ORIGINAL RESEARCH

ABC score: a new risk score that accurately predicts mortality in acute upper and lower gastrointestinal bleeding: an international multicentre study

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ABSTRACT

Objectives Existing scores are not accurate at predicting mortality in upper (UGIB) and lower (LGIB) gastrointestinal bleeding. We aimed to develop and validate a new pre-endoscopy score for predicting mortality in both UGIB and LGIB.

Design and setting International cohort study. Patients presenting to hospital with UGIB at six international centres were used to develop a risk score for predicting mortality using regression analyses. The score's performance in UGIB and LGIB was externally validated and compared with existing scores using four international datasets. We calculated areas under receiver operating characteristics curves (AUROCs), sensitivities, specificities and outcome among patients classified as low risk and high risk.

Participants and results We included 3012 UGIB patients in the development cohort, and 4019 UGIB and 2336 LGIB patients in the validation cohorts. Age, Blood tests and Comorbidities (ABC) score was closer associated with mortality in UGIB and LGIB (AUROCs: 0.81–84) than existing scores (AUROCs: 0.65–0.75; p≤0.02). In UGIB, patients with low ABC score (≤3), medium ABC score (4–7) and high ABC score (≥8) had 30-day mortality rates of 1.0%, 7.0% and 25%, respectively. Patients classified low risk using ABC score had lower mortality than those classified low risk with AIMS65 (threshold ≤1) (1.0 vs 4.5%; p<0.001). In LGIB, patients with low, medium and high ABC scores had in-hospital mortality rates of 0.6%, 6.3% and 18%, respectively.

Conclusions In contrast to previous scores, ABC score has good performance for predicting mortality in both UGIB and LGIB, allowing early identification and targeted management of patients at high or low risk of death.

Significance of this study

What is already known on this subject?

- Several risk scores have been developed to predict outcomes in patients with upper (UGIB) and lower gastrointestinal bleeding (LGIB).
- Recent studies have shown that the discriminative performance of existing scores for prediction of mortality in these patients is relatively poor.
- The recent UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report on gastrointestinal bleeding specifically recommended the development of one overall risk score that could be used in the assessment and management of all patients presenting with gastrointestinal bleeding from any source.

What are the new findings?

- Age, Blood tests and Comorbidities (ABC) score, a pre-endoscopy risk score based on patients age, blood tests and comorbidities, can accurately predict mortality in both UGIB and LGIB and is superior to the existing UGIB and LGIB scores at predicting this endpoint.
- ABC score enables early identification of 40% of patients with UGIB and 71% of patients with LGIB who are at very low risk (≤1%) of death within 30 days (for UGIB) or during hospitalisation (for LGIB).
- ABC score helps identify the 15% of patients with UGIB and 3% of patients with LGIB who are at very high risk of death (18%–25%) within 30 days (UGIB) or during hospitalisation (LGIB).

How might it impact on clinical practice in the foreseeable future?

- Implementation of ABC score may help the clinician in the early identification of patients with high mortality risk who would need close monitoring and potential targeted management, in addition to identifying patients for whom further active treatment may be considered futile.

INTRODUCTION

Bleeding from the upper or lower gastrointestinal tract is a common medical emergency. The incidence of upper gastrointestinal bleeding (UGIB) has been reported at 67–103 per 100 000 adults per year[1 2] with mortality rates decreasing to 2%–8%[2 3] in recent years.[4] Several pre-endoscopy and post-endoscopy risk scoring systems have been developed to predict a variety of outcomes including mortality,[4–6] need for hospital-based intervention[7] and need for endoscopic therapy.[8] Previous studies have shown that

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the Glasgow Blatchford Score (GBS) can predict patients who will require hospital-based intervention with high accuracy.[7 9–11] Implementation of GBS is associated with a 15%–20% reduction in the number of hospital admissions with UGIB,[10 11] and is therefore recommended to identify very low-risk patients who could be managed as outpatients.[12] In contrast, the discriminative performance of existing scores for prediction of mortality is relatively poor. AIMS65 and Progetto Nazionale Emorragia Digestiva (PNED) appear better at predicting mortality than GBS and Rockall score, but the reported area under the receiver operator characteristics curves (AUROCs) for all risk scores are generally no higher than 0.80, suggesting limited clinical utility in prediction of this endpoint.[5 6 9 13 14] In addition, PNED requires data on endoscopic findings and rebleeding for calculation, therefore, it cannot be used to assess risk at the time of patient presentation. The risk scores described above are shown in online supplementary appendix 1.

Acute lower gastrointestinal bleeding (LGIB) has an estimated incidence of 33 per 100 000 adults per year.[15] Compared with UGIB, LGIB tends to follow a more benign course with a lower need for haemostatic intervention and lower mortality.[16] Although risk scores have been developed to predict severe bleeding or mortality following LGIB,[17 18] a recent study showed that their discriminative ability to predict mortality is poor with AUROCs ranging from 0.66 (BLEED score) to 0.73 (AIMS65).[18] The newly developed Oakland Score seems promising in predicting safe discharge in LGIB and may be useful in predicting mortality alone.[18]

When assessing patients with gastrointestinal bleeding, it may be difficult to differentiate between UGIB and LGIB. Patients presenting with haematochezia may have a bleeding source in the upper gastrointestinal tract and presentation with black, tarry stool can be seen in patients with bleeding from the right colon. This may explain why no source of bleeding was identified in 17% of patients with UGIB in the 2007 UK audit[19] and why upper endoscopy was performed in 11% of patients with LGIB in the UK audit on LGIB.[16] Therefore, it would be helpful to clinicians to use one score for both acute UGIB and LGIB, as recommended in the recent UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report on GI bleeding.[20] Irrespective of bleeding source, accurate and early identification of patients at high risk of death could allow targeted management, including specialised care and early interventions that may improve outcome. At the other end of the spectrum, patients identified to be at very low risk of death may require less intensive management, which would help target resources to appropriate patients.

Based on a large international multicentre study, our aim was to develop a new pre-endoscopy risk score, which is more accurate than existing scores at predicting mortality in UGIB (part A). We then validated the performance of this new score in both UGIB and LGIB in several international external cohorts (part B), and last, we compared the discriminative ability of the new score in the validation cohorts with the optimal existing scores for predicting mortality in both UGIB and LGIB (part C).

