Chirurgia (2014) 109: 48-54
No. 1, January - February

Predictors for In-hospital Mortality and Need for Clinical Intervention in Upper GI Bleeding: A 5-year Observational Study

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Rezumat

Factori predictivi privind mortalitatea intraspitalicească și atitudinea terapeutică în hemoragiile digestive superioare: un studiu observațional de 5 ani

Introducere: Hemoragia digestivă superioară (HDS) este o urgență gastroenterologică cu potențial fatal, al cărei management depinde de stratificarea precoce a riscului pacienților.
Metodă: Am evaluat retrospectiv 151 pacienți cu HDS internați în spitalul nostru în perioada 1 ianuarie 2007 – 31 decembrie 2011, la care am calculat scorurile Rockall clinic și complet, Glasgow-Blatchford și Glasgow-Blatchford modificat. Am analizat performanța acestor scoruri în ceea ce privește predicția decesului pe durata spitalizării și a necesității de intervenții clinice.
Rezultate: Dintre cei 151 pacienți, 68.87% erau de sex masculin, iar media de vârstă a fost de 59,48 ani. 1 din 3 pacienți avea istoric de boală hepatică cronică, iar 1 din 8 avea istoric de HDS anterior. Clinic, 58,3% dintre pacienți au exteriorizat prin melenă, 18,5% prin hematemeză și 23,1% prin hematemeză și melenă. 22% din cazuri au fost hemoragii variceale iar restul non-variceale. 16 pacienți au decedat în timpul spitalizării. Cele 4 scoruri au arătat o valoare prognostică bună pentru decesul în timpul spitalizării și necesitatea de intervenții clinice, cea mai bună performanță având-o scorul Rockall complet (AUROC 0,849 și respectiv 0,653).
Concluzii: Scorurile Rockall și Blatchford sunt buni predictori ai mortalității și necesității de intervenție clinică, fiind utile pentru stratificarea pacienților cu HDS.

Cuvinte cheie: hemoragie digestivă superioară, scor de risc, Rockall, Glasgow-Blatchford, predictiv, mortalitate

Abstract

Background: Upper GI bleeding (UGIB) is a potentially life-threatening gastrointestinal emergency whose effective management depends on early risk stratification.
Methods: We retrospectively studied 151 patients admitted to our unit with UGIB between 1st January 2007 and 31st December 2011 and in whom we calculated the clinical and complete Rockall, the Glasgow-Blatchford and modified Glasgow-Blatchford risk scores. We performed an analysis of the predictive value of these scores for in-hospital mortality and need for clinical intervention.
Results: Of the 151 patients enrolled, 68.87% were male, and the mean age was 59.48 years. One in three patients had a history of chronic liver disease and one in eight had a previous episode of UGIB. Clinically, 58.3% of the patients presented with melena, 18.5% with hematemesis and 23.1% with both hematemesis and melena. 22% of cases were variceal hemorrhages and the other non-variceal. 16 patients died during hospitalization. The prognostic accuracy of all four scores for in-hospital death and need for clinical intervention was good, the complete Rockall score having the best performance (AUROC 0.849 and 0.653 respectively).
Conclusions: The Rockall and Blatchford scores were good predictors of mortality and need for clinical intervention in

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our study. The good predictive performance of these scores highlight the need for their use in day-to-day practice to select patients with likelihood of poor clinical outcome.

Key words: upper GI bleeding, risk score, rockall, glasgow-blatchford, predictor, mortality

Introduction

Upper GI bleeding (UGIB) is a potentially life-threatening gastrointestinal emergency that requires prompt evaluation and intervention. Effective management depends on using a risk stratification tool to identify low-risk and high-risk patients. Risk-stratification can be useful for initial triage, directing endoscopic timing and taking the decision of admission/discharge.

