## Outcome of Upper Gastrointestinal Hemorrhage According to the BLEED Risk Classification: a Two-year Prospective Survey

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Objective: Upper gastrointestinal bleeding (UGIB) is a common and serious medical emergency. The aim of this study was to predict UGIB patients' outcome according to a risk scoring system, independent of endoscopic findings, introduced by Kollef et al (BLEED: ongoing bleeding, elevated prothrombin time, erratic mental status, and unstable co-morbid disease).

**Design: Prospective study.** 

Setting: Sina university hospital.

Method: We studied all patients who presented with UGIB during 2000 to 2002. Patients meeting the BLEED criteria at their initial assessment were classified as high-risk (71) and all others were categorized as low-risk (50). In-hospital complications were defined as recurrent UGIB, surgery to control the source of hemorrhage and hospital mortality.

Results: There were 101 patients, aged  $55.7\pm20.8$  years. Re-bleeding, surgery and death occurred in 21 (20.8%), 28 (27.7%) and 14 (13.9%) of the patients, respectively. Therapeutic and diagnostic upper gastrointestinal endoscopy were performed in 7 (7%) and 83 (82.2%) of patients, respectively. Seventy percent were categorized as high-risk. There was significant difference in development of in-hospital complications, and death when considered individually, between the high and low-risk patients, but not in the rate of re-bleeding, length of hospital stay and transfused units of packed red blood cells. High-risk patients needed surgery more often than the low-risk cases but the difference was borderline significant (p=0.051). Low systolic blood pressure and elevated prothrombin time were independent predictors of in-hospital complications among BLEED criteria.

Conclusion: BLEED classification was capable of predicting in-hospital complications, especially mortality. It is, therefore, a helpful triage tool in centers where urgent endoscopy is hardly available.

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Upper gastrointestinal bleeding (UGIB) represents a common emergency in clinical practice with an incidence of 50-150 per 100,000 people per year<sup>1-5</sup>. The mortality rate of UGIB varies between 4% and 14%<sup>6-9</sup>. Re-bleeding is considered a risk factor of mortality and occurs in 10–30% of those successfully treated<sup>10</sup>. Different clinical and endoscopic factors associated with an increased risk for re-bleeding and mortality after admission because of UGIB have been described; although there is still considerable disagreement about the most important prognostic factors<sup>2, 6-8</sup>. Several risk scoring systems have also been proposed to classify patients into high and low risk groups for complications, like re-bleeding or mortality, based on multivariate analyses<sup>10-16</sup>. These scoring systems can be used to select low risk patients for early discharge or outpatient treatment, and to select high risk patients for intensive care treatment, which improves efficiency of current therapy. Unfortunately, the performance of most of these scoring systems has never been validated in a population of new patients. Validity can be separated into internal and external validity. External validity, which refers to the performance of the scoring system in patients outside the study context, it is especially important when scoring systems are used to predict outcome in daily practice, because it is well known that scoring systems (or models in general) perform less well in patient samples outside the clinical context in which these models are developed<sup>17</sup>.

One of the scoring systems for predicting the outcome of gastrointestinal (GI) bleeding has been introduced by Dr Kollef et al, who identified five predictors of risk for in-hospital complications and suggested they could be used to triage patients with upper and patients with lower GI hemorrhage<sup>18</sup>. The five predictors represented by the acronym "BLEED": ongoing bleeding, low blood pressure, elevated prothrombin time (PT), erratic mental status, and unstable co-morbid disease. They selected variables that are readily available at the time of triage, unlike most of the other risk classification systems, relying on the findings of endoscopy, which are seldom available at the time of admission<sup>10,11,19,20</sup>. Although using this risk scoring system as a model for defining risk factors for low-risk patients has been strongly recommended to clinicians by some other authors, its validity has not been tested, to our knowledge, in any survey, but the one by Kollef et al themselves<sup>18,21</sup>. The aim of this study was, to determine whether the BLEED criteria are able to predict complications (need for surgery, re-bleeding and death) after admission for UGIB in an Iranian patient population. We used BLEED scoring system to classify patients admitted to Sina hospital in Tehran, into different risk groups.

## METHOD

As we aimed to test the predictive value of BLEED criteria in UGIB patients, we used roughly the same method as the authors of the BLEED study<sup>18</sup>. However, we included patients under 18 years of age and those who developed UGIB during hospitalization for other reasons, in contrast to Kollef et al<sup>18</sup>.

