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Age, blood tests and comorbidities and AIMS65 risk scores outperform Glasgow-Blatchford and pre-endoscopic Rockall score in patients with upper gastrointestinal bleeding

Morarasu BC *et al.* Pre-endoscopic risk scores in upper GIB

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BACKGROUND

Upper gastrointestinal (GI) bleeding is a life-threatening condition with high mortality rates.

AIM

To compare the performance of pre-endoscopic risk scores in predicting the following primary outcomes: In-hospital mortality, intervention (endoscopic or surgical) and length of admission (≥ 7 d).

METHODS

We performed a retrospective analysis of 363 patients presenting with upper GI bleeding from December 2020 to January 2021. We calculated and compared the area under the receiver operating characteristics curves (AUROCs) of ⁴Glasgow-Blatchford score (GBS), pre-endoscopic Rockall score (PERS), albumin, international normalised ratio, altered mental status, systolic blood pressure, age older than 65 (AIMS65) and age, blood tests and comorbidities (ABC), including their optimal cut-off in variceal and non-variceal upper GI bleeding cohorts. We subsequently analyzed through a logistic binary regression model, if addition of lactate increased the score performance.

RESULTS

All scores had discriminative ability in predicting in-hospital mortality irrespective of study group. AIMS65 score had the best performance in the variceal bleeding group (AUROC = 0.772; $P < 0.001$), and ABC score (AUROC = 0.775; $P < 0.001$) in the non-variceal bleeding group. However, ABC score, at a cut-off value of 5.5, was the best predictor (AUROC = 0.770, $P = 0.001$) of in-hospital mortality in both populations. PERS score was a good predictor for endoscopic treatment (AUC = 0.604; $P = 0.046$) in the variceal population, while GBS score, (AUROC = 0.722; $P = 0.024$), outperformed the other scores in predicting surgical intervention. Addition of lactate to AIMS-65 score, increases by 5-fold the probability of in-hospital mortality ($P < 0.05$) and by 12-fold if added to GBS score ($P < 0.003$). No score proved to be a good predictor for length of admission.

CONCLUSION

ABC score is the most accurate in predicting in-hospital mortality in both mixed and non-variceal bleeding population. PERS and GBS should be used to determine need for endoscopic and surgical intervention, respectively. Lactate can be used as an additional tool to risk scores for predicting in-hospital mortality.

Key Words: Glasgow-Blatchford; Pre-endoscopic Rockall; Age older than 65; Age, blood tests and comorbidities; Risk score; Gastrointestinal bleeding

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Core Tip: Upper gastrointestinal (GI) bleeding is a life-threatening condition with high mortality rates. It represents one of the main reasons for presentation in the emergency department, having a major impact on both the patient and the clinician. This cohort study evaluates four of the mostly used pre-endoscopic risk scores by comparing them in two populations: Variceal and non-variceal upper GI bleeding, highlighting which one should be preferably used depending on the investigated outcome.

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INTRODUCTION

Upper gastrointestinal (GI) bleeding is defined as blood loss from the GI tract above the ligament of Treitz. It is a life-threatening condition with high mortality rates, of up to 15%^[1]. This is particularly important as emergency services are struggling with high patient flow^[2] and clinicians must promptly decide the need for admission, timing of endoscopy and level of care. It is generally recommended to perform endoscopy within 24 h of presentation^[3]. It plays a pivotal role in identifying the source of bleeding and it can achieve haemostasis in most cases. However, endoscopy may not be available in all centers or, if performed in low-risk patients, it may overcrowd the service with unnecessary urgent interventions.

European Society of Gastroenterology recommends immediate assessment of patient's haemodynamic status, transfusion strategy and risk stratification^[4]. The latter can be achieved by calculating GI bleeding risk scores which should predict several outcomes such as need for intervention, mortality, rebleeding rate or death^[5]. Pre-endoscopy risk scores have been increasingly used as they rely on limited number of parameters and may allow timely sequential decisions. Glasgow-Blatchford score (GBS)^[6] has been validated to identify low risk patients which may be managed as outpatients. PERS^[7] evaluates the risk of rebleeding and mortality, while albumin, international normalized ratio, altered mental status, systolic blood pressure, age older than 65 (AIMS65)^[8], determines the risk of death. Age, blood tests and comorbidities (ABC) is a relatively new risk score used to predict mortality in patients with both upper and lower GI bleeding^[9]. These scores have been previously compared, with a

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certain variability among studies, potentially due to the differences in population included. Moreover, there is limited data for variceal upper GI bleeding, with most of the studies including non-variceal cohorts^[10,11].

Venous lactate has been proven to be an important tool in critically ill patients, such as those with shock, trauma, or heart failure. It increases as a result of tissue hypoperfusion or hypoxia. Although not routinely used, it can predict in-hospital mortality, need for intensive care or surgical intervention, as well as rebleeding in patients with upper GI bleed^[12]. It may be used to improve performance of existing scoring systems^[13] and guide clinicians towards early triage of patients.

In this study, we aim to evaluate the performance of pre-endoscopic risk scores (GBS, PERS, AIMS65, and ABC) in patients with variceal and non-variceal upper GI bleeding for predicting the following primary outcomes: In-hospital mortality, type of intervention (endoscopic or surgical) and length of admission (≥ 7 d). We will further evaluate whether the addition of venous lactate improves the score performance in predicting the determined outcomes.

MATERIALS AND METHODS

We conducted a single centre cohort study, performed in a tertiary emergency hospital, "Saint Spiridon" Emergency University Hospital, Iasi, Romania. We retrospectively analysed all patients above 18 years old presenting to the emergency department (ED) with upper GI bleeding from January 2020 to December 2021.

Ethics statement

The study was approved by the Hospital's Ethics Committee. The "Saint Spiridon" Institutional Review Board approved this study, approval number 39/30.03.2022. Each patient signed our standard informed consent. We did not require additional consent as patient data is anonymous and the study included standard of care information.

