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Systematic Review

AIMS65 SCORING SYSTEM FOR PREDICTING CLINICAL OUTCOMES AMONG EMERGENCY DEPARTMENT PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING

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ABSTRACT

Introduction: Several scoring systems were developed for early risk stratification in Upper Gastrointestinal Bleeding (UGIB) patients. AIMS65 score is a scoring system that only consists of five parameters, it might be used in daily clinical practice because of rapid and easy to calculate within 12 hours of admission. **Objective:** To evaluate the AIMS65 scoring system as a predictor of mortality, rebleeding events, need for endoscopic therapy, blood transfusion, and ICU admission for all causes of UGIB. **Methods:** We conducted a systematic review on PubMed, ScienceDirect, ProQuest, and Cochrane Library databases from the 2012 to 2022 publication period. We included either prospective or retrospective cohort studies that reported UGIB with all kinds of aetiologies who presented in the emergency department (ED), reported discriminative performance for each outcome, and reported the optimal cut-off of AIMS65. The primary measurement of discriminative performance for clinical outcomes includes mortality, rebleeding incidents, need for endoscopic therapy, blood transfusion, and ICU admission. **Results:** We identified 351 published studies, of which 20 were included in this study. Most of the studies reported discriminative performance for predicting mortality, which amounts to about 18 out of 20 studies. Rebleeding prediction was reported in 11 studies, need for endoscopic therapy in 5 studies, blood transfusion in 7 studies, and ICU admission in 2 studies. Most of the studies reported fair to excellent discriminative performance for predicting mortality, but in contrast for predicting rebleeding, the need for endoscopic therapy, blood transfusion, and ICU admission. Cut-off values≥ 2 are frequently reported to distinguish between high-risk and low-risk patients in mortality. **Conclusion:** AIMS65 can be applied to patients with UGIB in ED for predicting mortality, but not applicable for predicting rebleeding events, the need for endoscopic therapy, blood transfusion, and ICU admission. It enhances early decision-making and triage for UGIB patients.

Keywords: AIMS65; Upper Gastrointestinal Bleeding (UGIB); Health Emergency Preparedness; Systematic Review.

ABSTRAK

Pendahuluan: Beberapa sistem skoring dikembangkan untuk stratifikasi risiko dini pada Pasien Perdarahan Gastrointestinal Bagian Atas (PSCBA). Skor AIMS65 adalah sistem skoring yang hanya terdiri dari lima parameter, dapat digunakan dalam praktik klinis sehari-hari karena cepat dan mudah dihitung dalam waktu 12 jam setelah admisi. **Tujuan:** Untuk mengevaluasi sistem penilaian AIMS65 sebagai prediktor mortalitas, kejadian perdarahan ulang, kebutuhan terapi endoskopi, transfusi darah, dan admisi ke ICU untuk semua penyebab PSCBA. **Metode:** Kami melakukan tinjauan sistematis melalui basis data *PubMed*, *ScienceDirect*, *ProQuest*, dan *Cochrane Library* dari periode publikasi 2012 hingga 2022. Kami memasukkan studi kohort prospektif atau retrospektif yang melaporkan UGIB dengan semua jenis etiologi yang dilaporkan di unit gawat darurat (UGD), melaporkan kemampuan diskriminatif untuk setiap hasil, dan melaporkan batas optimal AIMS65. Pengukuran utama kinerja diskriminatif untuk hasil klinis mencakup angka mortalitas, kejadian perdarahan ulang, kebutuhan terapi endoskopi, transfusi darah, dan admisi ke ICU. **Hasil:** Kami mengidentifikasi 351 penelitian yang dipublikasikan, 20 di antaranya diinklusi dalam penelitian ini. Sebagian besar penelitian melaporkan kinerja diskriminatif dalam memprediksi kematian, yaitu pada 18 dari 20 penelitian. Prediksi perdarahan ulang dilaporkan dalam 11 penelitian, kebutuhan terapi endoskopi dalam 5 penelitian, transfusi darah dalam 7 penelitian, dan admisi ke ICU dalam 2 penelitian. Sebagian besar penelitian melaporkan kinerja diskriminatif yang cukup baik hingga sangat baik dalam memprediksi angka kematian, namun berbeda dalam memprediksi perdarahan ulang, kebutuhan terapi endoskopi, transfusi darah, dan admisi ke ICU. Nilai batas ≥ 2 sering dilaporkan untuk membedakan antara pasien berisiko tinggi dan pasien berisiko rendah dalam hal kematian. **Kesimpulan:** AIMS65 dapat diterapkan pada pasien PSCBA di IGD untuk memprediksi mortalitas, namun tidak dapat diterapkan untuk memprediksi kejadian perdarahan ulang, kebutuhan terapi

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endoskopi, transfusi darah, dan admisi ke ICU. Ini dapat meningkatkan pengambilan keputusan dini dan triase untuk pasien dengan PSCBA.

Kata Kunci: AIMS65; Pasien Pendarahan Gastrointestinal Bagian Atas (PSCBA); Kesiapsiagaan Darurat Kesehatan; Tinjauan Sistematis.