From March 2000 till March 2002, all the patients admitted in the emergency ward with symptoms of hematemesis, melena, hematochezia, or blood admixture on nasogastric aspiration that were suspected of having acute UGIB were studied. We excluded the patients who were discharged from the hospital, and therefore, could not

be followed for the occurrence of complications.

### **Risk Classification Scheme and Main Outcome**

Patients with a primary diagnosis of acute UGIB were stratified into low-risk and high-risk categories according to the BLEED classification<sup>18</sup>. High-risk patients were defined according to the presence of any of the BLEED classification criteria: a) ongoing bleeding; b) low systolic blood pressure (BP) (i.e., <100 mm Hg, excluding orthostatic readings); c) elevated PT (i.e., >1.2 times the control value); d) erratic mental status; and e) presence of an unstable co-morbid disease.

The main outcome evaluated was the occurrence of an in-hospital complication, defined as either recurrent GI hemorrhage, surgical laparotomy to control the source of hemorrhage, or hospital mortality. Secondary outcomes were assessed, number units of packed red blood cells transfused and length of hospital stay.

Patients' characteristics were recorded: age, gender, BP, heart rate, history of peptic ulcer disease (PUD), use of warfarin, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), or aspirin; presentation of UGIB (melena, hematemesis, or hematochezia), findings from nasogastric tube aspiration, PT, hemoglobin, erratic or altered mental status, type of hospitalization (emergency vs. already admitted for other reasons) and identification of an unstable co-morbid disease. The final diagnosis was recorded for the patients according to endoscopic findings or laparotomy results.

### Definitions

Ongoing bleeding, at the time of patient evaluation in the emergency department, was defined as red blood through emesis or nasogastric tube aspirate or the ongoing spontaneous passage of red or maroon blood per rectum. Coffee grounds through emesis or nasogastric tube aspirate and the presence of formed maroon or black stool on digital-rectal examination were considered to indicate prior bleeding and not active, ongoing bleeding.

Erratic or altered mental status was defined by any notation in the emergency department medical record (e.g., by a nurse or physician) suggesting clouding of consciousness due to any cause (e.g., drugs or alcohol, primary central nervous system disorder, or a secondary disorder such as hepatic encephalopathy).

The use of aspirin, NSAIDs, corticosteroids, or warfarin was defined as the regular ingestion of any of these medications before hospital admission.

Mortality attributed to UGIB was defined as a death that could not be directly attributed to any other cause.

Re-bleeding after hospital admission was defined as recurrent hematemesis, melena, or hematochezia occurring after a period of 24 hours of stabilization, during which time no evidence of active bleeding was observed, and associated with a new decrease of >3.0% in hematocrit.

#### **Statistical Analysis**

Continuous variables were compared using Student's t-test and are expressed as mean  $\pm$  SD. The chi squared statistic or Fisher's exact test was used to compare categorical variables. P < 0.05 was considered statistically significant.

## RESULT

#### **Patient Population**

A total number of 102 patients were included (89 from emergency department and 13 were secondary bleeders), one patient was excluded due to discharge and transfer to another hospital. Overall, the mean age was  $55.7 \pm 20.8$  years (range: 7 to 89 years), 78 of the 101 patients were males. The baseline patients' characteristics and specific diagnoses for the episodes of acute UGIB are summarized in Table 1.

Table 1. Patients'	characteristics	and specific	diagnoses
Characteristic			

Age (yr)	$55.7 \pm 20.8$	
Male (n)	78	
Females (n)	23	
Mean arterial pressure < 100 mm Hg	22	
Heart rate $> 100$ beats/min	44	
Hemoglobin (g/dL)	$9.9 \pm 3.2$	
History of peptic ulcer disease	25	
Gastrointestinal malignancy	6	
Usage of drugs		
Using warfarin	3	
Using NSAIDs	10	
Using aspirin	24	
Using corticosteroids	3	
Presentation of upper gastrointestinal bleeding		
Hematemesis	76	
Melena	68	
Hematochezia	10	
Nasogastric tube aspirate		
Clear	13	
Coffee ground	60	
Red blood	27	
Specific diagnosis		
Duodenal ulcer	38	
Gastric ulcer	26	
Erosive gastritis	13	
Erosive esophagitis	3	
Varices	4	
Gastric cancer	6	
Stomal ulcer	2	
Ulcerated hiatal hernia	1	
Specific site undetermined <sup>a</sup>	8	

Data in the table represent the number of cases (among a total of 101 patients), except age and hemoglobin, that are presented as mean  $\pm$  SD. NSAIDs, Non-steroidal anti-inflammatory drugs.

