
>72 hours	(0.59) 8/134	(0.70) 1/141			
Hematemesis to endoscopy (duration)	(0.57) 0/131	(0.70) 17111	0.030^{2}		
<12 hours	(20.89) 28/134	(13.47)19/141	0.050		
12-24 hours	(35.07) 47/134	(35.46) 50/141			
24-72 hours	(42.53) 57/134	(44.97) 62/141			
>72 hours	(0.59) 8/134	(5.67) 8/141			
GCS	15/15/15 (15±1)	15/15/15 (15±1)	0.420^{1}		
Need of intensive care	(56.71) 76/134	(36.87) 52/141	0.420 0.001^2		
Blood transfusion	(45.52) 61/134	(70.21) 99/141	<0.001 ²		
	7.34/7.37/7.39 (7.36±0.05)		<0.001 <0.001 ¹		
pH (IQR & SD)		7.32/7.36/7.38 (7.35±0.05) 17.0/18.0/19.0 (17.6±3.1)	<0.001 <0.001 ¹		
Bicarbonate (IQR & SD) Stay duration (IQR & SD)	17.01/9.0/21.0 (18.8±3.2)				
	2/4/8 (6±7)	4/5/7 (7±5)	<0.001		
Hemoglobin (gms%)	$6.70/9.00/11.30 (9.05 \pm 3.06)$	6.30/7.50/8.80 (7.51±2.16)	$< 0.001^{1}$ 0.648^{2}		
Presence of shock	(34.32) 46/134	(36.17) 51/141			
Pulse rate (>100/min)	(38.05) 51/134	(38.58) 53/141	0.966^{2}		
BUN (IQR & SD)	$14.0/21.0/26.0 (22.4 \pm 13.0)$	17.0/23.0/30.8 (25.1±12.6)	0.0041		
Sr. creatinine (IQR & SD)	$0.90/1.00/1.20 (1.19 \pm 0.76)$	$0.92/1.10/1.30 (1.26\pm0.92)$	0.056^{1}		
Venous lactate (IQR & SD)	$1.10/1.70/2.83 (2.24 \pm 1.91)$	$1.60/2.20/3.78$ (2.85 ± 2.10)	< 0.0011		
ASA (at admission)	(24.2/) /2/42/	(40.47) 40/4/4	0.004^{2}		
1	(31.34) 42/134	(13.47) 19/141			
2	(35.07) 47/134	(47.51) 67/141			
3	(27.61) 37/134	(31.20) 44/141			
4	(5.97) 08/134	(42.55) 60/141			
Rebleeding episode	(14.2) 20/134	(18.43) 26/141	0.379^2		
Cause			< 0.0012		
Mallory Weiss	(14.17) 19/134	(0.00) 00/141			
Others	(13.68) 17/134	(16.31) 23/141			
Cirrhosis	(7.46) 10/134	(85.51) 120/141			
Neoplasia	(4.48) 6/134	(0.00) 00/141			

N is the number of non-missing value. ¹Kruskal-Wallis. ²Pearson. ³Wilcoxon.

IQR: interquartile range; SD: standard deviation; SBP: systolic blood pressure; WBC: white blood cell count; INR: international normalized ratio; GCS: Glasgow coma scale; BUN: blood urea nitrogen; ASA: American Society of Anesthesiology.

bleed. Out of 141 patents with variceal bleed, large varices were present in 94 (66.66%) cases. Gastroesophageal varices (GOV) were present in 26 (18.43%) patients; 19 (13.47%) had moderate to small varices and 2 (1.41%) had severe PHG.

Out of 134 cases of non-variceal bleed with positive stigmata of recent bleeding on endoscopy, 26 (19.40%) had erosive mucosal disease, 25 (18.65%) had Mallory Weiss tears, 24 (17.91%) had gastric ulcers, 22 (16.41%) had duodenal ulcers, 19 (14.17%) had esophagitis, 5 (3.77%) had pangastritis, 5 (3.77%) had pancreatitis, 2 (1.41%) had esophageal corrosive injury, 2 (1.41%) had Cameroon ulcer, 1 (0.77%) had esophageal candidiasis, 1 (0.77%) had esophageal ulcer.