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INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is a medical emergency case located between the oral cavity to the proximal treitz ligament. UGIB is clinically presented by haematemesis, coffee-ground emesis, and melena. Despite the improvement of overall mortality and morbidity rates in developing countries because of advanced diagnosis and treatment, the mortality rate of UGIB around the world in the past decade unchanged and varied between 3–14% (1). Patients with UGIB can present in either stable condition or requiring rapid management, such as resuscitation, blood transfusion, ICU admission, and endoscopic therapy depending on the clinical assessment of the patient. Endoscopy has an important role in the diagnostic and therapeutic of UGIB (2). Because of limited competent operators and equipment in all health facilities, most patients with UGIB do not receive rapid endoscopic intervention. Endoscopic procedures also have risks such as perforation and discomfort to patients so several considerations are needed to decide whether the patient needs an endoscopy or not (3).

The existing scoring system is considered helpful for physicians in the emergency department (ED) to enhance decision-making. A scoring system is able to guide earlier treatment or care for patients above the cut-off which is considered as a high risk, thus leading to improvements in mortality and morbidity rates (4,5). Several scoring systems were developed for early risk stratification in UGIB patients, such as the Glasgow Blatchford Score (GBS), Rockall Score, and AIMS65 (4,6). The Rockall Score requires an endoscopic component so it cannot be used for pre-endoscopic triage. The GBS and AIMS65 scoring systems are possible to overcome these problems because the prognostic parameters do not require endoscopic examination, but the GBS system has limitations compared to AIMS65 when used in clinical practice because it weighted each parameter so the outcome was often over-evaluated when calculated (7).

AIMS65 score is a more recent scoring system compared to the two others which only consists of 5 parameters, such as albumin levels, INR, changes in mental status, blood pressure, and age > 65 years old. It might be used in daily clinical practice because of rapid and easy to calculate within 12 hours of admission (7,8). As such, this systematic review aims to identify the AIMS65 scoring system for its ability to predict the prognosis including mortality rebleeding events, the need for therapy including endoscopic therapy, blood transfusion, and ICU admission for all causes of upper gastrointestinal bleeding based on predictive accuracy.

METHODS

Search Strategy

The literature search was conducted on four databases, including PubMed, ScienceDirect, ProQuest, and Cochrane Library with a publication period ranging from 2012 to 2022 using keywords related to "AIMS65" and "Upper Gastrointestinal Bleeding". Only studies written in English and

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full-text access articles were considered in this systematic review.

Eligibility Criteria

This study was conducted using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). We only included articles that match our eligibility criteria based on PICOS: (i) Population: all-cause UGIB patients admitted to the emergency department; (ii) Intervention: AIMS65 score; (iii) Comparison: not applicable; (iv) Outcomes: mortality, rebleeding, endoscopic therapy, blood transfusion, and ICU admission (v) Study design: a prospective or retrospective cohort. The analyzed variables were the discriminative performance of AIMS65 for each outcome, and the optimal cut-off should be reported to distinguish between low and high-risk patients. We excluded the AIMS65 score which validated variceal or non-variceal bleeding only. Furthermore, we exclude studies that measure discrimination ability for composite clinical outcomes. Two reviewers independently screened the titles and abstract based on inclusion and exclusion criteria, the discrepancies are solved by consensus and involve a third reviewer when needed. PICOS framework for inclusion studies can be seen in Table 1.

Table 1. PICOS framework

Population	All-cause UGIB patients admitted to the emergency department
Intervention	AIMS65 score
Comparison	Not applicable
Outcome	Mortality, rebleeding, endoscopic therapy, blood transfusion, ICU admission
Study design	Cohort

Data Extraction and Quality Assessment

The following data were extracted from each study: publication date, study design, sample size, and optimal cut-off, and we also extracted all performances of the score in terms of discrimination ability or AUC. The AUC thresholds to judge predictive ability have been described by other researchers: excellent (AUC ≥0.90); good (AUC ≥0.80 and <0.90); fair (AUC ≥0.70 and <0.80); and poor (AUC <0.70) (9). Calibration, sensitivity, specificity, positive predictive value, and negative predictive value were also reported if available. The extracted data from each study will be conducted for narrative synthesis. All included studies will be assessed by two independent reviewers. The risk of bias and concern for applicability were assessed using a Prediction-model Risk of Bias Assessment Tool (PROBAST). PROBAST was developed to assess the quality of primary studies on multivariable models in a systematic review. This tool evaluated the risk of bias using four domains (participants, predictor, outcome, and analysis) and concern for applicability using three domains (participants, predictor, outcome) then finally judged by criteria of 'low', 'high', and 'unclear'.

RESULTS AND DISCUSSION

Search Result

We identified 351 published studies in the initial literature search. From a total of 72 articles selected for full-text review, we only included 20 studies that reported optimal cut-off and discrimination ability of AIMS65 scores for predicting mortality, rebleeding, endoscopic therapy, blood transfusion, and ICU admission to conduct this systematic review. PRISMA flowchart for the selection studies process can be seen in Figure 1.

Study and Sample Characteristics

Total of 20 studies, 10 prospective cohort (6,10–18), 9 retrospective cohort (7,19–26), and 1 both prospective and retrospective cohort (27). The population ranged between 129 to

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4019. The studies recruited from several countries with a median age between 52 to 71 years old. All of the studies recruited only assessed ED patients and reported the discrimination ability of AUC. No study reported the calibration measurement for the clinical outcome of AIMS65 scores. Eighteen of the studies evaluate the accuracy of predicting mortality. Detailed characteristics of included studies can be seen in Table 2.