METHODS

Study design and population

This study was designed as an international cohort study with inclusion of patients with acute UGIB and LGIB. UGIB was defined as presentation with haematemesis, coffee-ground vomiting or melaena. LGIB was defined as presentation with red blood or clots per rectum, maroon-coloured stool or blood mixed in with stool, but any patient who had suspected UGIB based on findings at endoscopy were excluded.

Development of a pre-endoscopy risk score for predicting mortality in UGIB (part A)

We included prospectively collected data on consecutive patients presenting with UGIB between March 2014 and March 2015 at: Yale-New Haven Hospital (USA), Glasgow Royal Infirmary (UK), Royal Cornwall Hospital Truro (UK), Odense University Hospital (Denmark), Singapore General Hospital (Singapore) and Dunedin Hospital (New Zealand). Patients who developed UGIB while already inpatients for other reasons were not included. Patients with variceal bleeding were included at all sites.

Validation of the proposed risk score in UGIB and LGIB (part B)

External validation of the proposed score in UGIB was based on data from a national Italian database including prospectively collected data on consecutive patients presenting with UGIB at 50 Italian hospitals during the period January 2014 to December 2015, prospectively collected data on patients presenting with UGIB confirmed by endoscopy at Virgen de las Nieves University Hospital (Spain) between May 2011 and December 2016, and retrospectively collected data on consecutive patients presenting with UGIB at Emek Medical Center (Israel) between January 2016 and October 2017. Patients who developed UGIB while already inpatients for other reasons were included in the Italian and Spanish cohort. Inpatients were not included in the Israeli cohort. Patients with variceal bleeding were included in all cohorts.

Validation of the score in LGIB was performed using data from the National Comparative Audit of LGIB,[16] a prospectively collected database of patients presenting with LGIB at 143 UK hospitals between 1 September and 31 October 2015. This database has previously been described in detail.[16]

Comparison of the performance of the proposed risk score with optimal existing scores for predicting mortality (part C)

The discriminative ability of the new risk score for prediction of mortality in UGIB was compared with AIMS65, which is the optimal existing pre-endoscopic score at predicting mortality in UGIB.[9 21–23] In prediction of mortality in LGIB, the new score was compared with AIMS65, Glasgow Blatchford Score (GBS) and Oakland score. There are less published data on risk scores in LGIB, however, studies have suggested these three scores may be useful in LGIB.[17 18] We chose not to include Strate, BLEED and NOBLADS in this study, as AIMS65 was shown to be closer associated with mortality than these scores in a previous large study of LGIB.[18] All comparisons were undertaken using the same datasets as described in part B above.

Follow-up

Patients included in part A (risk score development) were followed up 30 days after hospital admission. The follow-up period used for assessing mortality in parts B and C (external validation) was 30 days in patients with UGIB, except in the Italian cohort where patients with variceal bleeding were followed for 42 days. Follow-up was performed by physicians, local research nurses or medical students using patient records, administrative data or contact with local general practitioners. In LGIB, we only had access to data on in-hospital mortality, up to a maximum of 28 days.

Table 1 Characteristics of patients, treatment and outcome in the ABC risk score development cohort (n=3012)

Age (years, median (IQR))	65 (30)
Sex (male)	1750 (58)
Comorbidity	
Ischaemic heart disease	580 (19)
Liver cirrhosis	353 (12)
Renal failure	266 (9)
Any malignancy	430 (14)
ASA score	
1	445 (15)
2	943 (32)
3	1338 (45)
4	232 (7.8)
5	18 (0.6)
Mean, (IQR)	2.5 (1)
Medication use	
Low-dose aspirin	705 (24)
Non-aspirin antiplatelets	214 (7.4)
Anticoagulants	343 (12)
NSAIDs	392 (13)
Circulatory status (median (IQR))	
Systolic blood pressure (mm Hg)	125 (32)
Pulse (beats/min)	89 (26)
Blood tests (median (IQR))	
Haemoglobin (g/L)	112 (49)
Urea (mmol/L)	8.2 (9.2)
Albumin (g/L)	36 (10)
Creatinine (µmol/L)	80 (44)
Findings at endoscopy	
Normal findings	296 (14)
Erosive disease	580 (28)
Gastric/duodenal ulcer	572 (28)
Variceal bleeding	142 (7)
Upper GI cancer	70 (3)
Not endoscoped	937 (31)
Treatment	
No of transfusions (mean, (IQR))	1.3 (2)
Endoscopic treatment	574 (19)
Surgery/embolisation	37 (1.2)
Outcome	
No need for intervention or death	1635 (54)
All-cause mortality	207 (6.8)
Bleeding-related mortality	69 (2.3)
Score (median, (IQR))	
AIMS65	1 (2)
PNED	2 (4)
Admission Rockall score	3 (3)
Full Rockall score	4 (3)
GBS	6 (9)
ABC score	3 (4)

Data are number of patients (%), unless otherwise stated.
Missing data: ABC score (n=343), AIMS65 (n=511), Admission Rockall score (n=43), Full Rockall score (n=1000), PNED (n=178), GBS (n=80), comorbidity (n=1), systolic blood pressure (n=41), pulse (n=38), haemoglobin (n=28), findings at endoscopy (n=2), total units of blood transfused (n=23), performance of endoscopic therapy (n=20), performance of surgery or embolisation (n=5), rebleeding (n=51), true low-risk status (n=28) and mortality (n=1).
ABC, age, blood tests and comorbidities; ASA, American Society of Anesthesiologists; GBS, Glasgow Blatchford score; GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; PNED, Progetto Nazionale Emorragia Digestive score.

Study outcomes

The outcome measures were predetermined. All-cause 30-day mortality was the primary outcome measure. Secondary outcome measures in part A included: (1) bleeding-related mortality, (2) non-bleeding-related mortality, (3) need for hospital-based intervention (treatment with transfusion, endoscopic treatment, surgery, angiography) or death, (4) need for haemostatic intervention and (5) rebleeding within 7 days.