There were 30 deaths overall, 12 (8.95%) in the non-variceal group (malignancy-3, gastric ulcer-3, erosive mucosal disease-2, Mallory Weiss tear-2 duodenal ulcer-2) and 18 (12.76%) in variceal group of which 15 had esophageal varices and 3 had gastroesophageal varices. This difference was not statistically significant.

Thirty day rebleeding was seen in 50 (16.33%) cases. It was more in the variceal group (18.4% vs 16.41%) but the difference was not statistically significant. Of these variceal cases, 16 (61%) had esophageal varices and 10 (38%) had GOV. Twenty two patients in non-variceal group had rebleeding episodes. Of these 6(27%) had gastric ulcers (IIa & IIb), 4 (18%) had esophagitis (2 grade D, 1 grade C, 1 grade B), 3 (13%) had duodenal ulcers, 3 (13%) had Dieulafoy's lesion, 2 (9%) had upper GI malignancy, 2 (9%) had pancreatitis while there were 2 (9%) patients had no stigmata of bleeding on endoscopy on both occasions, but had a consistent medical history of UGIB. Median duration of rebleed was on 2nd day. Overall 9 patients with rebleeding in both the groups had succumbed.

Endotherapy was done in 155 (51.66%) patients. The most commonly performed procedure was esophageal variceal ligation (EVL) in 108 patients.

Blood transfusion was required in 170 (56.66%) cases, significantly more in variceal bleed patients.

Failure of endoscopic therapy was seen in seven patients in variceal subgroup and 12 in non-variceal subgroup. All patients in variceal subgroup were with esophageal varices (100%). In non-variceal subgroup, esophagitis was found in five, was most commonly grade C and D, and followed by Duodenal ulcer (3), Hemosuccus Pancreaticus (2), Dieulafoy's lesion (1), and Gastric ulcer (1). Surgical and Radiological intervention was required in 14 patients. Five of the non-variceal group underwent emergency surgery (three had Dieulafoy's and one each had gastric and duodenal ulcers Forrest type Ib). Three patients with GOV (BRTO procedure), two with Hemosuccus Pancreaticus (Gastroduodenal and SMA pseudo aneurysm coiling) and one with Gastric cancer

(coiling) underwent interventional radiology. No cause was found on UGI endoscopy in three patients and they underwent diagnostic angiography.

Comparison of scores for death

In variceal subgroup Rockall and AIMS65 were found significant, though confidence intervals of Rockall reveal significant values than AIMS65. Rockall score >4 was more sensitive (94%) than others and had more NPV (96%) than others. (Refer FIGURE 2, Graph a; and TABLE 2).

Similarly in non-variceal group, all four scores were found to be significant. Overall PNED score significantly predicted events with accuracy than Rockall and GBS. Rockall >4 was more sensitive while PNED >6 was more specific. (Refer FIGURE 3 graph e; and TABLE 2).

Comparison of scores for rebleeding

In variceal group (Refer FIGURE 2 graph b; and TABLE 2) only Rockall and PNED were found to be modestly significant in predicting events. GBS and AIMS65 fared poorly in predicting events. PNED >7 had better accuracy in predicting events compared to other scores.

In non-variceal group (Refer FIGURE 3 graph f; and TABLE 2) all four scores were significant in performance. GBS had better AU-ROC 0.795 with cut-off >75 having high sensitivity and NPV. PNED score >7 had high specificity (87%) but modest sensitivity (43%).

Comparison of scores for blood transfusion

In variceal bleed patients, GBS (AUROC 0.648; CI-0.562 to 0.727, *P* value <0.0001) predicted events slightly better than other two scores) (See FIGURE 2 graph c; and TABLE 2). GBS >7 had a good sensitivity identifying patients requiring blood transfusion. AIMS65 score was not found significant (AUROC 0.58, CI -0.493 to 0.663, *P* value<0.0001).