<sup>a</sup> Specific sites of hemorrhage could not be identified by diagnostic procedures (e.g. endoscopy) or such procedures were not performed in these patients.

#### **Risk Stratification and Patient Outcomes**

During the study period, 21 (20.8%) of the patients developed recurrent GI hemorrhage; 28 (27.7%) underwent surgery to control their source of hemorrhage; and 14 (13.9%) died during their hospitalization. Upper GI endoscopy was performed in 7 (7%) and 83 (82.2%) of patients as a therapeutic and diagnostic measure, respectively. However, it was performed later than 24 hours after the initial presentation in the majority of cases (81 patients, 80%). Length of hospital stay was  $8.4 \pm 9.1$  days. Transfusion requirements were  $3 \pm 2.9$  units of packed red blood cells (RBCs) per patient.

Thirty patients were classified as low-risk, while 70% of the cases were high-risk. Fortythree patients developed at least one of the defined in-hospital complications, whereas 58/101 had no in-hospital complications. Table 2 shows the in-hospital complications and secondary outcomes stratified according to patient risk classification.

## Table 2. In-hospital complications and secondary patient outcomes according to risk classification

Complication/outcome	High-risk group (n=71)	Low-risk group $(n=30)$	p value
Major complications <sup>a</sup>	36 (50.7)	7 (23.3)	0.03
Mortality	14 (19.7)	0	0.001
Rebleeding	14 (19.7)	7 (23.3)	0.68
Surgery	24 (33.8)	4 (13.3)	0.05
Transfused units of packed RBCs	$3.1 \pm 3.1$	$2.7 \pm 2.6$	0.56
Length of hospital stay (days)	$9.2 \pm 10.1$	$6.6 \pm 5.2$	0.19

Values are given as number (%) or mean  $\pm$  SD. RBCs, red blood cells.

<sup>a</sup> Major complications are defined as either recurrent gastrointestinal hemorrhage, surgery to control the source of hemorrhage, or hospital mortality.

Table 3 represents a comparison of the BLEED classification criteria between patients with and patients without in-hospital complications. Table 4 summarizes the results of the multiple logistic regression analysis, using the five elements of the BLEED classification as independent variables and the occurrence of an in-hospital complication as the dependent variable.

BLEED Classification Criteria	In-hospital Complications (n=43)	No In-hospital Complications (n=58)	p Value
Ongoing bleeding	10 (23.3%)	0	0.001
Low systolic blood pressure	14 (32.6%)	8 (13.8%)	0.02
Elevated prothrombin time	20 (46.5%)	14 (24.1%)	0.02
Erratic mental status	7 (16.3%)	1 (1.7%)	0.007
Unstable co-morbid disease	26 (60.5%)	33 (56.9%)	0.71

# Table 3. Comparison between patients with and without in-hospital complications<sup>a</sup>

BLEED, ongoing bleeding, low systolic blood pressure, elevated prothrombin time, erratic mental status, unstable co morbid disease.

In-hospital complications are defined as either recurrent gastrointestinal hemorrhage, surgery to control the source of hemorrhage, or hospital mortality.

## Table 4. Independent predictors for in-hospital complications from the BLEED classification <sup>a</sup>

Variable	Adjusted Odds Ratio	95% CI	p Value
Ongoing bleeding	_	_	_
Low systolic blood pressure	3.11	1.05-9.26	0.04
Elevated prothrombin time	2.64	1.82-3.78	0.02
Erratic mental status	_	_	_
Unstable co morbid disease	-	-	-

BLEED, ongoing bleeding, low systolic blood pressure, elevated prothrombin time, erratic mental status, unstable co-morbid disease. CI, confidence interval.

<sup>a</sup> In-hospital complications are defined as either recurrent gastrointestinal hemorrhage, surgery to control the source of hemorrhage, or hospital mortality.

#### DISCUSSION

In this study, we assessed the risk for patients with acute UGIB introduced by Kollef et  $al^{18}$ . We demonstrated that the occurrence of an in-hospital complication (recurrent GI hemorrhage, surgery to control the source of hemorrhage, or hospital mortality) was predicted by the BLEED classification, using clinical data available at the time of initial evaluation in the emergency department (*p*=0.03, table 2). Our findings confirm the reliability of predicting outcome of UGIB patients by means of the BLEED scoring system.