Definitions

Definitions used in the study are provided in online supplementary appendix 2.

Data collection

Data were collected at each site by dedicated research nurses, doctors or medical students. A description of included variables is available in online supplementary appendix 3.

General treatment of patients

The general treatment of patients with UGIB and LGIB is described in online supplementary appendix 4.

Statistical analyses

Part A

Predictive factors for 30-day mortality were identified using logistic regression analysis. Regression models were constructed using backward elimination. Candidate variables with a $p>0.10$ were evaluated and excluded from the model in turn if a comparison of the full and reduced models using likelihood ratio tests were statistically insignificant. The order of elimination was determined by a combination of level of p value and clinical importance. Variables included in the regression models are described in online supplementary appendix 5. Continuous variables that were included in the final regression model were categorised according to thresholds closest associated with mortality in order to obtain an easily calculable score. Results are presented as ORs with 95% CIs. The appropriateness of the underlying assumptions (collinearity, linearity of independent variables and log odds) was examined graphically and statistically. Goodness of fit was evaluated using the Hosmer-Lemeshow test.

Based on the identified logistic regression model, a weighted risk score for prediction of 30-day mortality was generated. The discriminative ability for predicting outcomes was evaluated by ROC curves with 95% CIs. For the primary outcome, we also calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), outcome in classified low-risk and high-risk patients, and performed sensitivity analyses on the Age, Blood tests and Comorbidities (ABC) score thresholds. The performance of the developed new risk score was compared with AIMS65, PNED, admission and full Rockall scores, GBS and American Society of Anesthesiologists (ASA) score in the development cohort using AUROCs. The ROC curves were considered dependent and AUROCs were compared based on the method by DeLong *et al*.[24] Number and mortality rates of classified high-risk and low-risk patients and mortality were compared between scores.

Part B

External validation of the new score's ability to predict 30-day mortality in UGIB and LGIB, respectively, was performed by evaluating AUROCs, sensitivities, specificities, PPVs, NPVs and outcome in classified low-risk and high-risk patients.

Part C

The performance of the new score in predicting mortality in UGIB was compared with AIMS65, and in patients with LGIB it was compared with AIMS65, GBS and the Oakland score, using AUROC's. Number and mortality rates of classified

Table 2 Predictors of 30-day mortality

Variable	Univariate OR (95% CI)	Multivariate, adjusted OR (95% CI)	P value
Patients characteristics			
Age			
60–74 years	2.49 (1.65 to 3.78)	1.47 (0.88 to 2.44)	0.138
≥75 years	3.79 (2.60 to 5.52)	2.66 (1.62 to 4.37)	<0.001
Male sex	1.04 (0.78 to 1.38)	–	
Comorbidity			
ASA score			
3	5.07 (3.27 to 7.88)	1.80 (1.11 to 2.94)	0.018
≥4	18.7 (11.5 to 30.5)	3.99 (2.24 to 7.10)	<0.001
Ischaemic heart disease	1.45 (1.04 to 2.01)	–	
Cardiac failure	2.14 (1.45 to 3.16)	–	
Renal failure	2.36 (1.60 to 3.46)	–	
Liver cirrhosis	2.63 (1.87 to 3.69)	1.80 (1.11 to 2.90)	0.016
Any major comorbidity	2.96 (2.14 to 4.11)	–	
Any malignancy	3.73 (2.75 to 5.07)	–	
Disseminated malignancy	6.94 (4.81 to 10.0)	4.52 (2.82 to 7.25)	<0.001
Previous surgery for peptic ulcer	0.61 (0.36 to 1.05)	–	
Altered mental status	5.61 (4.07 to 7.75)	3.12 (2.10 to 4.63)	<0.001
Medication use			
Low-dose aspirin	1.17 (0.85 to 1.61)	–	
Other antithrombotics	1.30 (0.92 to 1.84)	–	
NSAIDs	0.31 (0.17 to 0.60)	–	
Symptoms of bleeding			
Coffee ground vomitting	(reference)		
Haematemesis of fresh blood	0.92 (0.68 to 1.22)	–	
Melaena	0.92 (0.69 to 1.22)	0.55 (0.39 to 0.78)	0.001
Haematochezia	0.80 (0.42 to 1.54)	–	
Syncope	1.45 (0.93 to 2.24)	–	
Haemodynamic status (median (IQR))			
Systolic blood pressure (mm Hg)	0.98 (0.97 to 0.99)	–	
Pulse >100 beats/min	1.64 (1.23 to 2.20)	1.57 (1.10 to 2.25)	0.014
Blood tests			
Haemoglobin (g/L)	0.99 (0.98 to 0.99)	–	
Urea >10 mmol/L	3.48 (2.57 to 4.71)	1.34 (0.88 to 2.04)	0.177
Albumin <30 g/L	5.42 (4.00 to 7.35)	3.18 (2.22 to 4.56)	<0.001
Creatinine			
100–150 µmol/L	3.01 (2.08 to 4.33)	1.61 (1.02 to 2.54)	0.043
>150 µmol/L	6.50 (4.64 to 9.12)	3.46 (2.17 to 5.51)	<0.001
Time variables			
Time from onset of symptoms	1.00 (1.00 to 1.00)	–	
Time from hospitalisation to EGD	1.00 (1.00 to 1.00)	–	

Variables registered with '-' in multivariate, adjusted ORs were removed from the model during backwards elimination (p>0.10). For details on how the variables were handled in the model please refer to the section on statistical methods.
ASA, American Society of Anesthesiologists; EGD, esophagogastroduodenoscopy; NSAIDs, non-steroidal anti-inflammatory drugs.

high-risk and low-risk patients were also compared between scores. Thresholds used for defining low-risk of mortality were: AIMS65 ≤1,[5 21] GBS≤1[9 11] and Oakland score ≤8.[18] Thresholds used for defining high risk were: AIMS65 ≥2[5 21] and GBS≥5.[9] Several GBS thresholds have been suggested previously, but we chose GBS≥5 as this threshold was associated with highest discriminative ability for predicting 30-day mortality in a large international multicentre study.[9]

Table 3 The ABC score for prediction of 30-day mortality

Variable	Assigned score
Age	
60–74 years	1
≥75 years	2
Blood tests	
Urea >10 mmol/L	1
Albumin <30 g/L	2
Creatinine	
100–150 µmol/L	1
>150 µmol/L	2
Comorbidity	
Altered mental status	2
Liver cirrhosis	2
Disseminated malignancy	4
ASA score	
3	1
≥4	3

ABC, age, blood tests and comorbidities; ASA, American Society of Anaesthesiologists.