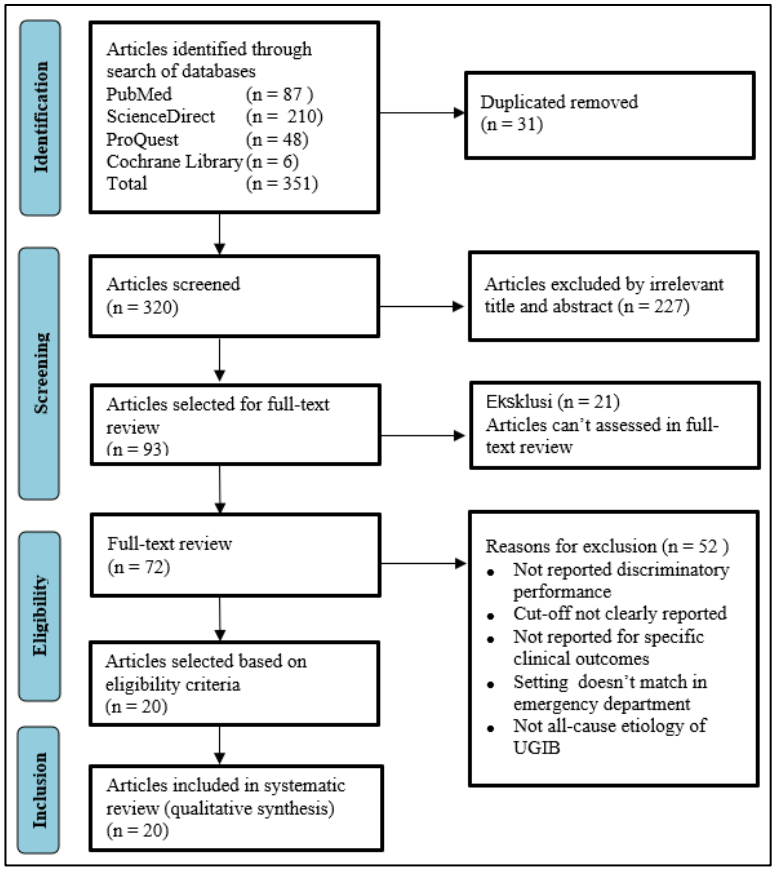

Figure 1. PRISMA flowchart

Table 2. Characteristics of Included Studies

First author, year	Design	Eligibility Criteria	Sample size	Male (%)	Median Age (IQR) Mean Age ± SD	Optimal Cut-off	Outcome
Hyett et al. 2013	Retrospective, single-center	UGIB based on ICD-9 codes	278	150 (54%)	63 (IQR 50–77)	(≥2)	Inpatient mortality
Thandassery et al. 2015	Retrospective, single-center	UGIB patients who underwent endoscopic evaluation within 12 hours; above 14 years of age	251	193 (76.8 %)	52 (IQR 15–84)	(≥2)	Blood transfusion, endoscopic therapy, ICU admission, rebleeding, mortality
Abougergi et al. 2016	Prospective, multicenter	Patients with UGIB either at the time of presentation to the hospital or if developed UGIB as an inpatient	*298*	197 (66%)	64 (IQR 52–75)	≥4	In-hospital mortality, 30-day mortality, in-hospital rebleeding, 30-day rebleeding
			309		64.6 ± 16.7	(≥1)	In-patient mortality,

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First author, year	Design	Eligibility Criteria	Sample size	Male (%)	Median Age (IQR) Mean Age ± SD	Optimal Cut-off	Outcome
Martı´nez-Cara et al. 2016	Prospective, single center	UGIB patients who underwent endoscopy; all patients received pantoprazole 80 mg iv as an initial bolus followed by a continuous infusion of 120 mg for the first 24 hours		214 (69.3 %)		(≥2)	Endoscopic therapy, blood transfusion, 6-month mortality
Robertson et al., 2016	Retrospective, single-center	UGIB based on ICD-10 codes	424	279 (66%)	71 (IQR 15–93)	(≥2)	In-hospital rebleeding,
						(≥3)	ICU admission, blood transfusion, in-hospital mortality
Zhong et al. 2016	Prospective, single center	Acute UGIB. Recurrent episode of UGIB; admission to the hospital and developed AUGIB for unrelated disease excluded	320	198 (61.9 %)	63 (IQR 42–79)	(≥2)	In-hospital mortality, in-patient rebleeding
Lau et al. 2016	Prospective, single center	UGIB patients who are not admitted to the hospital ward were excluded.	129	79 (61.2 %)	65.1 ± 21	(≥1)	In-patient mortality, blood transfusion
Zhao et al. 2017	Retrospective, single-center	UGIB patients above 65 years of age; endoscopic evaluation within 24 hours	293	170 (58%)	72.4 ± 6.3	(≥2)	In-patient mortality, rebleeding
Kalkan et al. 2017	Retrospective, single-center	Patient with the presence of overt endoscopic stigmata of UGIB; above 60 years of age	335	202 (60%)	72.9 ± 9	(≥2.5)	30-day mortality, rebleeding
Stanley et al. 2017	Propsektif, International multicenter	Patient with evidence of UGIB defined by haematemesis, coffee-ground vomiting, melaena. A patient who developed UGIB while an inpatient for another reader were excluded	3012	1750 (58%)	65 (IQR 24–90)	(≥2) (≥1)	30-day mortality, Endoscopic therapy
Tang et al. 2018	Retrospective, *single-center*	UGIB patients above 14 years of age. Patients who had been followed up for less than 30 days and were diagnosed other than UGIB were excluded	395	274 (69/4 %)	65 (IQR 50–77)	(≥2.5)	30-day mortality
Gu et al. 2018	Retrospective, single-center	UGIB patients who did not receive endoscopy examination as they had severe clinical symptoms and needed emergent clinical treatment	799	612 (77.22 %)	57.46 ± 18.04	(≥2)	In-hospital mortality
Shafaghi et al. 2019	Retrospective, single-center	UGIB patients above 18 years of age. Patients who didn't undergo endoscopy were excluded	563	345 (61.3 %)	60.53 ± 18.62	(≥2)	In-patient mortality, 30-day mortality, endoscopic intervention, blood transfusion
Redondo-Cerezo et al. 2020	Prospective, single center	UGIB patients were followed for 6 months after their discharge	547	367 (67.1 %)	64.1 ± 16.4	(≥2)	30-day mortality
						(≥1)	7-day rebleeding, endoscopic therapy

