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Original Article

Comparing AIMS65 Score With MEWS, qSOFA Score, Glasgow-Blatchford Score, and Rockall Score for Predicting Clinical Outcomes in Cirrhotic Patients With Upper Gastrointestinal Bleeding

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Background: The aim of our study was to compare the Age 65; International normalized ratio; Mental status; Shock (AIMS65) score with the Modified Early Warning Score (MEWS), quick Sepsis Related Organ Failure Assessment (qSOFA) score, Glasgow-Blatchford score (GBS), and the complete Rockall score (CRS) in predicting clinical outcomes in cirrhotic patients with upper gastrointestinal bleeding (UGIB).
Methods: A total of 442 consecutive cirrhotic patients admitted with UGIB during a 17-month period were retrospectively investigated. The primary outcome was in-hospital mortality. The secondary outcomes were rebleeding, intensive care unit (ICU) admission and development of infection. The area under receiver operating characteristic curve (AUC) for each system was analyzed.
Results: For prediction of mortality, the AUC of the AIMS65 score was greater than that of other scoring systems without statistical significance. For the prediction of rebleeding, the AIMS65 score was superior to qSOFA (0.65 vs. 0.56, p = 0.020). For the prediction of ICU admission, the AIMS65 score was superior to the GBS and CRS (0.77 vs. 0.63, p = 0.005 and 0.77 vs. 0.63, p = 0.007, respectively). For the prediction of the development of infection, the AIMS65 score was superior to CRS (0.73 vs. 0.60, p = 0.010).
Conclusions: In predicting in-hospital mortality among cirrhotic patients with UGIB, the AIMS65 score showed a trend of better performance than the MEWS, qSOFA score, GBS, and CRS. The AUCs of the AIMS65 score were greater than other four systems in predicting rebleeding, ICU admission and the development of infection.

Key words: *upper gastrointestinal bleeding, AIMS65, qSOFA, Glasgow-Blatchford score, Rockall score*

Introduction

Upper gastrointestinal bleeding (UGIB) is a frequent and fatal medical emergency, particularly among patients with cirrhosis, with a mortality rate of 5% to 17%.[1-8] However, there are few studies comparing these scoring systems in predicting adverse outcomes of UGIB in cirrhotic patients. Currently,

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most articles on the predictors of clinical outcomes for cirrhotic patients with UGIB have largely focused on variceal bleeding, which accounts for 55% to 87% of bleeding episodes.[5,6,8,9] The results of these studies may be of limited use when the bleeding source has not yet been identified on upper gastrointestinal (UGI) endoscopic examination. A simple, readily available, and precise scoring system to classify patients according to severity and to identify unstable patients would allow physicians to implement the correct treatment protocol for effective treatment and enable the proper allocation of resources.

Several scoring systems have been developed to predict the prognosis of UGIB. The Age 65; International normalized ratio; Mental status; Shock (AIMS65) score, a recently proposed scoring system to predict mortality in acute UGIB, has been validated as a simple, accurate, unweighted, non-endoscopic system with predictive value that is comparable or superior to the Glasgow-Blatchford score (GBS) and complete Rockall score (CRS), the two currently most widely used stratification tools in UGIB.[10-16] The Modified Early Warning Score (MEWS) system permits rapid calculation, based on clinical variables and may help to identify critical or potentially critical UGIB patients.[17]

Infection in cirrhotic patients with UGIB increases the risk of failure to control bleeding, the rebleeding rate, and mortality.[4,18-20] The quick Sepsis Related Organ Failure Assessment (qSOFA), also known as quickSOFA, is a novel scoring system developed to identify poor prognosis in patients with suspected infection.[21] Considering the significance of infection in patients with cirrhosis and the ability of the qSOFA for prognosis prediction in sepsis, qSOFA may help to recognize UGIB patients with possible unfavorable outcomes.

In this study, we compared the five most commonly used scoring systems—the AIMS65 score, MEWS, qSOFA score, GBS, and CRS—for predicting the clinical outcome of cirrhotic patients with UGIB from all sources. We hypothesized that the AIMS65 score had the potential to become the new standard risk score for cirrhotic patients with UGIB due to its simplicity, accuracy, and convenience. Outcomes were assessed in terms of in-hospital mortality, intensive care unit (ICU) admission, and the development of infection.

Methods

Study Design and Population

This was a retrospective study conducted in two hospitals: a medical center (Chang Gung Memorial Hospital, Linkou branch) and a regional hospital (Chang Gung Memorial Hospital, Chiayi branch); both hospitals were university-affiliated teaching hospitals. All adult (> 18-year-old) patients with cirrhosis presenting with UGIB to the emergency department (ED) of Chang Gung Memorial Hospital, Linkou branch between August 1, 2010 and December 31, 2010, and those presenting to the Chang Gung Memorial Hospital, Chiayi branch ED between January 1, 2011 and December 31, 2011, were reviewed for eligibility for inclusion.

The study was approved by the Institutional Review Board of each hospital and informed consent was waived.

