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Original Research Article

Predictors of Rebleeding and Mortality in Patients with Acute Upper Gastrointestinal Bleeding: A Prospective Study

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Abstract

Background: Acute upper gastrointestinal bleeding (UGIB) is a frequent emergency with clinically significant risks of rebleeding and mortality. Early identification of high-risk patients can lead to better triage, timing, monitoring and escalation of care. The main aim of study to identify clinical, laboratory, endoscopic and risk score predictors of rebleeding and mortality at 30 days in acute UGIB in a prospective study.

Methods: A prospective cohort of 286 consecutive adults with hematemesis and/or melena were standardizedly resuscitated, had their Glasgow-Blatchford (GBS) and AIMS65 scores calculated and underwent endoscopy within 24 hours if clinically appropriate, and their Rockall scores were calculated. The primary outcomes were rebleeding and all-cause mortality within 30 days. Multivariable logistic regression and ROC analysis were carried out.

Results: Mean age was 55.8 ± 16.7 years and 205 patients (71.7%) were male. The most common causes were peptic ulcer disease (41.6%) and variceal bleeding (24.1%). Thirty-seven patients (12.9%) experienced rebleeding and 23 patients (8.0%) died within 30 days. Independent predictors of rebleeding were shock index ≥1.0 (adjusted OR 2.78, 95% CI 1.27-6.08), hemoglobin <8 g/dL (OR 2.43, 95% CI 1.10-5.37), active/high-risk endoscopic bleeding stigmata (OR 3.61, 95% CI 1.58-8.22), and transfusion ≥3 units (OR 2.69, 95% CI 1.21-5.98). Mortality was independently associated with age ≥65 years (OR 2.94, 95% CI 1.15-7.51), systolic blood pressure ≤90 mmHg (OR 3.38, 95% CI 1.30-8.79), albumin <3.0 g/dL (OR 3.17, 95% CI 1.23-8.18), INR >1.5 (OR 2.76, 95% CI 1.08-7.04), and rebleeding (OR 4.52, 95% CI 1.78-11.50). AIMS65 had the best discrimination for mortality (AUC 0.82), and full Rockall and GBS were better for rebleeding (AUC 0.74 and 0.72).

Conclusions: Hemodynamic instability, severe anemia, high-risk endoscopic findings, and transfusion burden are predictive of rebleeding, while age, hypotension, hypoalbuminemia, coagulopathy, and rebleeding are predictive of mortality. Bedside scores and endoscopic findings give clinically useful risk stratification.

Keywords: Upper gastrointestinal bleeding; rebleeding; mortality; AIMS65; Glasgow-Blatchford score; Rockall score; endoscopy.

Introduction

Acute upper gastrointestinal bleeding (UGIB) is a common medical emergency that can be self-limited mucosal bleeding or exsanguinating bleeding. Although there have been improvements in resuscitation, endoscopic hemostasis, proton pump inhibitor therapy, vasoactive therapy for portal hypertensive bleeding and interventional radiology, mortality remains clinically significant, especially in older patients and those with significant comorbidities. Overall mortality is reported to be 2-10% in contemporary reviews, with outcome being increasingly dependent on physiologic reserve and comorbidity as well as the bleeding lesion itself [1]. Guidelines focus on early hemodynamic evaluation, transfusion of only small amounts in most patients, early risk stratification, and endoscopy within 24 hours after appropriate resuscitation [2]. The European Society of Gastrointestinal Endoscopy also suggests using the Glasgow-Blatchford score (GBS) to pre-endoscopy risk stratify patients, and that a GBS of ≤1 is a good threshold to consider outpatient management of very-low-risk patients [3]. The most important early decision in UGIB is not only what lesion is present but how likely the patient is to require intervention, rebleed, deteriorate or die. There are

several validated scores that focus on various aspects of this risk. The GBS was created to predict the need for treatment based on clinical and laboratory parameters that are available prior to endoscopy [4]. The Rockall score includes age, shock, comorbidity, diagnosis and endoscopic stigmata, and was first developed to assess the risk of death and rebleeding [5]. AIMS65 score is a simple clinical score that incorporates albumin <3.0 g/dL, INR >1.5, altered mental status, systolic blood pressure ≤90 mmHg and age >65 years and was developed as a predictor of inpatient mortality, length of stay and cost [6].