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First author, year	Design	Eligibility Criteria	Sample size	Male (%)	Median Age (IQR) Mean Age ± SD	Optimal Cut-off	Outcome
Saffouri et al. 2020	Prospective, international multicenter	UGIB patients who developed upper GI bleeding as inpatients were	3012	1746 (58%)	65 (IQR 24–90)	(≥1)	Blood transfusion
Liu et al. 2020	Prospective, multicenter	UGIB patients non-trauma; above 18 years	1072	779 (72.67 %)	61.41 ± 1577	(≥0.5)	90-day mortality, 90-day rebleeding
Lu et al. 2020	Retrospective, single-center	UGIB patients who are hospitalized within 48 hours of endoscopy; non-AUGIB cause death	284	197 (69.4 %)	64 (IQR 50–73)	(≥2)	In-hospital mortality
Sachan et al. 2021	Prospective, single center	UGIB patients above 18 years of age	268	222 (82.8 %)	48.49 ± 13.23	(≥2)	8-week mortality, rebleeding, blood transfusion
Chang et al. 2021	Prospective, single center	UGIB patients above 18 years of age. Patients who had a history of UGIB in the previous 3 months or had undergone endoscopy at another institution before admission were excluded	337	247 (73.3 %)	61.1 ± 16.5	(≥3)	In-hospital mortality
Laursen et al. 2021	Prospective and Retrospective, multicenter	Patients with acute UGIB are defined as presenting with haematemesis, coffee-ground vomiting, or melaena.	4019	2703 (67.25 %)	65 (IQR 30)	(≥2)	30-day rebleeding

Quality Assessment

All of the studies reported low concerns of applicability due to included studies having similar result in the review question. The analysis is the most common biased domain because the most studiesdo not report the calibration measurement of the AIMS65 score to predict clinical outcomes, therefore the judgment for all included studies is identified as high risk of bias. Quality assessment using PROBAST can be seen in Table 3.

Outcomes: Mortality prediction

From 20 studies that reported the discriminative performance of AIMS65 scores for predicting mortality, it was acceptable in general because the AUC showed ≥ 0.7 in most studies with a range from 0.65 to 0.955. 4 studies reported excellent discriminative performance, 5 studies reported good discriminative performance, 10 studies reported good discriminative performance, and only 3 studies reported poor discriminative performance. A total of 11 had data on sensitivity and specificity, ranging from 38% to 100% and 24% to 95.76%, respectively. PPV and NPV were available in 4 studies, ranging from 5.8% to 12% and 91% to 100%, respectively. Included studies were reported with various optimal cut-offs ranging from ≥ 0.5 to ≥ 4 with a frequently reported was ≥ 2. Mortality was reported on various follow-ups such as inpatient, in-hospital, 30-day, 8-week, 90-day, and 6-month. The predictive ability of AIMS65 to predict mortality can be seen in Table 4.

Outcomes: Rebleeding prediction

A total of 11 studies evaluated discriminative performance for rebleeding incidence. The AUC for rebleeding events prognosis ranged from 0.491 to 0.86.

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Table 3. Quality assessment by PROBAST

