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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)

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ABSTRACT

Background and aim: Upper gastrointestinal bleeding is a major cause of hospitalization and the most prevalent emergency worldwide, with a mortality rate of up to 14%. In Peru, there have not been any studies on the use of the Glasgow-Blatchford Scoring System to predict mortality in upper gastrointestinal bleeding. The aim of this study is to perform an external validation of the Glasgow-Blatchford Scoring System and to establish the best cutoff for predicting mortality in upper gastrointestinal bleeding in a hospital of Lima, Peru.

Methods: This was a longitudinal, retrospective, analytical validation study, with data from patients with a clinical and endoscopic diagnosis of upper gastrointestinal bleeding treated at the Gastrointestinal Hemorrhage Unit of the Hospital Nacional Edgardo Rebagliati Martins between June 2012 and December 2013. We calculated the area under the curve for the receiver operating characteristic of the Glasgow-Blatchford Scoring System to predict mortality with a 95% confidence interval.

Results: A total of 339 records were analyzed. 57.5% were male and the mean age (standard deviation) was 67.0 (15.7) years. The median of the Glasgow-Blatchford Scoring System obtained in the population was 12. The ROC analysis for death gave an area under the curve of 0.59 (95% CI 0.5-0.7). Stratifying by type of upper gastrointestinal bleeding resulted in an area under the curve of 0.66 (95% CI 0.53-0.78) for non-variceal type.

Conclusions: In this population, the Glasgow-Blatchford Scoring System has no diagnostic validity for predicting mortality.

Key words: Gastrointestinal hemorrhage. Upper gastrointestinal tract. Blatchford. Validation study.

INTRODUCTION

Upper gastrointestinal bleeding (UGB) is a major cause of hospitalization worldwide (1), with an average incidence rate of 34.45 per 100,000 person in Spain (2) and 50 to 100 cases per 100,000 in the United States (1-6). It is also a public health issue because of its high mortality rate, with values ranging between 3% and 14% (1,5-10).

In Latin America, Colombia reports a mortality rate of 9.5% (8) and in Peru, values of 3% (1) and 9.1% (12) have been measured in two reference hospitals. The magnitude of the numbers presented by this potentially deadly disease makes it the most prevalent gastroenterological emergency at all health care levels (3,13), so an early evaluation of patients is essential to establish an early diagnosis and set up an appropriate therapy.

To this end, scores have been created to predict the outcome of patients with UGB (10,14-17), stratified by risk of mortality or rebleeding and need for endoscopic treatment among other variables (9,10,14,16,18,19). These scores are useful as an initial tool for making oriented patient management decisions, either in or outpatient (15).

Among the existing scores, one of the most used to predict mortality and rebleeding in patients with UGB is the post-endoscopy Rockall Score, validated in Peru in 2009 (9,10,14,15,20,21). Another of the most used is the Glasgow-Blatchford Scoring System (GBSS), developed in 2000 and validated abroad (15,16,20,22,23) to determine the need for endoscopic or surgical treatment, as well as blood transfusion (9,14,16,17,20,22). However, unlike the post-endoscopy Rockall Score, it is based only on the use of clinical and laboratory data taken when the patient is admitted, and is based on measures of blood urea, hemoglobin, systolic blood pressure, pulse, presence of melena, syncope, liver disease and cardiac failure (16,24). It uses a graded scale from 0 to 23 according to the magnitude of the risk (16, 22).

The GBSS has been demonstrated to have a sensitivity of approximately 99% for identifying high-risk patients with UGB (9). Previous studies done in international settings have reported a correlation between the Rockall Score and GBSS for predicting mortality, with similar predictive values that allow for stratification of patients into low and high risk groups (3,15,21-23,25).

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While the assortment of scores available to predict risk in patients with UGB is extensive (20,22), most require endoscopic data for their application, which limits their use. In Peru, there are no studies that have evaluated the validity of GBSS for predicting mortality in patients with UGB. The post-endoscopy Rockall Score is the only score that has been validated locally (14), but it is limited to use only in hospital units with specialized endoscopy service.