Missing data

In part A of the study, the prevalence and pattern of missing data was evaluated and found not to be missing completely at random (Little's test: p<0.001). Missing data in the main cohort were handled using multiple imputation. All baseline and outcome variables were included in the imputation model and 20 imputations were used. In part B and C, we used complete case analysis.

Sample size determination

The required sample size for development of the risk score (part A) was estimated based on the work of Peduzzi *et al*[25] with 30-day mortality rate of 7% and expected inclusion of up to 10 covariates in the final regression model. Based on these assumptions, a minimum of 1450 patients were required.

Descriptive comparisons, level of significance and software used

Pearson's X^2 test and Fischer's exact test were used to compare proportions. Medians were compared using the Mann-Whitney U test. Data were analysed using STATA V.14.0 (StataCorp).

Patient and public involvement

Patients and the public were not involved in study design, conduct or reporting of the research.

Reporting guideline

Our report follows Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis guidelines.[26]

RESULTS

Part A

A total of 3012 patients were included in the risk score development cohort, with 2868 (95%), followed up for 30 days. The median age of patients was 65 years, 58% were men, mean ASA score was 2.5, median time to endoscopy was 19 hours and 30-day mortality was 6.8%. Patients' characteristics, endoscopic findings, interventions, outcomes and risk scores are summarised in table 1.

We found that age ≥75 years, creatinine >150 µmol/L, albumin <30 g/L, pulse >100 beats/min, altered mental status

Table 4 Characteristics of patients included in the external validation cohorts

Inclusion site	Israel (n=148)	Italy (n=3324)	Spain (n=547)	UK (n=2336)
Bleeding location	UGIB	UGIB	UGIB	LGIB
Patient characteristics				
Age, median (95% CI)	69 (30 to 87)	71 (40 to 89)	67 (36 to 87)	73 (29 to 91)
Male sex	94 (64)	2242 (68)	367 (67)	1124 (48)
Comorbidities				
Altered mental status	13 (8.8)	519 (17)	34 (6.2)	68 (3.1)
Liver cirrhosis	20 (14)	682 (21)	141 (26)	28 (1.2)
Disseminated malignancy	16 (11)	73 (2.2)	21 (3.8)	77 (3.3)
ASA score				
1	18 (12)	871 (26)	63 (12)	687 (30)
2	25 (17)	1148 (35)	111 (21)	928 (40)
3	87 (59)	1097 (33)	298 (55)	529 (23)
4	18 (12)	207 (6.2)	68 (13)	175 (7.6)
5	0 (0)	0 (0)	1 (0.2)	0 (0)
mean (95% CI)	2.7 (1 to 4)	2.2 (1 to 4)	2.7 (1 to 4)	2.1 (1 to 4)
Blood tests, median (95% CI)				
Haemoglobin, g/L	93.5 (54 to 137)	89 (53 to 139)	93 (55 to 141)	124 (69 to 158)
Albumin, g/L	35 (25 to 43)	32 (22 to 42)	32 (20 to 42)	38 (25 to 47)
Urea, mmol/L	25 (9.6 to 65)	20 (3.9 to 56)	24 (9.3 to 72)	6.3 (2.9 to 16.3)
Creatinine, µmol/L	75 (48 to 283)	88 (53 to 274)	80 (53 to 265)	80 (51 to 174)
Risk scores, median (95% CI)				
ABC score	4 (1 to 11)	4 (1 to 10)	5 (1 to 9)	2 (0 to 7)
AIMS65	1 (0 to 3)	1 (0 to 3)	1 (0 to 3)	1 (0 to 2)
Oakland score	–	–	–	14 (7–27)
AUROCs (95% CI) for mortality				
ABC score	0.91 (0.83 to 0.99)	0.80 (0.77 to 0.83)	0.81 (0.76 to 0.86)	0.84 (0.80 to 0.89)
AIMS65	0.83 (0.70 to 0.95)	0.62 (0.58 to 0.65)	0.75 (0.69 to 0.81)	0.75 (0.68 to 0.83)
Oakland score	–	–	–	0.69 (0.61 to 0.77)
Mortality*	6 (4.1)	223 (6.7)	51 (9.6)	52 (2.3)

Numbers are n(%) unless otherwise stated. Missing data in UGIB-validation cohorts: ABC score (n=593), AIMS65 (n=972), age (n=25), sex (n=20), albumin (n=378), haemoglobin (n=14), blood urea nitrogen (n=183), creatinine (n=163), altered mental status (n=770), liver cirrhosis (n=548), disseminated malignancy (n=547), ASA-score (n=7), and mortality (n=18). Missing data in LGIB-validation cohort: ABC score (n=552), AIMS65 (n=718), Oakland score (n=707), age (n=1), sex (n=10), albumin (n=393), haemoglobin (n=17), urea (n=71), creatinine (n=45), altered mental status (n=142), liver cirrhosis (n=10), disseminated malignancy (n=10), ASA-score (n=20), and mortality (n=35).

*Noted mortality rates reflect 30 day mortality in patients with UGIB and in-hospital mortality in patients with LGIB (see methods).

ABC, age, blood tests and comorbidities; ASA, American Society of Anesthesiologists; AUROC, area under receiving operator characteristics curves; LGIB, lower gastrointestinal bleeding; UGIB, upper gastrointestinal bleeding.

at presentation to hospital, ASA score >2, presence of liver cirrhosis and disseminated malignancy were all predictors of 30-day mortality (table 2). The Hosmer-Lemeshow goodness-of-fit test showed no indication of poor fit of the final regression model.