In non-variceal bleed patients all 4 scores were found to be significant. GBS (AUROC 0.839; CI-0.767 to 0.896, *P* value <0.0001) outperformed compared to other scores with optimal cut-off >7 having good sensitivity (81%), specificity (76%), and reasonable accuracy (see FIGURE 3 graph g; and TABLE 2).

Comparison of scores for need of Surgical or Radiological intervention-

In patient with variceal bleed, three scores, viz; AIMS65 (0.66), PNED (0.610), & GBS (0.604) were found to be significant. GBS >8 was 100% sensitive, had 100% NPV but marred by low specificity (kindly refer FIGURE 2 graph d; and TABLE 2).

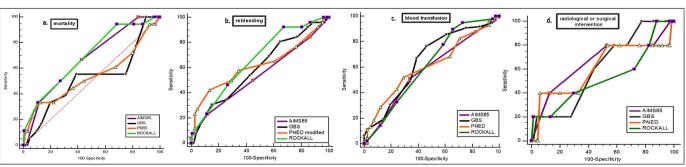


FIGURE 2. Showing graphs (a,b,c,d) comparing risk scores in predicting mortality, rebleeding, blood transfusion, radiological or surgical intervention in variceal bleed patients.

TABLE 2. Comparison of risk scores in variceal and non variceal bleed group for various outcomes.

Scores	AUROC	CI	optimal cut-offs	Sensitivity	Specificity	PLR	NLR	PPV	NPV
AUROC and	cut-offs of sco	res in variceal blee	d for mortality						
Rockall	0.691	0.609 to 0.771	>4	94.44	19.01	1.17	0.29	14.8	95.8
GBS	0.52	0.433 to 0.605	>8	56.23	43.55	1.18	0.35	12.88	88.1
PNED	0.537	0.450 to 0.622	>8	33.33	87.6	2.69	0.76	28.6	89.8
AIMS65	0.674	0.589 to 0.751	>1	66.67	57.02	1.55	0.58	18.7	92
AUROC and	cut-offs of sco	res in non-variceal	bleed for mortality						
Rockall	0.761	0.681 to 0.829	>4	90.91	58.59	2.2	0.16	15.9	98.7
GBS	0.729	0.647 to 0.801	>10	72.73	75.78	3	0.36	20.5	97
PNED	0.768	0.689 to 0.835	>6	63.64	89.84	6.27	0.4	35	96.6
AIMS65	0.688	0.603 to 0.763	>1	45.45	89.06	4.16	0.61	26.3	95
AUROC and	cut-offs of sco	res in variceal blee	d for rebleeding						
Rockall	0.662	0.577 to 0.740	>4	94.44	19.01	1.17	0.29	14.8	95.8
GBS	0.597	0.510 to 0.679	>5	92.31	32.74	1.37	0.23	24	94.9
PNED	0.652	0.567 to 0.731	>7	42.31	87.61	3.41	0.66	44	86.8
AIMS65	0.54	0.454 to 0.625	>2	23.08	87.61	1.86	0.88	30	83.2
AUROC and	cut-offs of sco	res in non-variceal	bleed for rebleeding						
Rockall	0.715	0.633 to 0.788	>3	82.61	52.99	1.76	0.33	25.7	93.9
GBS	0.795	0.719 to 0.859	>7	91.67	56.41	2.1	0.15	30.1	97.1
PNED	0.734	0.652 to 0.805	>5	50	91.45	5.85	0.55	52.4	90.7
AIMS65	0.634	0.548 to 0.714	>0	63.64	65.81	1.86	0.55	25.9	90.6
AUROC and	cut-offs of sco	res in variceal bleed	d for need of blood tr	ansfusion					
Rockall	0.614	0.528 to 0.695	>4	89.8	34.15	1.36	0.3	76.5	58.3
GBS	0.648	0.562 to 0.727	>7	90.91	24.39	1.2	0.37	74.4	52.6
PNED	0.611	0.525 to 0.692	>5	52.04	70.73	1.78	0.68	81	38.2
AIMS65	0.58	0.493 to 0.663	>1	51.02	65.85	1.49	0.74	78.1	36
AUROC and	cut-offs of sco	res in non-variceal	bleed for need of blo	od transfusion					
Rockall	0.732	0.650 to 0.804	>3	72.06	65.28	2.08	0.43	66.2	71.2
GBS	0.839	0.767 to 0.896	>7	81.16	76.39	3.44	0.25	76.7	80.9
PNED	0.779	0.701 to 0.845	>2	71.64	77.78	3.22	0.36	75	74.7
AIMS65	0.677	0.592 to 0.754	>0	56.72	77.78	2.55	0.56	70.4	65.9
AUROC and	cut-offs of sco	res in variceal bleed	d for need of surgical	or radiological	intervention				
Rockall	0.527	0.440 to 0.612	>8	20	98.51	13.4	0.81	33.3	97.1
GBS	0.604	0.518 to 0.686	>8	100	22.39	1.29	0	4.6	100
PNED	0.61	0.524 to 0.692	≤2	40	94.03	6.7	0.64	20	97.7
AIMS65	0.66	0.575 to 0.738	≤0	40	87.31	3.15	0.69	10.5	97.5
AUROC and	cut-offs of sco	res in non-variceal	bleed for need of sur	gical or radiolo	gical interventi	on			
Rockall	0.619	0.533 to 0.700	>4	75	56.06	1.71	0.45	9.4	97.4
GBS	0.847	0.777 to 0.903	>9	87.5	66.67	2.62	0.19	13.7	98.9
PNED	0.852	0.781 to 0.906	>2	100	57.25	2.34	0	12.5	100
AIMS65	0.544	0.458 to 0.629	>0	50	61.83	1.31	0.81	7.4	95.3

