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Validation and Comparison of Risk Scoring Systems in Predicting Clinical Outcomes in Patients with Upper Gastrointestinal Bleeding

Sukanya Bhrugumalla,[1]Bhushan Chopade[2], Sumaswi Angadi[3], Ravichandra Nuggahalli[4], Chaudhary Vineet[5]

[1]Associate Professor in Medical Gastroenterology, Nizam's Institute of Medical Sciences, Hyderabad

[2]Consultant Gastroenterologist, Chintamani Hospital, Jalgaon

[3]Assistant Professor in Medical Gastroenterology, Nizam's Institute of Medical Sciences, Hyderabad

[4]Consultant Gastroenterologist, DRM Hospital, Mysuru

[5]Consultant Gastroenterologist, Max Superspeciality Hospital, Thane

Abstract

Background: Upper gastrointestinal bleeding (UGIB) is a common cause of admission to hospitals worldwide with an annual incidence of 80-140/100,000 population (1) and mortality of 10%. (2) Rebleed and mortality depend not only on the etiology of blood loss but also on factors like age and co morbidities. The proportion of patients who are “low risk” ranges from 20% to 70%. (3) Many of these patients end up with unwarranted prolonged hospital stay. Early risk stratification is essential for optimal management and utilization of resources. Many scoring systems have been developed to identify patients at the low risk. We undertook this study to validate and compare various scores in predicting the outcome in Indian population.

Material and Methods: This single centre, prospective, observational study was conducted among patients presenting with upper GI bleed to a university teaching hospital in South India. Consecutive patients of UGI bleed were screened and recruited.

Results:110 patients (87 males, 23 females), mean age 47.78±15.54 years were recruited. 8 patients died. Rebleeding rates were similar in survivors vs. non survivors (p=0.625). Mean age of non survivors was higher than survivors, 62.25 vs 46.65 years (p=0.005). Commonest cause of bleed was esophageal varices; commonest endoscopic intervention was endoscopic variceal ligation. AIMS65, post endoscopy Rockall and T scores were excellent predictors of

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mortality (AUROC 0.956, 0.934, 0.908 respectively). GBS was the only score with good prediction of rebleeding. (AUROC 0.859).

Conclusion: All scores were good predictors of mortality with AIMS65 being the best at a cut-off of >2. GBS was good for predicting rebleed. None of the scores could predict need for endoscopic intervention.

Short title: Validation of various risk scoring systems in Upper GI bleed.

Keywords: Mortality; Rebleed rate; Risk scoring systems; Upper GI bleed.

Corresponding Author: Sukanya Bhrugumalla, Associate Professor in Medical Gastroenterology, Nizam's Institute of Medical Sciences, Hyderabad.

Introduction

Upper gastrointestinal bleeding (UGIB) is a common cause of admission to hospitals worldwide with an annual incidence of 80-140/100,000 population,[1] and a mortality of 10%[2] Most epidemiological studies on UGIB come from UK and other European nations. Studies from India on incidence are scarce. In most cases, hospital admission is considered mandatory until the risk of further hemorrhage recedes. In published literature, the proportion of patients with non-variceal upper gastrointestinal bleed (UGIB) who are considered "low risk" ranges from 20% to 70%.[3] Most patients with UGIB have a self-limiting illness and uncomplicated hospital stay. Despite this low risk many patients remain admitted, often longer than necessary thereby exposing them to an increased risk of hospital-acquired infections. It also leads to financial burden to the patients due to cost of hospitalization and loss of wages during hospitalization. Even healthcare resources and personnel involved in treating these patients are put under strain.

Although endoscopic findings can identify individuals at a high risk of rebleeding, overall mortality is often due to other factors such as age and co-morbid illnesses. Therefore, risk stratification in patients with UGIB is very important. Scoring systems for prediction of complications serve this purpose. Scoring system with high sensitivity and high negative predictive value for mortality and complications can help in identifying patients at low risk, who can be managed as outpatient.

Many risk assessment scores have been developed to predict clinically relevant outcomes like mortality, need for hospital-based intervention, rebleeding, and lengths of hospital stay. Out of them Rockall,[4] and Glasgow-Blatchford score (GBS),[5] are the best known and widely used scores in prediction of several clinically important outcomes. Recently Saltzman

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JR et al have designed AIMS65 score,[6] to predict hospital mortality. It has also been validated in many studies. Current guidelines,[7] recommend early risk stratification in patients presenting with UGIB to facilitate accurate triage and assist in decisions such as timing of endoscopy, discharge planning, and level of care,[7,8] but uncertainty remains about their exact role in clinical practice.