Patient management

Each patient presenting with upper GI bleed exteriorised as hematemesis, coffee ground vomiting or melena was fully assessed by the emergency medicine physician, including past medical history and complete clinical examination. Immediate venous catheterization and fluid resuscitation was performed as indicated following primary assessment. Subsequent full work-up with blood tests (full blood count, haemoglobin (Hb), platelets, INR, aPTT, albumin, ALT, AST, urea, creatinine, and venous lactate), and other investigations (as indicated) were performed within 24 h from presentation. Hemodynamically stable patients with a Hb ≤ 7 g/dL had at least one unit of red blood cell concentrate transfused, with more than one unit in those with severely lower Hb. A higher Hb threshold (Hb ≤ 8 g/dL) was used for patients with associated cardiovascular disease. Post-transfusion target Hb was between 7-9 g/dL. In case of major transfusion protocol, severe liver disease, drug-induced coagulopathy with active bleeding, patients received both red cell concentrate and fresh frozen plasma. Endoscopy was performed within 24 h of ED arrival in all patients included in analysis. Forrest classification was used to describe peptic ulcer disease, with Baveno and Sarin's classification for gastroesophageal varices. Those with suspected variceal bleeding had endoscopic evaluation and management within 6 h to 12 h, after initial appropriate fluid resuscitation. In those with non-variceal upper GI bleeding, endoscopy was performed within the first 12 h to 24 h with no patient being postponed more than 24 h. However, we would perform the intervention earlier guided by the patient's clinical status and the clinician's preference. Patients with non-variceal upper GI bleeding received an infusion with proton pump inhibitors (PPIs), while those with variceal bleeding were treated with Somatostatin. Endoscopic treatment was performed depending on the cause of bleeding. For non-variceal upper GI bleed there was a combined approach with injection therapy (dilute epinephrine) and mechanic therapy (thermal coagulation or haemostatic clip) for FIa, Fib, and FIIa, with clot removal in FIIf lesions. In variceal bleeding, endoscopic ligation was the main approach. Surgical treatment was performed in cases where endoscopic treatment failed, such as actively bleeding malignant lesion, vascular fistula, or in patients with bleeding perforated

ulcer. Need for admission was established by the gastroenterology and general surgery teams on-call guided by the patient's clinical status, comorbidities, and high risk of rebleeding and mortality (GBS score ≥ 2 in non-variceal patients and all patients with stigmata of variceal bleeding irrespective of risk score).

Data collection

Initially, a ward clerk extracted all data from ED's computer data. Further exclusion of duplicates/incomplete files was performed. We extracted from the patient's records and electronic files, the following data: age, gender, comorbidities (heart failure, atrial fibrillation, hypertension, coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease, asthma, liver cirrhosis, active malignancy, hepatocarcinoma, and cerebral vascular disease), symptoms on presentation (hematemesis, melena, coffee ground vomiting, abdominal pain, and syncope), vital signs (systolic blood pressure, heart rate), blood parameters needed to calculate the GBS, PERS, AIMS65 and ABC scores, venous lactate level, source of bleeding if identified by endoscopy (variceal bleeding- oesophageal and/or gastric varices and non-variceal bleeding- gastric/duodenal ulcer, severe/erosive gastritis or duodenitis, severe/erosive esophagitis, Mallory Weiss syndrome, GI malignancy, angiodysplasia, Dieulafoy lesion), type of endoscopic intervention (no intervention, injection therapy, mechanical intervention) or surgical intervention, length of admission (number of days), need for transfusion on admission and in-hospital survival. Venous lactate was measured using Radiometer ABL 90 Series I393-09.

Patients were excluded if they were unable to undergo/did not consent for endoscopy or surgical intervention, had a final diagnosis of non-upper GI bleeding, were also diagnosed with sepsis, pregnancy, severe trauma, were taking Metformin, had incomplete data for score calculation or venous lactate was not determined.

Statistical analysis

² Statistical analysis was performed using SPSS software for Windows (v.22.0; SPSS, Chicago, IL, United States). The statistical methods of this study were reviewed by I.L. Rusu, biomedical statistician. Nominal variables are presented as frequencies and percentages, and continuous variables as the mean \pm SD. We were able to apply all tests as the score values are homogenous, median value is similar to the mean value and skewness test had $[-2 \div 2]$ interval. ³ Categorical variables were presented as percentages and compared using Chi-square test. A *P* value of < 0.05 was considered statistically significant. We determined the scores' ability to predict each investigated outcome by calculating the area under the receiver operating characteristics curves (AUROCs), including optimal cut-off value with specificity and sensitivity and 95% confidence intervals. AUROCs were determined significant for a value above 0.600. Subsequently, we analysed through a logistic binary regression model, if addition of lactate to the risk scores increased the probability of previously determined outcomes.

RESULTS

A total of 1046 medical records were considered eligible (Figure 1). We excluded duplicates or patients with more than one presentation within the study period. After applying the exclusion criteria, the study ended with a cohort of 363 patients with upper GI bleeding with a mean age of 60 years old and a predominance of male sex ($n = 240$, 66.1%). Non-variceal bleeding was the main cause of presentation ($n = 236$, 65%). Liver cirrhosis is the most frequent associated comorbidity in the entire group ($n = 139$, 38.3%), and 2.5% ($n = 9$) of patients had associated hepatocarcinoma (Table 1). The main symptom of presentation was haematemesis in patients with variceal bleeding and melena in the non-variceal group. Approximately 9% of our patients had chronic treatment with antiplatelets ($n = 36$, 9.9%) or oral anticoagulation ($n = 32$, 8.9%). Gastric/duodenal ulcer was the main cause of GI bleeding ($n = 151$, 41.6%), followed by oesophageal varices ($n = 115$, 31.7%). Most patients in variceal bleeding group required mechanical endoscopic therapy with band ligation ($n = 48$, 13.2%) and only 2 patients (0.6%) had variceal sclerotherapy. In the non-variceal bleeding group, dual therapy

with thermal anticoagulation and local administration of dilute Adrenaline was the main type of endoscopic intervention ($n = 29$, 8.0%). Failed endoscopy was recorded in approximately 4.7% ($n = 17$) of patients. Only 9 patients in the non-variceal group required surgical intervention, in most cases due to actively bleeding perforated duodenal ulcer, inability to achieve local haemostasis in diffuse bleeding induced by malignancy or fistulas. Approximately 31% ($n = 112$) of the population in both groups required transfusion. In-hospital mortality had an overall rate of 9.4% ($n = 34$), most cases ($n = 16$, 12.6%) were in the variceal group (Table 1). The direct cause of death was hypovolaemic shock secondary to upper GI bleeding (in most cases variceal). There were several cases of perforated duodenal ulcer which required emergency surgery, but with poor outcome. One patient developed ventilator associated pneumonia, and another one, acute myocardial infarction, both of them, however in context of the patient presenting with major GI bleed.