AUROC's: Area under receiver operating curve; CI: confidence intervals; PLR: positive likelihood ratio, NLR: negative likelihood ratio; PPV: positive predictive value; NPV: negative predictive value; GBS: Glasgow Blatchford score, PNED: Progetto Nazionale Emorrhagica Digestiva score.

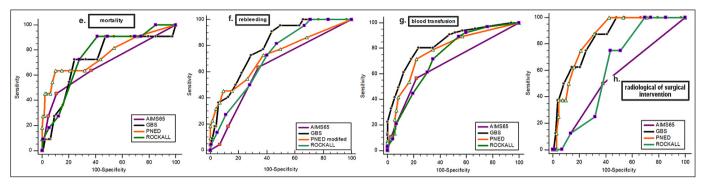


FIGURE 3. Showing graphs (e, f, g, h) comparing risk scores predicting mortality, rebleeding, blood transfusion, radiological or surgical intervention in non-variceal bleed patients.

In case of non-variceal bleeding, PNED (0.852) and GBS (0.847) performed fairly in predicting need of surgical and radiological intervention. PNED score >2 had 100 % sensitivity and 57% specificity. AIMS65 and Rockall were not found significant (kindly refer FIGURE 3 graph h; and TABLE 2).

DISCUSSION

Hospital admission rates for UGIB vary from place to place. Etiology and comorbidities also vary. This is due to local referral bias, inhomogeneity of protocols used and the way scores are applied in hospitals to manage these patients. Insufficient validation or complexity of use has been cited as problems in using these scoring systems. Hence locally validated scores should be applied in clinical practice. Blatchford score performing better than Rockall to predict high risk adverse events in one population may not be applicable to another population.

