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Original Research Article

RISK PREDICTION IN PATIENTS WITH ACUTE VARICEAL BLEED – A META-ANALYSIS

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Abstract

Background: Risk stratification is necessary for acute variceal bleeding (AVB), a potentially fatal disease, in order to direct therapeutic treatment. It's still up for debate which risk system would most correctly represent the prognosis. Our goal was to perform a meta-analysis of the predictive usefulness of MELD, CTP, Rockall (clinical and complete scores), GBS and AIMS65. **Materials and Methods:** A search was conducted using PubMed, Web of Science, Embase, Cochrane library. There were twenty-eight articles in the study. The predicted accuracy was combined using the MedCalc and Meta-DiSc softwares. **Result:** In terms of in-hospital mortality, the combined AUCs for CTP, AIMS65, MELD, Full-Rockall, and GBS were 0.824, 0.793, 0.788, 0.75, and 0.683, in that order. CTP had the specificity of 0.666 (95% CI: 0.635–0.696) and has highest sensitivity of 0.910 (95% CI: 0.864–0.944). With a sensitivity of 0.679 (95% CI: 0.617–0.736) and a specificity of 0.774 (95% CI: 0.749–0.798), AIMS65 demonstrated the highest specificity. AUCs for follow-up mortality were 0.798, 0.77, 0.746, 0.704, 0.678, and 0.618 for MELD, AIMS65, CTP, Clinical Rockall, Full-Rockall, and GBS, respectively. CTP was better With the highest specificity (0.806, 95% CI: 0.763–0.843) and a better sensitivity of 0.722 (95% CI: 0.628–0.804). GBS showed highest sensitivity of 0.800 (95% CI:0.696–0.881)with specificity of 0.412 (95% CI:0.368–0.457) . Regarding re-bleeding, none of the scores fared well. **Conclusion:** Our systematic evaluation could not identify any risk scores that were optimal. When it came to determining which AVB patients were at low risk during follow-up and which ones were at high risk of dying in the hospital, CTP outperformed other risk ratings. Guidelines have recommended the use of GBS to risk stratification of patients with upper gastrointestinal bleeding,In this study ability of GBS was limited as we studied only variceal bleeding.

INTRODUCTION

The incidence of acute variceal bleeding (AVB), which is second only to peptic ulcers in terms of causes of acute upper gastrointestinal bleeding (AUGIB), is quite high.[1] They most frequently result from portal hypertension,[2] which is frequently associated with cirrhosis.

Varices occur at rate of 5–15% per year are detected in 50% of cirrhotic cases.[3] Every episode of variceal hemorrhage has a 6-week death rate of about 20%.[3] Treatment that is prompt and accurate can lower death rates. It is proposed that risk stratification scores should be used as soon as possible in patients with AUGIB including ulcer and non-variceal bleeding.[4–6]

The AIMS65 score, the Rockall score, and the Glasgow-Blatchford score (GBS) are used scores to predict upper gastrointestinal hemorrhage. The GBS was created and approved in 2000 to forecast mortality, rebleeding while hospitalized, and the need for intervention.[7]

The Rockall score, which comes in two forms—clinical and full—was developed in 1996 to forecast both death and re-bleeding.[8] The AIMS65 score was created and validated by Saltzman et al. in 2011 as a

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predictor of in-hospital death.[9] A useful method for assessing the prognosis of chronic liver disease, particularly cirrhosis, is the Child-Pugh score (CTP).[10] The model for end-stage liver disease (MELD) is another scoring system for determining how serious chronic liver disease is. It is frequently utilized procedure and rank the order of priority for receiving a liver transplant.[11,12] The two staging system's ability to predict the outcomes of AVB patients had been documented in earlier research, but it was unclear which would be more accurate in predicting the prognosis.[13,14] Our goal is to perform a comprehensive analysis of the predictive significance of GBS, AIMS65, Rockall (both clinical and full Rockall scores), CTP, and MELD in risk stratification for AVB patients with regard to death and re-bleeding.