The validation of a score based on clinical and laboratory data routinely obtained without the need for endoscopic findings will allow for early classification of patients according to their risk of mortality, it will be significant for guiding the decision-making process for the appropriate and early management of UGB, especially in settings with poor resources and low health coverage like in Peru, where endoscopy services are not available at all health care levels (12). The early recognition of high risk patients could prevent complications that increase mortality and expenditure for health systems, and also avoid the overload of emergency departments by accelerating referral to critical units, gastrointestinal hemorrhage services, and hospital discharge, among others.

The aim of this study is to perform the external validation of the GBSS and, thereby, establish the best cutoff for predicting mortality in patients with UGB at a national referral hospital in Lima, Peru.

MATERIALS AND METHODS

Study design

We conducted a longitudinal, retrospective, analytical study to evaluate the diagnostic accuracy of a clinical prediction score and to establish the best cutoff. To do this, we used data from patients with UGB who were seen at Hospital Nacional Edgardo Rebagliati Martins (HNERM), between June 2012 and December 2013. We obtained data from the emergency admission notes located in the clinical records of patients who were in the Gastrointestinal Hemorrhage Unit (GHU).

Setting

The study was executed at the GHU of the HNERM, which is the primary referral center of the Peruvian Social Security (EsSalud). This center has the highest complexity level of health care and is located in Jesus Maria, Lima, Peru (26).

Study population

The study population corresponds to the patients admitted for UGB emergency, who underwent an upper endoscopy and had clinical (presence of hematemesis, melena, coffee pot vomiting, rectal bleeding or hematochezia) (14) and endoscopic diagnostic (signs of active or recent bleeding established according to the Forrest Classification) (24) of variceal and non-variceal UGB. We excluded patients under 18 years old and those with insufficient data to complete the variables required for calculating the score of the GBSS (Table I).

Sample size

The sample size was calculated using the PASS program (Power Analysis and Sample Size Software). According to the literature reviewed, the area under the curve (AUC) for GBSS and mortality ranges between 0.7 and 0.9 (3,12,17,22); so the average value of 0.8 was used as our expected value. Using a range of confidence interval (CI) of 0.3 for the AUC and assuming a prevalence of the reference (mortality) equal to 9.1% (12), with a statistical power of 80% and an alpha level of .05, a sample size of 308 records of patients with UGB, of which 28 should be fatal cases, was estimated.

Sample design and recruitment of patients

The sampling frame used was the records of patients with UGB in the medical registries from the GHU. The sampling units were

Table I. Glasgow-Blatchford Scoring System (20)

Admission risk factor	*Score*
Blood urea (mmol/L)	
≥ 6.5 to < 8.0	2
≥ 8.0 to < 10.0	3
≥ 10.0 to < 25.0	4
≥ 25	6
Hemoglobin for men (g/dL)	
≥ 12.0 to < 13.0	1
≥ 10.0 to < 12.0	3
< 10.0	6
Hemoglobin for women (g/dL)	
≥ 10.0 to < 12.0	1
< 10.0	6
Systolic blood pressure (mmHg)	
100-109	1
90-99	2
< 90	3
Other markers	
Pulse ≥ 100 beats/minute	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

Modified from Pang et al. (20).

the admissions notes for patients admitted to the emergency room who had an endoscopy at GHU. We conducted a non-probabilistic, consecutive sampling based on the number of patients' records with UGB available at the GHU. We identified cases with UGB sequentially, starting with patients admitted in December 2013 and going back to attain the calculated sample size.

The inclusion of patients and data collection was independent of the outcome assessment of the patient with UGB (discharge with survival *versus* hospital discharge with death, obtained from the hospital demographic database). Mortality was defined as the death of the patient within up to 30 days after the bleeding episode.

Glasgow-Blatchford Scoring System

The value of GBSS for each patient was obtained according to the points given from the parameters of blood urea, hemoglobin, systolic blood pressure, pulse, presence of melena, syncope, liver disease and cardiac failure (16,24). Its measurement scale is from 0 to 23 points and was recorded as a discrete numerical variable (Table I).