GBS had the highest mean value in the mixed population (12.32), as well as in the two main study groups (12.98 in variceal bleeding and 11.97 in non-variceal bleeding), most patients being at high risk of intervention. ABC score showed a medium risk (mean value 5.02) of mortality rate, as well as AIMS65 (mean value 1.52). Mean PERS is consistent with an 11% chance of mortality prior to endoscopy (Table 2).

We have performed linear regression analysis of each pre-endoscopic score against each determined outcome. AIMS65 score is influenced by the following variables: mortality, endoscopic and surgical intervention (Model 4: $r = 0.316$; $P = 0.007$), as well as length of stay, with an Y point $3.959 - 0.961 \text{ Death} - 0.148 \text{ Endoscopy} + 0.057 \text{ Surgery} - 0.291 \text{ d}$ (Table 3). PERS score is influenced by mortality and endoscopic intervention (Model 2: $r = 0.243$; $P = 0.009$), with an Y point $6.227 - 1.961 \text{ Death} - 0.512 \text{ Endoscopy}$ (Table 4). ABC score is influenced by mortality and endoscopic intervention (Model 2: $r = 0.324$; $P = 0.006$), with an Y point $11.161 - 2.466 \text{ Death} - 0.815 \text{ Endoscopy}$ (Table 5). GBS score is influenced by mortality and endoscopic intervention (Model 2: $r = 0.241$; $P = 0.007$), with an Y point $18.557 - 2.231 \text{ Death} - 1.127 \text{ Endoscopy}$ (Table 6).

In-hospital mortality

All scores had discriminative ability in predicting in-hospital mortality irrespective of study group (AUROC > 0.600). AIMS-65 score had the best performance for the variceal bleeding group (AUROC 0.772; $P < 0.001$) (Figure 2A, Table 7), and ABC (AUROC 0.775; $P < 0.001$) in the non-variceal bleed (Figure 2B, Table 7).

The optimal cut-off value for predicting in-patient mortality was calculated for each score depending on the type of bleeding. For variceal bleeding, an AIMS 65 score above 1 with sensitivity of 90% and specificity of 73% (AUC = 0.772; 95%CI: 0.673-0.871; $P = 0.001$) and GBS score above 10.5 with a sensitivity of 93.8% and specificity of 81% (AUC = 0.752; 95%CI: 0.621-0.883; $P = 0.001$). PERS and ABC scores had similar cut-off values, of 3.5 and 5.5, respectively, irrespective of type of bleeding, but with slight variations in sensitivity (PERS: 87.5% variceal group, 77.8% non-variceal group; ABC: 80% variceal group, 77.8% non-variceal group) and specificity (PERS: 64% variceal group, 56% non-variceal group; ABC: 76.7% variceal group, 65.1% non-variceal group). In the non-variceal bleeding group, the optimal cut-off value for in-hospital mortality was 1.5 for AIMS65 score, with sensitivity of 66.7% and specificity of 57% (AUC = 0.693; 95%CI: 0.577-0.810; $P = 0.006$), and 12.5 for GBS score with sensitivity of 66.7% and specificity of 52.8% (AUC = 0.657; 95%CI: 0.505-0.808; $P = 0.027$) (Table 7).

We have determined the best scoring system for in-patient mortality in the included population for both variceal and non-variceal bleeding. ABC showed the highest AUROC, 0.770 (Figure 2C), as being the best predictor for in-patient mortality in the entire population, at a cut-off value of 5.5 with a sensitivity of 88.2% and a specificity of 59.6% (95%CI: 0.700-0.840; $P = 0.001$) (Table 8).

Type of intervention

Endoscopic intervention: For variceal bleeding patients, only PERS score, at a cut-off value above 3.5 was a good predictor for endoscopic treatment with a sensitivity of 76.5% and specificity of 40% (AUC = 0.604; 95%CI: 0.506-0.703; $P = 0.046$) (Figure 2D).

No score performed as a good predictor for endoscopic intervention in non-variceal bleeding group (Table 9).

Surgical intervention: In the non-variceal bleeding group, all risk scores were good predictors for surgical intervention, with an AUROC > 0.600 (Figure 2E). However, only GBS score, at a cut-off value above 12.5 with a sensitivity of 66.7% and specificity of 52.8% (AUC = 0.722; 95%CI: 0.541-0.903; $P = 0.024$), had statistical significance (Table 9). No patient in the variceal bleeding group underwent surgical intervention.

Length of admission (> 7 d)

No score proved to be a good predictor for length of admission, due to their low AUROC < 600 (Table 10).

Role of venous lactate

Logistic regression model showed that lactate is an independent predictor for the determined outcomes. It did not show, however, good performance in predicting variceal or non-variceal bleeding, either due to low sensitivity (64.3%) and specificity (53.2%) or a low AUROC (0.357) (Figure 3, Table 11). For the variceal bleeding population, addition of lactate to AIMS65 score, leads to a 5-fold increase in probability of in-hospital mortality ($P < 0.05$). For non-variceal bleeding, addition of lactate to GBS score showed a 12-fold increase in probability of in-hospital mortality ($P < 0.003$). In terms of intervention, higher level of venous lactate increases by 5.5 times the probability of endoscopic intervention and by 2 the probability for surgical intervention ($P = 0.001$) (Table 12).

DISCUSSION

To our knowledge, this is the first study to compare four of the most representative pre-endoscopic risk scores, AIMS65, PERS, GBS and the relatively new ABC score in

variceal and non-variceal GI bleeding cohort. Our aim was to identify which score would be preferably used depending on source of bleeding.

Prognostic risk scores could be a key step in the initial evaluation of upper GI bleeding patient in order to establish which one is at high risk of death. It should further identify likelihood of blood transfusion, endoscopic or surgical treatment, need for intensive care unit admission and cost of care in an attempt to decrease the burden over ED. Moreover, the routine determination of venous lactate should be used in determining probability of in-patient mortality, both as an independent predictor, and in association with certain risk scores.

Our cohort included a total of 363 patients, out of which 9.4% ($n = 34$) died, most of them ($n = 16$, 12.6%) in the variceal bleeding group. The mortality rate in our group is high, but similar to the one reported in other studies^[14]. The pre-endoscopic risk scores should be considered as a key step to improve these numbers. When we analyzed the performance of risk scores according to in-patient mortality, ABC score had the best performance in both mixed and non-variceal bleeding group, with AIMS65 in variceal bleeding cohort. For endoscopic treatment, only PERS showed good discriminative value in the variceal bleeding group. In terms of surgical intervention, all determined scores had good performance, but only GBS had statistical significance. No score proved to be good in determining length of admission.