Survey Content and Administration

The medical records of all adult cirrhotic patients presenting with UGIB to the ED were reviewed. The diagnosis of UGI bleeding was made based on the following clinical manifestations: hematemesis, vomiting with coffee ground substance, melena, or blood from nasogastric tube aspiration. The diagnosis of liver cirrhosis was confirmed based on compatible abdomen sonographic findings accompanied by laboratory findings of hepatic dysfunction or clinical findings of portal hypertension. Child–Pugh classification (CP classification) A, B, or C was used to classify the severity of cirrhosis.[22] CP classification A denotes good hepatic function, CP classification B denotes intermediate hepatic function, and CP classification C poor function. Shock was defined as signs of shock at ED triage, including systolic blood pressure < 100 mmHg and pulse rate > 100 beats/min. All patients underwent UGI endoscopy to confirm the source of hemorrhage. Variceal bleeding was diagnosed via endoscopic findings, including active hemorrhage from any varices, the presence of a clot over any varices, or the presence of blood in the stomach with varices as the only potential source of bleeding. Those patients not diagnosed as having variceal bleeding were classified as having non-variceal bleeding. Patients were excluded if endoscopy was not performed. All cirrhot-

ic patients with UGI bleeding were treated following a standardized protocol, including fluid resuscitation, vasoactive drugs, antibiotics, and high-dose acid suppression therapy, according to each hospital practice guidelines. Clinical variables, including age, sex, clinical presentation of bleeding, vital signs, laboratory data, comorbidities, findings on endoscopic examination, the need for ICU admission, development of infection, rebleeding, and in-hospital mortality were recorded. ICU admission was indicated when a patient had respiratory failure with mechanical ventilation support or had signs of hemodynamic instability despite adequate fluid resuscitation and medical treatment. The development of infection in our study was defined as any clinical symptoms and signs of suspected infections, such as systemic inflammatory response syndrome,[21] spontaneous bacterial peritonitis, urinary tract infection, pneumonia on chest radiograph, plus a positive bacterial culture of any specimen, including sputum, urine, blood, and ascites during hospitalization for UGIB. Rebleeding was defined as any of the following: (1) repeated endoscopy within 3 days, (2) continuous blood transfusion for more than 3 days, or (3) surgical intervention to control bleeding within 3 days. The AIMS65 score, MEWS, qSOFA score, GBS, and CRS were calculated for all patients enrolled in the study. The methods for calculating these scores were based on the original articles[21,23-26] (Supplement Tables 1–4).

The primary outcome was in-hospital mortality. The secondary outcomes were rate of rebleeding, ICU admission, and development of infection.

Statistical Analysis

Statistical analysis was performed using MedCalc Statistical Software version 17.0.4 (MedCalc Software bvba, Ostend, Belgium). Normally distributed data are presented as mean with standard deviation (SD) and data with skewed distribution are expressed as median and interquartile ranges (IQR). Receiver operating characteristic (ROC) curves were generated for primary and secondary outcomes and the area under the ROC curve (AUC) was calculated for each score and outcome. The optimal thresholds of the AIMS65 score, MEWS, qSOFA score, GBS, and CRS were identified as the threshold associated with the highest Youden index. The difference between two AUC values was analyzed using the method set out by DeLong et al.[27] The difference was considered significant if the p value was < 0.05.

Sensitivity Analysis

To test the robustness of the main results, several additional analyses were conducted. A subgroup analysis was conducted by stratifying causes of bleeding into variceal bleeding and non-variceal bleeding.

Results

Fig. 1 illustrates the selection process of study participants. A total of 442 patients with cirrhosis were enrolled in the study and underwent endoscopy for UGIB. Of these, over half (51.6%) were male and 31.2% were over 65 years of age. The mean level of hemoglobin was 9.1 (± 2.4) g/dL. The median AIMS65 score, MEWS, qSOFA score, GBS, and CRS was 1 (IQR = 0–2), 3 (IQR = 1–4), 0 (IQR = 0–1), 10 (IQR = 8–13), and 9 (IQR = 7–9), respectively. Of the 442 patients, 27 died (in-hospital mortality rate 6.1%). The clinical characteristics and demographic data of patients are shown in Table 1. The ROC curve and AUC, with 95% confidence interval (CI) and p value, are shown in Table 2. Comparisons between each two scoring systems regarding in-hospital mortality, rebleeding, ICU admission rate, and development of infection, are presented in Table 3.

For the prediction of mortality, the AUC was obtained for the AIMS65 score = 0.76 (95% CI = 0.71–0.80), MEWS = 0.67 (95% CI = 0.62–0.71), qSOFA score = 0.71 (95% CI = 0.67–0.75), GBS = 0.71 (95% CI = 0.66–0.75), and CRS = 0.64 (95% CI = 0.60–0.69). The AUC of the AIMS65 score was greater than that of the other scoring systems, without statistical significance (Table 3).