The proposed risk score for prediction of 30-day mortality was based on patient ABC score and is shown in table 3. Although blood urea nitrogen at presentation to hospital was found not to be a significant predictor for mortality in the multivariate adjusted model, it was kept in the regression model because it improved identification of patients in low risk of death in the derived risk score. Despite being associated with mortality, tachycardia and melaena (table 2) were not included in the final score because these variables did not increase the score's ability to predict mortality.

The ABC score showed good discriminative ability for prediction of 30-day mortality (AUROC (95% CI) 0.86 (0.84 to 0.89)) in the development cohort. There were no differences in performance of the score between sites. Based on AUROCs, the ABC score was better at predicting 30-day mortality as compared with PNED (AUROC (95% CI) 0.79 (0.76 to 0.82); p<0.001), AIMS65 (AUROC (95% CI) 0.79 (0.76 to 0.82); p<0.001), admission Rockall score (AUROC (95% CI) 0.76 (0.73 to 0.79); p<0.001), ASA score (AUROC (95% CI) 0.74 (0.71 to 0.77); p<0.001), full Rockall score (AUROC (95% CI) 0.72 [0.68 to 0.77); p<0.001) and GBS (AUROC (95% CI) 0.69 (0.66 to 0.72); p<0.001) in the development cohort (online supplementary figure 1). The ABC score performed similarly well in predicting bleeding-related and non-bleeding-related mortality (AUROCs: 0.85 vs 0.85).

There was a clear association between ABC score and mortality. Patients with a score of ≤3 (56% of patients) had a very low (0.7%) risk of death within 30 days. Patients with a score of 4–7 (34% of patients) had a mortality rate of 9.3%, and patients with a score of ≥8 (10% of patients) had a very high mortality rate of 34%. Results of sensitivity analyses on the thresholds for defining low-risk and high-risk patients are available in online supplementary table 1A and B. Baseline characteristics and management of patients with high ABC score in relation to survival is shown in online supplementary table 2.

The ABC score was less accurate at predicting need for hospital-based intervention (AUROC (95% CI) 0.75 (0.74 to

Table 5 Discriminative abilities for ABC score and AIMS65 and outcomes in classified low-risk and high-risk patients according to cohort

Cohort	Development (n=3012)		Validation (n=4019)		Validation (n=2336)	
Bleeding site	UGIB		UGIB		LGIB	
Risk score	ABC score	AIMS65	ABC score	AIMS65	ABC score	AIMS65
Mean score (95% CI)	3.5 (0 to 9)	1.0 (0 to 3)	4.5(1 to 10)	1.4 (0 to 3)	2.6 (0 to 7)	0.9 (0 to 2)
AUROC (95% CI)	0.86 (0.84 to 0.89)	0.79 (0.76 to 0.82)	0.81 (0.78 to 0.83)	0.65 (0.62 to 0.69)	0.84 (0.79 to 0.89)	0.75 (0.68 to 0.83)
Sensitivity (low risk)	0.60	0.76	0.43	0.60	0.73	0.81
Specificity (low risk)	0.94	0.66	0.94	0.63	0.84	0.58
PPV (low risk)	0.99	0.97	0.99	0.96	0.99	0.99
NPV (low-risk)	0.15	0.18	0.12	0.11	0.076	0.073
No (%) classified low-risk patients	1498 (56)	1829 (73)	1369 (40)	1781 (58)	1275 (71)	1296 (80)
Mortality in classified low-risk patients; n(%)*	11 (0.7)	62 (3.4)	14 (1.0)	79 (4.5)	7 (0.6)	17 (1.3)
Sensitivity (high risk)	0.49	0.66	0.52	0.63	0.22	0.58
Specificity (high risk)	0.93	0.76	0.88	0.60	0.97	0.81
PPV (high risk)	0.34	0.18	0.25	0.11	0.18	0.073
NPV (high risk)	0.96	0.97	0.96	0.96	0.98	0.99
No (%) classified high-risk patients	267 (10)	672 (27)	519 (15)	1266 (42)	56 (3.1)	322 (20)
Mortality in classified high-risk patients; n(%)*	91 (34)	121 (18)	129 (25)	133 (11)	10 (18)	23 (7.3)

*Noted mortality rates reflect 30-day mortality in patients with UGIB and in-hospital mortality in patients with LGIB (see the Methods section).
ABC, age, blood tests and comorbidities; AUROC, area under receiver operating characteristics curves; LGIB, lower gastrointestinal bleeding; NPV, negative predictive values; PPV, positive predictive values; UGIB, upper gastrointestinal bleeding.

0.77)), need for haemostatic intervention (AUROC (95% CI) 0.68 (0.65 to 0.70)) and rebleeding within 7 days (AUROC (95% CI]) 0.63 (0.59 to 0.67)).

Part B

A total of 4019 patients with UGIB and 2336 patients with LGIB were included in the external validation cohorts. Patients with UGIB had a median age of 70 years, 66% were males, the mean ASA score was 2.3 and 30-day mortality rate was 7.0%. There were differences in age (mean age ranging from 67 to 71 years; p<0.001), ASA score (mean ASA score ranging from 2.2 to 2.7; p<0.001), frequency of liver cirrhosis (ranging from 14% to 26%; p=0.001), frequency of disseminated malignancy (ranging from 2.2% to 11%; p<0.001) and frequency of altered mental status (ranging from 6.2% to 17%; p<0.001) between the UGIB validation cohorts. Patients with LGIB had a median age of 73 years, 48% were males, mean ASA score was 2.1 and in-hospital mortality rate was 2.3%. Further data on patients' characteristics and risk scores according to site are shown in table 4.