When comparing the two cohorts and their AUROC values, AIMS65 had the best accuracy in predicting in-patient mortality for patients with variceal bleeding. AIMS65 includes clinical parameters and regular laboratory tests which are fast and simple to be performed in ED settings. We determined an AUROC of 0.772 (95%CI: 0.673-0.871; $P = 0.001$), which was similar to other studies^[15,16], but lower than other cohorts^[10,17]. AIMS65 was also reported in other studies as the only score to provide accurate risk assessment for variceal GI bleeding population^[18] in comparison to other scores, such as GBS or full Rockall (endoscopic) score. In our research, AIMS65 was superior to GBS, but the latter performed better than ABC or PERS score, which had the lowest AUROC, of 0.705. Previous reports compared both GBS and full Rockall score in predicting

outcomes in patients with variceal bleeding, with similar results as ours^[19]. The substrate for GBS inferiority in comparison to AIMS65, might be explained by the lack of liver disease history as some patients' first presentation of liver cirrhosis is with variceal bleeding. Moreover, AIMS65 includes level of serum albumin and INR, which reflect liver function. Other reports comparing different other specific scores used in patients with liver cirrhosis (MELD-model for end-stage liver disease, ⁶APACHE II-acute physiology and chronic health evaluation II, qSOFA-quick sepsis related organ failure assessment) confirmed higher accuracy of AIMS65 in predicting in-hospital mortality^[1]. Similar predictive power for in-hospital mortality of AIMS65 score, Child-Pugh score (CTP) and MELD score was found in a metanalysis performed on a variceal bleeding population^[20].

The ABC score was recently validated to predict 30 d mortality in patients with both upper and lower GI bleed. Based on patient's age, kidney, and liver (albumin) function, and associated comorbidities, it can classify patients at low, medium, or high risk of mortality. Although there is limited literature data, the ABC score showed better performance when compared to AIMS65 and full Rockall score on a mixed population (variceal and non-variceal) GI bleeding^[9,21]. Interestingly, in our study, the score had the highest performance (AUROC 0.770) in predicting in-patient mortality in the entire population (variceal and non-variceal), as well as non-variceal bleeding when compared to AIMS65, PERS and GBS. This is particularly important as no previous investigations compared the scores' ability to predict mortality by type of GI bleeding (variceal *vs* non-variceal). Our findings also support previous evidence that ABC performs better than GBS or AIMS65 score^[22], also outperforming Progetto Nazionale Emorragia Digestive (PNED) and Rockall score^[23]. Looking at the other three scores, our results show that AIMS65 is superior to GBS and PERS, but with no significant difference in the AUROC value. In non-variceal upper GI bleeding, other investigators support a better predictive power for AIMS65 when compared to other scores^[24]. In contrast, GBS and PERS are the most widely used pre-endoscopic scoring system in clinical practice, with most studies in non-variceal upper GI bleeding cohorts. GBS has been previously reported to

perform less than PERS in predicting mortality^[25,26], similar to our cohort, where GBS had the lowest AUROC of 0.657. However, for practical reasons, we consider that ABC score, at a cut-off value of 5.5 can be used to determine in-hospital mortality in both populations.

The cut-off value of each score was determined as it is a key determinant in predicting outcomes. There are significant variations among different studies, probably due to population characteristics, moment, and type of therapeutic interventions^[27]. For in-patient mortality, we determined a cut-off value of 1 for AIMS65 score in patients with variceal bleeding. This should label the patients as high category of emergency and limit the waiting time until assessment as much as possible. Cut-off values of 1^[27], 2^[24], or 3^[28] were previously reported in different populations, with similar results for European cohorts. For those presenting with non-variceal upper GI bleed, an ABC score of 5.5 classifies them as high risk. Similar to our findings, another study reported a cut-off value of 5.5 for ABC score in predicting 30-d mortality^[29] associated with a 13.1% risk of mortality.

Regarding endoscopic intervention, no score performed as a good predictor in the non-variceal bleeding group, due to an AUROC < 0.600. This is consistent with previous reports where AUROC levels were around 0.500^[30], but other investigators showed better performance (AUROC 0.750, sensitivity 80.4%, specificity 57.4%)^[31]. We found that PERS score, at a cut-off value above 3.5 showed good performance for predicting endoscopic treatment in variceal bleeding patients, with a sensitivity of 76.5% and specificity of 40%, and a relatively low AUROC (AUC = 0.604; 95%CI: 0.506-0.703; $P = 0.046$). Rockall score can be calculated after endoscopy (full Rockall), or prior to it (PERS). The pre-endoscopic score relies on vital signs, patient's age and comorbidities and it was previously validated to predict in-patient mortality. On the other hand, the full Rockall score can be used as a predictor of endoscopic treatment at a cut-off value > 3.5^[32]. This is particularly important as the latter score includes endoscopic findings which plays a major role in the diagnosis and treatment of such patients. All patients included in our cohort have been investigated endoscopically

within the first 24 h of presentation. As previously mentioned, timing of endoscopy is of paramount importance in patients with high risk of further bleeding and mortality and it should be performed within 12 h, especially in patients with variceal bleed. On the other hand, very early endoscopy (less than 6 h) does not appear to reduce mortality or further risk of bleeding^[33].

Although our AUROC values were low, we agree with most previously reported data which showed better performance of GBS in predicting endoscopic intervention in patients with GI bleeding^[20]. We did not find any study to evaluate the ABC score against this outcome. Further larger studies may be needed.

Nowadays, less surgical interventions are performed in upper GI bleeding, mainly due to advances in types of endoscopic treatment and interventional radiology. All patients requiring surgical intervention in our population ($n = 9$) are in the non-variceal group. The main reason is failure of endoscopic treatment and lack of availability of endovascular therapies. All scores showed good predictive value for surgical intervention with an AUROC > 0.600. Our study is the first to compare such outcome for all investigated scores. However, only GBS score, at a cut-off value above 12.5 with a sensitivity of 66.7% and specificity of 52.8% had statistical significance. GBS has been validated to be a good predictor for need of treatment, which consisted of either endoscopy, surgery or interventional radiology^[34].