The in-hospital mortality cutoff point that maximized the sum of the sensitivity and specificity was 1 for the AIMS65 score (sensitivity = 0.78, specificity = 0.67, total = 1.45), 4 for MEWS (sensitivity = 0.41, specificity = 0.88, total = 1.29), 0 for qSOFA (sensitivity = 0.74, specificity = 0.65, total = 1.39), 9 for GBS (sensitivity = 0.96, specificity = 0.47, total = 1.43), and 7 for CRS (sensitivity = 0.89, specificity = 0.34, total = 1.23).

For the prediction of rebleeding, the AUC was obtained for the AIMS65 score = 0.65 (95% CI = 0.60–0.70), MEWS = 0.58 (95% CI = 0.53–0.64), qSOFA = 0.56 (95% CI = 0.51–0.62), GBS = 0.62

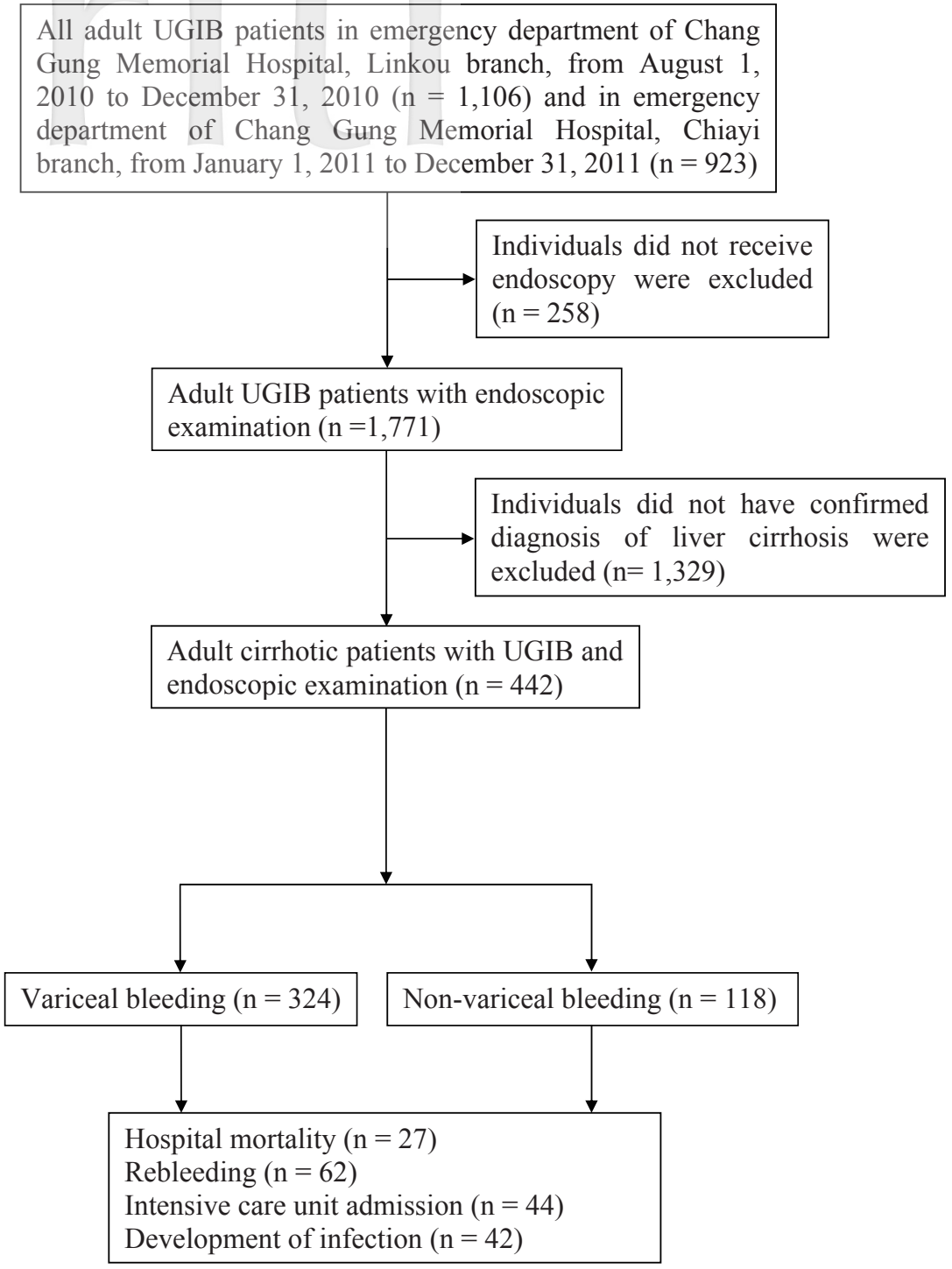

Fig. 1. Flow chart of identification of study participants. Patients enrolled in the study; number of patients included in and excluded from the study. Adult patients with upper gastrointestinal bleeding (UGIB) were included. Individuals who did not receive endoscopy and those who did not have a confirmed diagnosis of liver cirrhosis were excluded.