However, no single score is best for all outcomes. Comparisons of AIMS65 and GBS have been made in prospective multicenter studies, and AIMS65 has been found to be useful for mortality, while GBS may be more useful for transfusion or intervention needs [7]. Other validation studies have found similar or moderate discrimination for rebleeding in AIMS65, GBS and Rockall systems [8]. Recent Indian data also show that performance is case dependent, particularly if variceal bleeding is a significant proportion of presentations [9]. Therefore, local prospective evaluation is still clinically relevant. Rebleeding is a special case that needs to be addressed as it is a consequence and a risk factor for death. Hemodynamic instability, low hemoglobin, active bleeding, large ulcer size, and high-risk ulcer location have been found to be consistently associated with recurrent bleeding after endoscopic therapy in peptic ulcer bleeding [10]. The Forrest classification remains prognostic for rebleeding, especially for ulcers with active bleeding or large stigmata [11]. Older prospective studies also showed that shock, hematemesis, cirrhosis, ulcer size and location, and endoscopic stigmata could stratify patients into significantly different groups of risk for rebleeding [12].

The difficulty in routine practice is that patients with acute UGIB are heterogeneous. The risk of lesions varies with peptic ulcer disease, varices, erosions, malignancy, Mallory-Weiss tears, and portal hypertensive gastropathy, and age, liver disease, renal dysfunction, anticoagulation, and shock affect outcomes. A practical prediction strategy should therefore combine bedside physiology, validated scores, and endoscopic features, not just one variable, with reserve.

The aim of this prospective study was to determine the independent predictors of 30-day rebleeding and all-cause mortality in consecutive adults with acute UGIB. A secondary aim was to assess the discriminatory ability of the AIMS65, GBS and Rockall scores in a mixed variceal and nonvariceal population for these outcomes.

Materials and Methods

Participants and study design: Consecutive adults presenting to the emergency department of Aanvi Endoscopy and Surgery Centre, Bharuch & Dr K C Patel Medical College and Research Institute, Bharuch with acute UGIB (defined as hematemesis, coffee ground vomiting, melena or hematochezia with a suspected upper gastrointestinal source) were enrolled in this prospective observational study. Patients under 18 years of age, those with bleeding due to recent upper gastrointestinal surgery, and those who had been treated for definitive endoscopic hemostasis elsewhere were excluded.

Initial assessment and management: Airway and circulation were assessed on arrival and two large bore intravenous lines were inserted where indicated. Baseline variables consisted of age, sex, presenting symptom, comorbidities, cirrhosis, antiplatelet/anticoagulant exposure, systolic and diastolic blood pressure, heart rate, mental status, and shock index (heart rate/systolic blood pressure). Laboratory parameters measured were hemoglobin, platelet count, urea, creatinine, albumin, bilirubin and INR. Transfusion of packed red blood cells (PRBC) was given based on the patient's hemodynamic status, hemoglobin level, continued bleeding, and cardiovascular comorbidities. Vasoactive therapy, antibiotic prophylaxis and intravenous proton-pump inhibitor (PPI) therapy were started when variceal bleeding was suspected and nonvariceal bleeding was suspected, respectively.

Risk scores and endoscopy: GBS and AIMS65 were determined at presentation. Pre-endoscopic Rockall score was used prior to endoscopy and the complete Rockall score was used following the endoscopic diagnosis and stigmata. The upper gastrointestinal endoscopy was directed within 24 hours of stabilization, and earlier endoscopy was at the discretion of the treating team if there was continued severe bleeding. Forrest stigmata were used to classify peptic ulcers.

When clinically high risk, high-risk nonvariceal stigmata were defined as active spurting/oozing, nonbleeding visible vessel, or adherent clot. High-risk endoscopic bleeding was also defined as variceal active bleeding or as evidence of recent hemorrhage that needed endoscopic therapy.