In our study variceal bleeding (47%) was most common cause of UGIB with chronic liver disease (43.33%) followed by Coronary artery disease (CAD) (6%) as the most common etiology. This was in consonance with a study from north India (45% & 13% respectively)(4). Studies from eastern and southern India and all studies from the west report non-variceal as the most common cause with duodenal ulcer leading the list(2,5,7,13,14). Various international studies have reported an incidence ranging from 3%–43% for variceal bleed but overall significantly lower than non-variceal bleed (2,7,13,14). In our study 25 cases had negative endoscopy. Chen et al. argued that presence of endoscopic stigmata are related to time of endoscopy from presentation, mean hemoglobin values and ASA status(15). In our study presence of painless bleed (P<0.001), coffee colored vomitus (P=0.002), presence of ascites (P<0.001), pedal edema (P<0.001) and history of previous bleed (P<0.001) correlated with the presence of variceal bleed. Other laboratory parameters that also correlated with variceal bleed were: hemoglobin <7.5 gms (P<0.001), pH<7.35 (P<0.001), serum bicarbonate level <17.6 mmol/L (*P*<0.001), serum albumin <2.75 gms% (*P*<0.001), platelet count $< 1.2 \text{ lacs/}\mu\text{L}$ (P < 0.001), high INR 1.35 (P < 0.001), BUN > 25mmol/L (P<0.001), ASA status (P<0.001). Similar findings were reported by Goenka et al. and Lahiff et al. (3,16)

We have compared four scores that appeared most promising. Two of them were clinical or pre-endoscopic, i.e. AIMS65 and GBS, and two had both clinical and endoscopic variables, i.e. Rockall and PNED. Rockall score is the most validated one^(4,17). For need of treatment GBS is validated better than Rockall^(15,18). In certain populations AIMS65 is useful in predicting mortality and rebleed-

ing risk⁽¹⁹⁾. Derived from non-variceal bleed database, PNED score is not validated in variceal population till date⁽²⁰⁾.

We compared these scores for predicting the four most concerned outcomes at the time of hospital admission. Patients were investigated at the time of presentation, after endoscopy as well as in follow-up period. They were sub grouped into variceal and non-variceal populations. Alcohol was the most common etiology of varices due to chronic liver disease as has been reported from north India and Thailand^(4,21). In predicting mortality in the variceal group. Rockall score had the maximum AUROC 0.691; the other score that was found significant was AIMS65. On comparing with non-variceal population these scores were less sensitive and specific. This is in agreement with the findings of Lahiff et al. (16). It showed that high comorbidities, low hemoglobin, younger age and low systolic blood pressures are associated with worse outcomes such as rebleeding. In the same study, Rockall score had better predictive value for rebleeding and mortality, while no patient with GBS of score 0 had adverse clinical outcome. This is in agreement with our findings where Rockall was found significant. However, Kate et al. from south India compared Partial Rockall, Complete Rockall, GBS and Modified GBS and found GBS (AUROC 0.833) as the best predictor⁽⁴⁾. In the variceal bleeding group, GBS (AUROC 0.736) was found to be significant while clinical and complete Rockall could not achieve significance. This was in contrast to our study where Rockall achieved statistical significance while GBS did not. Another study on only variceal bleeding patients comparing AIMS65, GBS and Rockall score found similar predictive values (0.70 vs 0.64 vs 0.66) for mortality but, AIMS65 better (0.74 vs 0.60 vs 0.67) at predicting rebleeding while GBS for need of intervention or transfusion. We found only Rockall and AIMS65 significant in predicting death in the variceal group. In predicting need of transfusion or any intervention GBS was significant. In another prospective study by Choe et al. showed variceal bleed accounted 22%, which was higher than most of western studies. It compared AIMS65, Rockall, GBS scores and found all three were statistically significant in predicting mortality in variceal and non-variceal bleeding (AUROC 0.705 vs 0.804, 0.665 vs 0.661, 0.665 vs 0.679, respectively). In his study, for predicting rebleeding Rockall score (AUROC 0.723) performed better than GBS (AUROC 0.634) and AIMS65 was not found significant⁽²²⁾. This echoed similar finding to our study that AIMS65 overall is not useful for predicting rebleed. In overall cases, Rockall score was only found to be significant (AUROC 0.701) and was also recommended for use in their population subset in predicting mortality while GBS for predicting need of intervention which is in sync with our study^(21,23). In the Italian PNED study done in over 1300 patients with non-variceal

bleed, odds ratio of rebleeding were twice in patients on antiplatelets and anticoagulants⁽¹⁷⁾. It showed that this 10 point score was significantly better than Rockall in predicting rebleed (AUROC 0.81 vs 0.66). We had modified this score by removing rebleeding points in patients who had already suffered rebleeding. It was found to be statistically significant in predicting rebleed in the variceal sub-group.