Author	Risk of Bias				Applicability			Overall	
	1	2	3	4	5	6	7	Risk of bias	Applicability
(19)	+	?	?	-	+	+	+	-	+
Thandassery et al., 2015	+	?	?	-	+	+	+	-	+
Abougergi et al., 2016	+	+	+	-	+	+	+	-	+
Martı´nez-Cara et al., 2016	+	+	+	-	+	+	+	-	+
Robertson et al, 2016	+	+	?	-	+	+	+	-	+
Zhong et al., 2016	+	+	+	-	+	+	+	-	+
Lau et al., 2016	+	+	-	-	+	+	+	-	+
Zhao et al., 2017	-	?	-	-	+	+	+	-	-
Kalkan dkk., 2017	-	+	-	-	+	+	+	-	-
Stanley et al., 2017	+	-	+	-	+	+	+	-	+
Tang et al., 2018	+	+	+	-	+	+	+	-	+
Gu et al., 2018	+	-	+	-	+	+	+	-	+
Shafaghi et al., 2019	+	-	?	-	+	+	+	-	+
Redondo-Cerezo et al., 2020	+	+	?	-	+	+	+	-	+
Saffouri et al., 2020	+	-	?	-	+	+	+	-	+
Rao et al., 2020	-	-	+	-	+	+	+	-	+
Liu et al., 2020	+	+	+	-	+	+	+	-	+
Lu et al., 2020	+	?	?	-	+	+	+	-	+
Sachan et al., 2021	+	+	+	-	+	+	+	-	+
Chang et al., 2021	+	+	?	-	+	+	+	-	+
Laursen et al., 2021	+	?	+	-	+	+	+	-	+

*PROBAST = Prediction model Risk Of Bias Assessment Tool, ROB; risk of bias

*1, risk of bias for participants; 2, risk of bias for predictor; 3, risk of bias for outcome; 4, risk of bias for analysis; 5, concern applicability for participants; 6, concern applicability for predictor; 7, concern applicability for outcome

*(+) indicates low ROB/low concern regarding applicability; (−) indicates high ROB/high concern regarding applicability; and (?) indicates unclear ROB/unclear concern regarding applicability.

There is only one study that reported fair and good discrimination performance with optimal cut-offs≥ 2 and ≥ 2.5, respectively.The remaining studies reported poor discriminative performance with optimal cut-off ranging from ≥ 0.5 to ≥ 3. Sensitivity and specificity were available in 6 studies, and they ranged from 57%-78.9% and 35.52% - 89.4%, respectively. PPV and NPV were available only in 1 study with the value of 14.25% and 92.29%. Follow-up time for rebleeding varies in all studies, such as inpatient, in-hospital, 7-day, 30-day, and 90-day. The predictive ability of AIMS65 to predict rebleeding can be seen in Table 5. postoperative pain between the experimental and placebo groups.

Outcomes: Need for endoscopic therapy prediction

Five studies consistently found the poor discriminative performance of AIMS65 scores for predicting the need for endoscopy therapy with the AUC ranging from 0.48 to 0.63. Three studies reported optimal cut-off was ≥ 1 and two studies reported optimal cut-off was ≥ 2. Of 5 studies, only 2 studies included sensitivity and specificity, those 2 studies also reported PPV and NPV. The predictive ability of AIMS65 to predict the need for endoscopic therapy can be seen in Table 6.

Outcomes: Need for blood transfusion

Seven studies reported blood transfusion prediction with the AUC ranged from 0.57 to 0.72. Only 2 optimal cut-offs were reported for blood transfusion specifically ≥ 1 and ≥ 2. Two studies reported fair discrimination performance with different optimal cut-offs of ≥ 1 and ≥ 2 respectively. Five remaining studies reported poor discrimination for rebleeding events. The predictive ability of AIMS65 to predict blood transfusion can be seen in Table 7.

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Table 4. Predictive Ability of AIMS65 to Predict Mortality

Study	Optimal Cut-off	Follow-up	AUC and Category	Sensitivity/ Specificity (%)	PPV/ NPV (%)
Hyett et al.	≥2	Inpatient mortality	0.93 (95% CI, 0.89–0.96) (Excellent)	83/48	NS
Thandassery et al.	≥2	NS	0.74 (95% CI, 0.63–0.85) (Fair)	NS	NS
Abougergi et al.	≥4 ≥4	In-hospital mortality 30-day mortality	0.85 (95% CI, 0.81–0.89) (Good) 0.74 (95% CI, 0.70–0.79) (Fair)	NS NS	NS NS
Martı´nez-Cara et al.	≥1 ≥2	Inpatient mortality 6-month mortality	0.76 (95% CI, 0.68–0.83) (Fair) 0.74 (95% CI, 0.66–0.82) (Fair)	100/24 38/89	12/100 31/91
Robertson et al.	≥3	Inpatient mortality	0.80 (95% CI, 0.69–0.91) (Good)	72/77	NS
Zhong et al.	≥2	In-hospital mortality	0.786, 95% CI, 0.670-0.903) (Fair)	NS	NS
Lau et al.	≥1	Inpatient mortality	0.83 (95% CI, 0.67–0.99) (Good)	100/48	5.8/100
Zhao et al.	≥2	Inpatient mortality	0.833 (95% CI, 0.785–0.874) (Good)	96/54	NS
Kalkan et al.	≥2.5	30-day mortality	0.88 (Good)	79.6/89.2	NS
Stanley et al.	≥2	30-day mortality	0.78 (95% CI, 0.75–0.81) (Fair)	65.8/76.2	18/96.6
Tang et al.	≥2.5	30-day mortality	0.907 (95% CI, 0.874–0.934) (Excellent)	70.73/95.76	NS
Stokbro et al.	≥1	30-day mortality	0.74 (Fair)	NS	NS
Gu et al.	≥2	In-hospital mortality	0.91 (95% CI, 0.84–0.98) (Excellent)	NS	NS
Shafaghi et al.	≥2	Inpatient mortality	0.675 (95%CI 0.545–0.806) (Poor)	57.1/79.5	NS
Redondo-Cerezo et al.	≥2	30-day mortality	0.75 (95% CI, 0.69–0.81) (Fair)	NS	NS
Liu et al.	≥0.5	90-day mortality	0.672 (95% CI, 0.624–0.721) (Poor)	87.18/36.44	14.39/ 95.87
Lu et al.	≥2	In-hospital mortality	0.955 (95%CI, 0.923–0.976) (Excellent)	NS	NS
Sachan et al.	≥2	8-week mortality	0.725 (95%CI, 0.656–0.794) (Fair)	80.3/53.9	NS
Chang et al.	≥3	In-hospital mortality	0.747 (95% CI, 0.630–0.863) (Fair)	NS	NS
Laursen et al.	≥2	30-day mortality	0.65 (95% CI, 0.62–0.69) (Poor)	NS	NS