In the present study, high and low-risk groups were not different according to hospital stay and transfusion requirements (table 2), in contrast to the BLEED survey. Our patients (both the high and low-risk groups) stayed in hospital longer than those in study of Kollef Et al<sup>18</sup>. In that study, high-risk patients spent an average of 8 days, compared to 4 days for the low-risk group. High-risk cases in our study received less blood transfusion compared to their counterparts in study of Kollef et al. The opposite was true for the low-risk patients, who were transfused with an average of 2.7 vs. 1.6 and 1.1 units of packed RBCs in our study and the study of Kollef et al respectively.

We found that among different elements of the BLEED classification, low systolic BP and elevated PT independently predicted the occurrence of in-hospital complications (table 4). In BLEED study, low systolic BP, ongoing bleeding and unstable co-morbid disease were independent predictors of complications in Barnes hospital; In Jewish hospital the factors capable of independent prediction of outcome were elevated PT, erratic mental status, and ongoing bleeding<sup>18</sup>.

Although Kollef et al tested the predictability of in-hospital complications considered together as a single variable, they did not discuss in their publication the predictability of each complication individually<sup>18</sup>. We examined this by analyzing the effect of risk group on the occurrence of death, surgery or rebleeding as separate entities and found a statistically significant relationship only for prediction of mortality (table 2). Although high-risk patients needed surgery more often than the low-risk cases, the difference was borderline (p=0.051).

There have been differences in both baseline characteristics (table 1) and the frequency of in-hospital complications between this study and those in Kollef study. Our patients were younger compared to the cases in Barnes (mean age  $63.4 \pm 17.5$  years) and Jewish hospitals (mean age  $69.1 \pm 18$  years). This could be in part due to inclusion of the patients under 18 years in the present study, while Kollef et al had excluded them<sup>18</sup>. Males constituted 78% of the patient population in the present study and fewer than half of the cases in the Barnes and Jewish hospitals<sup>18</sup>. However, 74.4% and 57% of the patients in the Ontario GI bleed study and the British national audit of acute UGIB were male, respectively<sup>22,23</sup>.

In this study, seventy percent was classified as high-risk, compared to 50.1% and 39.5% of the patients in Barnes and Jewish hospitals, respectively<sup>18</sup>. Our center being a tertiary care center, admitting patients referred from other hospitals in the capital, most of them have been referred due to difficulties in management, may partially account for the high percentage of high-risk patients. Furthermore, 13 cases were included who had developed UGIB while being hospitalized for other diseases, and, therefore, have contributed to the increase in the subgroup of patients with co-morbid diseases, thereby increasing the number of high-risk group. The complications of UGIB were also more common in the present study, in comparison with BLEED study, in which 2.8% of patients (both upper and lower GI bleeding cases) died, 15.3% developed recurrent UGIB, 6.5% underwent surgery and 18.7% developed at least one of the three complications<sup>18</sup>. The mortality rate of UGIB was 14% in the British national audit, and 13.9% in a large survey in Amsterdam, almost similar to the present study<sup>9,23</sup>. Re-bleeding occurs in 10-30% of those UGIB subjects that have been successfully treated<sup>10</sup>. Nevertheless, surgery to control source of hemorrhage has been more widely used in our study than the BLEED survey and Amsterdam study, both reporting operations in approximately 7% of their cases<sup>9,18</sup>. The reason for the high rate of surgery in our center is the less common application of upper GI endoscopy as a treatment modality (7%), it has become the primary modality employed in the management of UGIB<sup>24</sup>. Moreover, the majority of the patients in our center underwent endoscopy (either diagnostic or therapeutic) after more than 24 hours of admission, which is later than the recommended "*early*" endoscopy<sup>24</sup>. This emphasizes the importance of a risk scoring system independent of endoscopic findings in countries like Iran, where urgent endoscopy is less commonly available in most circumstances.

#### CONCLUSION

We found BLEED risk scoring system to be capable of predicting the in-hospital complications due to UGIB, and in particular the occurrence of mortality. Our results confirm the findings by Kollef et al; the BLEED criteria are helpful tools for triage of UGIB cases, without endoscopic findings that are hardly available at the time of admission at our center and many centers in the developing countries.