No risk score proved to be a good predictor for length of stay (> 7 d) as it had poor statistic power, with an AUROC below 0.600. Similar low discriminative abilities were previously reported for PNED, full and PERS, GBS and AIMS65 score, with an AUROC close to 0.600^[15].

Lactate is an independent predictor for in-hospital mortality, need for intensive care unit admission, recurrence of bleeding or need for surgical intervention^[12,13]. We are of the opinion that lactate could be implemented as a standard test in all patients with upper GI bleeding. In variceal bleeding patients, levels of lactate might be higher due to associated liver insufficiency, large volume of bleeding and subsequent hypovolemia^[13,35]. On the other hand, in patients with less dramatic clinical

presentation, lactate could be used as a tool for early detection of GI bleeding^[36,37]. In our cohort it was an independent predictor of mortality and intervention (endoscopy and surgery). There is, however, disparity among studies evaluating role of lactate in addition to risk scores. It seems that incorporation of arterial lactate in PERS and GBS showed a statistically significant improvement in their ability to predict mortality, but with a low AUROC^[38]. In contrast, when taking into account venous lactate level, the power of discrimination for GBS and PERS for in-patient mortality showed better performance and an AUROC > 700. The difference between levels of arterial and venous lactate (which has higher levels) might be a determinant factor for study results variability^[39]. In our population, addition of lactate to GBS score showed a 12-fold increase in probability of in-hospital mortality ($P < 0.003$), but this only applies to the non-variceal bleeding group. In case of patients presenting with variceal upper GI bleeding, addition of lactate to AIMS65 score, leads to a 5-fold increase in determining the probability of in-hospital mortality ($P < 0.05$). Similar findings are supported by another retrospective study where the modified L-AIMS65 score (AIMS65 combining lactate) had higher AUC for rate of rebleeding and 30 days mortality. Unfortunately, it did not show statistical significance^[40].

In terms of type of intervention, adding lactate to the regression model of non-variceal bleeding population does not improve the prediction value of any of the determined scores.

There are several limitations of our study. It is a single center, retrospective analysis based on clinical records data which may lead to selection bias. The decision of intervention was based on the clinical judgement of emergency medicine physician. Hospital admission was indicated by the gastroenterologist and surgeon on call. We excluded a large number of patients, mainly due to lack of availability in albumin and venous lactate level. Also, irrespective of their statistical power, risk scores are tools which cannot replace appropriate clinical evaluation, decision making process and the need for an individualized approach of each patient.

CONCLUSION

ABC score is the most accurate in predicting in-hospital mortality in both mixed and non-variceal bleeding population. AIMS65 had the best performance in predicting in-patient mortality in patients with variceal upper GI bleeding, however, for practicality, we advise the use of ABC score for both populations. In terms of intervention, PERS and GBS should be used to determine need for endoscopic and surgical intervention. Lactate can be used in conjunction to AIMS65 and GBS score to predict in-patient mortality and intervention. Although GBS is currently largely used, further studies are needed to investigate the relatively new ABC score regarding its role in daily clinical practice and possible implementation in guidelines.

ARTICLE HIGHLIGHTS

Research background

Upper gastrointestinal (GI) bleeding patients require immediate assessment at the time of arrival in the emergency department (ED). A comprehensive, however fast approach regarding haemodynamic status, transfusion strategy and need for intervention should be performed. This can be achieved by calculating GI bleeding risk scores which should be able to predict several outcomes such as need for intervention, mortality, rebleeding rate or death. Pre-endoscopy risk scores have proved to be a reliable tool which may allow timely sequential decisions. Glasgow-Blatchford score (GBS) has been validated to identify low risk patients which may be managed as outpatients. Pre-endoscopic Rockall score (PERS) evaluates the risk of rebleeding and mortality, while albumin, international normalized ratio, altered mental status, systolic blood pressure, age older than 65 (AIMS65), determines the risk of death. Age, blood tests and comorbidities (ABC) is a relatively new risk score used to predict mortality in patients with both upper and lower GI bleeding. There is a certain variability among these risk scores, potentially due to the differences in population included. Moreover, there is limited data for variceal upper GI bleeding. Venous lactate is another important tool in critically ill patients, such as those with shock, trauma, or heart failure. It has been

shown to predict in-hospital mortality, need for intensive care or surgical intervention, as well as rebleeding rate in patients with upper GI bleed. It may be used to improve performance of existing scoring systems and guide clinicians towards early triage of patients.

Research motivation

As emergency services are struggling with high patient flow, clinicians must promptly decide appropriate management in patients with upper GI bleeding. A standardized approach and protocols should attempt to quickly assess the need for admission, timing of endoscopy and level of care. It is generally recommended to perform endoscopy within 24 h of presentation as it plays a pivotal role in identifying the source of bleeding and it can achieve haemostasis in most cases. Unfortunately, it may not be available in all centers or, if performed in low-risk patients, it may overcrowd the service with unnecessary urgent interventions. Hence, we need a standardized tool to guide the emergency medicine clinician for appropriate referral and management of patients. This should reduce the burden and costs on the healthcare system and on-call physicians.

Research objectives

To evaluate the performance of pre-endoscopic risk scores (GBS, PERS, AIMS65, and ABC) in patients with variceal and non-variceal upper GI bleeding for predicting the following primary outcomes: In-hospital mortality, type of intervention (endoscopic or surgical) and length of admission (≥ 7 d). We will further evaluate whether the addition of venous lactate improves the score performance in predicting the determined outcomes.

Research methods

We retrospectively analyzed all patients above 18 years old presenting to the emergency department (ED) with upper GI bleeding from January 2020 to December 2021. Each patient presenting with exteriorized upper GI bleed was fully assessed by the

emergency medicine physician. Immediate venous catheterization and fluid resuscitation was performed and full work-up with blood tests (full blood count, coagulation parameters, liver, kidney function, venous lactate), and other investigations were performed within 24 h from presentation. Patients with a Hb \leq 7 g/dL had at least one unit of red blood cell concentrate transfused, with a higher Hb threshold (Hb \leq 8 g/dL) for patients with associated cardiovascular disease. Post-transfusion target Hb was between 7-9 g/dL. Endoscopy was performed within 24 h of ED arrival in all patients included in analysis. Forrest classification was used to describe peptic ulcer disease, with Baveno and Sarin's classification for gastroesophageal varices. Patients with non-variceal upper GI bleeding received an infusion with PPIs, while those with variceal bleeding were treated with Somatostatin. Endoscopic treatment was performed depending on the cause of bleeding. A combined approach with injection therapy (dilute epinephrine) and mechanic therapy (thermal coagulation or haemostatic clip) was used for FIa, FIb, and FIIa, with clot removal in FIIf lesions. In variceal bleeding, endoscopic ligation was the main approach. Surgical treatment was performed in cases where endoscopic treatment failed. The need for admission was established by the gastroenterology and general surgery teams on-call.