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

Table 5. Predictive Ability of AIMS65 to Predict Rebleeding

Study	Optimal Cut-off	Follow-up	AUC and Category	Sensitivity/ Specificity (%)	PPV/ NPV (%)
Hyett et al.	≥2	Inpatient rebleeding	0.63 (95% CI, 0.57–0.69) (Poor)	57/73	NS
Thandassery et al.	≥2	NS	0.53 (95% CI, 0.40–0.66) (Poor)	NS	NS
Abougergi et al.	≥3 ≥3	In-hospital rebleeding 30-day rebleeding	0.69 (95% CI, 0.63–0.74) (Poor) 0.63 (95% CI, 0.57–0.69) (Poor)	NS NS	NS NS
Robertson et al.	≥2	In-hospital rebleeding	0.61 (95% CI, 0.51–0.70) (Poor)	76/44	NS
Zhong et al.	≥2	Inpatient rebleeding	0.735 (95% CI, 0.667-0.802) (Fair)	NS	NS
Zhao et al.	≥2	NS	0.646 (95% CI, 0.588–0.700) (Poor)	74/52	NS
Kalkan et al.	≥2.5	NS	0.86 (Good)	75.5/89.4	NS
Shafaghi et al.	≥2	30-day rebleeding	0.491 (95% CI 0.369–0.614) (Poor)	NS	NS
Redondo-Cerezo et al.	≥1	7 day-rebleeding	0.64 (95% CI, 0.59–0.68) (Poor)	NS	NS
Liu et al.	≥0.5	90-day rebleeding	0.585 (95% CI, 0.537–0.634) (Poor)	78.29/35.52	14.25/9 2.29
Sachan et al.	≥2	NS	0.626 (95% CI, 0.546–0.707) (Poor)	78.9/48.3	NS

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

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Outcomes: Need for ICU admission

Discriminative performance for ICU admission was only presented in 2 studies, Thandassery et al reported an AUC for ICU admission to be 0.61, and Robertson et al (x) reported an AUC of 0.74 for ICU admission. All of the studies reported optimal cut-off was ≥ 2. Only Robertson et al reported sensitivity and specificity of about 88% and 47%. The predictive ability of AIMS65 to predict ICU admission can be seen in Table 8.

Discussion

We conducted a systematic review to assess the predictive accuracy of AIMS65 as pre-endoscopic risk scoring in emergency department's UGIB patients for mortality, rebleeding, need for endoscopic therapy, blood transfusion, and ICU admission. AIMS65 is a scoring system developed by Saltzman et al. on 29.222 patients to predict inpatient mortality in UGIB patients (8). A total of 20 studies included in this systematic review reported a various follow-up time to predict mortality indicating that AIMS65 had an acceptable discriminative performance in most studies. Hyett et al. reported excellent discriminative performance for inpatient mortality using optimal cut-off ≥ 2. This is not surprising even though the accuracy showed better performance than the derived study because AIMS65 was established for that (19). Zhao et al using the same optimal cut-off reported good discrimination for inpatient mortality for elderly UGIB patients above 65 years in which they had at least one comorbid, and also reported in non-survival patients they had significantly lower hemoglobin levels (21). Lau et al. and Martı´nez-Cara et al. reported good and fair discriminative performance for inpatient mortality using cutoff ≥ 1 (11,13).

Martı´nez-Cara et al. also reported fair discriminative performance for 6-month mortality using cut-off ≥ 2. Extending time to follow-up was considered because patients with UGIB could challenge the precarious clinical balance of frail patients, such as patients with cirrhotic and cardiovascular diseases with the result that cause delayed death (11). Robertson et al. using cut-off ≥ 3 showed good discriminative performance in predicting inpatient mortality (20). Zhong et al. and Gu et al. reported good and excellent discriminative performance using cut-off ≥ 2 in predicting in-hospital mortality in the Chinese population (12,24). Chang et al. reported fair discriminative performance using cut-off ≥ 3 in predicting in-hospital mortality and specified that AIMS65 showed significant predictive accuracy in variceal bleeding than non-variceal bleeding (18). Abougergi et al. reported discriminative performance ≥ 0.7 using optimal cut-off ≥ 4 not only for in-hospital mortality but also for 30-day mortality (10).