In our study serum lactate levels correlated with mortality risk and levels were significant in the variceal subgroup. This was similar to other western studies⁽²⁴⁾. Other scores validated in a few studies are Model for end stage liver disease (MELD) and MELD-Na⁽²⁵⁻²⁸⁾. Mortality risk is <5% with MELD<11⁽²⁵⁾. Chavez et al. found MELD more accurate than Rockall in predicting mortality while GBS as significant predictor of rebleeding⁽²⁵⁾. Turnes et al.; showed risk of first episode of bleeding could be minimized with beta blockers⁽²⁸⁾. However, a study comparing AIMS65, Rockall, GBS and MELD found AIMS65 in variceal population found all scores significant, but AIMS65(AUROC 0.808) as more accurate than others in predicting six week mortality⁽⁹⁾.

Strength of the study

It is a prospective study comparing four popular scores in patients with bleeding varices.

Limitations of the study

It is a single centre study and needs to be validated in a larger population. Need of endoscopy couldn't be assessed as all patients underwent endoscopy.

CONCLUSION

We conclude from our study that risk scores have lower predictive potential in acute variceal bleed. Rockall score has remained robust in predicting mortality and rebleed. In predicting requirement of transfusion and intervention, GBS has remained the key score. For predicting all events except mortality in the variceal subset PNED score was significant. AIMS65 was significant in predicting mortality in variceal subgroup as well. High serum lactate levels also corroborates with mortality risk.

Authors' contribution

Chandnani S: study concept and design, drafting the manuscript. Rathi P: critical revision of the manuscript for important intellectual content. Sonthalia N, Udgirkar SS, Contractor Q: critical revision of the manuscript for important intellectual content. Jain S: statistical review of manuscript.

Orcid

Sanjay Chandnani. Orcid: 0000-0001-8270-7680. Pravin Rathi. Orcid: 0000-0002-1095-3652.

Suhas Sudhakarrao Udgirkar. Orcid: 0000-0002-1275-4833.

Nikhil Sonthalia. Orcid: 0000-0002-5439-2084. Qais Contractor. Orcid: 0000-0001-7191-8589. Samit Jain. Orcid: 0000-0002-8097-5291.

Chandnani S, Rathi P, Udgirkar SS, Sonthalia N, Contractor Q, Jain S. Utilidade clínica dos escores de risco no sangramento varicoso. Arq Gastroenterol. 2019:56(3):286-93.

RESUMO - Contexto - O sangramento varicoso permanece como importante causa de sangramento gastrointestinal superior. Vários escores são utilizados na estratificação do risco para sangramento não varicoso. Sua utilidade em pacientes de sangramento varicoso não é clara. Objetivo - Este estudo tem como objetivo comparar a probabilidade desses escores em prever vários desfechos na mesma população. Estudar característica e validar o AIMS65, o Rockall, a Pontuação de Glasgow Blatchford (GBS), o escore Progetto Nazionale Emorragia Digestiva (PNED), na pontuação em hemorragia gastrointestinal varicosa superior (UGIB) em pacientes para prever vários resultados em nossa população. Métodos - Um total de 300 indivíduos com UGIB foram rastreados prospectivamente. Destes, 141 pacientes com sangramento varicoso foram submetidos à avaliação clínica, hematológica e endoscopia tendo seus escores de risco calculados e comparados aos casos não-varicosos. Todos os casos foram acompanhados por 30 dias para mortalidade, necessidade de transfusão sanguínea por ressangramento ou de necessidade de intervenção radiológica ou cirúrgica. Resultados – O sangramento varicoso (141) foi mais comum do que não varicoso (134) e em 25 teve endoscopia negativa. No grupo varicoso, a cirrose foi a etiologia mais comum (85%). A distribuição da idade e do sexo foi semelhante em ambos os grupos. Presença de vômito colorido em borra de café (P=0,002), sangramento indolor (P=0.001), edema (P=0.001), ascite (P=0.001), hemoglobina <7.5 GMS (P<0.001), pH <7.35 (P<0.001), nível de bicarbonato sérico <17,6 mmol/L (P<0,001), albumina sérica <2,75 GMS% (P<0,001), contagem plaquetária <1,2 Lacs/μL (P<0,001), INR elevada 1,35 (P<0,001), Bun >25 mmol/L (P<0,001) e estado ASA (P<0,001), lactato elevado >2,85 mmol/L (P=0,001) foram significativos. Entretanto, nenhum fator foi encontrado como significativo na análise multivariada. Rockall foi significativo em prever a mortalidade e ressangrar. O AIMS65 também foi significativo em prever a mortalidade e ressangrar. icante na predição da mortalidade. O GBS foi significativo na predição de transfusão sanguínea e necessidade de intervenção. O escore de PNED foi significante em todos os eventos, exceto mortalidade. Conclusão - Todos os quatro escores apresentaram menor potencial preditivo na predição de eventos em sangramento varicoso. Entretanto, o AIMS65 e o escore de Rockall foram significantes na predição da mortalidade, enquanto o GBS na predição da necessidade de transfusão e intervenção. O escore de PNED foi significante em todos os eventos, exceto mortalidade.