Several studies have validated and compared these scores but it is still not clear which one is superior. While a number of studies are available from the Western population on the utility of these scores, the data from India is minuscule. We undertook this study to compare and validate these scores in effectively predicting clinically relevant outcomes in our population of patients.

Material and Methods

This was a single centre, prospective, observational study conducted in a university teaching hospital in South India from January 2018 – December 2018 after Institutional ethics committee approval.

Inclusion criteria

Patients with UGIB, defined by hematemesis, coffee-ground vomiting, or melena were screened and recruited after obtaining informed consent.

Exclusion criteria

1. Subjects who did not undergo endoscopy.
2. Subjects who had normal endoscopy.
3. Age < than 18 years.
4. Subjects who had bleeding from iatrogenic lesions such as after endoscopic resection.
5. Subjects in whom parameters for scoring systems could not be obtained.

Patients fulfilling the inclusion and exclusion criteria were serially recruited into study. Clinical examination was performed and appropriate investigations sent. After resuscitation and stabilization, UGI endoscopy was performed within 24 hours of presentation. All clinical, laboratory, endoscopic and therapeutic details were recorded in the study proforma. Pre-endoscopic Rockall, post-endoscopic Rockall, GBS and AIMS65 scores were calculated using android app ‘MD Calc’. T score was calculated manually. All patients received standard care as per guidelines. Patients were followed for a period of 6 weeks and their clinical outcome including rebleeding was documented. Telephonic follow up was done for patients unable to attend the outpatient clinic.

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Definitions:

Hematemesis,[2] was defined as vomiting of bright red blood or coffee-ground emesis. Melaena,[2] was defined as black tarry stool.

Rebleeding was defined by the presence of fresh hematemesis and/or melaena associated with development of shock or a reduction in hemoglobin concentration greater than 2 g/dL over 24 hours necessitating repeat endoscopy, surgery or any interventional radiology procedure.

Altered mental status,[6] was defined as a Glasgow Coma Scale score of less than 14.

Heart failure: Patients with low ejection fraction on 2D echo or clinical signs of heart failure (Bilateral basal crepts, X-ray showing pulmonary edema).

Liver disease: Patients with radiological and/or clinical signs of liver disease.

Endoscopy: All endoscopies were performed with Olympus GIF-XP170 series scope and were done by endoscopists with more than 7 years' experience.

Endoscopic variceal ligation (EVL): EVL was done using multiband ligator (Wilson -Cook/ EndoVu).

Glue injection: Glue used was n-Butyl Cyanoacrylate (M/s Samarth life sciences Pvt. Ltd)

Hemoclips: Hemoclips used were EZ clips (Olympus India limited)

Endoscopic injection therapy: It was done by injecting Inj. Adrenaline (1:10,000)

Score calculation: Pre-endoscopic Rockall, post-endoscopic Rockall, GBS and AIMS65 scores were calculated using android app 'MD Calc'. T score was calculated manually.

Statistical Analysis

Statistical analysis was performed using the SPSS (statistical package for social performance) v 20 software. Comparison of two independent variables with normal distribution was done using students (t) test and of independent variables with non- normal distribution using Mann. Whitney U test. Difference was considered statistically significant when p-value was <0.05. Each score's ability to predict the predetermined outcome was computed using area under the receiver operating characteristic curve (AUROCs) and 95% confidence intervals. The optimal score thresholds to predict patients at very low risk of rebleeding and mortality and thus being suitable for outpatient management were identified based on a sensitivity of 90% or more. The sensitivity, specificity, positive predictive value and negative predictive value of each score were calculated from the cutoff point obtained.

Results

110 patients (87 males, 23 females), age (mean±SD) 47.78 ± 15.54 years were recruited. There were 8 (7.3%) deaths and 102 (92.7%) survivors. 19 patients (17.27%) had re-bleed.

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There was no significant difference in mortality between re- bleeders and non-re-bleeders (10.6 vs 6.6, p=0.625). Co-morbidities were seen in 86 (78.18%) patients. Many patients had more than 1 co-morbidity. CLD was most common co-morbidity (n=66), followed by diabetes mellitus (n=24), renal dysfunction (n=17), hypertension (n=20), cardiac disorder (n=16), cerebrovascular disease (n=5) and respiratory disorder (n=2). 71(64.54%) patients needed blood transfusion; re-bleeders more than non-re-bleeders (94.7% vs 58%). There was no difference in the symptoms at presentation or gender distribution between survivors and non-survivors. There was a significant difference in age, pulse rate, blood pressure, inotrope requirement between survivors and non-survivors. Hemoglobin and prothrombin time at admission were not a predictor of mortality. Serum albumin and blood urea were significantly different between survivors and non-survivors. Mortality in those who needed transfusion was more than those who did not require transfusion. [Table 1]

Table 1: Demographic, clinical and laboratory parameters.