Table 1. Characteristics of patients

	All n (%)	Variceal bleeding n (%)	Non-variceal bleeding n (%)	*p* value
Number of patients	442 (100.0)	324 (73.3)	118 (26.7)	
Age > 65 years	138 (31.2)	84 (25.9)	54 (45.8)	< 0.001*
Male sex	228 (51.6)	152 (46.9)	76 (64.4)	0.001*
Endoscopic findings				
Esophageal varices	345 (78.0)	303 (93.5)	42 (35.5)	< 0.001*
Gastric varices	184 (41.6)	153 (47.2)	31 (26.2)	< 0.001*
Gastric ulcer	120 (27.1)	49 (15.1)	71 (60.2)	< 0.001*
Duodenal ulcer	66 (14.9)	18 (5.6)	48 (40.7)	< 0.001*
Causes of bleeding				
Esophageal varices	295 (66.7)	295 (91.0)	—	—
Gastric varices	29 (6.6)	29 (9.0)	—	—
Gastric ulcer	64 (14.5)	—	64 (54.2)	—
Duodenal ulcer	45 (10.2)	—	45 (38.1)	—
Other	9 (2.0)	—	9 (7.6)	—
Child–Pugh class of liver cirrhosis				
Child–Pugh class A	158 (35.7)	104 (32.1)	54 (45.8)	0.008*
Child–Pugh class B	169 (38.2)	139 (42.9)	30 (25.4)	< 0.001*
Child–Pugh class C	115 (26.0)	81 (25.0)	34 (28.8)	0.419
Comorbidities				
Heart failure	22 (5.0)	14 (4.3)	8 (6.8)	0.283
Ischemic heart disease	61 (13.8)	24 (7.4)	37 (31.4)	< 0.001*
Renal failure	73 (16.5)	42 (13.0)	31 (26.3)	< 0.001*
Metastatic cancer	66 (14.9)	45 (13.9)	21 (17.8)	0.308
Hemodynamic status at triage				
Shock[a]	54 (12.2)	43 (13.3)	11 (9.3)	0.262
Treatment				
Blood transfusion	196 (44.3)	147 (45.4)	49 (41.5)	0.472
Fresh frozen plasma	84 (19.0)	76 (23.5)	8 (6.8)	< 0.001*
Endoscopic treatment	243 (55.0)	212 (65.4)	31 (26.3)	< 0.001*
Outcomes				
Mortality	27 (6.1)	18 (5.6)	9 (7.6)	0.421
Rebleeding	62 (19.9)	58 (21.8)	4 (8.9)	0.002*
ICU admission	44 (10.0)	39 (12.0)	5 (4.2)	0.015*
Development of infection	42 (9.5)	36 (11.1)	6 (5.1)	0.056

ICU: intensive care unit.
[a]Shock was defined as signs of shock at emergency department triage, including systolic blood pressure < 100 mmHg and pulse rate > 100 beats/min.
*$p < 0.05$.

Table 2. Age 65; International normalized ratio; Mental status; Shock, Modified Early Warning Score, quick Sepsis Organ Failure Assessment, Glasgow-Blatchford score, and Rockall score for the outcomes

Outcome and scoring system	AUC	95% CI
Mortality		
AIMS65	0.76	0.71–0.80
MEWS	0.67	0.62–0.71
qSOFA	0.72	0.67–0.75
GBS	0.71	0.66–0.75
CRS	0.64	0.60–0.69
Rebleeding		
AIMS65	0.65	0.60–0.70
MEWS	0.58	0.53–0.64
qSOFA	0.56	0.51–0.62
GBS	0.62	0.57–0.68
CRS	0.58	0.52–0.63
ICU admission		
AIMS65	0.77	0.73–0.81
MEWS	0.74	0.69–0.78
qSOFA	0.75	0.70–0.79
GBS	0.63	0.58–0.67
CRS	0.63	0.59–0.68
Development of infection		
AIMS65	0.73	0.69–0.77
MEWS	0.69	0.65–0.74
qSOFA	0.71	0.66–0.75
GBS	0.64	0.60–0.69
CRS	0.60	0.55–0.64

AIMS65: Age 65; International normalized ratio; Mental status; Shock; AUC: area under receiver operating characteristic curve; CI: confidence interval; CRS: complete Rockall score; GBS: Glasgow-Blatchford score; ICU: intensive care unit; MEWS: Modified Early Warning Score; qSOFA: quick Sepsis Organ Failure Assessment.

(95% CI = 0.57–0.68), and CRS = 0.58 (95% CI = 0.52–0.63). The AIMS65 score was comparable to the MEWS, GBS, and CRS (p = 0.141, 0.440, and 0.074, respectively) and superior to the qSOFA (p = 0.020) in predicting rebleeding (Table 3).

