External validation of Glasgow-Blatchford, modified Glasgow-Blatchford and CANUKA scores to identify low-risk patients with upper gastrointestinal bleeding in emergency departments: a retrospective cohort study

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ABSTRACT

Background: Upper gastrointestinal bleeding (UGIB) is a medical emergency with an approximate mortality of 10%, which results in a high hospitalization rate. The Glasgow-Blatchford score (GBS) is recommended to identify low-risk patients who can be discharged from the emergency department (ED). A modified GBS (mGBS) and CANUKA score have recently been proposed but have not been well studied. The aim of this study was to assess whether the use of GBS, mGBS or CANUKA score could identify patients at low-risk of death or need for intervention.

Methods: A single-center retrospective study was performed including patients with suspected UGIB visiting the ED of Saint-Antoine hospital (Paris, France) from January 2016 to December 2018. Demographic and medical data needed to calculate GBS and CANUKA were collected, as well as outcomes data. Need for intervention was defined as the need for blood transfusion, endoscopic hemostasis or rebleeding within 7 days. In-hospital mortality was also collected. Sensitivity, specificity and predictive values were measured for the score thresholds of interest.

Results: A total of 386 patients were included. Median age was 60 years [38-78], 65.3% (n=252) were male and 60% (n=233) were hospitalized. A GBS $\leq$ 1, mGBS = 0 and CANUKA $\leq$ 2 categorized 24.9%, 18.2% and 18.9% of patients as low-risk, respectively. There was a need for intervention in 2.2%, 4.6% and 0% of those patients categorized as low-risk by GBS, mGBS and CANUKA, respectively. No deaths occurred in the patients identified as low-risk, regardless of the score used. All scores had a high sensitivity and negative predictive value.

Conclusions: In patients with UGIB, the use of a GBS $\leq$ 1 or CANUKA score $\leq$ 2 appears to be safe for identifying patients at low risk of death or need for intervention.

KEY MESSAGES

- **What is already known on this topic** ?

The Glasgow-Blatchford score (GBS) is recommended to identify low-risk patients who can be discharged from the emergency department (ED). A modified GBS (mGBS) and CANUKA score have recently been proposed but studies are scarce.

- **What this study adds** ?

GBS, mGBS and CANUKA scores identified about 20% of patients at low risk for complications (death or need for intervention). The use of a GBS ≤ 1 or CANUKA score ≤ 2 appears to be safe for identifying patients at low risk for complications.

- **How this study might affect research, practice or policy ?**

Low-risk patients, as identified using the GBS and CANUKA score, could be considered for safe discharge from the ED and management as outpatients.

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a common medical emergency, with an incidence of 100-150 per 100 000 adults per year and a mortality of 5 to 14 %.[1-3] Considering these risks, more than 80% of patients are hospitalized for monitoring, blood transfusion, endoscopy and/or hemostatic procedures. However, studies have shown that a portion of patients have a low risk of requiring any intervention or dying within 30 days.[4-6] Appropriate stratification of patients with UGIB could therefore improve medical decisions, such as timing to endoscopy and need for hospitalization.

Several scoring systems have been developed to evaluate patients with UGIB, the most commonly used being the Rockall Score (RS) and the Glasgow-Blatchford Score (GBS) (Figure 1). Initially designed to detect patients at high risk of complications, they were later evaluated to identify those at low risk who would not require in-hospital care.[4, 5] Studies have shown the GBS as superior to the RS or other existing scores for this purpose.[6-8] According to international guidelines, a GBS $\leq$ 1 would allow identification of patients at low risk of complications who could safely be managed as outpatients.[9-11] Despite several studies validating its use and the potential economic benefit by reducing the number of hospitalizations related to UGIB, the GBS has never been studied in France and its practice is not widespread.

A modified Glasgow-Blatchford score (mGBS) has also been proposed, removing the subjective components of the GBS (Figure 1), and it appears to perform as well as the full GBS with a proposed threshold $\leq$ 1 to identify low-risk patients, although publications are scarce.[12-14] Furthermore, a new score has recently been proposed, the CANUKA (Figure 2), which would more accurately identify patients at low risk for adverse outcomes with a validated threshold $\leq$

1.[15] However, the authors suggested the possibility of choosing a threshold ≤ 2 to identify a larger number of low-risk patients. Other scores such as the AIMS65 exist, but have not been validated to identify low-risk patients. At this time, no other published studies have assessed the CANUKA score in patients with suspected upper GI bleeding from any cause and the GBS, mGBS, and CANUKA score have never been compared in the same population.