Despite significant advances in diagnosis and treatment [acid suppressors, endoscopic haemostatic techniques and recognition of Helicobacter pylori as an etiologic agent of peptic ulcers (1)] and the shift of management from the OR to the endoscopy lab (2) (thus avoiding surgical complications), mortality rate from UGIB hasn't changed much in the last decades (3). This is probably due to an increase in age of patients with UGIB (with a high likelihood of severe comorbid illnesses and a high vulnerability to hemodynamic changes from an acute bleeding) and a rise of NSAID (non-steroidal anti-inflammatory drug) associated-UGIB. Death in UGIB patients is mostly related to hypovolemic shock, severe comorbidities with poor overall health status, and failure to control bleeding.

In order to optimize management of UGIB, multiple clinical prediction models have been proposed as a tool to identify patients at risk for poor outcome. The ideal risk score should be easy to calculate early after presentation and should have a good accuracy to predict outcomes.

The goal is to select low-risk patients who can be managed on an outpatient basis (and thus reduce costs), and the high-risk ones, who require hospital admission, clinical and endoscopic interventions. The most frequently used risk scoring system in UGIB is the Rockall score (4) – *Table 1*, which was described in 1996, following analysis of data from a large English audit; the score was developed to assess the risk of death following presentation with UGIB and incorporates patient age, hemodynamics, comorbidities and endoscopic findings. Another frequently used scoring system is the Glasgow Blatchford Score (GBS) - *Table 2*, which was developed in 2000 to predict the need for hospital based intervention (transfusion, endoscopic therapy or surgery) or death following UGIB (5).

Material and Method

Aim

Our goal was to compare the current risk stratification tools for patients with upper GI bleeding, in terms of in-hospital mortality and the need for clinical intervention. We also tried to study the cause of death in patients with UGIB.

Study design

We conducted a retrospective study on 151 patients admitted to our unit with a diagnosis of UGIB, according to ICD-10 codes, over a period of 5 years, between 1st January 2007 and 31st December 2011.

Clinical, biological and endoscopic data were collected from their charts. We calculated the clinical and complete Rockall, the Glasgow-Blatchford and modified Glasgow-Blatchford risk scores and performed an analysis of their predictive value for in-hospital mortality and need for clinical intervention (blood transfusions, endoscopic or surgical treatment).

Statistical analysis

Accuracy to predict mortality and the need for clinical intervention was evaluated by the area under the receiver operating characteristic curve (AUROC) with 95% confidence

Table 1. *Rockall score (4)*

Component	0	1	2	3
Age	< 60	60-79	≥ 80	—
Hemodynamics				
Pulse	< 100	≥ 100		—
Systolic BP	≥ 100	≥ 100	< 100	—
Comorbidities	None		IHD, cardiac failure, other major comorbidity	Renal or liver failure, disseminated malignancy
Diagnosis	MW or no esion and no stigmata	All other diagnoses	Malignant lesions of UGIT	—
Stigmata of hemorrhage	No stigmata or dark spot on ulcer	—	Blood in UGIT, adherent clot, visible/spurting vessel	—

UGIT: Upper gastrointestinal tract; IHD: Ischemic heart disease; MW: Mallory-Weiss tear; GI: Gastrointestinal; BP: Blood pressure

Table 2. *Glasgow-Blatchford score (5)*

Admission risk marker	Score
Blood urea (mmol/L)	2
6.5-8	3
8-10	4
10-25	6
> 25	
Hb (g/L) in men	
120-130	1
100-120	3
< 100	6
Hb (g/L) in women	
100-120	1
< 100	6
Systolic BP (mmHg)	
100-109	1
90-99	2
< 90	3
Pulse ≥ 100/min	1
History and comorbidities	
Melena	1
Syncope	2
Hepatic disease	2
Cardiac failure	2

interval (CI). We also reported the predictive value of the risk stratification scores in variceal vs. non-variceal bleeding. The significance level was chosen at $\alpha = 0.05$. Statistical analysis was performed using SPSS Statistics 17.0.