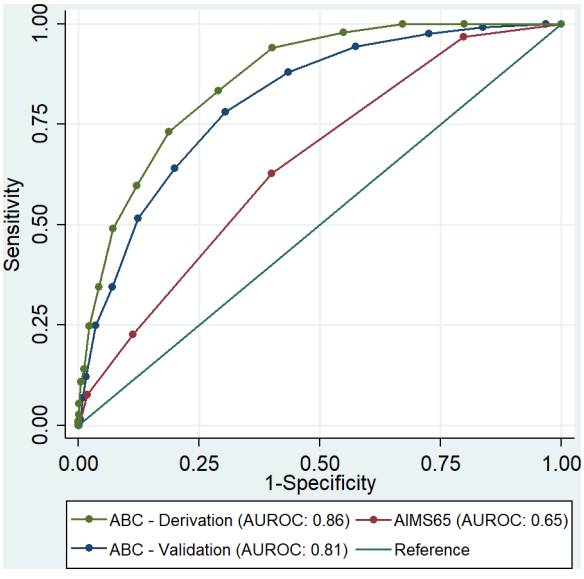

Figure 1 Comparison of ABC score and AIMS65 in prediction of 30-day mortality in UGIB. ABC, age, blood tests and comorbidities; AUROC, areas under receiver operating characteristics curve; UGIB, upper gastrointestinal bleeding.

The ABC score was closely associated with 30-day mortality in the UGIB-validation cohort (AUROC (95% CI) 0.81 (0.78 to 0.83)). There was no statistically significant difference in the performance of the ABC score between centres with AUROCs (95% CI) ranging from 0.91 (0.83 to 0.99) in Israel to 0.81 (0.76 to 0.86) in Spain and 0.80 (0.77 to 0.83) in Italy (p=0.06). Patients with low ABC score ≤3 (n=1369; 40%), medium ABC score 4–7 (n=1538; 45%) and high ABC score ≥8 (n=519; 15%) had 30-day mortality rates of 1.0% (n=14), 7.0% (n=107) and 25% (n=129), respectively.

In the LGIB-validation cohort, the ABC score was also closely associated with mortality, with AUROC (95% CI) 0.84 (0.79 to 0.89). Patients with low ABC score ≤3 (n=1275; 71%), medium ABC score 4–7 (n=453; 25%) and high ABC score ≥8 (n=56; 3%) had in-hospital mortality rates of 0.6% (n=7), 6.3% (n=28) and 18% (n=10), respectively.

Sensitivities, specificities, PPV and NPVs for prediction of low and high risk of mortality, as well as outcomes among patients classified as low and high risk using ABC score are shown in table 5. Mortality rates in UGIB and LGIB per ABC score value are shown in online supplementary table 3.

The distribution of each ABC score component in UGIB patients classified low, medium and high risk is shown in online supplementary table 4. Among classified high-risk patients, 11% had disseminated malignancy and 34% had an ASA score of 4. Thus, these two factors were present in less than half of classified high-risk patients. Presence of either renal failure (creatinine >150 µmol/L), ASA score of 4 or disseminated malignancy was also common (32%) among patients with a medium ABC score, where these patients had a 30-day mortality rate of 13%.

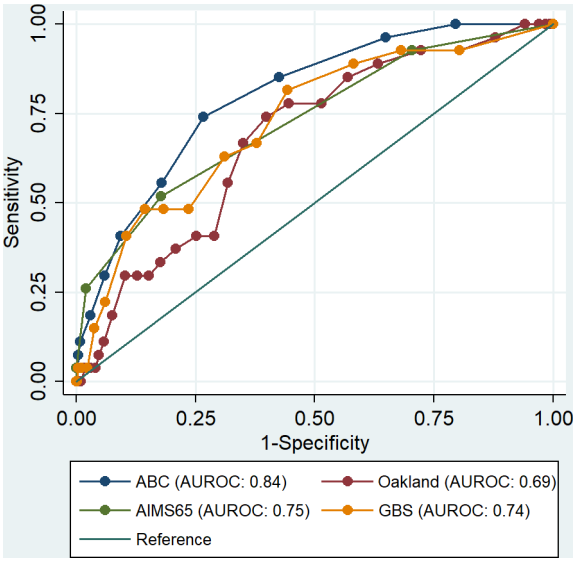

Figure 2 Comparison of ABC score, AIMS65, GBS and Oakland score in prediction of mortality in LGIB. ABC, age, blood tests and comorbidities; AUROC, areas under receiver operating characteristics curves; GBS, Glasgow Blatchford Score; LGIB, lower gastrointestinal bleeding.

Part C

In the UGIB validation cohorts, AIMS65 had an overall AUROC (95% CI) for predicting 30-day mortality of 0.65 (0.62 to 0.69] ranging from 0.83 (0.70 to 0.95) in Israel to 0.75 (0.69 to 0.81) in Spain and 0.62 (0.58 to 0.65) in Italy (p<0.001). Compared with AIMS65, the ABC score was more closely associated with 30 day mortality in UGIB (AUROC (95% CI): 0.81 vs 0.65; p<0.001; see figure 1).

In LGIB the ABC score (AUROC (95% CI) 0.84 (0.80 to 0.89)) was also more closely associated with mortality than AIMS65 (AUROC (95% CI) 0.75 (0.68 to 0.83); p=0.022), GBS (AUROC (95% CI) 0.74 (0.67 to 0.81); p=0.0017), and Oakland score (AUROC (95% CI) 0.69 (0.61 to 0.77); p=0.0023; see figure 2).

Sensitivities, specificities, PPV and NPVs for prediction of low and high risk of mortality as well as outcomes among classified low-risk and high-risk patients using AIMS65 are compared with ABC score in table 5. Outcomes among classified medium-risk patients using ABC score in each cohort are shown in online supplementary table 5. Sensitivities, specificities, PPV and NPVs for prediction of low risk and high risk of mortality as well as outcomes among classified low-risk and high-risk patients using GBS are available in online supplementary table 6.

In the UGIB-validation cohort, using traditional cut-offs for the existing scores, AIMS65 classified a higher proportion of patients as being at low risk of death within 30 days compared with ABC score (58% vs 40%; p<0.001), but patients classified as low risk using AIMS65 had a higher mortality rate compared with those classified as low risk by ABC score (4.5% vs 1.0%; p<0.001). AIMS65 classified a much higher proportion of patients as being at high risk of death within 30 days than ABC score (42% vs 15%; p<0.001). However, the associated 30-day mortality rate in patients classified as high risk using AIMS65 was relatively low compared with ABC score (11% vs 25%; p<0.001).