Endoscopic treatment: Endoscopic hemostasis was performed in a standard fashion based on the type of lesion. Combination injection plus thermal/mechanical therapy was preferred for peptic ulcer bleeding for active bleeding, and clip/thermal therapy for visible vessels. Esophageal variceal bleeding was treated by band ligation and gastric variceal bleeding was treated by appropriate endoscopic or radiologic strategy. Repeat resuscitation and repeat endoscopy were performed

when this did not stop the bleeding, which was followed by angiographic embolization or surgery if these failed.

Outcomes: Recurrent hematemesis or melena with hemodynamic instability, decrease in hemoglobin of ≥2 g/dL after stabilization, or requirement for repeat endoscopic, radiologic, or surgical hemostasis for bleeding after the initial control was considered rebleeding within 30 days. All-cause 30-day mortality was the second primary outcome. Other outcomes were transfusion requirement, admission to intensive care unit, endoscopic intervention, length of stay, and radiologic or surgical rescue.

Data analysis: SPSS version 29.0 was used for statistical analysis.

Results

Two hundred eighty-six patients were included. Mean age was 55.8 ± 16.7 years and 205 (71.7%) were male. Hematemesis occurred in 59.4%, melena in 73.8%, and both in 38.5%. Cirrhosis was present in 75 patients (26.2%), chronic kidney disease in 31 (10.8%), and known ischemic heart disease in 35 (12.2%). Mean admission hemoglobin was 8.7 ± 2.4 g/dL. Eighty-one patients (28.3%) presented with systolic blood pressure ≤100 mmHg and 59 (20.6%) had a shock index ≥1.0.

Endoscopy identified peptic ulcer disease in 119 patients (41.6%), esophageal or gastric variceal bleeding in 69 (24.1%), erosive gastritis/duodenitis in 44 (15.4%), Mallory-Weiss tear in 19 (6.6%), upper gastrointestinal malignancy in 15 (5.2%), and other causes in 20 (7.0%). Endoscopic hemostatic therapy was required in 142 patients (49.7%). The median GBS was 10 (IQR 6-13), median AIMS65 was 1 (IQR 0-2), and median full Rockall score was 5 (IQR 3-7).

Thirty-seven patients (12.9%) experienced rebleeding within 30 days; 29 events occurred during the index hospitalization and eight after discharge. Rebleeding was significantly more frequent in patients with shock index ≥1.0, hemoglobin <8 g/dL, active/high-risk endoscopic stigmata, and transfusion of at least three units. On multivariable analysis, these four variables remained independently associated with recurrent bleeding. Patients who rebled had a longer mean hospital stay (8.9 ± 4.8 vs 5.2 ± 3.1 days, p<0.001) and were more likely to require ICU care and repeat endoscopy.

Twenty-three patients (8.0%) died within 30 days. Causes of death included uncontrolled or recurrent hemorrhage with multiorgan failure (n=8), decompensated liver disease/sepsis (n=8), cardiopulmonary events (n=5), and advanced malignancy-related deterioration (n=2). Mortality was higher in patients aged ≥65 years, those with systolic pressure ≤90 mmHg, albumin <3.0 g/dL, INR >1.5, altered mental status, and those who developed rebleeding. In adjusted analysis, age ≥65 years, severe hypotension, hypoalbuminemia, INR >1.5, and rebleeding were independent predictors.

For mortality, AIMS65 showed the highest AUC at 0.82 (95% CI 0.74-0.90), followed by full Rockall at 0.80 and GBS at 0.74. For rebleeding, full Rockall had an AUC of 0.74, GBS 0.72, and AIMS65 0.66. An AIMS65 score ≥2 identified a high-mortality subgroup, while GBS ≤1 identified a small low-risk subgroup without death or need for urgent hemostatic intervention in this cohort.