Results

Patient characteristics

Of the 151 patients enrolled, 68.87% were male and 31.13% female, with a mean age of 59.48 ± 13.41 (range 23-88). Assessment of risk factors for UGIB revealed that 13.2% were active smokers and 21.9% reported chronic alcohol intake. One in three patients (31.79%) had a history of chronic liver disease (alcoholic, viral) and one in eight (12.58%) had a previous episode of UGIB (47.36% of the rebleeders were cirrhotic patients with previous variceal bleeding, and most of the others were patients with gastric ulcers and angiodysplasia). Regarding drug-related GI bleeding risk, 17.9% of patients were on NSAID, 5.3% on antiplatelets, 6% on oral anticoagulant and 1.2% on combinations of these. Clinically, 58.3% of the patients presented with melena, 18.5% with hematemesis (fresh blood or coffee-ground emesis) and 23.1% with both hematemesis and melena; there was no patient presenting with hematochezia with positive gastric lavage – *Table 3*. Mean hemoglobin was lower in patients presenting with both hematemesis and melena (9.03 g/dl vs. 9.89 g/dl in those presenting with melena only and 9.46 g/dl in those with hematemesis only), signifying a greater blood loss; this group of patients also had the least favorable hemodynamic status.

Table 3.

Patient characteristics	No. of patients (%)
Gender	
Female	47 (31,13)
Age: mean (min-max)	59 (23-88)
UGIB type	
Variceal	34 (22.51)
Non-variceal	117 (77.49)
Risk factors	
Smoking	20 (13.24)
Chronic alcohol	33 (21.85)
Previous UGIB	19 (12.58)
Presentation	
Hematemesis	28 (18.54)
Melena	88 (58.27)
Both	35 (23.17)
Comorbidities	
Heart failure	43 (28.47)
Liver disease	48 (31,79)

22.51% of cases were variceal hemorrhages and the rest of 77.49% non-variceal. Most patients (58%) had stigmata of recent bleeding, while only 7% were active bleeders – *Table 4*. 16 patients died during hospitalization (most of them having esophageal varices or gastric tumors) and the mean LOS was 8 days (range 1-39). 37.5% of deceased patients had a LOS of less than 3 days, reflecting a high likelihood of death in the severely ill. A significant proportion of survivors also had short LOS, but this was due to mild UGIB.

Predictive value of risk stratification tools

Among the clinical and biologic parameters, an increased heart rate (HR), low systolic blood pressure (SYS-BP) or high ALT were associated with a greater mortality risk. The first two reflect a greater amount of blood loss and hemodynamic instability, which are known to be associated with poor outcome. The predictive value of high ALT can be explained by its association with chronic liver disease and the likelihood of variceal bleeding in these patients – *Table 5*.

Table 4. *Endoscopic findings*

	N=151
Esophageal varices	34 (22.5%)
Gastric ulcer	27 (17.8%)
Duodenal ulcer	41 (27.1%)
Hemorrhagic gastritis	42 (27.8%)
Malignancy	18 (11.9%)
Angiodysplasia	9 (5.9%)
Mallory-Weiss tear	4 (2.6%)
Others*	13 (8.6%)

Some patients had more than 1 finding.

Others: esophagitis (5), duodenitis (5), portal hypertensive gastropathy (3)

Table 5.

	Deceased (n=16)	Survived (n=135)	p value
Female gender	31,25%	31,11%	0.9910
Age	61,87±12,43	59,20±13,23	0.4432
Platelet count (x10^3)	247.00±175.64	231.13±115.30	0.6255
HR (bpm)	94.18±12.98	86.22±14.44	0.0369
SYS BP (mmHg)	100.62±22.42	118.26±20.64	0.0016
Creatinin (mg/dl)	1.08±0.34	1.21±1.07	0.61317
ALT (U/l)	63.02±44.98	32.96±29.78	0.0004
Hb (g/dl)	8.62±2.77	9.78±2.61	0.09703
INR	1.42±0.50	1.31±0.61	0.4911
Algover score	1.63±0.21	1.70±0.26	0.3134
clinical RS	4.06±1.52	2.39±1.71	0.0002
full RS	6.75±2.11	3.74±1.92	<0.00001
GBS	11.37±5.03	8.61±4.00	0.0122
mGBS	8.62±3.96	6.44±.51	0.0218