Research results

The final study included 363 patients with upper GI bleeding with a mean age of 60 years old and a predominance of male sex. Non-variceal bleeding was the main cause of presentation, liver cirrhosis the most frequently associated comorbidity in the entire group. The main symptom of presentation was haematemesis in patients with variceal bleeding and melena in the non-variceal group. Approximately 9% of our patients had chronic treatment with antiplatelets or oral anticoagulation. Gastric/duodenal ulcer was the main cause of GI bleeding. Most patients in variceal bleeding group required mechanical endoscopic therapy with band ligation and only 2 patients had variceal sclerotherapy. In the non-variceal bleeding group, dual therapy with thermal anticoagulation and local administration of dilute Adrenaline was the main type of

endoscopic intervention. Failed endoscopy was recorded in approximately 4.7% of patients. Only 9 patients in the non-variceal group required surgical intervention. In-hospital mortality had an overall rate of 9.4%, most cases were in the variceal group. All scores had discriminative ability in predicting in-hospital mortality irrespective of study group. AIMS-65 score had the best performance for the variceal bleeding group and ABC in the non-variceal bleed. The optimal cut-off value for predicting in-patient mortality was calculated for each score depending on the type of bleeding. For variceal bleeding, an AIMS65 score above 1 with sensitivity of 90% and specificity of 73% and ABC score with a cut-off value of 5.5 and specificity. In the non-variceal bleeding group, the optimal cut-off value for in-hospital mortality was 1.5 for AIMS65 score, with sensitivity of 66.7% and specificity of 57%. We have determined the best scoring system for in-patient mortality in the included population for both variceal and non-variceal bleeding. ABC as being the best predictor for in-patient mortality in the entire population. For variceal bleeding patients, only PERS score, at a cut-off value above 3.5 was a good predictor for endoscopic treatment with a sensitivity of 76.5% and specificity of 40%. Venous lactate did not show good performance in predicting variceal bleeding, due to low sensitivity (64.3%) and specificity (53.2%). However, logistic regression model showed it is an independent predictor for the determined outcomes. For the variceal bleeding population, addition of lactate to AIMS65 score, leads to a 5-fold increase in probability of in-hospital mortality. For non-variceal bleeding, addition of lactate to GBS score showed a 12-fold increase in probability of in-hospital mortality. In terms of intervention, higher level of venous lactate increases by 5.5 times the probability of endoscopic intervention and by 2 the probability for surgical intervention.

Research conclusions

To our knowledge, this is the first study to compare four of the most representative pre-endoscopic risk scores, AIMS65, PERS, GBS and the relatively new ABC score in variceal and non-variceal GI bleeding cohort. ABC score is the most accurate in

predicting in-hospital mortality in both mixed and non-variceal bleeding population. AIMS65 had the best performance in predicting in-patient mortality in patients with variceal upper GI bleeding, however, for practicality, we advise the use of ABC score for both populations. In terms of intervention, PERS and GBS should be used to determine the need for endoscopic and surgical intervention. Lactate can be used in conjunction to AIMS65 and GBS score to predict in-patient mortality and intervention.

Research perspectives

Although GBS is currently largely used, further studies are needed to investigate the relatively new ABC score regarding its role in daily clinical practice and possible implementation in guidelines.

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Figure Legends

Figure 1 Flow diagram of patient selection.

Figure 2 Receiver operating characteristics curve of age older than 65, pre-endoscopic Rockall score, age, blood tests and comorbidities, and Glasgow-Blatchford score predictors of in-hospital mortality. A: Variceal bleed; B: Non-variceal bleed; C: Mixed variceal and non-variceal bleeding population; D: Variceal bleeding group; E: Non-variceal bleeding group.

Figure 3 Receiver operating characteristics curve. Lactate as a predictor for variceal bleed compared to non-variceal bleeding group.

Table 1 Descriptive analysis of demographical data, clinical findings, type of intervention and outcome by type of bleeding, *n* (%)

Parameters	All cases, <i>n</i> = 363 (%)	Variceal bleeding, <i>n</i> = 127 (34%)	Non- variceal bleeding, <i>n</i> = 236 (65%)	<i>P</i> value for Chi-Square tests
Demographical data				
Age, yr; median/interval	60.90; 61/19-93	57.24; 57.50/19-88	62.87; 63/21-93	0.001
> 60 yr	201 (55.4)	56 (44.1)	145 (61.4)	0.002
Male	240 (66.1)	85 (66.9)	155 (65.7)	0.810
Comorbidities				
Heart failure	75 (20.7)	9 (7.1)	66 (28.0)	0.001
Atrial fibrillation	52 (14.3)	8 (6.3)	44 (18.6)	0.001
Arterial hypertension	119 (32.8)	22 (17.3)	97 (41.1)	0.001
Coronary artery disease	61 (16.8)	4 (3.1)	57 (24.2)	0.001
Diabetes mellitus	49 (13.5)	18 (14.2)	31 (13.1)	0.783
COPD	9 (2.5)	1 (0.8)	8 (3.4)	0.096
Asthma	3 (0.8)	0 (0.0)	3 (1.3)	0.107
Kidney disease	30 (8.3)	2 (1.6)	28 (11.9)	0.001
Liver cirrhosis	139 (38.3)	99 (78.0)	40 (16.9)	0.001
Active malignancy	25 (6.9)	12 (9.4)	13 (5.5)	0.166
Hepatocarcinoma	9 (2.5)	8 (6.2)	1 (0.5)	
Cerebral vascular disease	24 (6.6)	2 (1.6)	22 (9.3)	0.002
Symptoms				
Haematemesis	279 (76.9)	115 (90.6)	164 (69.5)	0.001
Melena	267 (73.6)	89 (70.1)	178 (75.4)	0.274
Abdominal pain	60 (16.5)	19 (15.0)	41 (17.4)	0.553
Syncope	12 (3.3)	2 (1.6)	10 (4.2)	0.151
Presyncope	8 (2.2)	2 (1.6)	6 (2.5)	0.539
Other symptoms	36 (9.9)	12 (9.4)	24 (10.2)	0.826
Chronic treatment				
Antiplatelets	36 (9.9)			0.002

