

Scoring Systems and Risk Stratification in Cirrhotic Patients with Acute Variceal Bleeding "Scoring in Variceal Bleeding"

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Abstract

Objectives: To find the most accurate, suitable and applicable scoring system used for prediction of outcome in cirrhotic patients with bleeding varices.

Methods: This prospective study included 120 cirrhotic patients with acute variceal bleeding, admitted at Department of Tropical Medicine and Gastroenterology in Sohag University Hospital over a one-year period (1/2015 to 1/2016). Clinical, laboratory and endoscopic parameters were studied, Child-Pugh (CTP) classification score, Model for end-stage liver disease (MELD) score, Acute physiology and chronic health evaluation II (APACHE II) score, sequential organ failure assessment (SOFA) score and AIMS65 score were calculated for all patients, univariate, multivariate analysis and performance was performed for all taken parameters and the scores.

Results: The 120 patients (92 male, 28 female) admitted during the study period, eight patients (6.67%) died in hospital. Higher age, presence of encephalopathy, rebleeding, and higher serum bilirubin were independent factors associated with higher hospital mortality. The largest area under the receiver operator curve (AUROC) was for AIMS65 score and SOFA score followed by MELD score and APACHEII score then Child score all of which achieved very good performance (AUROC > 0.8). AIMS 65 score has the best sensitivity, specificity negative and positive predictive values. Although AIMS65 score was not significantly different from MELD, SOFA, and APACHEII scores, it was the best among them in prediction of mortality.

Conclusions: AIMS65 score is best simple and applicable scoring system to independently predict mortality in those patients.

Keywords: AIMS65; Liver cirrosis; Variceal bleeding

Introduction

Acute upper gastrointestinal (GI) bleeding is a frequent cause of hospital emergency admissions worldwide [1]. Acute variceal hemorrhage (AVH) is the most dangerous complication of portal hypertension as it is associated with significantly higher morbidity and mortality [2]. The prognosis for cirrhotic patients associated with liver disease severity [3]. Child-pugh classification used to assess the severity of liver disease, higher scores significantly affects survival time. The mortality rate after the first episode of bleeding ranges from 15% to 80% and is higher with child's class B and C (60% to 80%) than with class A (15%) [4]. Many factors have been studied and found to be associated with increased risk of mortality in patients with bleeding varices [5]. When cirrhotic patients admitted to intensive care unit, the use of liver prognostic models as child-pugh and MELD scores were found to be poor predictors of outcome [6]. But in patients with acute variceal hemorrhage it still remains unclear if these models could do well for risk stratification among this group of patients.

Our aim is to evaluate the outcome of patients presented to our tertiary referral center with acute variceal bleeding and to study the best of the prognostic models for prediction of this outcome.

Patients and Methods

This prospective study included all adult cirrhotic patients admitted to Sohag University Hospital, Tropical Medicine Department with acute variceal bleeding (in the form of haematemesis, melena, and/or bloody fluids either as vomitus or drained by nasogastric tube) from 1/2015 to 1/2016.

The study was approved by the local ethics committee in Sohag faculty of medicine.

Inclusion criteria

Cirrhotic patients presented by bleeding varices (esophageal, fundal or both).

Exclusion criteria

Patients diagnosed to have other causes of upper GIT bleeding (such as: peptic ulcer disease, reflux esophagitis, erosions, antral vascular ectasia) previously or at endoscopy after admission.

A complete history, thorough physical examination, monitoring of vital signs, to all patients were done.

Liver function and serum creatinine were assessed on admission and serially during hospitalization. Complete blood count, serum

electrolytes, arterial blood gases, and number of units of blood received were recorded.

All patients underwent upper endoscopy and therapy was initiated according to the endoscopic findings, all the endoscopic finding were described according to the Japanese research society for portal hypertension [7].

Urine analysis, chest X-ray, and ascitic fluid analysis, were performed to detect sources of infection.

All patients underwent abdominal ultra-sonography and testing for the surface antigen of the hepatitis B virus (HBsAg) and hepatitis C virus antibodies (HCV Abs).

Prognostic scores were calculated from data collected on the 1st day of admission. Child-Turcotte-Pugh (CTP) score, model for end-stage liver disease (MELD), acute physiology and chronic health evaluation II (APACHE II) score and sepsis-associated organ failure assessment (SOFA) score were calculated according to the Pugh modification [8], United Network of Organ Sharing adjustments [9], Knaus et al. [10] Vincent et al. [11].

AIMS65 score was calculated according to Saltzman et al. [12], it was recently developed, this risk score could predicts in-hospital mortality, length of stay, and cost in patients with acute UGIB. The new score compromised from the following parameters: level of albumin less than 3.0 g/d L (A), international normalized ratio (INR) more than 1.5 (I), mental status alteration (M), systolic blood pressure \leq 90 mmHg (S), and age more than sixty five years. When more than two components of AIMS65 are present, the mortality risk is considered to be high.

Hypovolaemic shock

It was defined as the presence of decrease in systolic blood pressure into <90 mmHg; tachycardia > 100 beats/minute; and a decreased central venous pressure or jugular venous pressure [13].

Rebleeding is recurrent vomiting of blood, and/or melena with shock and/or decrease of at least 2 g/d L in hemoglobin concentration after initial treatment, resuscitation and/or indicated endoscopic therapy [14].

Transfusion requirements

The whole blood units and/or blood products needed to the admitted patient on the day of admission or five days afterword [15].