The overall accuracy of the scoring systems was good, the full Rockall score being the best predictor for mortality (AUROC 0.849 [95% CI 0.739-0.959]), followed by the clinical Rockall score (AUROC 0.748 [95% CI 0.626-0.869]), GBS (AUROC 0.656 [95% CI 0.499-0.814]) and modified GBS (AUROC 0.655 [95% CI 0.499-0.810]) – *Fig. 1*.

Regarding the need for clinical intervention (transfusions or endoscopic treatment – clips, epinephrine injection, banding or argon-plasma coagulation), all four scores had a similar performance: full RS – 0.653 [95% CI 0.552-0.754]), clinical RS (AUROC 0.614 [95% CI 0.508-0.720]), Glasgow-Blatchford score (AUROC 0.604 [95% CI 0.508-0.701]) and modified GBS (AUROC 0.605 [95% CI 0.507-0.702]) – *Fig. 2*.

The predictive value of the scores increased significantly when considering only variceal bleeding patients: AUROC 0.903 for clinical RS, 0.955 for full RS, 0.824 for GBS and 0.766 for mGBS.

Analysis of fatal cases

Among the 16 cases of UGIB-related deaths, 5 (31.25%) were females, with an average age of 61.87 years. Mortality rates were similar in both sexes – 5/47 (10.63%) in females, 11/104 (10.57%) in males. 8 out of the 16 patients (50%) had chronic liver disease, and 5 (31.25%) were oncologic patients (advanced gastric, liver or pulmonary malignancy). Mean

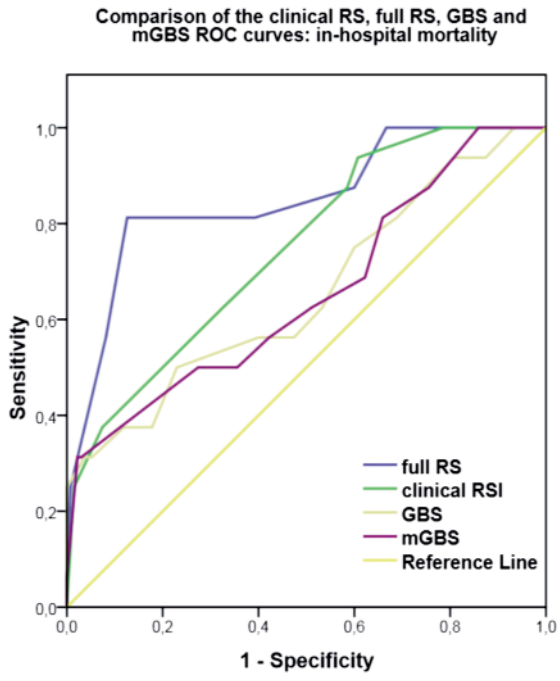

Figure 1.

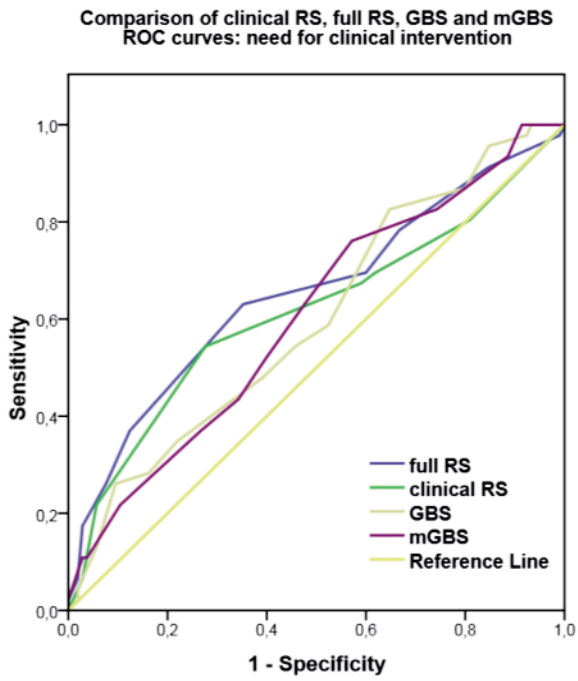

Figure 2.