Table 6. Predictive Ability of AIMS65 to Predict the Need for Endoscopic Therapy

Study	Optimal Cut-off	AUC and Category	Sensitivity/ Specificity (%)	PPV/NPV(%)
Thandassery et al.	≥2	0.48 (95% CI, 0.39–0.56) (Poor)	NS	NS
Martı´nez-Cara et al.	≥1	0.62 (95% CI, 0.56–0.68) (Poor)	87/28	45/76
Stanley et al.	≥1	0.63 (95% CI, 0.60–0.65) (Poor)	79.7/38.7	25.9/87.6
Shafaghi et al.	≥2	0.562 (95% CI, 0.487–0.637) (Poor)	NS	NS
Redondo-Cerezo et al.	≥1	0.59 (95% CI, 0.54–0.64) (Poor)	NS	NS

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

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Table 7. Predictive Ability of AIMS65 to Predict Blood Transfusion

Study	Optimal Cut-off	AUC and Category	Sensitivity/ Specificity (%)	PPV/NPV(%)
Thandassery et al.	≥2	0.60 (95% CI, 0.51–0.67) (Poor)	NS	NS
Martı´nez-Cara et al.	≥1	0.71 (95% CI, 0.65–0.77) (Fair)	88/37	69/64
Robertson et al.	≥2	0.72 (95% CI, 0.67–0.77) (Fair)	71/63	NS
Lau et al.	≥1	0.57 (95% CI, 0.43–0.68) (Poor)	60.9/48.1	20.3/8.5
Shafaghi et al.	≥2	0.674 (95% CI 0.628–0.721) (Poor)	NS	NS
Saffouri et al.	≥1	0.692 (95% CI, 0.663–0.720) (Poor)	NS	NS
Sachan et al.	≥2	0.643 (95% CI, 0.574–0.711) (Poor)	68.1/55.4	NS

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

Table 8. Predictive Ability of AIMS65 to Predict ICU Admission

Study	Optimal Cut-off	AUC and Category	Sensitivity/ Specificity (%)	PPV/NPV(%)
Thandassery et al	≥2	0.61 (95% CI, 0.52–0.70) (Poor)	NS	NS
Robertson et al.	≥2	0.74 (95% CI, 0.68–0.80) (Fair)	88/47	NS

*AUC, area under the curve; PPV, positive predictive value; NPV; negative predictive value, NS; not stated.
*AUC thresholds : excellent (AUC ≥0.90), good (AUC ≥0.80 and <0.90), fair (AUC ≥0.70 and <0.80), and poor (AUC <0.70)

Stanley et al. (n = 3012) is the only study that collected data from six countries. The study reported fair discriminative performance for 30-day mortality using cut-off ≥ 2 and stated that AIMS65 scores had a lack of measurement for albumin that led to an underestimation of the accuracy of AIMS65 scores to identify low-risk patients. Redondo-Cerezo et al. using a similar cut-off reported fair discriminative and stated that low albumin levels might be a surrogate marker of severe comorbidities that lead to adverse outcomes (6,14). Kalkan et al. and Tang et al. used a cut-off ≥ 2.5 in predicting 30-day mortality.

Kalkan et al. reported good discriminative performance in which the population included in those studies only ≥ 60 years old, It also stated that increased risk of mortality was associated with serum albumin, hemoglobin level, multiple medications, and creatinine level, age, and comorbidity in which multiple medications and elevated creatinine level was an independent risk factor for mortality (22). Sachan et al. reported fair discriminative performance in 8-week mortality using cut-off ≥ 2. This study reported the most common etiology for UGIB was variceal bleeding, replacing peptic ulcer disease in most studies that reported the etiology of all-cause UGIB. Thandassery et al. using optimal cut-off≥ 2 reported the mortality incidence of AIMS65 in scores 0, 1, 2, 3, and 4 are about 3%, 7.8%, 20%, 36%, and 40%, respectively (7,17).

Despite most included studies reporting fair to excellent discriminative performance for mortality, three studies reported poor discriminative performance. Shafaghi et al. using a cut-off value ≥ 2 for inpatient mortality stated although albumin is an independent risk factor that is included in the variable, the albumin threshold is not the best to get one point in AIMS65 scores. This study reported that 41.14% of patients in the non-survival group had albumin ranging between 3 to 3.5 so changing the Albumin threshold to 3 to 3.5 in AIMS65 increased its discriminative performance to predicting mortality from 0.67 to 0.72 (25). Liu et al using cut-off ≥ 0.5 for 90-day mortality stated that AIMS65 had a lower discriminative performance compared with

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ABC scores (0.672 vs 0.722) but had a sensitivity higher than ABC score (87.18% vs 76.07%) (16). The largest international multicenter cohort by Laursen et al. in 2021 (n=4019) collected data from Israel, Spanyol, and Italy showed poor discriminative performance in predicting 30-day mortality in the Italian population in a setting with the largest population in this study. This condition affects the overall discriminative performance of AIMS65 scores in this study. The lower predictive accuracy of AIMS65 in the Italian cohort may be explained by a high proportion of cirrhotic in high-risk patients about 21% (27).

Accuracy of scores for predicting rebleeding events showed fair and good discriminative performance by Zhong et al. and Kalkan et al. Kalkan et al. stated that AIMS65 using a cut-off score ≥ 2.5 predicted rebleeding with 75.5% sensitivity and 89.4% specificity (12,22). However, the remaining studies reported poor discriminative performance for rebleeding events. Studies using cut-off value ≥ 2 with sensitivity and specificity reported are Hyett et al. about 57% and 73%, Robertson et al about 76% and 44%, Zhao et al. about 74% and 52%, and Sachan et al. about 78.9% and 48.3%. It showed inconsistent sensitivity and specificity that led to hesitation for its predictive ability in terms of discriminative performance (17,19–21).