#### REFERENCES

- 1. Johnston SJ, Jones PF, Kyle J, et al. Epidemiology and course of gastrointestinal haemorrhage in north-east Scotland. Br Med J 1973; 3:655–60.
- 2. Schiller KF, Truelove SC, Williams DG. Haematemesis and melaena, with special reference to factors influencing the outcome. Br Med J 1970; 2:7–14.
- 3. Cutler JA, MendeloV AI. Upper gastrointestinal bleeding. Nature and magnitude of the problem in the US. Dig Dis Sci 1981; 26:90–6S.
- 4. Wara P. Endoscopic management of the bleeding ulcer. A survey. Dan Med Bull 1986; 33:1–11.
- Yavorski RT, Wong RK, Maydonovitch C, et al. Analysis of 3,294 cases of upper gastrointestinal bleeding in military medical facilities. Am J Gastroenterol 1995; 90:568–73.
- 6. Morgan AG, Clamp SE.OMGE international upper gastrointestinal bleeding survey, 1978–1986. Scand J Gastroenterol Suppl 1988; 144:51–8.
- Katschinski B, Logan R, Davies J, et al. Prognostic factors in upper gastrointestinal bleeding. Dig Dis Sci 1994; 39:706–12.
- Branicki FJ, Coleman SY, Fok PJ, et al. Bleeding peptic ulcer: a prospective evaluation of risk factors for re-bleeding and mortality. World J Surg 1990;14:262-70
- Vreeburg EM, Snel P, Bruijne JW, et al. Acute upper gastrointestinal bleeding in the Amsterdam area; incidence, diagnosis and clinical outcome. Am J Gastroenterol 1997; 92:236–43.
- Saeed ZA, Ramirez FC, Hepps KS, et al. Prospective validation of the Baylor bleeding score for predicting the likelihood of rebleeding after endoscopic hemostasis of peptic ulcers. Gastrointest Endosc 1995; 41:561–5.
- 11. Rockall TA, Logan RFA, Devlin HB, et al. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996; 38:316–21.
- 12. Bordley DR, Mushlin AI, Dolan JG, J et al. Early clinical signs identify low-risk patients with acute upper gastrointestinal hemorrhage. JAMA 1985; 253:3282–5.
- Schein M, Gecelter G. APACHE II score in massive upper gastrointestinal haemorrhge from peptic ulcer: prognostic value and potential clinical applications. Br J Surg 1989; 76:733–6.
- 14. Pimpl W, Boeckl O, Waclawiczek HW, et al. Estimation of the mortality rate of patients with severe gastroduodenal hemorrhage with the aid of a new scoring system. Endoscopy 1987; 19:101–6.
- Clason AE, Macleod DAD, Elton RA. Clinical factors in the prediction of further hemorrhage or mortality in acute upper gastrointestinal haemorrhage. Br J Surg 1986; 73:985–7.
- 16. Morgan AG, McAdam WA, Walmsley GL, et al. Clinical findings, early endoscopy, and multivariate analysis in patients bleeding from the upper

gastrointestinal tract. Br Med J 1977; 2:237-40.

- Lemeshow S, Le Gall J. Modeling the severity of illness of ICU patients. A systems update. JAMA 1994; 272:1049–55
- Kollef MH, O'Brien JD, Zuckerman GR, et al. BLEED: A classification tool to predict outcomes in patients with acute upper and lower gastrointestinal hemorrhage. Crit Care Med 1997; 25:1125-32.
- 19. Laine L, Peterson WL: Bleeding peptic ulcer. N Engl J Med 1994; 331:717-26.
- 20. Longstreth GF, Feitelberg SP: Outpatient care of selected patients with acute non-variceal upper gastrointestinal hemorrhage. Lancet 1995; 3345:108-111.
- 21. Zimmerman JE. Triage for patients with gastrointestinal hemorrhage: Patients who don't need intensive care. Crit Care Med 1997; 25:1101-2.
- Marshall JK, Collins SM, Gafni A. Demographic Predictors of Resource Utilization for Bleeding Peptic Ulcer Disease: The Ontario GI Bleed Study. J Clin Gastroenterol 1999; 29:165-70.
- 23. Rockall TA, Logan RFA, Devlin HB, et al. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the UK. Br Med J 1995; 311:222-6.
- 24. Exon DJ, Sydney Chung SC. Endoscopic therapy for upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol 2004; 18:77-98.