MATERIALS AND METHODS

Search strategy: The terms "risk score" and "variceal bleeding" were looked up in from the start until December 2023, PubMed, Web of Science, Embase, the Cochrane library, were all included.

Study selection: Articles that are eligible should fulfil the following requirements:

1. Adults (~18 years old) with verified AVB presentations using a fundal, oesophageal, or upper GI endoscopy.
2. The GBS, AIMS65, Rockall (clinical and complete scores), CTP and MELD scores studies were all included in this meta-analysis.
3. Every risk score ought to align with the globally acknowledged norm. Duplicate articles, reviews, letters to the editor, case reports, animal research, and children's studies were among the exclusion criteria.

Measures of outcome: Re-bleeding and mortality were among the results. Overall death, including in-hospital death and follow-up death within three months was referred to as mortality.

Re-bleeding was defined as variceal bleeding following a 24 hours of clinically stable period with haemostasis. Categorized as in-hospital re-bleeding and follow-up re-bleeding,(follow-up re-bleeding is within three months). A seven-day follow-up period was deemed to be in the hospital.

Data abstraction: Abstract Data was taken from of publications that were eligible. In theory, data from tests with an AUC (Area Under Curve) less than 0.5 were excluded from the meta-analysis.[15]

Quality assessment: The quality and bias risk of the included articles were evaluated using the QUADAS-2 program.[16] This tool assesses the possibility of bias stemming from four factors: research flow and scheduling, reference standard, index test, and patient selection. The reference standards pertain to the patient outcomes within the follow-up.

Statistical analysis: The AUC was primarily used to evaluate each scoring system's capacity to forecast the outcomes (mortality and re-bleeding). According to this meta-analysis, AUCs and SEs (standard error) were applied. In the event that the studies did not publish the SEs, the calculation was as follows: SE 1/4 upper limit of 95% CI – lower limit of 95% CI / (2*1.96).[17] The predictive power of a pooled AUC of 0.5 was deemed to be zero, whereas values between 0.5 and 0.7 were deemed to have poor predictive power, values between 0.7 and 0.9 were deemed to have excellent predictive power, and a value of 1 was deemed to be a perfect measure.[18]

RESULTS

Selection of studies: The electronic search yielded up 121 articles in total. The 59 duplicates were eliminated, and then the lefts were scanned using inclusion and exclusion criteria. After reviewing the abstracts and titles, we decided to eliminate 20 studies. A total of 42 papers were reviewed in full. 4 evaluations were disqualified due to the incorrect study type. 8 studies studied other scores which were new or not validated and needed further research. Additionally 2 studies was disqualified because an endoscope was not used to confirm the UGIB. Finally, there were 28 articles included in the research.[13,14,19–44] Refer to [Figure 1].

Ynopsis of the articles that are included

This review contained twenty-eight studies [Table 5]. The included studies were released between 2005 and 2024. Every study was carried out over a three-month period to evaluate mortality and re-bleeding outcomes. Of the 28 investigations, 11 were prospective in nature. Sensitivity and specificity values were published in nine research.[19,21,26,27,32,34,36,38,42] For every study, there were AUCs and 95% CIs.