Aspirin	22 (6.1)	1 (0.8)	21 (8.9)	
Clopidogrel	7 (1.9)	0 (0)	7 (3.0)	
DAPT (aspirin clopidogrel or aspirin ticagrelor)	6 (1.7)	1 (0.8)	5 (2.1)	
Ticagrelor	1 (0.3)	0 (0)	1 (0.4)	
No treatment	327 (90.1)	125 (98.4)	202 (85.6)	
Anticoagulation	32 (8.9)			0.003
DOAC	22 (6.1)	0 (0)	22 (9.3)	
VKA	10 (2.8)	3 (2.4)	7 (3.0)	
No treatment	331 (91.2)	124 (97.6)	207 (87.7)	
Source of GI bleeding				
Ulcerative and erosive lesions	25 (6.9)	0 (0)	25 (10.6)	0.001
Severe/erosive esophagitis	27 (7.4)	0 (0)	27 (11.4)	
Severe/erosive gastritis/duodenitis	151 (41.6)	0 (0)	151 (64)	
Vascular lesions (angiodysplasia)	6 (1.7)	0 (0)	6 (2.5)	
Mass lesions	12 (3.3)	0 (0)	12 (5)	
Traumatic lesions (Mallory Weiss tear)	9 (2.4)	0 (0)	9 (3.8)	
Lesion unidentified/ Dieulafoy	6 (1.6)	0 (0)	6 (2.7)	
Oesophageal varices	115 (31.7)	115 (90.5)	0 (0)	0.003
Gastric varices	12 (3.3)	12 (9.5)	0 (0)	
Intervention				
Injection therapy (dilute epinephrine) with thermal coagulation	29 (8.0)	0 (0.0)	28 (11.9)	0.001
Mechanical endoscopic therapy	59 (16.3)	50 (39.4)	9 (3.8)	0.001
Haemostatic clip	9 (2.5)	0 (0)	9 (3.8)	
Variceal ligation	48 (13.2)	48 (37.7)	0 (0)	
Variceal sclerotherapy	2 (0.6)	2 (1.6)	0 (0)	

Failed endoscopic therapy	17 (4.7)	9 (7)	8 (3.4)	0.001
Surgical interventions	9 (2.5)	0 (0)	9 (3.8)	0.026
Transfusion				
Transfusions	112 (30.9)	38 (29.9)	74 (31.5)	0.758
In-hospital mortality				
Death	34 (9.4)	16 (12.6)	18 (7.7)	0.131

COPD: DAPT: DOAC: VKA: GI: Gastrointestinal.

Table 2 Mean values of scores in variceal and non-variceal bleed

Scores	All cases, <i>n</i> = 363 mean	Variceal bleeding, <i>n</i> = 127 mean (SD)	Non-variceal bleeding, <i>n</i> = 236 mean (SD)	<i>P</i> values for <i>t</i> -Student test
AIMS-65	1.52	1.74 (0.95)	1.40 (1.05)	0.003
PERS	3.30	3.76 (1.35)	3.06 (1.70)	0.001
ABC	5.02	5.83 (2.42)	4.59 (2.51)	0.001
GBS	12.32	12.98 (2.90)	11.97 (3.74)	0.008

AIMS65: Age older than 65; PERS: Pre-endoscopic Rockall score; ABC: Age, blood tests and comorbidities; GBS: Glasgow-Blatchford score.

Table 3 Linear regression analysis of age older than 65 score against each determined outcome

Model	R	R square	Adjusted R square	Std. error of the estimate	Change statistics				
					R square change	F change	df1	df2	Sig. F change
1	0.261 (a)	0.068	0.065	0.994	0.068	260.305	1	361	0.000
2	0.281 (b)	0.079	0.074	0.989	0.011	40.320	1	360	0.038
3	0.286 (c)	0.082	0.074	0.989	0.003	10.010	1	359	0.316
4	0.316 (d)	0.100	0.090	0.981	0.018	70.290	1	358	0.007

Table 4 Linear regression analysis of pre-endoscopic Rockall score against each determined outcome

Model	R	R square	Adjusted R square	Std. error of the estimate	Change statistics				
					R square change	F change	df1	df2	Sig. F change
1	0.202 (a)	0.041	0.038	10.588	0.041	150.411	1	361	0.000
2	0.243 (b)	0.059	0.054	10.575	0.018	60.987	1	360	0.009
3	0.248 (c)	0.062	0.054	10.575	0.002	0.941	1	359	0.333
4	0.260 (d)	0.068	0.057	10.572	0.006	20.359	1	358	0.125

Table 5 Linear regression analysis of age, blood tests and comorbidities score against each determined outcome

Model	R	R square	Adjusted R square	Std. error of the estimate	Change statistics				
					R square change	F change	df1	df2	Sig. F change
1	0.294 (a)	0.087	0.084	20.435	0.087	340.206	1	361	0.000
2	0.324 (b)	0.105	0.100	20.413	0.019	70.543	1	360	0.006
3	0.329 (c)	0.108	0.101	20.413	0.003	10.241	1	359	0.266
4	0.334 (d)	0.111	0.101	20.412	0.003	10.183	1	358	0.277

Table 6 Linear regression analysis of Glasgow-Blatchford score against each determined outcome

Model	R	R square	Adjusted R square	Std. error of the estimate	Change statistics					
					R square change	F change	df1	df2	Sig.	F change
1	0.198	0.039	0.036	30.434	0.039	140.659	1	361	0.000	
	(a)									
2	0.241	0.058	0.053	30.405	0.019	70.250	1	360	0.007	
	(b)									
3	0.256	0.065	0.058	30.396	0.007	20.873	1	359	0.091	
	(c)									
4	0.273	0.075	0.064	30.384	0.009	30.534	1	358	0.061	
	(d)									

Table 7 Analysis of area under the receiver operating characteristics curve, cut-off value, 95% confidence interval for in-hospital mortality

Test result variable	Area	Cut off	Std. error(a)	Asymptotic Sig.(b)	Asymptotic confidence interval	95%
Variceal bleed						
AIMS-65	0.772	1.0	0.051	0.001	0.673-0.871	
PERS	0.705	3.5	0.067	0.008	0.573-0.837	
ABC	0.744	5.5	0.052	0.002	0.642-0.845	
GBS	0.752	10.5	0.067	0.001	0.621-0.883	
Non-variceal bleed						
AIMS-65	0.693	1.5	0.059	0.006	0.577-0.810	
PERS	0.680	3.5	0.053	0.011	0.576-0.785	
ABC	0.775	5.5	0.051	0.001	0.675-0.874	
GBS	0.657	12.5	0.077	0.027	0.505-0.808	

AIMS65: Age older than 65; PERS: Pre-endoscopic Rockall score; ABC: Age, blood tests and comorbidities; GBS: Glasgow-Blatchford score.