Ethics

The protocol was submitted for review by both Ethics Committees from the Universidad Peruana de Ciencias Aplicadas and HNERM. This investigation was a retrospective study of secondary data recorded routinely and did not require informed consent because it did not involve performing any invasive medical procedure that would have exposed the population to a potential additional risk besides their underlying disease (UGB). For these reasons, we believe that it corresponds to a minimal risk study that was worthy of a partial review by the ethics committees mentioned above.

Confidentiality and anonymity of patients were maintained, removing personal identifiers (affiliation information) found in the clinical assessment records.

Data collection

Permissions were obtained from the GHU of HNERM, Ethics Committee from Universidad Peruana de Ciencias Aplicadas and Ethics Committee from HNERM.

We collected data from patients' records inside the medical register for endoscopy located at the GHU. These records were selected according to the inclusion and exclusion criteria specified above and the data were collected in the same unit, using a computer with a Microsoft Excel database.

Data analysis

Microsoft Excel was used to track data and STATA 13.0 for statistical analysis. In addition, we used the QxMD Calculate application for mobile devices to calculate the score of GBSS from the data collected.

We carried out a descriptive analysis of categorical and numerical variables using means and standard deviations.

The scores of GBSS throughout the study population were calculated and presented using means and standard deviations for each component; the median and interquartile range was calculated for the final score.

The ROC analysis for external validation of GBSS was used to predict mortality and to establish the best cutoff, as well as its values of sensitivity, specificity, and likelihood ratios.

With the values obtained from the GBSS, we calculated the sensitivity and specificity for each one and constructed a curve whose area represents the diagnostic validity of GBSS for mortality prediction based on values ranging between 0.5 and 1 (0.5 corresponds to a test without discriminating diagnostic value and 1 to an idealized test free of diagnostic classification error) (27). According to the score obtained, we determined its usefulness for distinguishing between individuals experiencing the event of interest (UGB mortality) versus those who do not in each of the values found. In this case, according to the Youden index, the best cutoff jointly determines the highest estimated sensitivity and specificity that graphically correspond to the point closest to the upper left corner ROC curve, where sensitivity = 100% and specificity = 100% (28). The results are presented as values of area under the ROC curve, with 95% CI and likelihood ratio.

RESULTS

Between June 2012 and December 2013, 916 patients were admitted to the HNERM emergency room with a suspected diagnosis of UGB. Of these, 543 met clinical and endoscopic criteria for UGB. Two hundred and four patients were excluded for being younger than 18 years of age (15 patients) or for not having enough data to complete the variables of interest in the study (189 patients). In the end, 339 records of patients who met the selection criteria mentioned above were included in the analysis (Fig. 1).

The mean age (standard deviation) was 67.0 (15.7) years and 57.5% were male. Of the total sample, 67.0% suffered from non-variceal UGB and 8.9% of the patients died. Among the key endoscopic findings, gastric and duodenal ulcers (54.9%) and esophageal varices (35.7%) stand out. Population characteristics and other important endoscopic findings can be seen in tables II and III.

Comparing the data from patients included in the study with those excluded for having insufficient records to complete the GBSS (189 patients), both groups were similar in terms of sex (60.9% were males), mean age [66.6 (16.9)] and predominant type of UGB (73.6% were non-variceal). In addition, from the patients we could obtain the mortality data in this group, it is known that 5.45% died.

The median of GBSS obtained in the population was 12, with minimum and maximum values of 0 and 20. Only one patient had a score of 0 and 70.8% of the population scored equal to or greater than 10 (Table IV).

We performed a simple nonparametric ROC analysis for the entire sample, considering both patients with variceal and non-variceal UGB types. The AUC was equal to 0.59 (95% CI 0.5-0.7) (Fig. 2). We then performed a logistic