Table 1: Baseline characteristics and outcomes

Variable	Overall n=286	Rebleeding n=37	No rebleeding n=249	p value
Age, years	55.8 ± 16.7	59.7 ± 15.2	55.2 ± 16.9	0.115
Male sex	205 (71.7%)	28 (75.7%)	177 (71.1%)	0.566
Systolic BP ≤90 mmHg	46 (16.1%)	13 (35.1%)	33 (13.3%)	0.001
Shock index ≥1.0	59 (20.6%)	17 (45.9%)	42 (16.9%)	<0.001
Hemoglobin <8 g/dL	108 (37.8%)	22 (59.5%)	86 (34.5%)	0.004
Cirrhosis	75 (26.2%)	13 (35.1%)	62 (24.9%)	0.185
High-risk endoscopic stigmata	104 (36.4%)	24 (64.9%)	80 (32.1%)	<0.001
Transfusion ≥3 units	91 (31.8%)	21 (56.8%)	70 (28.1%)	<0.001

Table 2: Multivariable predictors of 30-day rebleeding

Predictor	Adjusted OR	95% CI	p value
Shock index ≥1.0	2.78	1.27-6.08	0.010
Hemoglobin <8 g/dL	2.43	1.10-5.37	0.028
High-risk endoscopic stigmata	3.61	1.58-8.22	0.002
Transfusion ≥3 units	2.69	1.21-5.98	0.015
Cirrhosis	1.48	0.67-3.29	0.333

Table 3: Predictors of 30-day mortality and risk-score performance

Variable	Adjusted OR / AUC	95% CI	p value
Age ≥65 years	2.94	1.15-7.51	0.024
Systolic BP ≤90 mmHg	3.38	1.30-8.79	0.013
Albumin <3.0 g/dL	3.17	1.23-8.18	0.017
INR >1.5	2.76	1.08-7.04	0.034
Rebleeding	4.52	1.78-11.50	0.002
AIMS65 for mortality	AUC 0.82	0.74-0.90	<0.001
Full Rockall for mortality	AUC 0.80	0.71-0.88	<0.001
GBS for mortality	AUC 0.74	0.64-0.84	<0.001
Full Rockall for rebleeding	AUC 0.74	0.66-0.82	<0.001
GBS for rebleeding	AUC 0.72	0.63-0.81	<0.001

Discussion

This prospective cohort shows that the risk factors for rebleeding and mortality following acute UGIB are partially overlapping but not identical. Hemodynamic compromise, severe anemia, high-risk endoscopic bleeding stigmata and higher transfusion requirement were most strongly associated with rebleeding. Mortality, however, was a measure of physiologic reserve and systemic vulnerability: age ≥65 years, severe hypotension, hypoalbuminemia, coagulopathy, and rebleeding were independent risk factors for death. The results confirm the idea of a multi-layered risk assessment instead of a single score.

The rebleeding rate of 12.9% and mortality of 8.0% observed are consistent with a tertiary-care population with both nonvariceal and variceal bleeding. Despite the improved mortality rates achieved in many patients with contemporary guideline-based care, patients with shock and/or significant comorbidities remain overrepresented for poor outcomes. The ACG guideline highlights the importance of early risk assessment, appropriate resuscitation, and restrictive transfusion for the majority of patients and endoscopy within 24 hours [2]. Our results confirm these priorities as the best early predictors were evident at the time of first presentation.

Shock index was independently related to rebleeding when other clinical parameters were taken into account. The shock index combines tachycardic compensation and can show signs of circulatory stress prior to severe hypotension, as compared to blood pressure alone. Hemoglobin <8 g/dL also predicted recurrent bleeding. Admission hemoglobin is affected by timing and fluid shifts, but if the anemia is severe and there is obvious bleeding, then there is likely significant blood loss or reserve depletion. Hemodynamic instability and low hemoglobin were previously found to be recurrent predictors of peptic ulcer bleeding after endoscopic treatment in a prior meta-analysis [10]. Our model showed the highest adjusted association with rebleeding for high-risk endoscopic stigmata. This is anticipated as it is a lesion level finding of active bleeding, a visible vessel, or significant stigmata, which indicate that the hemostatic defect is not stable. The classification of Forrest, which is based on the presence of active bleeding and major stigmata, still has significant predictive value for recurrent bleeding, even in the era of endoscopic hemostasis [11]. In a similar study, prospective work by Guglielmi et al. also found that Forrest class, hemodynamic status, ulcer size and location, and cirrhosis were significant factors in the risk of post-endoscopic rebleeding [12].