The rebleeding cutoff point that maximized the sum of the sensitivity and specificity was 1 for the AIMS65 score (sensitivity = 0.54, specificity = 0.66, total = 1.20), 1 for MEWS (sensitivity = 0.82, specificity = 0.33, total = 1.15), 1 for qSOFA (sensitivity =

Table 3. Comparison of receiver operation curve curves for Age 65; International normalized ratio; Mental status; Shock, Modified Early Warning Score, quick Sepsis Organ Failure Assessment, Glasgow-Blatchford score, and complete Rockall score

Outcome and scoring system	DBA	p value
Mortality		
AIMS65 vs. MEWS	0.087	0.140
AIMS65 vs. qSOFA	0.045	0.442
AIMS65 vs. GBS	0.051	0.365
AIMS65 vs. CRS	0.113	0.070
MEWS vs. qSOFA	0.043	0.351
MEWS vs. GBS	0.037	0.527
MEWS vs. CRS	0.026	0.670
qSOFA vs. GBS	0.006	0.904
qSOFA vs. CRS	0.069	0.274
GBS vs. CRS	0.063	0.204
Rebleeding		
AIMS65 vs. MEWS	0.068	0.141
AIMS65 vs. qSOFA	0.087	0.020*
AIMS65 vs. GBS	0.029	0.440
AIMS65 vs. CRS	0.074	0.074
MEWS vs. qSOFA	0.019	0.568
MEWS vs. GBS	0.039	0.391
MEWS vs. CRS	0.005	0.894
qSOFA vs. GBS	0.058	0.121
qSOFA vs. CRS	0.013	0.729
GBS vs. CRS	0.044	0.276
ICU admission		
AIMS65 vs. MEWS	0.033	0.561
AIMS65 vs. qSOFA	0.022	0.645
AIMS65 vs. GBS	0.142	0.005*
AIMS65 vs. CRS	0.136	0.007*
MEWS vs. qSOFA	0.011	0.724
MEWS vs. GBS	0.109	0.030*
MEWS vs. CRS	0.103	0.047*
qSOFA vs. GBS	0.120	0.005*
qSOFA vs. CRS	0.114	0.012*
GBS vs. CRS	0.006	0.909
Development of infection		
AIMS65 vs. MEWS	0.032	0.534
AIMS65 vs. qSOFA	0.024	0.566
AIMS65 vs. GBS	0.085	0.090

Table 3. Comparison of receiver operation curve curves for Age 65; International normalized ratio; Mental status; Shock, Modified Early Warning Score, quick Sepsis Organ Failure Assessment, Glasgow-Blatchford score, and complete Rockall score (Continued)

Outcome and scoring system	DBA	*p* value
AIMS65 vs. CRS	0.134	0.010*
MEWS vs. qSOFA	0.008	0.804
MEWS vs. GBS	0.053	0.266
MEWS vs. CRS	0.048	0.035*
qSOFA vs. GBS	0.061	0.157
qSOFA vs. CRS	0.110	0.022*
GBS vs. CRS	0.048	0.309

AIMS65: Age 65; International normalized ratio; Mental status; Shock; CRS: complete Rockall score; DBA: difference between area; GBS: Glasgow-Blatchford score; ICU: intensive care unit; MEWS: Modified Early Warning Score; qSOFA: quick Sepsis Organ Failure Assessment.
*$p < 0.05$.

0.22, specificity = 0.91, total = 1.13), 7 for GBS (sensitivity = 0.93, specificity = 0.24, total = 1.17), and 8 for CRS (sensitivity = 0.61, specificity = 0.52, total = 1.13).

For the prediction of ICU admission, the AUC was obtained for the AIMS65 score = 0.77 (95% CI = 0.73–0.81), MEWS = 0.74 (95% CI = 0.69–0.78), qSOFA = 0.75 (95% CI = 0.70–0.79), GBS = 0.63 (95% CI = 0.58–0.67), and CRS = 0.63 (95% CI = 0.59–0.68). The AIMS65 score was comparable to the MEWS and qSOFA ($p = 0.561$ and 0.645, respectively) and superior to the GBS and CRS ($p = 0.005$ and 0.007, respectively) in predicting ICU admission (Table 3).

The ICU admission cutoff point that maximized the sum of the sensitivity and specificity was 2 for the AIMS65 score (sensitivity = 0.46, specificity = 0.93, total = 1.39), 4 for MEWS (sensitivity = 0.55, specificity = 0.91, total = 1.46), 0 for qSOFA (sensitivity = 0.75, specificity = 0.66, total = 1.41), 10 for GBS (sensitivity = 0.75, specificity = 0.54, total = 1.29), and 8 for CRS (sensitivity = 0.68, specificity = 0.51, total = 1.19).

For predicting the development of infection, the AUC was obtained for the AIMS65 score = 0.73 (95% CI = 0.69–0.77), MEWS = 0.69 (95% CI = 0.65–0.74), qSOFA = 0.71 (95% CI = 0.66–0.75), GBS = 0.64 (95% CI = 0.60–0.69), and CRS = 0.60 (95% CI = 0.55–0.64). The AIMS65 score was comparable to the MEWS, qSOFA, and GBS ($p = 0.534$, 0.566, and 0.090 respectively) and superior to the CRS ($p = 0.010$) in predicting the development of infection (Table 3).