Table 8 Analysis of area under the receiver operating characteristics curve, cut-off value, 95% confidence interval for in-patient mortality in mixed variceal and non-variceal bleeding population

Scores	Cut off	Sensitivity	Specificity	Area	Std. error	Asymptotic Sig.	Asymptotic 95% confidence interval
AIMS-65	1.50	82.4	52.6	0.730	0.041	0.001	0.650-0.809
PERS	3.50	82.4	49.2	0.696	0.042	0.001	0.615-0.778
ABC	5.50	88.2	59.6	0.770	0.036	0.001	0.700-0.840
GBS	12.50	76.5	47.7	0.704	0.052	0.001	0.602-0.805

AIMS65: Age older than 65; PERS: Pre-endoscopic Rockall score; ABC: Age, blood tests and comorbidities; GBS: Glasgow-Blatchford score.

Table 9 Analysis of area under the receiver operating characteristics curve, cut-off value, 95% confidence interval for intervention

Test result variable	Area	Cut off	Std. error(a)	Asymptotic Sig.(b)	Asymptotic confidence interval	95%
Endoscopy-variceal bleed						
AIMS-65	0.538		0.051	0.470	0.437-0.638	
PERS	0.604	3.5	0.050	0.046	0.506-0.703	
ABC	0.553		0.052	0.313	0.452-0.654	
GBS	0.538		0.052	0.468	0.437-0.639	
Surgical intervention-non-variceal bleed						
AIMS-65	0.621	1.5	0.081	0.218	0.461-0.781	
PERS	0.624	3.5	0.088	0.208	0.451-0.796	
ABC	0.657	5.5	0.079	0.111	0.502-0.811	
GBS	0.722	12.5	0.092	0.024	0.541-0.903	

AIMS65: Age older than 65; PERS: Pre-endoscopic Rockall score; ABC: Age, blood tests and comorbidities; GBS: Glasgow-Blatchford score.

Table 10 Analysis of area under the receiver operating characteristics curve, cut-off value, 95% confidence interval for length of admission (over 7 d)

Test variable	result	Area	Std. error(a)	Asymptotic Sig.(b)	Asymptotic confidence interval	95%
Variceal bleeding						
AIMS65		0.516	0.053	0.768	0.412-0.619	
PERS		0.497	0.054	0.960	0.391-0.604	
ABC		0.434	0.053	0.215	0.330-0.538	
GBS		0.496	0.053	0.946	0.393-0.600	
Non-variceal bleeding						
AIMS65		0.587	0.037	0.024	0.514-0.660	
PERS		0.557	0.038	0.139	0.482-0.631	
ABC		0.550	0.039	0.194	0.473-0.627	
GBS		0.566	0.038	0.084	0.491-0.641	

AIMS65: Age older than 65; PERS: Pre-endoscopic Rockall score; ABC: Age, blood tests and comorbidities; GBS: Glasgow-Blatchford score.

Table 11 Analysis of area under the receiver operating characteristics curve, cut-off value, 95% confidence interval of venous lactate in variceal and non-variceal bleed

Venous lactate	Cut off	Area	Std. error	Asymptotic Sig.	Asymptotic confidence interval	95%
Variceal bleed	2.05	0.643	0.030	0.001	0.585-0.701	
Non variceal bleed	2.45	0.357	0.030	0.001	0.299-0.415	

Table 12 Logistic regression model for age older than 65, pre-endoscopic Rockall score, age, blood tests and comorbidities, Glasgow-Blatchford score and lactate

Logistic models	regression	Independent variable	Odds ratio (95%CI)	P value
In-hospital mortality (Yes/No)				
Adjusted model bleed	variceal	AIMS-65	1.434 (1.202-1.930)	0.032
		PERS	1.028 (0.591-1.789)	0.922
		ABC	0.799 (0.608-1.049)	0.106
		GBS	0.915 (0.740-1.132)	0.415
		Venous lactate	4.944 (2.207-11.008)	0.001
Adjusted model, non-variceal bleed	non-	AIMS-65	0.716 (0.374-1.372)	0.314
		PERS	0.965 (0.669-1.393)	0.850
		ABC	0.824 (0.627-1.084)	0.167
		GBS	1.159 (1.053-1.276)	0.003
		Venous lactate	11.720 (3.437-39.968)	0.001
Endoscopy (Yes/No)				
Adjusted model bleed	variceal	AIMS-65	1.049 (0.688-1.599)	0.823
		PERS	0.762 (0.544-1.067)	0.113
		ABC	1.025 (0.850-1.236)	0.794
		GBS	1.029 (0.905-1.171)	0.659
		Venous lactate	2.222 (0.531-9.305)	0.274
Adjusted model, non-variceal bleed	non	AIMS-65	0.860 (0.533-1.388)	0.537
		PERS	1.205 (0.904-1.604)	0.203
		ABC	0.931 (0.743-1.166)	0.533
		GBS	0.982 (0.891-1.083)	0.721
		Venous lactate	5.550 (1.943-15.853)	0.001
Surgical	intervention			

(Yes/No)					
Adjusted	model	non	AIMS-65	0.928 (0.533-1.388)	0.870
variceal bleed					
			PERS	0.870 (0.904-1.604)	0.663
			ABC	1.255 (0.743-1.166)	0.280
			GBS	1.214 (0.891-1.083)	0.130
			Venous lactate	2.002 (1.002-2.047)	0.001

AIMS65: Age older than 65; PERS: Pre-endoscopic Rockall score; ABC: Age, blood tests and comorbidities; GBS: Glasgow-Blatchford score.

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