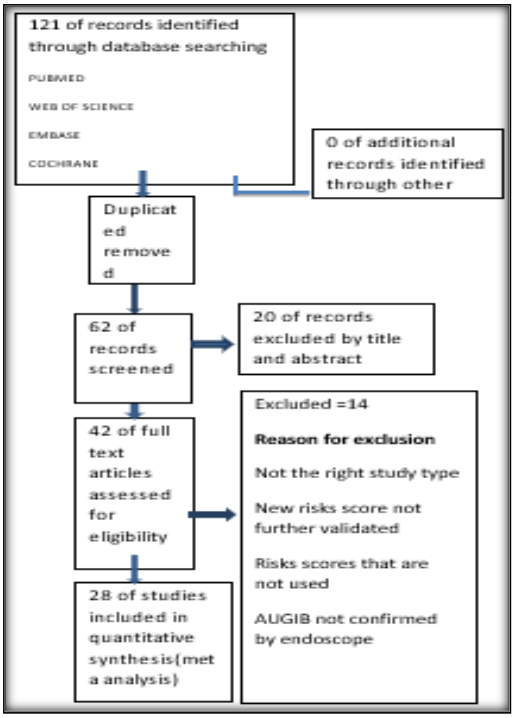

Figure 1: Flowchart showing the process for selecting eligible studies in this meta-analysis

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Risk of bias / quality of studies: Four studies failed to state whether patients were enrolled consecutively nor provided exclusion criteria, which raised concerns bias in patient selection is highly likely.[20,22,23,44] Bias in the index test was minimal.

Outcomes of meta-analysis: There was no heterogeneity in this study due to the threshold effect, (according to the diagnostic threshold analysis). The MedCalc version's 15.2 aggregated AUC values are shown in Tables 1,2,3 and 4. Information was arranged according to follow-up duration.

Mortality

In terms of in-hospital mortality, the pooled AUCs for CTP, AIMS65, MELD, Full-Rockall, and GBS were 0.824, 0.793, 0.788, 0.75, and 0.683, respectively (Table 1). MELD, AIMS65, CTP, Clinical Rockall, Full-Rockall, and GBS each had a pooled AUC of 0.798, 0.77, 0.746, 0.704, 0.678, and 0.618 for follow-up mortality [Table 3]. With regard to overall mortality, CTP demonstrated strong specificity (0.707, 95% CI: 0.682–0.731) and a high sensitivity (0.848, 95% CI: 0.805–0.885).

We performed a subgroup analysis based on follow-up time. CTP demonstrated a strong sensitivity of 0.910 (95% CI: 0.864–0.944) and specificity of 0.666 (95% CI: 0.635–0.696) with respect to in-hospital mortality. As for follow-up mortality, GBS had the highest sensitivity of 0.800 (95% CI: 0.696–0.881) and a specificity of 0.412 (95% CI: 0.368–0.457) [Table 3].

AIMS65 demonstrated the greatest value of 0.766 (95% CI: 0.745–0.787) for total mortality specificity and 0.660 (95% CI: 0.606–0.710) for sensitivity. Within subgroup analysis. The results indicate that, in terms of follow-up time, AIMS65 had the highest specificity in terms of in-hospital mortality, with a sensitivity of 0.679 (95% CI: 0.617–0.736) and a specificity of 0.774 (95% CI: 0.749–0.798), while CTP had the highest specificity in terms of follow-up mortality, with a sensitivity of 0.722 (0.628–0.804), as shown in [Table 2]

Re-bleeding

As for re-bleeding, none of the scores fared particularly well. Clinical Rockall had the strongest predictive value of AUC (0.689, 95% CI: 0.627–0.752) for in-hospital recurrent bleeding [Table 3]. AIMS65 had the greatest predictive value of AUC (0.682, 95% CI: 0.614–0.750) for follow-up re-bleeding [Table 4]. Regardless of the follow-up period, no score demonstrated high predictive value with an AUC greater than 0.7.

Table 1: predicting in hospital mortality.

Scores	N (studies)	AUC	SE	95%CI	P value
CTP	9	0.824	0.0102	0.804–0.844	<.001
AIMS65	8	0.793	0.0475	0.700– 0.886	<.001
MELD	10	0.788	0.0269	0.735–0.840	<.001
Full-Rockall	5	0.75	0.0474	0.657–0.843	<.001
GBS	7	0.683	0.0364	0.611–0.754	<.001