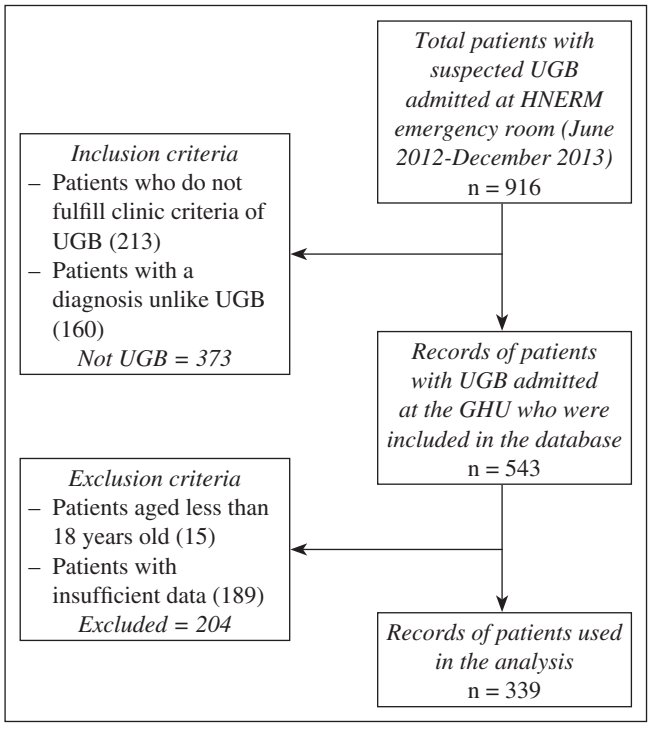

Fig. 1. Flowchart of enrollment of patients.

Table III. Endoscopic findings in patients with UGB

Endoscopic diagnosis	*n*	*%*
Esophageal varices	121	35.7
Grade I	25	7.4
Grade II	39	11.5
Grade III	44	13.0
Grade IV	13	3.8
Gastric varices	27	8.0
Ulcers	186	54.9
Gastric	100	29.5
Duodenal	86	25.4
Erosive gastritis	46	13.6
Neoplasm	12	3.5
Mallory Weiss syndrome	6	1.8
Portal hypertensive gastropathy	9	2.7
Angiodysplasia	15	4.4
Erosive esophagitis	15	4.4
Others*	5	1.5

Patients could have more than one endoscopic diagnosis; absolute and relative total is not equal to 100%. *Others: Dieulafoy's lesion, gastric polips, duodenal polips, pyloric stenosis and Zenker diverticulum.

regression using mortality as the dependent variable and the GBSS as the independent variable and adjusted for gender and type of UGB. In this multivariate analysis, none of the variables were statistically significant and the estimated adjusted AUC post-logistic regression was 0.60 (95% CI 0.5-0.7).

Finally, we conducted a simple nonparametric ROC analysis stratified by type of UGB. In the case of subjects with non-variceal UGB (n = 227, mortality = 18/227 = 7.9%), the AUC obtained was 0.66 (95% CI 0.5-0.8) (Fig. 3), whereas for subjects with variceal UGB (n = 112, mortality = 12/112 = 10.7%) the AUC was 0.49 (95% CI 0.3-0.7) (Fig. 4). In this case, the best GBSS cutoff to predict mortality in patients with non-variceal UGB would be 12 (Table V).

Table II. Population demographics and clinical characteristics

Variable		*n*	*%*
Sex			
	Male	195	57.5
Age			
	Mean; standard deviation	67.0; 15.7	
	Minimun value; maximum value	[19; 94]	
UGB type	Non-variceal	227	67.0
History of prior bleeding*		120	42.3
Deaths		30	8.9

*This analysis was performed with 284 records of patients with UGB.

DISCUSSION

The findings of this study show that the GBSS used in patients with variceal and non-variceal UGB type lacks adequate diagnostic accuracy for predicting mortality (AUC 0.59; 95% CI 0.5-0.7). This goes hand in hand with the findings by Laursen et al., who found a low specificity when evaluating the GBSS solely for predicting mortality within 30 days after the episode of UGB (AUC of 0.71; 95% CI 0.7-0.8) (30). Similarly, Kim et al. showed that the Forrest Classification had higher specificity than the GBSS in predicting mortality (50.23 *vs.* 1.83, respectively) (18).

The lack of diagnostic validity previously found has been attributed to the deaths evaluated within 30 days after the episode of UGB that were originated by causes that were not directly related to gastrointestinal bleeding, such as infections or stroke (30). The differences on the ability of GBSS to predict mortality as compared to other scales could be due to measurement of mortality only during the first 30 days after the UGB and the association with a history of rebleeding (18,30).