The aim of this study was to validate whether the use of the GBS, mGBS or CANUKA score could identify emergency department (ED) patients at low-risk of death or need for intervention.

METHODS

Study design

This retrospective, observational, single-center study was conducted at Saint-Antoine Hospital's ED in France from January 1, 2016 to December 31, 2018. This study fell within the scope of the reference methodology MR-004 of the French legislation which allows use of routinely collected data for research. Patients have the right to oppose the use of their personal data. No patient opposed use of the data. The protocol was registered in the *Assistance Publique-Hôpitaux de Paris (APHP)* studies registry (number 20210423183709 and 20210423190021) and approved by the Data Protection Officer for *APHP.Sorbonne Université*. The STROBE guidelines for reporting observational studies and TRIPOD guidelines for reporting validation studies were followed.[17,18]

Population

All adult patients who presented at the ED with suspected UGIB (defined by the reason for consultation « hematemesis » or « melena/hematochezia » from the French ED nurse

classification [16]) were eligible. All patients whose reason for consultation was not suggestive of UGIB, such as hematochezia evocative of lower GI bleeding, hemoptysis, epistaxis, or bowel obstruction, were excluded after review of their medical report by two independent emergency physicians (CP and ZD). In case of disagreement, the patient was excluded. All remaining patients were included in the study.

Data collection

Each patient's electronic hospital record was reviewed using Orbis®, Urqual® and Stare® software, with analysis of ED reports, biological results, imaging and endoscopy reports, and any hospitalization reports following the ED visit, including free text. The following data were abstracted from the record to calculate GBS, mGBS and CANUKA score: age, gender, symptoms (hematemesis, melena, hematochezia, syncope), medical history (liver disease/cirrhosis, heart disease, malignancy), heart rate and blood pressure, laboratory results (hemoglobin, urea). Data concerning endoscopy, final diagnosis, patient outcome (discharge or hospitalization), need for intervention within 7 days (blood transfusion, rebleeding, endoscopic hemostasis) and in-hospital mortality (censored at 30 days) were also collected.

Hematemesis, melena, hematochezia and syncope were defined as present if they were observed by a health professional or reported by the patient. Liver and heart disease were defined by known history or clinical, biological or radiological evidence at presentation to the ED. Malignancy was defined by a current diagnosis or a treatment for cancer within the last 12 months. Symptoms and comorbidities were considered absent if they were not mentioned in the medical record. Blood transfusion was defined as administration of at least one red blood cell within 7 days. Rebleeding was defined as a new episode of bleeding occurring within 7 days after the initial bleeding had stopped, based on clinical evidence (hematemesis, melena, hematochezia)

or a fall in hemoglobin concentration of more than 2 g/dL. Endoscopic hemostasis was defined as the use of any hemostatic procedure during endoscopy within 7 days. Discharge was defined as an ED stay of less than 24 hours. For the discharged patients, their electronic medical records (shared by the 38 hospitals of the *Assistance Publique-Hôpitaux de Paris* of which 17 have an adult ED in the greater Paris area) were accessed up to 30 days after their initial ED visit. If there was no new visit or hospitalization related to UGIB, the patient was considered without complication.

Two independent junior emergency physicians collected these data for all patients in similar but separate Excel® spreadsheet (CP and ZD) (Supplemental Material). They knew the aim of the study and were not blinded to the assessed scores or to patient outcomes, as they were also the study investigators. One meeting was planned at the end of the data collection; in case of discordance on any data, the medical report was reviewed with a senior emergency physician (PCT) to obtain a consensus. As all the data needed for this study were routinely collected, the expected number of missing data was low and they were therefore not imputed. The choice of the study period was pragmatic; it included the last 3 years for which data were available before a change of information system.

Data analysis

Patient characteristics were described by median, first and third quartiles for quantitative variables, and numbers and percentages for qualitative variables. Scores were calculated only for patients with no missing data. The performance of the scores in identifying patients who had complications or not was determined through calculation of sensitivity, specificity, positive predictive value, negative predictive value. Sensitivity was the proportion of patients who had an event (death or therapeutic intervention) that were identified as high-risk by the scores.

Specificity was the proportion of patients identified as low-risk among patients who did not have an event. Positive predictive value was the proportion of patients with an event among those deemed high-risk by the score. Negative predictive value was the proportion of patients with no event among patients categorized by the score as low-risk. All the 95% confidence intervals (CI95) were calculated using a binomial exact method. The inter-rater reliability (identical coding for both raters) was measured for each variable by a Cohen's kappa (κ) and it CI95 was calculed by Clopper-Pearson method.