Three or more units of transfusion was also independently associated with rebleeding. The amount of transfusion is partly a reflection of the severity and duration of the initial bleed, and not necessarily a risk factor. It incorporates continuous blood loss, hemodynamic instability, and failure to achieve stabilization of hemoglobin. Clinically, if a high transfusion burden is observed, it should be closely monitored and a low threshold should be set for repeat evaluation should new melena, tachycardia, hypotension or hemoglobin drop occur.

The pattern of mortality was a bit different. The best discrimination for death in this cohort was achieved by AIMS65. This is consistent with the original derivation study, where albumin, INR, altered mental status, systolic pressure, and age were chosen as the specific variables to predict inpatient mortality [6]. AIMS65 was also shown to discriminate better than GBS for inpatient mortality and length of stay in a prospective multicenter comparison [7]. Similarly, Robertson et al. found that AIMS65 was superior to GBS and pre-endoscopy Rockall in predicting mortality but not clearly superior in predicting composite clinical outcomes [8].

The significance of hypoalbuminemia and INR >1.5 may be more due to systemic illness than severity of bleeding. Low albumin can be a sign of cirrhosis, malnutrition, inflammation, or chronic disease, and coagulopathy can be a sign of impaired liver synthesis or exposure to

anticoagulants. These factors help to recognize patients who are at risk of poor tolerance of an acute hemorrhage and who may continue to be at risk even after apparent endoscopic control. AIMS65 has been validated for use in India and has been found to be superior to GBS for mortality, while GBS may be superior for transfusion and rebleeding, particularly in populations with significant variceal disease [9]. This is consistent with our results, which split performance into the same categories. The best independent post-presentation predictor of mortality was rebleeding. Clinically important because it's an intermediate event that can be modified. Optimal initial endoscopic hemostasis, high dose acid suppression for high-risk ulcer bleeding, vasoactive therapy and band ligation for varices, and prompt repeat endoscopy or radiologic embolization may therefore affect survival. If rebleeding occurs, the patient's risk profile should be re-evaluated at the time of the rebleeding event, and not treated as a repeat event.

The comparative score analysis indicates that each score should be used for the task for which it is best suited. GBS is still very useful prior to endoscopy to identify low-risk patients and to predict the need for resources, as it was originally designed to do [4] and as it is still recommended in the guidelines [3]. AIMS65 is easy to use and is especially appropriate for mortality risk.

However, the addition of diagnosis and stigmata to Full Rockall adds value after endoscopy, which may account for its relatively good rebleeding performance. A practical approach might then be to use GBS at triage, AIMS65 to identify patients with systemic mortality risk, and endoscopic/full Rockall information once the lesion has been characterised.

There are limitations to the study. Biological heterogeneity was present as it was single center and included both variceal and nonvariceal bleeding. This enhances the relevance of the real world, but can decrease lesion-specific precision. The mortality was not large, so that only a few covariates can be incorporated into a stable mortality model.

There was no standardisation of management decisions regarding transfusion or admission to the ICU, except that they were clinician-dependent. The full Rockall score can only be used after endoscopy and is not available to inform the earliest triage decisions. Lastly, the study measured outcomes at 30 days only and did not measure longer-term mortality due to liver disease or malignancy.

The strengths are the prospective enrollment, the use of three widely used risk scores, calculated in a standard way, the inclusion of both clinical and endoscopic predictors, the explicit definitions of outcomes at 30 days, and the use of multivariable modeling. The results offer a clinically sensible risk profile: severity of active bleeding and lesion instability are associated with recurrent bleeding, whereas age, shock, hepatic/synthetic reserve and rebleeding are associated with death.

The findings together support dynamic risk stratification instead of a single risk stratification. The risk level of a patient starts with bedside physiology and lab data, is more specific after endoscopy, and should be re-calculated if rebleeding occurs.

Conclusion

In acute upper gastrointestinal bleeding, shock index ≥1.0, hemoglobin <8 g/dL, high-risk endoscopic stigmata, and a transfusion requirement of at least three units independently predicted 30-day rebleeding. Mortality was independently associated with older age, severe hypotension, hypoalbuminemia, INR >1.5, and rebleeding. AIMS65 performed best for mortality, whereas full Rockall and GBS were more informative for rebleeding, supporting a combined and dynamic approach to risk stratification.

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