When using traditional cut-offs in the LGIB-validation cohort, AIMS65 classified a higher proportion of LGIB patients as being at low risk of death than ABC score (80% vs 71%; p<0.001). There was no statistically significant difference in mortality among patients classified low risk using AIMS65 score compared with ABC (1.3% vs 0.6%; p=0.06). When using the threshold validated for predicting safe hospital discharge (≤8), the Oakland score classified 11% (187/1692) of LGIB patients as being at low risk of poor outcome with an associated in-hospital mortality rate of 0.5% (n=1). Compared with ABC score, the Oakland score identified a considerably lower number of low-risk patients (11% vs 71%; p<0.001) and the mortality rate among classified low-risk patients was similar for these scores (0.5% vs 0.6%). When comparing ABC and GBS, ABC identified a higher number of low-risk patients (71% vs 32%; p<0.001) and mortality rates were similar among classified low-risk patients (0.6% vs 0.4%). AIMS65 classified a higher proportion of LGIB patients as being at high risk of death compared with ABC score (20% vs 3.1%; p<0.001). However, LGIB patients classified as high risk using AIMS65 had a lower 30-day mortality compared with those classified as high risk by ABC score (7.3% vs 18%; p=0.019). Likewise, GBS ≥5 classified a higher proportion of LGIB patients as being at high risk of death compared with ABC score (55% vs 3.1%; p<0.001), but mortality rate was low for classified high-risk patients when compared with ABC (3.7% vs 18%; p<0.001).

DISCUSSION

In this international, multicentre study we developed a new risk score that can be calculated early after patient presentation and performs well in predicting mortality in patients with both UGIB and LGIB. It is superior to the existing optimal risk scores for predicting this endpoint in UGIB and LGIB and can discriminate between patients at low, medium and high risk of mortality. Although patients with UGIB and those with LGIB are sometimes managed by different clinical teams, it is useful to have one score that can predict mortality in both conditions, especially because an accurate diagnosis of the location of bleeding (UGIB vs LGIB) cannot always be made at presentation. Indeed, the UK NCEPOD report criticised the separation of hospital care of patients with UGIB and LGIB and specifically recommended the development of one risk score to manage all patients presenting with gastrointestinal bleeding.[20] Thus, the new ABC score represents an accurate score to assess risk of mortality following presentation with acute gastrointestinal bleeding, regardless of the source.

The ABC score enables early identification of the 15% of patients with UGIB and 3% of patients with LGIB who are at very high risk of death (18%–25%) within 30 days or during hospitalisation, respectively. AIMS65 classified 42% of UGIB patients in our validation cohort as being at high risk of death. However, this high proportion results in a relatively low mortality rate (11%), limiting its clinical utility. Similar clinical advantages of the ABC score in identifying patients at high risk of death were found in patients with LGIB. Early identification of patients with an ABC score of ≥8 enables clinicians to target appropriate management to patients at high risk of death. Elderly patients and those with existing comorbidities are known to be at high risk of mortality after gastrointestinal bleeding[4] and most die of non-bleeding-related causes.[27] Therefore, management should focus on both bleeding and non-bleeding related conditions. Specialised care may be important as underlined by Sanders, who showed that treatment of UGIB patients in a specialised GI-bleeding unit was associated with a 37% reduction in mortality.[28] This may include transfer to higher level or specialist care for closer monitoring, consideration of earlier endoscopy, use of prophylactic embolisation after endoscopic control of bleeding in patients with high-risk lesions,[29] careful screening for infection, early resumption of antithrombotic drugs if appropriate,[30] and involvement

with relevant specialists in cases with unstable comorbidities. It is important to underline that current evidence on specific interventions in high-risk patients remains limited and future studies are needed to demonstrate that early interventions in patients with a high ABC score improve outcomes.

Regarding low-risk patients, ABC score helps to identify 40% of patients with UGIB and 71% of patients with LGIB who are at very low risk (≤1%) of death within 30 days (for UGIB) or during hospitalisation (for LGIB). The ABC score appears more attractive for identifying UGIB patients at low risk of death than AIMS65, because patients classified as 'low risk' using AIMS65 have a fourfold higher mortality rate compared with ABC score (4.5% vs 1.0%). However, when considering outpatient management for very low-risk patients we believe that GBS remains the best risk score for determining this specific management strategy, as 13%–18% of patients with a low ABC score or AIMS65 required endoscopic therapy in our development cohort (data not shown). Despite this, the ability to accurately predict patient mortality remains very useful to clinicians.

The strengths of the development of the ABC score in our study lies in the consecutive inclusion of a large number of patients presenting with UGIB at six international centres over four continents. Limitations include the fact that a high number of patients (31%) did not undergo endoscopy. We do not believe this had a major effect on the development of the ABC score, as 95% of patients were followed up for 30 days after presentation and a post hoc analysis showed that performance of ABC score was similar in centres with low (<10%) versus centres with high (>30%) rates of non-performance of endoscopy (AUROCs (95% CIs) 0.85 (0.80 to 0.90) vs 0.88 (0.85 to 0.91); p=0.33). The exact reasons for not performing endoscopy were unknown, but it may be that the patient was so ill that the clinician felt they would not survive the procedure or it was deemed inappropriate. At the other end the spectrum, many lower-risk patients did not attend the planned outpatient endoscopy. Our findings are in accordance with a national UK audit on UGIB where 26% of patients notified to gastroenterologists did not have inpatient endoscopy.[31] Although there may be a relatively high frequency of low-risk patients in our development cohort, our validation data indicate that this did not have any effect on our overall findings. The strengths of the external validation of the ABC score in UGIB lie in inclusion of patients at three international centres with no substantial difference in the discriminative performance of the ABC score between sites.

In contrast to many previous studies, we included patients who presented with gastrointestinal bleeding while already inpatients in several of our external validation cohorts, which may have had an impact on our findings as such patients are known to have a higher risk of death. We acknowledge that this may seem confusing and could lead to problems with heterogeneity. However, there were no significant differences in performance of ABC score between sites, therefore, we believe our results show that the ABC score can be used to estimate risk of death in both patients presenting to hospital with gastrointestinal bleeding and existing inpatients who bleed. Inpatient status was not registered in our validation cohorts, therefore, we were unable to perform sensitivity analyses comparing the performance of the risk scores between patients presenting with gastrointestinal bleeding versus inpatients with bleeding. Previous international studies described significant differences in patients' characteristics between countries,[9 11] and we found differences in age and comorbidity between our UGIB validation cohorts. Although these differences may have had an impact on the performance of the ABC score, the external validity seems high as ABC score had similar performance in the validation cohorts. Our ABC score development cohort only included patients with UGIB as we initially did not have access to a high-quality LGIB dataset.