RESULTS

During the study period, 386 patients were identified as presenting to the ED for UGIB and included in our study (Figure 3). Patient characteristics are shown in Table 1. Median age was 60 years [38-78] and 252 (65.3%) were male. The main symptom was hematemesis in 248 patients (64.2%), melena in 133 (34.5%) and hematochezia in 5 (1.3%). Cardiac failure, hepatic disease and malignancy were reported in 10.1%, 21% and 10.6% of the patients, respectively. Two hundred and fifteen patients (55.7%) had an upper gastrointestinal endoscopy (UGE), of which more than half (n=114, 29.5%) were performed during their ED stay. Two hundred and thirty-three patients (60.4%) were hospitalized, a third of them (n=78, 20.2%) in intensive care unit. One hundred and twenty patients (31.1%) received a blood transfusion and 81 (21%) required endoscopic hemostasis. Forty-one (10.6%) had rebleeding, 15% (n=6/41) of whom did not require intervention or die. Patients' characteristics and outcomes according to their disposition are shown in Supplemental Table 2. Death or need for intervention occurred in 63.9% (n=149/233) of hospitalized patients *versus* 7.8% (n=12/153) of discharged patients. The main

etiologies of the bleeding were peptic disease in 24.8% of patients, Mallory-Weiss syndrome in 15.3% and portal hypertension in 9.6%. In 146 patients (37.8%), the cause remained unknown. Overall and inpatient mortality were 3.1% and 4.3%, respectively. Inter-rater reliability was very good for presence of melena (κ=0.979, CI95 0.958-0.991), syncope (κ=0.914, CI95 0.882-0.946) and hepatic disease history (κ=0.969, CI95 0.950-0.985), and perfect (κ=1) for all other variables.

Table 1. Patients' characteristics according to their outcomes

	Total n=386	Death or need for intervention n=161	No death or need for intervention n=225
Age (years), median [Q1Q3]	60 [38-78]	70 [58-83]	46 [31-72]
Male sex, n(%)	252 (65.3)	109 (68)	143 (64)
Symptoms, n(%)			
Hematemesis	248 (64.2)	78 (48.4)	170 (75.6)
Melena	178 (46.1)	107 (66.5)	71 (31.6)
Hematochezia	5 (1.3)	5 (3.1)	0
Syncope	26 (6.7)	16 (9.9)	10 (4.4)
Medical history, n(%)			
Liver disease	81 (21)	55 (34.2)	26 (11.6)
Heart disease	39 (10.1)	32 (19.9)	7 (3.1)
Malignancy[a]	41 (10.6)	27 (16.8)	14 (6.3)
Vital parameters, median [Q1Q3]			
Heart rate (/min)	87 [73-102]	86 [74-103]	88 [73-102]
Systolic blood pressure (mmHg)	127 [113-143]	119 [105-134]	134 [121-149]
Laboratory results, median [Q1Q3]			
Hemoglobin (g/dL)[b]	11.8 [8.9-13.9]	8.7 [7.4-10.4]	13.4 [11.9-14.8]
Urea (mmol/L)[c]	7.1 [4.7-11.7]	10.9 [7.6-15.6]	5.4 [4-7.6]
Endoscopy, n(%)	215 (55.7)	133 (82.6)	82 (36.4)
Scores, median [Q1Q3]			
GBS[c]	6 [1-11]	11 [8-13]	2 [1-5]
mGBS[c]	5 [1-9]	9.5 [7-11]	1 [0-4]
CANUKA[d]	6 [3-9]	9 [7-10]	4 [2-6]

[a]2 missing data, [b]12 missing data, [c]29 missing data, [d]31 missing data
Q1Q3: first and third quartiles, GBS: Glasgow-Blatchford score

The GBS could be calculated for 357 patients (29 had missing data, including 27 discharged and 2 hospitalized patients). The median GBS was 6 [1-11] and 89 patients (24.9%) were classified as low-risk with a GBS ≤ 1, including 48 with a GBS = 0 and 41 with a GBS = 1. Two patients had a recurrence of their bleeding within 7 days, resulting in 2 events for 89 patients (2.2%, CI95 0.3-7.9%). None of them required blood transfusions, an endoscopic hemostasis procedure or died. The median mGBS was 5 [1-9]. One hundred and eleven patients (31.1%) were classified as low-risk with a mGBS ≤ 1, six of whom (5.4%, CI95 2.0-11.4%) required interventions and none died. Using a threshold of 0, 65 patients (18.2 %) were classified as low-risk and three (4.6%, CI95 1.0-12.9%) required intervention. The CANUKA score could be calculated for 355 patients (31 had missing data, including 29 discharged and 2 hospitalized patients). The median CANUKA score was 6 [3-9] and 31 (8.7%) patients were classified as low-risk with a CANUKA ≤ 1. Using a threshold ≤ 2, 67 patients (18.9%) were identified as low-risk. No intervention or deaths were recorded in these patients (0%, CI95 0-5.4%). The 2 x 2 tables for calculation of test characteristics are shown in Supplemental Table 3. Sensitivity, specificity, positive and negative predictive values of different scores to categorize patients as high-risk or low-risk and predict death or need for intervention are presented in Table 2. All scores had a high sensitivity and negative predictive value, but a low specificity and positive predictive value.