Parameter	**Survivors**	**Non-Survivors**	**P value**
Age (years±SD)	46.65± 15.147	62.25± 11.399	0.005
Pulse (beats/minute	100±16	121±10.5	0.001
Systolic Blood pressure (mm Hg)	103.6±11.6	87.2±12.8	<0.001
Hemoglobin (gram/dL)	7.98±2.67	7.44±1.68	0.573
Vasopressor support (%)	8.83	75	<0.001
Albumin (g/dL)	3.4±2.95	2.54±0.44	0.409
INR	1.5±0.5	1.7±0.58	0.354
Urea	48.48±32.12	87.5±39.7	0.002
Blood transfusion (%)	61.76	100	0.049

All patients underwent endoscopy within 24 hours of arrival in hospital. The commonest endoscopic finding was esophageal varices (61.8%) followed by portal hypertensive gastropathy (24.54%) and gastroesophagealvarices (20.9%). [Table 2]

Table 2: Source of GI bleed on endoscopy

Endoscopic finding	**Number**	**Percentage**
Esophageal varices	68	61.8%

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Portal hypertensive gastropathy	27	24.54%
Gastroesophagealvarices	23	20.9%
Duodenal ulcer	13	11.8%
Gastric ulcer	7	6.36%
Erosions	7	6.36%
Isolated gastric varices	4	3.63%
Malignancy	4	3.63%
GAVE	3	2.73%
Mallory Weiss tear	3	2.7%
Hemosuccuspancreaticus	2	1.81%
Barrett's esophagus	1	0.9%

GAVE: Gastric Antral Vascular ectasia 57 patients underwent endoscopic intervention, commonest being endoscopic variceal ligation followed by glue injection. [Table 3]

Table 3: Modality of endoscopic intervention

Endoscopic intervention	**Number**	**Percent**
EVL	34	59.65 %
Glue injection	10	17.54 %
Endoscopic injection	5	8.77 %
Endoscopic hemoclip	4	7 %
EVL + glue	3	5.20 %
Endoscopic injection + hemoclip	1	1.75 %
Total	57	100%

EVL: Endoscopic variceal ligation. ROC curves for various bleeding scores were plotted and AUROC of different scores for prediction of mortality calculated. All scores performed good for predicting mortality with AUROC >0.8. For prediction of mortality AIMS65 was superior to the others with AUROC of 0.956 (95% CI: 0.914-0.998) p value <0.001. AUROCs for post-endoscopy Rockall score, GBS, T score and Pre-endoscopy Rockall scores were 0.934, 0.908, 0.865 and 0.828 respectively. [Table 4, Figure 1]

No patient in non-survivor group had Pre-RS score <5, post-RS < 7, GBS< 14, AIMS65 <3 and T score >4. [Table 4]

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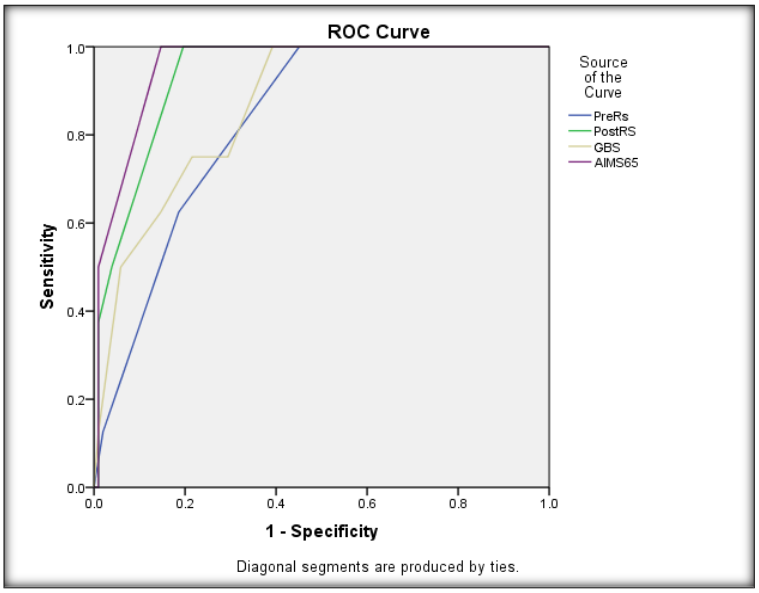

Figure 1: Receiver-operating characteristic curves (ROCs) for the AIMS65, Glasgow–Blatchford, and Pre and post endoscopic Rockall risk scores as predictors of mortality.