The cutoff point for development of infection that maximized the sum of the sensitivity and specificity was 1 for the AIMS65 score (sensitivity = 0.66, specificity = 0.68, total = 1.34), 3 for MEWS (sensitivity = 0.52, specificity = 0.75, total = 1.27), 0 for qSOFA (sensitivity = 0.71, specificity = 0.65, total = 1.36), 9 for GBS (sensitivity = 0.76, specificity = 0.47, total = 1.23), and 7 for CRS (sensitivity = 0.88, specificity = 0.34, total = 1.22).

Sensitivity Analysis

The results of subgroup analysis presented that the AIMS65 was a better scoring system in predicting in-hospital mortality in both variceal bleeding group and non-variceal bleeding group than others (Supplement Tables 5 and 6).

Discussion

In Table 1, significant differences between the two groups (variceal bleeding and non-variceal bleeding) were noted in many variables, including age, sex, endoscopic findings, CP classification, comorbidities, and treatments. The reason for the differences in variables is that the pathophysiology is quite different between variceal and non-variceal.[28] In non-variceal bleeding, the causes of bleeding are mainly owing to ulcerative or erosive lesions whereas variceal bleeding mostly results from complications of portal hypertension.[29] In addition, in patients with non-variceal bleeding, a history of *Helicobacter pylori* infection or use of nonsteroidal anti-inflammatory drugs and aspirin is prevalent; in patients with variceal bleeding, a history of liver disease or alcohol abuse is more common.[6,30] In our study, the higher proportion of patients with CP classification A implies that there were possibly fewer complications of portal hypertension, such as seen in variceal bleeding. A higher proportion of patients with ischemic heart disease in the non-variceal bleeding group suggests a possible greater use of low-dose aspirin, increasing the risk of ulcer bleeding.[31] The slightly higher rate of mortality in the non-variceal bleeding group may be due to more older-aged patients or a higher proportion of patients with comorbidities of ischemic heart disease and renal disease.[6] In fact, although the mortality was slightly

higher in the group with non-variceal bleeding, no significance was noted as compared with the variceal bleeding group ($p = 0.421$). Further prospective studies including a large number of patients and focusing on cirrhotic patients with UGIB are needed.

The results of the present study showed that the AIMS65 score had the greatest AUC values, compared with the MEWS, qSOFA, GBS, and CRS, for detecting in-hospital mortality. After adjusting the p value to < 0.1, the AIMS65 score was superior to the CRS ($p = 0.070$). There are few studies comparing scoring systems among cirrhotic patients with UGIB, and most of these studies have focused on variceal bleeding. The AIMS65 score is comparable to the CRS in predicting in-hospital mortality[11,12] and superior to the GBS and pre-endoscopy Rockall score (PRS)[10,12,13,15,16] in serial UGIB studies. Among studies of variceal bleeding, the AIMS65 score has been found to be more accurate than the CRS in predicting in-hospital mortality,[32] and is comparable to the PRS and GBS in predicting 30-day mortality.[33] Previous reports have indicated that the AIMS65 score is superior to the SOFA score, model for end-stage liver disease (MELD) score, Acute Physiology and Chronic Health Evaluation (APACHE) II score, and CP classification in predicting mortality in patients with variceal bleeding.[34] In a recent study, Bozkurt et al.[17] confirmed that the MEWS was as effective as the GBS and Rockall score in predicting in-hospital mortality. To the best of our knowledge, the present study is the first to include the qSOFA and MEWS for the prediction of mortality in cirrhotic patients with UGIB, and our findings suggest that the AIMS65 score is comparable to other scoring systems.

In this study, we did not find any differences in performance between the AIMS65 score, MEWS, GBS, and CRS in the prediction of rebleeding; however, the AIMS65 score was superior to the qSOFA score (0.65 vs. 0.56, $p = 0.020$). The AUC values of these five scoring systems were between 0.56 and 0.65, implying that the clinical application of these systems in predicting rebleeding is limited. In agreement with a prospective study in Denmark, our data revealed similar performance of the CRS to detect rebleeding; the authors of that study found similarly low AUC values.[35] Also similar to our report, a recent investigation in Peru revealed that the GBS, CRS, and AIMS65 score were comparable in predicting rebleeding.[36] Recent prospective research in China has demonstrated that the AIMS65 score had better performance for predicting rebleeding than the GBS (AUC = 0.74 vs. 0.62, $p = 0.01$).[37] In contrast, another report from Mexico showed that the GBS (AUC = 0.76) was a better scoring system than the CRS (AUC = 0.69) and AIMS65 score (AUC = 0.66) for prediction of rebleeding, although no significant difference was noted ($p = 0.28$).[38] These discrepant findings in reports from different countries suggest that a new scoring system with performance that is superior to the current five scoring systems for rebleeding is required.