DESCRITORES - Trato gastrointestinal superior. Varizes esofágicas e gástricas. Endoscopia. Valor preditivo dos testes. Confiabilidade dos dados.

REFERENCES

- Button LA, Roberts SE, Evans PA, Goldacre MJ, Akbari A, D'silva R, et al. Hospitalized incidence and case fatality for upper gastrointestinal bleeding from 1999 to 2007: a record linkage study. Aliment Pharmacol Ther. 2011;33:64-76.
- Singh SP, Panigrahi MK. Spectrum of upper gastrointestinal hemorrhage in coastal Odisha. Trop Gastroenterol. 2013;34:14-7.
- Parvez MN, Goenka MK, Tiwari IK, Goenka U. Spectrum of upper gastrointestinal bleed: An experience from Eastern India. Dig Endosc. 2016;7:55.
- Sharma V, Jeyaraman P, Rana SS, Gupta R, Malhotra S, Bhalla A, Bhasin DK. Utility of clinical and complete Rockall score in Indian patients with upper gastrointestinal bleeding. Trop Gastroenterol. 2017;37:276-82.
- Anchu AC, Mohsina S, Sureshkumar S, Mahalakshmy T, Kate V. External validation of scoring systems in risk stratification of upper gastrointestinal bleeding. Indian J Gastroenterol. 2017;36:105-12.
- Shrestha UK, Sapkota S. Etiology and adverse outcome predictors of upper gastrointestinal bleeding in 589 patients in Nepal. Dig Dis Sci. 2014;59:814-22.
- Dworzynski K, Pollit V, Kelsey A, Higgins B, Palmer K. Management of acute upper gastrointestinal bleeding: summary of Upper gastrointestinal bleeding risk scores NICE guidance. BMJ. 2012;344: e3412.
- Sarin SK, Kumar A, Angus PW, Baijal SS, Baik SK, Bayraktar Y, et al. Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations. Hepatol Int. 2011;5:607-24.
- Wang F, Cui S, Wang F, Li F, Tang F, Zhang X, Gao Y, Lv H. Different scoring systems to predict 6-week mortality in cirrhosis patients with acute variceal bleeding: a retrospective analysis of 202 patients. Scand J Gastroenterol. 2018:53: 885.00
- Mohammad AN, Morsy KH, Ali MA. Variceal bleeding in cirrhotic patients: What is the best prognostic score?. Turk J Gastroenterol. 2016;27:464-9.
- Lee JG, Turnipseed S, Romano PS, Vigil H, Azari R, Melnikoff N, et al. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. Gastrointest Endosc. 1999;50:755-61.
- Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Use of endoscopy for management of acute upper gastrointestinal bleeding in the UK: results of a nationwide audit. Gut. 2010;59:1022-9.
- Stanley AJ, Laine L, Dalton HR, Ngu JH, Schultz M, Abazi R, et al. Comparison of risk scoring systems for patients presenting with upper gastrointestinal bleeding: international multicentre prospective study. BMJ. 2017;356:i6432.
- Cassana A, Scialom S, Segura ER, Chacaltana A. Validation of the Glasgow-Blatchford Scoring System to predict mortality in patients with upper gastrointestinal bleeding in a hospital of Lima, Peru (June 2012-December 2013). Rev Esp Enferm Dig. 2015;107:476-82.