Note: In contrast to other scores, lower values of T score indicate bad prognosis hence ROC of T score was not clubbed with other scores

Table 4: Comparison of Sensitivity, Specificity, PPV, NPV and AUROC of various scores for prediction of mortality

Score	Cut-off	Sensitivity	Specificity	PPV	NPV	AUROC
Pre RS	>3	100	55	14.8	100	0.828
Post RS	>6	100	80.4	28.6	100	0.934
GBS	>13	100	60.8	16.7	100	0.865
AIMS65	>2	100	85	34	100	0.956
T Score	<7	87.5	77.5	23.3	98.8	0.908
Key: Pre RS-Pre endoscopic Rockall score, Post RS- Post-endoscopic Rockall score, GBS-Glasgow Blatchford score, PPV- Positive predictive value, NPV- Negative predictive value.						

GBS was the only good predictor of rebleed with AUROC of 0.859. All the other scores failed to predict rebleed. [Table 5]

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Table 5: Comparison of AUROC values of various scores in predicting rebleed

Score	AUROC	Std. Error	p value	95% CI
Pre-RS	0.449	0.065	0.487	0.323 - 0.576
Post-RS	0.528	0.07	0.704	0.39 - 0.666
GBS	0.859	0.046	<0.001	0.768 - 0.95
AIMS65	0.523	0.073	0.752	0.38 - 0.666
T score	0.75	0.062	0.06	0.64 – 0.872
Key: Pre RS-Pre endoscopic Rockall score, Post RS-Post-endoscopic Rockall score, GBS-Glasgow Blatchford score				

Discussion

Mean age in present study was 47.78 ± 15.54 as against western studies where the study cohort was much older.[40] with mean age of 60 years. This can be an observation bias or due to a relatively young population in India. Mortality rate in our cohort was 7.27% which is comparable to previously published studies. Mortality rates have ranged between 2.6,[9] to 14%,[10] in various studies with an older cohort of study population having higher mortality.[10] Presence of multiple co morbidities especially coronary artery disease, renal dysfunction in elderly have been implicated as cause for higher mortality and hence many of the risk predictor scores include co morbidities as one of the parameters. 78.18% of our patients had co morbidities. Re bleeding rate in our study group was 17.3% which is slightly higher than other large studies.[11,12] Both of these can be explained by the predominance of portal hypertension in our patients. Due to low overall mortality, we could not do statistical analysis of mortality in those with co-morbidities versus those without. We found that AIMS65 with an AUROC of 0.956 was the best predictor of mortality. We hypothesize that such a good AUROC for AIMS65 is likely due to the predominance of portal hypertension related bleed in our study as some components of AIMS65 like albumin, prothrombin time are also components of Child Pugh score which is used for assessing severity of liver disease. So, someone with a higher Child Pugh score would have high mortality and the same would be picked up by AIMS65 score as well. However, similar results were seen in various other studies from India,[13] other Asian countries.[14,15] and the west,[16,17,18] with AUROCs ranging from 0.77 to 0.93, regardless of the etiology. This may be due to the fact that AIMS65 was developed with the aim of predicting mortality as against a score like GBS which was developed with the intention of predicting need for clinical intervention. In our study Post

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endoscopy Rockall (AUROC 0.934) and GBS (AUROC of 0.865) were also good predictors of mortality. GBS and post endoscopy Rockall scores were good alternative predictors of mortality in most other studies also.[14,15,17,19,20] As expected, GBS with a AUROC 0.859 was the only good predictor for rebleed. All the other scores fared poorly in predicting rebleed.

Conclusion

GI bleeding is a leading cause of GI emergencies. The spectrum of etiology is evolving from predominance of ulcer related bleed to more of portal hypertension related bleeding probably due to the widespread use of proton pump inhibitors. Most patients are low risk for bleed hence it is important to have good predictive scores for triaging patients at admission itself for optimal utilization of resources. Co-morbidities play a major role in mortality hence predictor scores which include co-morbidities have shown better accuracy than others. AIMS65 was best score in predicting mortality in patients with upper gastrointestinal bleed with optimal cut-off being >2. All other studied scores also predicted mortality well. GBS was a good predictor of re bleeding while other scores did not fare well. We hypothesize that triaging for all patients presenting with GI bleed should be done at admission with AIMS65 and GBS and all those at low risk should be managed on outpatient basis. The main drawback of the study was the predominance of portal hypertension as the etiology which could have impacted the results. Larger sample size with a more representative study population is needed to validate the results of this study.

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