Table 2 scores for in-hospital rebleed

Scores	N (studies)	AUC	SE	95%CI	P value
Clinical Rockall	2	0.689	0.0318	0.627–0.752	<.001
CTP	2	0.688	0.0307	0.627–0.748	<.001
MELD	3	0.586	0.0383	0.511–0.661	<.001
GBS	3	0.576	0.0247	0.528–0.624	<.001
AIMS65	4	0.557	0.0208	0.516–0.597	<.001

Table 3: predicting follow-up mortality

Scores	N (studies)	AUC	SE	95%CI	P value
MELD	11	0.798	0.0134	0.772–0.824	<.001
AIMS65	9	0.77	0.0214	0.728–0.812	<.001
Clinical Rockall	3	0.704	0.0292	0.647–0.761	<.001
CTP	10	0.746	0.0358	0.675–0.816	<.001
Full-Rockall	6	0.678	0.0365	0.606–0.749	<.001
GBS	7	0.618	0.0183	0.5820.654	<.001

Table 4: scores for follow up re-bleeding

Scores	N (studies)	AUC	SE	95%CI	P value
AIMS65	7	0.682	0.0347	0.614–0.750	<.001
CTP	2	0.661	0.0335	0.595–0.727	<.001
MELD	4	0.648	0.0533	0.544–0.753	<.001
GBS	6	0.578	0.0197	0.540–0.617	<.001
Clinical Rockall	3	0.616	0.041	0.536–0.696	<.001
Full-Rockall	5	0.610	0.0217	0.567–0.652	<.001

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Table 5

First author, study	Country	Number of patients	Males (%)	Age (year) (mean ± SD or range)	Risk scores	Outcomes
Zhao,[14]	Australia	379	224 (59.1%)	53:7 ± 1:3	Child–Pugh MELD	In-hospital death
Robertson,[42]	Australia	222	173 (78%)	56 (18–88)	AIMS65 clinical Rockall full Rockall MELD Child–Pugh	In-patient mortality, 6-week mortality and in-patient rebleeding,
Chang,[41]	Thailand	70	55(78.6%)	56.1 ± 12.7	AIMS65 GBS full Rockall	In-hospital death and in-hospital rebleeding
Buckholz,[40]	New York	223	156 (70%)	61 (–)	Child–Pugh MELD	6-week mortality
Tantai,[38]	China	330	203(61.5%)	54.9 ± 12.7	Child–Pugh MELD clinical Rockall GBS AIMS65	In-hospital rebleeding and in-hospital mortality
Rout,[37]	India	572	474 (82.9%)	43.5 ± 13.6	Clinical Rockall full Rockall, GBS AIMS65	42-d mortality and 42-d rebleeding
Chandnani,[36]	India	141	40 (28.36)	–	Full Rockall, GBS AIMS65	30-d death and 30-d rebleeding
Wang,[34]	China	202	150 (74.3%)	56.8 ± 11.8	AIMS65 GBS full Rockall MELD Child–Pugh	6-week mortality
Mandal,[33]	USA	75	51(67.7%)	52.5 (–)	Child–Pugh MELD	In-hospital mortality
Hassanien,[32]	Egypt	714	500 (70%)	57.59 ± 0.46	Child–Pugh MELD AIMS65	In-hospital mortality
Iino,[31]	Japan	47	39 (83.0%)	60 (56–67)	GBS Child–Pugh MELD	1-week mortality and 6-week mortality
Fortune,[30]	USA	70	53(75.7%)	51 (48–57)	Child–Pugh MELD	6-week mortality
Choe,[29]	Korea	286	198 (69.2%)	57.9 (23–97)	GBS, full Rockall; AIMS65	In-hospital mortality, 30-d mortality and 30-d rebleeding
Mohammad,[27]	Egypt	120	92 (76.67%)	56.94 ± 9.20	Child–Pugh AIMS65: MELD	In-hospital mortality
Budimir,[26]	Croatia	225	162 (72%)	61.3 ± 11.57	GBS clinical Rockall AIMS65	30-d rebleeding and 30-d mortality
Reed,[25]	Scotland	71	43 (61%)	56 (–)	GBS full Rockall clinical Rockall	3-month mortality and 3-month rebleed
Sempere,[21]	Spain	201	142 (70.6%)	59.48 ± 11.78	Child–Pugh MELD score	6-week mortality and 3-month mortality
Flores,[13]	Mexico	212	145(68.4%)	53 ± 12	Child–Pugh MELD score	In-hospital mortality
Dunckley,[20]	-	63	-	-	MELD, full Rockall Child–Pugh GBS	In-patient mortality and 30-d rebleed
Amitrano,[19]	Italy	172	108 (62.79%)	61.3 ± 11.4	MELD Child–Pugh	6-week mortality and 3-month mortality
Su,[43]	China	182	89 (48.9%)	59.7 ± 11.9	MELD GBS AIMS65	In-hospital mortality and in-hospital rebleed
Wang,[22]	China	365	290 (79.5%)	48.8 (25–85)	MELD Child–Pugh	3-month rebleeding
Guo,[44]	China	82	49 (59.8%)	56.74 ± 6.41	MELD AIMS65	2-month mortality and 2-month rebleeding
Gao,[39]	China	270	105 (38.9%)	69.5 (50–86)	GBS AIMS65	In-hospital rebleeding and in-hospital mortality
Jin,[35]	China	110	71 (64.5%)	53.5 ± 18.2	MELD, AIMS65	6-week mortality and 6-week rebleeding
Wang,[28]	China	152	108 (71.1%)	53.56 ± 15.93	AIMS65	30-d mortality and 30-d rebleeding