A simple and accurate scoring system to predict ICU admission is crucial for physicians, to enable them to commence appropriate resuscitation and make prompt specialist referral for urgent endoscopy. Previous studies have reported various results regarding this aspect. Hyett et al.[16] reported that the AIMS65 score had greater AUC values than the GBS, although this was not statistically significant (AUC = 0.69 vs. 0.63, $p = 0.35$). A prospective study from Turkey[14] revealed that the GBS had superior discriminatory power compared with the AIMS65 score (AUC = 0.80 vs. 0.75, $p = 0.137$) for composite clinical outcomes, defined as the need for surgical or endoscopic intervention, rebleeding, ICU admission, or in-hospital mortality, although this was not statistically significant. A more recent study conducted by Robertson et al.[12] showed that the AIMS65 score was superior to all other scores, including the GBS, PRS, and CRS (AUC = 0.74 vs. 0.70 vs. 0.62 vs. 0.71, respectively). There are limited reports on scoring systems or factors predicting ICU admission in patients with variceal bleeding and cirrhotic patients with UGIB from all sources.

Our study showed that the differences in AUC values between the AIMS65 score and GBS and between the AIMS65 and CRS in predicting ICU admission were statistically significant ($p = 0.005$ and 0.007, respectively). Furthermore, no differences were noted in AUC values between the AIMS65 score and MEWS or between the AIMS65 and qSOFA scores. The AIMS65, MEWS, and qSOFA may be valuable for early risk stratification of cirrhotic patients with UGIB, to prioritize ICU admission.

It is known that bacterial infection is frequently diagnosed in cirrhotic patients with UGIB, including those with variceal and non-variceal bleeding.[2,18-20] Bacterial infection is independently associated with multiple adverse outcomes (failure to control bleeding, recurrent bleeding episodes, in-hospital mortality) in cirrhotic patients with UGIB.[4,18-20] Timely antibiotic

prophylaxis reduces the infection rate, in-hospital mortality, rebleeding episodes, days of hospitalization, and improves patient outcome.[1,2,38,39] A scoring system identifying patient groups that are likely to develop infection is crucial for physicians to select the most effective antibiotic and promptly administer antibiotic prophylaxis. The results of our study indicate that the AIMS65 score had greater AUC values than those of the MEWS and qSOFA scores, although without statistical significance. However, the difference in AUC values between the AIMS65 score and CRS was significant ($p = 0.010$). The AIMS65 score may be the most appropriate tool to predict the development of infection in cirrhotic patients with UGIB in the ED.

Limitations

There are several limitations to this study. First, our study had a retrospective design and some data were unavailable or incomplete. However, we enrolled consecutive patients who fulfilled clearly defined inclusion criteria. We also reviewed individual charts using a standardized data collection tool to minimize variability. Second, our study included only two institutions. However, these were large-scale hospitals and urgent endoscopy is available 24 hours, 7 days a week in both hospitals. Therefore, patients with UGIB in critical condition are frequently transferred from neighboring cities to these hospitals.

Conclusions

The AIMS65 score is a better predictor of in-hospital mortality among cirrhotic patients with UGIB than the MEWS, qSOFA score, GBS, and CRS. The AUC values of the AIMS65 score were greater than those of the other four systems in predicting rebleeding, ICU admission, and the development of infection. This study proved that the AIMS65 score can be applied to cirrhotic patient with all-source UGIB for the prediction of outcomes. The AIMS65 score is a simple, unweighted score, which is easy to calculate and does not rely on endoscopic examination.

Conflicts of Interest Statement

There are no conflicts of interest in this study.

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Author Contributions

Yi-Chen Lai, Yi-Chuan Chen, Ming-Szu Hung and Yu-Han Chen conceived the study, designed the method. Yi-Chuan Chen and Ming-Szu Hung supervised the conduct of the data collection. Yi-Chuan Chen and Ming-Szu Hung undertook recruitment of participating centers and patients and managed the data, including quality control. Yi-Chuan Chen and Ming-Szu Hung provided statistical advice on study design and analyzed the data; Yi-Chuan Chen chaired the data oversight committee. Yi-Chen Lai, Yi-Chuan Chen, Ming-Szu Hung, and Yu-Han Chen drafted the manuscript, and all authors contributed substantially to its revision. Yi-Chuan Chen takes responsibility for the paper as a whole.

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Supplement Table 1. Age 65; International normalized ratio; Mental status; Shock and Glasgow-Blatchford score

Variables	Score
AIMS65	
Albumin < 3.0 mg/dL	1
INR > 1.5	1
Altered mental status	1
SBP < 90 mmHg	1
Age > 65 years	1
Maximum	5
Glasgow-Blatchford score	
Blood urea nitrogen (mg/dL)	
18.2–22.3	2
22.4–27.9	3
28.0–69.9	4
≥ 70.0	6
Hemoglobin, men (g/dL)	
12.0–12.9	1
10.0–11.9	3
< 10.0	6
Hemoglobin, women (g/dL)	
10.0–11.9	1
< 10.0	6
SBP (mmHg)	
100–109	1
90–99	2
< 90	3
Other markers	
Pulse ≥ 100/min	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease	2
Heart failure	2
Maximum	23

AIMS65: Age 65; International normalized ratio; Mental status; Shock; INR: international normalized ratio; SBP: systolic blood pressure.