Table IV. Glasgow-Blatchford Scoring System of patients

	n	*(%)*	*Mean*	*Standard deviation*	*Minimum and maximum value*
Male sex	195	57,5			
Hemoglobin (men)			8.7	2.2	[4; 16.3]
Hemoglobin (women)			8.4	2.2	[3.8; 14.5]
Blood urea			73.5	51.9	[7.0; 3.3]
Melena	245	72.3			
Syncope	28	8.3			
Pulse			86.5	15.6	[52; 137]
Systolic blood pressure			113.3	21.6	[60; 200]
Hepatic disease	101	29.8			
Cardiac failure	13	3.8			
Total score			12*	10-14†	[0; 20]

*Median. †Interquartile range.

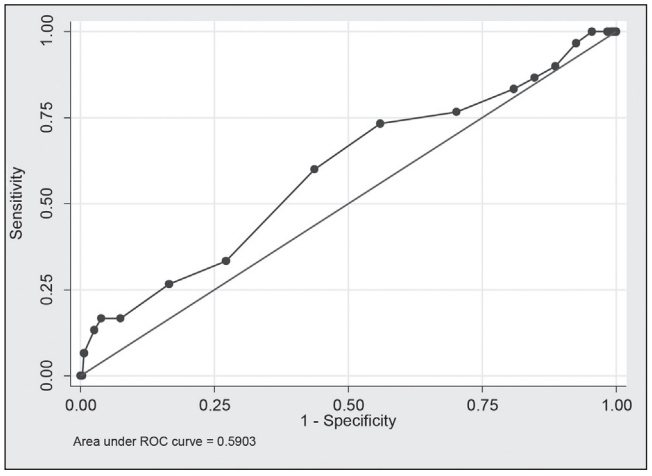

Fig. 2. Glasgow-Blatchford Scoring System ROC curve* for mortality in patients with variceal and non-variceal UGB.
*AUC is 0.59 (95% CI 0.5-0.7).

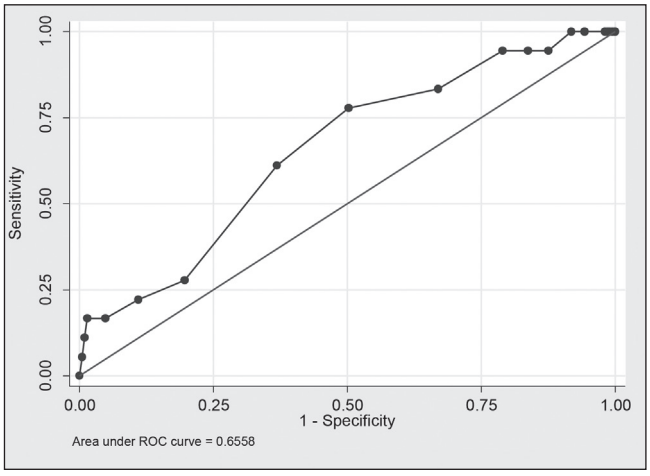

Fig. 3. Glasgow-Blatchford Scoring System ROC curve* for mortality in patients with non-variceal UGB.
*AUC is 0.66 (95% CI 0.5-0.8).

On the other hand, since HNERM is a national referral hospital, it is possible that a proportion of patients admitted to their emergency with suspected UGB come referred from other health care centers, where there may have received some stabilizing treatment. This may have affected the initial values of the parameters measured by the GBSS enough to influence our analyses. Unfortunately, we do not have tools to know this. The level of complexity of this center may also explain the high frequency of patients with high values on the GBSS.

By exploring the ROC analysis stratified by type of UGB, we showed that the ability of GBSS to predict mortality in patients with non-variceal UGB is higher than in variceal UGB [AUC of 0.66 (95% CI 0.5-0.8) *versus* AUC 0.49 (95% CI 0.3-0.7), respectively]. While the value reached in the first subgroup is not of a high diagnostic accuracy, the difference between the two groups is consistent with that previously reported, since the type of UGB has been considered an independent predictor of hospital death. This is because the variceal UGB type is associated with chronic liver disease and Child Pugh Score Class C correlates with mortality with an OR of 11 (1.4 to 87.2; p = 0.005) (7). In this case, the Child Pugh Score was not assessed because it is not data routinely collected in the GHU.