- Chen YI, Wyse J, Barkun A, Bardou M, Gralnek IM, Martel M. Can the Presence of Endoscopic High-Risk Stigmata be Bredicted before Endoscopy? A Multivariable Analysis Using the RUGBE Database. Canadian Journal of Gastroenterology and Hepatology. 2014;28:301.
- Lahiff C, Shields W, Cretu I, Mahmud N, McKiernan S, Norris S, et al. Upper gastrointestinal bleeding: predictors of risk in a mixed patient group including variceal and nonvariceal haemorrhage. Eur J Gastroenterol Hepatol. 2012;24:149-54.
- Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut. 1996;38:316-21.
- Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper gastrointestinal haemorrhage. The Lancet. 2000;356:1318-21.
- Saltzman JR, Tabak YP, Hyett BH, Sun X, Travis AC, Johannes RS. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. Gastrointest Endosc. 2011;74:1215-24.
- Marmo R, Koch M, Cipolletta L, Capurso L, Grossi E, Cestari R, et al. Predicting mortality in non-variceal upper gastrointestinal bleeders: validation of the Italian PNED Score and Prospective Comparison with the Rockall Score. Am J Gastroenterol. 2010;105:1284.
- Thanapirom K, Ridtitid W, Rerknimitr R, Thungsuk R, Noophun P, Wongjitrat C, et al. Prospective comparison of three risk scoring systems in non-variceal and variceal upper gastrointestinal bleeding. Journal of gastroenterology and hepatology. 2016;31:761-7.
- Choe JW, Kim SY, Hyun JJ, Jung SW, Jung YK, Koo JS, et al. Is the AIMS65 65 Score Useful in Predicting Clinical Outcomes in Korean Patients with Variceal and Non-variceal Upper Gastrointestinal Bleeding. Gut Liver. 2017;11:813.
- Laursen SB, Hansen JM, De Muckadell OB. The Glasgow Blatchford score is the most accurate assessment of patients with upper gastrointestinal hemorrhage. Clin Gastroenterol Hepatol. 2012;10:1130-5.
- Shah A, Chisolm-Straker M, Alexander A, Rattu M, Dikdan S, Manini AF. Prognostic use of lactate to predict inpatient mortality in acute gastrointestinal hemorrhage. Am J Emerg Med. 2014;32:752-5.
- Reverter E, Tandon P, Augustin S, Turon F, Casu S, Bastiampillai R, et al. A MELD-based model to determine risk of mortality among patients with acute variceal bleeding. Gastroenterology. 2014;146:412-9.
- Altamirano J, Zapata L, Augustin S, Muntaner L, González-Angulo A, Ortiz AL, et al. Predicting 6-week mortality after acute variceal bleeding: role of classification and regression tree analysis. Ann Hepatol. 2009;8:308-15.
- Wang J, Wang AJ, Li BM, Liu ZJ, Chen L, Wang H, Shi F, Zhu X. MELD-Na: effective in predicting rebleeding in cirrhosis after cessation of esophageal variceal hemorrhage by endoscopic therapy. J Clin Gastroenterol. 2014;48:870-7.
- Turnes J, Garcia-Pagan JC, Abraldes JG, Hernandez-Guerra M, Dell'Era A, Bosch J. Pharmacological reduction of portal pressure and long-term risk of first variceal bleeding in patients with cirrhosis. Am J Gastroenterol. 2006;101:506.