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Jiang,[24]	China	101	62 (61.4%)	63.6 ± 14.8	Child–Pugh MELD	30-d mortality
Fang,[23]	China	104	57 (54.8%)	53.2 ± 8.6	Child–Pugh MELD	3-month mortality and 3-month rebleeding

DISCUSSION

AVB is a major emergency because of its rapid bleeding, high death rate, and high rate of re-bleeding. It is the liver cirrhosis consequence that poses the greatest risk to life. The death and re-bleeding rate of AVB have decreased recently due to the on-going development of new medications, endoscopic intervention, and other innovative diagnostic and treatment technologies. In spite of this, 20% of cases still result in death after six weeks.[3]

Good predictive value was demonstrated by CTP, AIMS65, and MELD for in-hospital mortality and follow-up mortality. Full-Rockall showed good predictive power for in-hospital mortality has low predictive power for follow-up mortality. Clinical Rockall demonstrated a strong ability to predict follow-up mortality. Regardless of the duration of follow-up, GBS has poor predictive power. Regarding re bleeding, no score exhibited strong predictive ability.

CTP (child-turcotte-pugh)

The straightforward and conventional CTP score and categorization have been used for a long time to assess prognosis, surgical risk, and liver function reserve.[10]

In this study, we examined CTP's predictive usefulness in predicting AVB patients' outcomes. According to the data, CTP had the best predictive power for in-hospital mortality, with a pooled AUC value of 0.824. With a specificity of 0.666 (95% CI: 0.635–0.696) and the best pooled sensitivity (0.910, 95% CI: 0.864–0.944), CTP outperformed other risk scores in identifying hospitalized patients who were at high risk of mortality. With a pooled AUC value of 0.746 for follow-up mortality, there was a small drop in predictive power. Possessing a high sensitivity of 0.722 and High pooled specificity of 0.806, Significant ramifications for healthcare were caused by the effectiveness of CTP in triaging low-risk patients for early release or less extensive treatment.