Other limitations of this study were that the analysis was not stratified by the presence of prior bleeding or the age of patients because these variables are not considered within the parameters of GBSS. While Chiu et al. report that rebleeding (OR 1.63, 95% CI 1.1-2.4) and older age (OR 1.47, 95% CI 1.1-2.0) in patients with UGB are predictors of mortality (31), this study was conducted

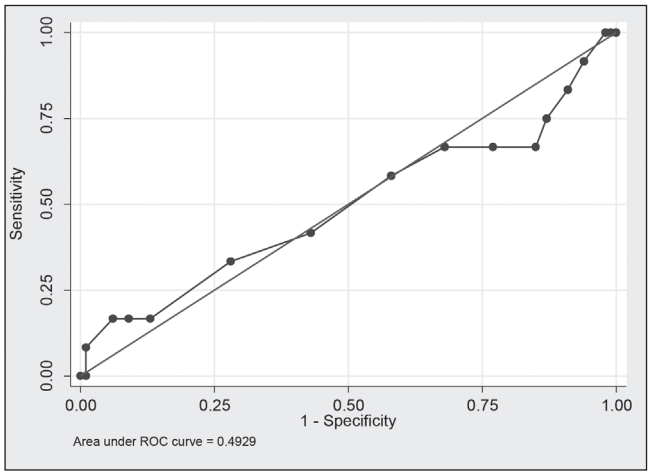

Fig. 4. Glasgow-Blatchford Scoring System ROC curve* for mortality in patients with variceal UGB.
*AUC is 0.49 (95% CI 0.3-0.7).

Table V. ROC analysis, sensitivity, specificity and likelihood ratio of Glasgow-Blatchford Scoring System for mortality

Cutoff	*Sensitivity (%)*	*Specificity (%)*	*LR+**	*LR-†*
≥ 0	100.0	0.0	1.0	
≥ 1	100.0	0.3	1.0	0.0
≥ 2	100.0	0.7	1.0	0.0
≥ 4	100.0	1.0	1.0	0.0
≥ 5	100.0	1.6	1.0	0.0
≥ 6	100.0	4.5	1.0	0.0
≥ 7	96.7	7.4	1.0	0.4
≥ 8	90.0	11.3	1.0	0.9
≥ 9	86.7	15.2	1.0	0.9
≥ 10	83.3	19.1	1.0	0.9
≥ 11	76.8	29.8	1.1	0.8
≥ 12	73.3	44.0	1.3	0.6
≥ 13	60.0	56.3	1.4	0.7
≥ 14	33.3	72.8	1.2	0.9
≥ 15	26.7	83.5	1.6	0.9
≥ 16	16.7	92.6	2.2	0.9
≥ 17	16.7	96.1	4.3	0.9
≥ 18	13.3	97.4	5.2	0.9
≥ 19	6.7	99.3	10.3	0.9
≥ 20	0.0	99.7	0.0	1.0
> 20	0.0	100.0		1.0

*Positive likelihood ratio. †Negative likelihood ratio.

in patients with gastrointestinal bleeding due solely to peptic ulcers. Also, in the logistic regression model for the original development of GBSS, it was not found that age constituted an independent risk factor for mortality when considering the other corresponding variables in the analysis (16). On the other hand, the mortality of patients was studied only as a dichotomous categorical variable and not the causes of the death or the interval where it occurred.

This study was the first external validation of the GBSS for predicting mortality in patients with UGB nationwide. For further studies we recommend analyzing other variables associated with increased risk of UGB mortality that could influence the validation of the GBSS, such as the history of rebleeding or the Child Pugh Score of chronic liver disease, among others. Additionally, the diagnostic validity of the GBSS contrasting with the post-endoscopy Rockall Score for predicting mortality could be explored, studying the causes of deaths and assessing whether there is an association with the type of endoscopic treatment received.

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