hemoglobin level was lower in these patients compared to survivors (8.62 vs. 9.78 g/dl, p=0.09). 7/16 (43.75%) of patients had hemodynamic decompensation following the upper GI bleed. Regarding the source of bleeding, 5 (31.25%) were variceal and the other 11 (68.75%) were non-variceal.

68.75% of patients were transferred to the ICU during their admission and 40% required blood transfusions. In most cases, the cause of death was liver or kidney failure; one patient died from pulmonary embolism and one from neurologic complications of polyradiculoneuritis. The mean interval between the UGIB and death was 5.07 days. In our cohort, comorbid illness was the major cause of death, and not the actual UGIB.

Discussions

Upper GI bleeding is one of the most frequent emergencies in gastroenterology. The most common causes are peptic ulcer disease and esophageal varices (these two etiologies accounted for 60.92% cases in our study). Other causes include tumors, esophagitis, Mallory-Weiss tear, gastritis or vascular malformations such as angiodysplasia or Dieulafoy lesions [the latter can be found anywhere in the GI tract, including the colon (6)].

Initial assessment including medical history, vital signs, lab values and endoscopy is very important for risk-stratification (in terms of outcomes, rebleeding, need for transfusions or endoscopic treatment), as some patients may have a mild, self-limiting UGIB from a Mallory-Weiss tear, while others may have massive variceal bleeding with hemodynamic instability.

As stated by Yavorski RT et al (7), comorbidities, rather than actual bleeding, are the major cause of death in UGIB patients: almost all patients who die after UGIB (98.3%) have at least one comorbidity and in approximately 3 out of 4 cases (72.3%) this is the primary cause of death. In our cohort of patients presenting with UGIB, liver failure and malignancy were associated with a high likelihood of death. Exsanguination has been recognized as a cause of death in UGIB patients, but it is quite rare nowadays. Active spurters on endoscopy (Forrest Ia), variceal bleeders, patients with large ulcers (especially those located posteriorly in the duodenum) or aorto-enteric fistula are at great risk of massive hemorrage which can lead to hypovolemic shock and ultimately to death if not treated promptly. Failure of primary hemostasis with continued bleeding and rebleeding are also associated with a high mortality risk.

According to the summary of predictors for mortality in UGIB conducted by Chiu and Ng (2), the most frequently reported risk factors are advanced age, presence of comorbidities (cardiac disease, liver or renal failure, malignancy), hemodynamic collapse and low hemoglobin. In our study, tachycardia, hypotension and increased ALT were associated with a higher mortality risk. The same review done by Chiu and Ng concluded that encephalopathy, prothrombin time, albumin and bilirubin levels were important predictors for mortality in variceal bleeding. All these parameters are included in the Child-Pugh score: Afessa and Kulibis (8) reported that the Child-Pugh grade was a good predictor for clinical outcomes in patients with variceal UGIB, with an AUROC value of 0.76 (compared to Gatta and Garden scores, with AUROC values of 0.70 and 0.71 respectively).

Several scoring systems have been developed to stratify UGIB patients – some of them are pre-endoscopic scores [clinical Rockall (4), Glasgow-Blatchford score (5) with its age-extended and modified versions, Cambridge score (9), ANN (10)], while others are post-endoscopic [full Rockall, Cedar-Sinai (11), Baylor (12), Almela (13)]. Besides age, gender, hemodynamics, comorbidities and time from symptoms, the post-endoscopic scores include the endoscopic findings (characteristics of the bleeding lesion, severity of hemorrhage), which makes them valuable to predict rebleeding.