Among patients included in the LGIB validation cohort, 26% were treated with blood transfusion, and in-patient flexible sigmoidoscopy or colonoscopy was only performed in 25% of patients.[16] This may indicate that these patients in general had minor bleeding episodes. Furthermore, we only had access to mortality during hospitalisation in LGIB patients. Thus, future international studies assessing the ABC score in predicting 30 days mortality after LGIB in higher-risk cohorts are needed to further validate our findings. We were not able to compare the performance of ABC score with GBS in our UGIB-validation sample, but previous studies have found that GBS only has low ability to predict mortality following UGIB (AUROCs 0.64–71).[9 13 14 21 22] Likewise, we did not have the required data to evaluate the clinical prediction tool recently described by Sengupta *et al*, that in the original study had an AUROC of 0.72 for predicting 30 days mortality in LGIB.[32]

In clinical practice patients with an ASA score of 4, disseminated malignancy or renal failure (creatinine >150 µmol/L) will intuitively be perceived as being at very high risk of death. One or more of these factors were present in 32% of patients with a medium ABC score, but these patients had a relatively low 30 days mortality rate of 13%. As presented in online supplementary table 4, the frequencies of all risk factors increased with increasing ABC score and less than half of classified high-risk patients had an ASA score of 4 or disseminated malignancy. Therefore, ABC score seems to add more to risk assessment than the intuitive clinical impression. This is also supported by the finding that ABC score had significantly higher ability to predict mortality than ASA score in our derivation cohort. Although use of ASA score could be associated with inter-rater reliability,[33] our findings indicate that ABC score is externally valid.

The AUROC for AIMS65 in predicting mortality in our Italian UGIB validation cohort was lower than those reported in some previous studies. However, most of the previous studies that described a good or excellent performance of AIMS65 for predicting mortality focused on prediction of in-hospital mortality,[21–23] were single-centre[21 23] and/or small studies (n<300).[21 22] The influence of length of follow-up is underlined by Abougergi *et al* who found that AIMS65 had an AUROC for predicting in-hospital mortality of 0.85, but the value for predicting 30 days mortality was only 0.74,[22] which matches the level from our Spanish cohort, and also the value from a recent large international study.[9] The lower ability of AIMS65 to predict mortality in our Italian cohort may be explained by inclusion of inpatients with UGIB (18%), in addition to higher-risk patient characteristics including a high proportion of cirrhotic patients (21%), frequent presentation with altered mental status (17%) and older age (median: 71 years).

Ideally, we would have one risk score for assessing patients with gastrointestinal bleeding that could predict all outcomes of interest. However, this seems impossible when using traditional risk scores, because main predictors differ between outcomes. Age and comorbidity are strong predictors for mortality as shown in this study, but these factors are not closely associated with rebleeding.[34] Likewise, hypotension is a strong predictor of rebleeding[34] but is not significant in predicting 30-day mortality (table 2). We believe this explains why GBS performs well in predicting need for hospital-based intervention and ABC score for predicting mortality but not vice versa. Thus, at present, we need to use two risk scores for predicting these two important outcomes in UGIB. In the future, this problem may be solved

by use of machine learning models that may be able to predict multiple outcomes of interest.[35]

Although several risk scores have been developed for assessment of patients with gastrointestinal bleeding, no risk score has been widely accepted in clinical practice. A study from Canada published in 2013 described that the Rockall score was recorded in less than 2% of medical records.[36] The main reason that the vast majority of previously published scores have not implemented is most likely due to the low discriminative ability of these scores to predict outcomes and that implementation may not affect management. GBS is the only score that has been shown in several studies to have a high ability to predict outcomes of interest (need for hospital-based intervention)[9–11 13] and where implementation has been shown to improve outcomes (reduced rate of hospital admission, length of hospital stay and cost utilisation).[10 37] Use of risk scores (specifically GBS) in patients presenting with UGIB is now recommended by the European Society of Gastrointestinal Endoscopy,[12] the Asia-Pacific working group[38] and the International consensus group.[39] Consistent recommendations from major evidence-based guidelines should be translated into clinical practice. This may be facilitated by embedding automatically generated risk scores into the electronic medical record.

In conclusion, we developed and validated the ABC score; a new pre-endoscopy risk score that can be used early after presentation to estimate mortality in patients with UGIB or LGIB. This was developed in a multicentre study, has been externally validated in several other international centres and appears superior to existing risk scores for gastrointestinal bleeding. Use of the ABC score to identify patients at high, or very low risk of death, allows focused patient management as appropriate and provides useful prognostic information for patients and relatives.

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Contributors The study was designed by SBL and AS. VB collected data. SBL and AS wrote the paper with considerable input from KO, LL, IG, VJ, IAM, JN, ER-C, RM, HRD and MS. All coauthors approved the final manuscript. SBL is the study guarantor.

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Competing interests IG is a consultant, has a financial interest and is a member of the Medical Advisory Board of MOTUS GI. IG is a consultant for Boston Scientific, Symbionix and GI View. KO has received editorial fees for reviews on the same topic.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from West of Scotland Ethics committee, San Carlo Borromeo Hospital Milan and the Helsinki Committee at Emek Medical Center. Furthermore, each participating centre obtained approval from their local research committee or review board. Due to the observational, non-interventional nature of the study, the ethical committee (and local committees and boards) agreed that individual patient consent was not required. The UK LGIB cohort data were collected as part of a national audit that collected no patient identifiers and involved no clinical interventions; thus, ethical approval was not required for the primary study nor for subsequent use of data.

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Data availability statement Data are available on reasonable request. Relevant anonymised patient-level data are available from the corresponding author SBL. Consent was not obtained but the presented data are anonymised and risk of identification is low.

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