Table 2. Performance of scores and thresholds in prediction of death or need for intervention

Score	Low-risk patients		High-risk patients		Sensitivity	Specificity	PPV	NPV
	Cut-off	n (%)	Cut-off	n (%)	% [IC95]	% [IC95]	% [IC95]	% [IC95]
GBS	≤ 1	89 (24.9)	> 1	268 (75.1)	98.6 [94.9-99.8]	40.1 [33.5-46.9]	51.5 [45.3-57.6]	97.8 [92.1-99.7]
mGBS	0	65 (18.2)	> 0	292 (81.8)	98.2 [94.8-99.6]	32.3 [25.7-39.4]	55.5 [49.6-61.3]	95.4 [87.1-99.0]
	≤ 1	111 (31.1)	> 1	246 (68.9)	95.2 [89.8-98.2]	45.3 [38.7-51.9]	48.4 [42.0-54.8]	94.6 [88.6-98.0]
CANUKA	≤ 1	31 (8.7)	> 1	324 (91.3)	100 [98.1-100]	19.3 [13.5-26.2]	59.9 [54.3-65.3]	100 88.8-100]
	≤ 2	67 (18.9)	> 2	288 (81.1)	100 [97.7-100]	34.0 [27.4-41.1]	54.9 [48.9-60.7]	100 [94.6-100]

PPV: positive predictive value; NPV: negative predictive value; GBS: Glasgow-Blatchford score

DISCUSSION

The GBS, mGBS and CANUKA scores in our ED population categorized 17-25% of patients at low-risk of death or need for intervention, which is similar to prior studies.[6-8, 12, 15, 19] There was a need for intervention in 2.2% for patients with GBS ≤ 1, 4.6% of patients with mGBS = 0 and no patient with CANUKA ≤ 2. No deaths occurred in the low-risk patients, independent of the score used.

These results support the hypothesis that low-risk patients identified with the GBS and CANUKA score could be considered for safe discharge and management as outpatients, as suggested by previously published data.[6-8, 12-14, 19] GBS ≤ 1 identified the largest number of low-risk patients with a low need for intervention and it is appropriate that it is recommended in European and international guidelines.[9-11] Although it has the advantage of excluding subjective items, the mGBS appears to be slightly less useful for this purpose with fewer low-risk patients

identified and more need for intervention. In contrast, the CANUKA ≤ 2 identified fewer low-risk patients than the GBS ≤ 1, yet appears to be the safest score, as previously shown;[15] its use should be more extensively investigated.

The benefit of using these scores to identify patients at low-risk of death or need for intervention is to reduce the number of unnecessary hospitalizations. Indeed, the number of ED patients is constantly increasing, due in particular to the ageing of the population, and the adequate use of hospital beds has become a major public health issue. In our study, low-risk patients have a hospitalization rate of about 20%, but it reaches more than 50% in the literature.[20] Although some patients may be hospitalized for reasons other than their UGIB, some authors estimated that the use of these scores could reduce hospital admissions by 15-20%.[19] According to results in our single centre study, this rate would rather be around 7.5% (17 patients with GBS ≤ 1 among 233 hospitalized). Although our data support the possibility of using GBS ≤ 1 or CANUKA ≤ 2 to identify patients at low risk of complication who may not require hospitalization or urgent intervention, the clinical acumen of the emergency physician should predominate in the decision of patient disposition. In addition, medical follow-up of discharged patients should be ensured by setting up a post-emergency pathway with the opportunity to consult a gastroenterologist or to perform an outpatient UGE.