They are of great value in stratifying high-risk and low-risk patients, thus optimizing medical resources in emergency departments: for example, a GBS score of 0 can accurately select patients with UGIB who can be treated on an outpatient basis (14). Similarly, a full Rockall score of 0 or 1 is associated with low rebleeding rate (3.4-4.9%) and 0% mortality (4); on the other hand, a Rockall score of more than 7 has a significantly higher risk for rebleeding/mortality, according to Chiu PW et al (15).

Data from clinical trials revealed heterogeneous results for the predictive value of these scores regarding mortality, risk for rebleeding or need for clinical intervention (blood transfusions, endoscopic or surgical treatment) – *Table* 6.

Of these, GBS seems to be the most accurate in identifying those patients who require hospital-based intervention and those suited for early discharge and outpatient care; patients with a GBS ≤ 2 can be managed safely as outpatients, according to Le Jeune et al (18). GBS can also select patients who benefit from early endoscopy. Although endoscopy is recommended in the first 24h in UGIB, there is a subgroup of patients who require emergency endoscopy – those with variceal bleeding, advanced age, hemorrhagic shock, prosthetic aortic graft or severe comorbidities. Although a randomized trial of 93 patients who were assigned to either urgent (before admission) or elective endoscopy (after admission) did not show a reduction in resource utilization or improved outcomes from early endoscopy, the study conducted by Lim LG (21) revealed a survival benefit for patients with a GBS ≥ 12 who underwent endoscopy in the first 12 hours.

Concerning the prediction of mortality for the Rockall score, we found similar results in our cohort (AUROC 0.748 for the clinical RS and 0.849 for the complete RS) as those in other studies (see *Table* 6). AIMS65 is a novel, simple risk score with good accuracy, which needs further validation.

As highlighted in Stanley's review (25), the current risk scores for UGIB seem to perform better in low-risk patients than high-risk ones. An accurate identification of this low-risk subgroup (full Rockall ≤ 2, GBS =0-1) is very important for saving healthcare resources, as these patients can be safely discharged early.

The limitations of this study consist of the relatively small sample size, especially in the variceal bleeding subgroup [the rate of variceal bleeds has been on the decline in

Table 6. *Predictive value of risk scores in UGIB*

	AUROC for	Stanley (14)	Cheng (16)	Camellini (17)	Le Jeune (18)	Stanley (19)	Others
clinical RS	mortality/rebleed	0.70*	0.59		0.75	0.76	0.73/0.61 (20)
	clinical intervention		0.66			0.63	
full RS	mortality/rebleed	0.81*	0.69	0.85/0.68		0.79	
	clinical intervention		0.75			0.76	
GBS	mortality/rebleed	0.90 *	0.81		0.92	0.74	0.81 (21) 0.93** (22)
	clinical intervention		0.86			0.79	
mGBS	mortality/rebleed		0.83				
	clinical intervention		0.85				
Baylor	mortality/rebleed			0.78/0.59			
Cedar-Sinai	mortality/rebleed			0.81/0.67			
AIMS65	mortality/rebleed						0.77 (23)
ANN	mortality/rebleed						0.95*** (24)

RS – Rockall score, GBS – Glasgow-Blatchford score, mGBS – modified Glasgow-Blatchford score

* composite endpoint: mortality and need for clinical intervention; ** AUROC for 30-day mortality or hospital-based intervention;

*** AUROC for 30-day mortality

the last couple of years, due to consistency in primary and secondary prophylaxis, as reported by Jammal et al (26)] and the lack of some parameters needed to calculate other risk scores (such as albumin for AIMS65).

Conclusions

Our study showed that both Rockall and GBS scores are useful as risk stratification tools for UGIB patients, having good predictive accuracy for mortality and need for clinical intervention. The two scoring systems had a very good performance for variceal bleeders in particular.

By using these scores we can safely split UGIB patients into low-risk (and direct them for outpatient endoscopy) and high-risk (who require prompt, intensive, in-hospital intervention), thus optimizing healthcare resources.

Conflicts of interest and source of funding

None.

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