Supplement Table 2. Rockall score[a]

Variable	Score			
	0	1	2	3
Age (years)	< 60	60–79	≥ 80	
Shock		HR > 100	SBP < 100 mmHg	
Comorbidity			IHD, CHF, any major comorbidity	Renal failure, liver failure, metastatic malignancy
Diagnosis	Mallory–Weiss tear or no lesion observed	Peptic ulcer disease, erosive esophagitis	UGI tract malignancy	
Stigmata of recent hemorrhage	Clean-based ulcer, flat pigmented spot		Blood in UGI tract, clot, visible vessel, bleeding	

CHF: congestive heart failure; HR, heart rate; IHD: ischemic heart disease; SBP: systolic blood pressure; UGI: upper gastrointestinal.
[a]Pre-endoscopic Rockall score = score of age + score of shock + score of comorbidity (maximum score = 7); complete Rockall score = clinical Rockall score + score of diagnosis + score of stigmata of recent hemorrhage (maximum score = 11).

Supplement Table 3. Quick Sepsis Related Organ Failure Assessment[a]

	Score[a]
Altered mental status (Glasgow Coma Scale < 15)	1
respiratory rate ≥ 22	1
SBP ≤ 100 mmHg	1

SBP: systolic blood pressure.
[a]Maximum score = 3.

Supplement Table 4. Modified Early Warning Score

	3	2	1	0	1	2	3
SBP (mmHg)	< 70	71–80	81–100	101–199		≥ 200	
HR (bpm)		< 40	41–50	51–100	101–110	111–129	≥ 130
Respiratory rate (bpm)		< 9		9–14	15–20	21–29	≥ 30
Temperature (°C)		< 35.0		35.0–38.4		≥ 38.5	
AVPU score				Alert	Reaction to voice	Reaction to pain	Unresponsive

AVPU: alert, voice, pain, unresponsive scale; HR: heart rate; SBP: systolic blood pressure.

Supplement Table 5. Age 65; International normalized ratio; Mental status; Shock, Modified Early Warning Score, quick Sepsis Related Organ Failure Assessment, Glasgow-Blatchford score, and Rockall score for the outcomes in variceal bleeding group

Outcome and scoring system	AUC	95% CI
Mortality		
AIMS65	0.75	0.70–0.79
MEWS	0.64	0.59–0.70
qSOFA	0.75	0.70–0.80
GBS	0.75	0.70–0.80
CRS	0.60	0.54–0.65
Rebleeding		
AIMS65	0.64	0.58–0.70
MEWS	0.59	0.53–0.65
qSOFA	0.57	0.51–0.63
GBS	0.64	0.58–0.69
CRS	0.56	0.50–0.63
ICU admission		
AIMS65	0.78	0.73–0.82
MEWS	0.72	0.67–0.77
qSOFA	0.74	0.69–0.79
GBS	0.60	0.54–0.65
CRS	0.61	0.56–0.66
Development of infection		
AIMS65	0.76	0.71–0.80
MEWS	0.68	0.62–0.73
qSOFA	0.72	0.67–0.77
GBS	0.62	0.57–0.66
CRS	0.58	0.52–0.63

AIMS65: Age 65; International normalized ratio; Mental status; Shock; AUC: area under the curve; CI: confidence interval; CRS: complete Rockall score; GBS: Glasgow-Blatchford score; ICU: intensive care unit; MEWS, Modified Early Warning Score; qSOFA, quick Sepsis Organ Failure Assessment.

Supplement Table 6. Age 65; International normalized ratio; Mental status; Shock, Modified Early Warning Score, quick Sepsis Related Organ Failure Assessment, Glasgow-Blatchford score, and Rockall score for the outcomes in non-variceal bleeding group

Outcome andscoring system	AUC	95% CI
Mortality		
AIMS65	0.81	0.72–0.88
MEWS	0.73	0.64–0.81
qSOFA	0.63	0.54–0.72
GBS	0.63	0.54–0.72
CRS	0.77	0.68–0.84
Rebleeding		
AIMS65	0.70	0.55–0.83
MEWS	0.54	0.38–0.69
qSOFA	0.54	0.39–0.69
GBS	0.52	0.32–0.67
CRS	0.63	0.48–0.77
ICU admission		
AIMS65	0.82	0.73–0.88
MEWS	0.80	0.72–0.87
qSOFA	0.78	0.69–0.85
GBS	0.65	0.55–0.73
CRS	0.61	0.51–0.70
Development of infection		
AIMS65	0.66	0.57–0.74
MEWS	0.66	0.58–0.74
qSOFA	0.62	0.53–0.71
GBS	0.61	0.52–0.70
CRS	0.65	0.55–0.73

AIMS65: Age 65; International normalized ratio; Mental status; Shock; AUC: area under the curve; CI: confidence interval; CRS: complete Rockall score; GBS: Glasgow-Blatchford score; ICU: intensive care unit; MEWS: Modified Early Warning Score; qSOFA: quick Sepsis Organ Failure Assessment.