Thandassery et al. using a similar cut-off reported that rebleeding events are not linear with increases in scores. Scores 0, 1, 2, 3, and 4 are reported around 6.1%, 10.9%, 15%, 4%, and 20%, respectively. The need for endoscopic therapy showed poor discriminative performance in all included studies. Martı´nez-Cara et al stated that AIMS65 is an optimal scoring for low-risk patients, especially if the goal is to avoid endoscopy. It was caused by 16 patients with AIMS65 scores of 0 still needing endoscopic therapy. Thandassery et al. reported no significant difference between low-risk (< 2) and high-risk (≥ 2) patients in need of endoscopic therapy (26.1% vs 21.8%). This study also reported about 37 patients with a score of 0 and 15 patients with a score of 1 still required endoscopic therapy. Most studies are concerned about biases because the need for endoscopic therapy is carried out due to early endoscopic examination by a physician (7,11).

Blood transfusions showed fair discriminative only in two studies. Martı´nez-Cara et al. using optimal cut-off ≥ 1 stated about 30% of non-survival patients had cardiovascular disease, which may affect the need for blood transfusion. Lau et al using optimal cut-off ≥ 1 showed poor discrimination performance. It may be explained because hemoglobin level is not included as a variable component that led to an inability to predict the need for blood transfusion. Blood transfusion requirements, as an endpoint for UGIB, have an essential role in resuscitation rather than intervention. It may raise questions as to whether the need for blood transfusion should be included as an endpoint (11,13). ICU admission was only reported in 2 studies with different discriminative performances. Robertson et al. showed fair discriminative performance (AUC 0.74) and reported that patients managed in the general ward who required ICU admission are about 56 (13.2%) patients. Thandassery et al. showed poor discriminative performance (AUC 0.61). It is also stated although significant difference in the number of low-risk and high-risk patients in ICU admission (16.8% vs 38.2%, p=0.001), the study reported 11 (8.3%) patients with a score of 0 and 22 (34.3%) patients with a score 1 underwent admission to ICU. ICU admission has an important role in the management of UGIB patients in critical condition or requires

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close monitoring to improve their quality of life, while low-risk patients on AIMS65 scores do not avoid the chances admitted to ICU (7,20).

A good scoring system shows a good fit between the probabilities calculated using the scoring system and the outcomes observed. Discriminative performance is an essential indicator of predictive accuracy to overcome a lack of accuracy using sensitivity or specificity only. A cut-off for each scoring system is also important to distinguish low-risk and high-risk in predicting clinical outcomes (28). Unfortunately, cut-off values were reported almost differently for each included study. The reason for the inconsistent cut-off value from the studies included is difficult to explain. However, this condition might be due to some differences in those studies such as participant's ethnicity, UGIB etiology, use of medical treatment before endoscopy, time of endoscopy, and adherence to the guidelines regarding endoscopic therapy (23,24).

This systematic review shows a lack of evidence for discriminative performance ranging from fair to excellent in predicting rebleeding events, the need for endoscopic treatment, blood transfusion, and ICU admission. AIMS65 only showed sufficient evidence of fair to excellent discriminative performance in predicting mortality. It is clinically important because knowing which patients are at a true high risk of mortality can help to guide limited resources such as emergency endoscopy or ICU beds. AIMS65 included variables that are easily remembered, obtained, and less subjective. Furthermore, the variables are non-weighted and easy to calculate within 12 hours as part of the initial evaluation in ED. This is very potent to ensure objective assessment and applicable to enhance decision-making than individual clinical judgment only as an early risk stratification assessment (2,4,7).

All studies included in this study were conducted in the Emergency Departments, so it fits in line with the main objective of this review. We also determined, especially for clinical outcomes that it might be favorable to consider it as decision-support rather than composite outcomes. To our knowledge, this review is among the few that systematically synthesize on specific topic of AIMS65 score in patients with UGIB. Additionally, all included studies were very recent and publicized from 2012 to 2022.

However, this study has some limitations. First, the clinical outcomes of the need for intervention are limited to the need for endoscopic therapy, blood transfusion, and ICU admission. Surgery and radiology may be considered as clinical outcomes for this study. Second, lack of studies that reported long-term mortality or rebleeding events. There is only one study that reported mortality for 6 months. Another limitation is all included studies do not report calibration performance in analysis. Knowing that the included studies were designed as a validation study, recent impact analysis studies are needed to evaluate the usefulness of the score in a clinical setting in terms of patient satisfaction or resource/time allocation.

CONCLUSION

In conclusion, AIMS65 is a simple, non-dependent-to-endoscopic examination, and easily calculated, so it is practical for UGIB cases in the emergency department. AIMS65 showed fair to excellent evidence in predicting mortality, but the evidence for predicting rebleeding events, the need for endoscopic therapy, blood transfusion, and ICU admission, says otherwise. However, AIMS65 still has a

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critically important role in early decision-making and triage for UGIB patients.

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Conflict of Interest
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