Our study population was predominantly male (65%), with a median age of 60 years, similar to the data found in various French and international studies.[2, 3, 6-8, 12-15, 19, 21] Our hospitalization rate was much lower than those found in the literature (around 80%). This could be explained because some studies only included patients who presented with a confirmed bleeding as assessed by the physician or had UGE, who might have more severe bleeding. This

high proportion of discharged patients may explain our lower UGE rate (56%) compared to other studies (>75%).[2, 3, 7, 19] On the other hand, 79% of hospitalized patients had an UGE and one in five patients required endoscopic hemostasis, which is consistent with the literature.[8, 19] More than half of UGE were performed during the ED stay, which includes the observation unit where patients can be admitted for up to 24 hours, before being hospitalized or discharged. One third of our patients received a blood transfusion and one in ten had a rebleeding, in line with values found in some studies [2, 6, 12, 13, 19] while other studies have shown higher rates of up to 76% transfusion and 26% rebleeding.[14, 21] This may be related to the larger number of non-severe patients included in our study, but also to differences in transfusion protocols or definitions of rebleeding. The mortality rate was lower than those found in the literature (between 5 and 11%),[2, 3, 6-8, 14, 15, 19] which could also be explained by the lesser severity of our patients, but also because our study took place in a reference center for the management of gastrointestinal bleeding, likely allowing optimization of the management.

Our study found a lower rate of bleeding related to gastroesophageal varices compared to other French studies, usually around 20%.[2, 3] This could partially be explained by our lower proportion of patients who have undergone UGE, limiting the possibility of an accurate diagnosis. It should be noted that in hospitalized patients, of whom nearly 80% had an UGE, these figures are within the values found in the literature. It is also possible that since the publication of these older studies, there has been an improvement in the management of cirrhotic patients at risk of UGIB, through the optimized use of beta-blockers or transjugular intrahepatic portosystemic shunts.

Limitations

This study has some limitations, mainly associated with its retrospective methodology. As far as possible, we have followed the recommendations for the presentation of this study design conducted in EDs.[22, 23] First, patients were identified according to the reason for consultation as defined by the triage nurse. Some patients consulting for UGIB may have been registered under another reason for consultation such as "vomiting", "anemia", "shock/hypotension" or "abdominal pain", and may not have been included, which may have led to a selection bias. Nevertheless, this recruitment has the advantage of including all types of patients, including the less severe ones. Second, some variables included in the GBS and CANUKA may be subjective, such as the occurrence of melena or syncope, self-reported by patients and not necessarily witnessed by a healthcare professional. Some medical conditions may also be unreported by patients. Thus, it is possible that some patients' scores may be inaccurate. However, this reflects real life and should not compromise their use. Third, the inclusion of rebleeding in the definition of "need for intervention" is questionable. Indeed, the 2 patients with GBS ≤ 1 identified as rebleeding did not require therapeutic intervention and did not die. However, we had chosen this definition because it is the one used in the original article describing GBS.[5] Without considering rebleeding, the results would be even more favorable to GBS and mGBS since the number of interventions would be 0 and 4 (3.6%), respectively, with a threshold ≤ 1. Fourth, the reviewers were junior emergency physicians and did not receive standardized training. They knew the aim of the study and were not blind to the assessed scores or outcomes. Nevertheless, the majority of the variables were not subject to interpretation by the chart abstractors and inter-rater reliability was excellent. Fifth, there is a possible center effect due to our single-center study conducted in a reference hospital for management of gastrointestinal bleeding. The typology of patients and their management could be different in other centers, which may limit generalization of the results. Sixth, there are missing data that do not allow the calculation of scores for all

patients, mainly because some patients did not have a blood sample. These patients were younger, had fewer comorbidities, were less frequently hospitalized and had fewer complications. Seventh, the number of complications (rebleeding, transfusion, hemostatic procedure, death) may have been underestimated in discharged patients who could have reconsulted in another hospital. These patients were less severe (Supplemental Table 2), and we believe that this risk remains low, especially since we have access to the medical reports of all the *Assistance Publique-Hôpitaux de Paris* hospitals. Finally, the confidence intervals are slightly wide due to a small sample size and the scarcity of events.

CONCLUSION

In patients with UGIB, the use of a GBS ≤ 1 or CANUKA score ≤ 2 appears to be safe for identifying patients at low risk of death or need for intervention, who could be discharged from the ED. Prospective multicenter studies are needed to validate these results and confirm the safety of use of the Glasgow-Blatchford and CANUKA scores, as well as to study the medico-economic implications of their application.

LEGENDS

Figure 1. Full and modified Glasgow-Blatchford scores

Figure 2. CANUKA score

Figure 3. Flowchart of patient inclusion.

Note: Eligible patients were selected based on their reason for consultation, either hematemesis or a reason combining melena and hematochezia. The majority of patients identified by the combined reason had hematochezia and were suspected of having lower gastrointestinal bleeding and not upper gastrointestinal bleeding, which explains the large number of patients excluded in this category.

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