MELD (model for end stage liver disease)

Malinchoc was the one who first proposed MELD, and Malinchoc and Kamath later modified and enhanced it.[11,12] Forman stated that the MELD score was a useful addition to the prognostic toolkit and that it was likely to overthrow the Child-Turcotte-Pugh technique as the gold standard for predicting chronic liver disease.[45] On the other hand, Cholongitas claimed that in non-transplant environments, MELD did not outperform the Child–Turcotte–Pugh score.[46] In terms of in-hospital mortality, MELD's pooled AUC value was lower than CTP's (AUC: 0.788 vs. 0.824), but it was greatest (0.798) in terms of follow-up mortality. Consequently, MELD outperformed CTP in predicting outpatient outcomes in 3-month but underperformed it in predicting in-hospital mortality.

GBS (Glasgow Blatchford score): Stanley proposed that UGIB patients with an area under the ROC curve of 0.90 might be safely managed as out patients by using the GBS.[47] According to a prospective, international, multi center research with 3012 patients, GBS had the highest accuracy (AUC: 0.86) in predicting intervention or death.[48] There were only 143 individuals with AVB in that study, and they made up just 7% of all patients who had endoscopied. The outcomes of our meta-analysis varied when AVB patients were the only ones included. GBS had no AUC value greater than 0.7 and shown poor predictive potential for both death and re-bleeding outcomes. The reason could be GBS was formulated in most ANVUGIB, who typically had a milder illness and a better prognosis.

AIMS65 (albumin,INR, mental status, systolic BP, Age > 65): Its primary purpose is to evaluate the UGIB patient fatality rate.[9] In 278 UGIB patients, Hyett et al. compared the AIMS65 and GBS scores and found that the AIMS65 score was better in predicting inpatient mortality (AUC, 0.93 vs. 0.68, p <.001).[49] The findings of this meta-analysis, which focused solely on AVB patients, were consistent with earlier studies. With a pooled AUC value of 0.77 in follow-up mortality and 0.793 in hospitalization, AIMS65 outperformed GBS.

Rock all: The Rockall score was created and established in 1996,[8] on the basis of a prospective, unselected, multicentre research. In rock all score Our meta-analysis's findings for AVB patients showed a pooled AUC value of 0.75 for in-hospital mortality, the Full Rockall score demonstrated strong predictive power. On the other hand, follow-up mortality was modest (AUC: 0.678). The application of complete Rockall scores was limited because not all patients had the opportunity to undergo endoscopy. The clinical Rockall score emerged as a solution to such issue. On the other hand, the included publications about the clinical Rockall score showed a decrease (n ¼ 3) in comparison to other risk scores and the in-hospital mortality meta-analysis could not be completed. Given that the follow-up mortality pooled AUC was 0.704, the clinical Rockall score was found to have a modest predictive ability.

Limitation

A limitation of this meta-analysis is small number of included studies of clinical and full Rockall scores when pooling sensitivity and specificity. The majority of the AVB patients had cirrhosis. But there are other possible causes of cirrhosis, such as alcoholism, viruses that cause hepatitis, and so on. Furthermore, patients with AVB were included in

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several trials due to both portal hypertension from other causes and cirrhosis. The distinct etiology of gastric and oesophageal varices may lead to bias in selection. Because varied follow-up times were used in the trials, there was substantial clinical heterogeneity. A machine learning algorithm for UGIB powered by artificial intelligence was created and tested by Shung Dennis L. It demonstrated 100% sensitivity and 26% specificity.[50] Patients with AVB may benefit from a similar method.

CONCLUSION

Our comprehensive evaluation yielded no optimal identification of risk scores (CTP, MELD, GBS, AMIS65, full Rockall, andclinical Rockall). Compared to other risk ratings, CTP was better in determining which AVB patients are at low risk of dying during follow-up and which are at high risk of dying in the hospital. It has been suggested by guidelines that individuals with upper gastrointestinal bleeding should be risk-stratified using GBS. However, particular caution should be exercised when it is suspected that
stomach and oesophageal varices are the source of upper gastrointestinal bleeding.Because this meta-analysis revealed that GBS has a limited capacity to predict AVB patients' death and rebleeding. Further studies are required to confirm it in the future. Future research in artificial intelligence could be crucial in helping to risk-stratify AVB patients..

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