Blood transfusions initiated when the hemoglobin is less than 7 g/dL when there is no associated illness, our aim is to reach a level ≥ 7 g/dL. However, in patients presenting with UGIB and suffering from coronary artery disease, we need to reach hemoglobin level ≥ 9 g/dL to avoid adverse events of significant anemia. Fresh frozen plasma (FFP) or platelets transfused to patients with coagulopathy or uncontrolled bleeding and/or a severe thrombocytopenia ($<50,000/\mu\text{L}$) [16].

Esophageal balloon temponade

It was used when bleeding is rapid with haemodynamic instability before endoscopy.

Statistical analysis

Chi squared test or Fisher's exact test were used to analyze the data as appropriate. Univariate and multivariate analysis will be performed using logistic regression models.

Results

A total of 120 patients (92 male, 28 female) were admitted to our department over a period of one year due to acute upper GIT bleeding with bleeding attributed to gastroesophageal varices (GEV).

Demographic, clinical, laboratory, and endoscopic data are shown in Table 1.

The etiology of liver cirrhosis was HCV in 95 patients (79.17%) HBV in 5 patients (4.17%), infection with HBV and HCV in 2 patients (1.67%) and unknown in 18 patients (15%).

Infections were present in 16 patients including chest infection, spontaneous bacterial peritonitis (SBP), and bed sores. Hepatic encephalopathy was found in 28 patients, rebleeding occurred in 8 patients and, portal vein thrombosis (PVT) in 7 patients from 23 patients diagnosed hepatocellular carcinoma (HCC).

As regard the endoscopic findings: Esophageal varices were found in 105 patients, gastric varices were found in 6 patients, while 9 patients were found to have both gastric and esophageal varices.

Endoscopic interventions the patients, 107 patients had band ligation, 9 had histoacryle injection and 4 patients had both band ligation and histoacryle injection.

In our study 8 patients (6.67%) died, clinical characteristic of studied population in survivors and non survivors is shown in Table 1.

Parameter	Survivors 112 (93.33%)	Non- survivors 8 (6.67%)	P value
Age Mean (SD)	56.94 (9.20)	64.75 (16.69)	0.03*
Male Sex	85(75.89%)	7(87.50%)	0.68
Female sex	27(24.11%)	1(12.5%)	
Hypovolemic shock at admission	16 (14.29%)	3 (37.50%)	0.11
Melena	95 (84.82%)	8 (100%)	0.6
Presence of encephalopathy	20 (17.86%)	8 (100%)	$< 0.0001^*$
Need for balloon temponade	57 (50.89%)	5 (62.50%)	0.72
Presence of infection	11 (9.82%)	5 (62.50%)	0.001*

Re-bleeding	4 (3.57%)	4 (50.00%)	0.001*
No. of transfused blood units Mean (SD)	1.18 (1.57)	0.88 (0.83)	0.99
HCC	22 (19.64%)	1 (12.50%)	1
Etiology of cirrhosis			
HCV	89 (79.46%)	6 (75.00%)	0.77
HBV	5 (4.46%)	0	
HBV &HCV	2 (1.79%)	0	
Unknown	16 (14.29%)	2 (25.00%)	
Co-morbidity			
No	73 (65.18%)	5 (62.50%)	0.43
DM	32 (28.57%)	2 (25.00%)	
DM, HTN	2 (1.79%)	1 (12.50%)	
DM, HTN, COPD	1 (0.89%)	0	
HTN	4 (3.57%)	0	
Albumin Mean (SD)	2.72 (0.55)	2.23 (0.25)	0.01*
Bilirubin Mean(SD)	1.85 (1.48)	4.94 (2.87)	0.001*
INR Mean (SD)	1.38 (0.21)	1.56 (0.14)	0.02*
Prothrombin time Mean (SD)	15.71 (2.39)	17.58 (1.24)	0.03*
Prothrombin concentration Mean (SD)	64.39 (12.81)	52.56 (5.52)	0.01*
S. creatinine Mean (SD)	1.25 (0.53)	1.79 (0.66)	0.02*
Size of varices			
F1	9 (8.04%)	1 (12.50%)	0.98
F2	68 (60.71%)	4 (50.00%)	
F3	26 (23.21%)	3 (37.50%)	
Esophagus F1- Gastric F1	2 (1.79%)	0	
Esophagus F1- Gastric F2	2 (1.79%)	0	
Esophagus F2- Gastric F2	2 (1.79%)	0	
Esophagus F3- Gastric F1	2 (1.79%)	0	
Esophagus F3- Gastric F2	1 (0.89%)	0	
Endoscopic intervention			
Band ligation	99 (88.39%)	8 (100%)	
Histoacyl injection	9 (8.04%)	0	
Both	4 (3.57%)	0	

*Statistically Significant

Table 1: Comparing demographic, clinical, laboratory and endoscopic findings in survivors and non-survivors.

There was a significant difference between survivors and non survivors as regard the presence of encephalopathy ($p < 0.0001$), infection ($p=0.001$) and rebleeding ($p=0.001$) (Table 1).

Upon studying the laboratory and endoscopic characteristics in survivors and non-survivors we found that:

The non survivors had significantly lower albumin level ($2.23 (\pm 0.25)$ Vs. $2.72 (\pm 0.55)$, mg/dl, $p=0.01$) and higher bilirubin ($4.94 (\pm 2.87)$ vs. $1.85 (\pm 1.48)$ mg/ dl, $p=0.001$), with higher INR ($1.56 (\pm 0.14)$ vs. $1.38 (\pm 0.21)$, $p=0.02$) with more prolonged prothrombin time ($p=0.03$) and decreased prothrombin concentration ($p=0.01$).

Site, size of varices or type of endoscopic therapy didn't influence mortality (Table 1).

Hospital mortality was significantly high with Child C (87.5% vs. 26.79%) ($p=0.001$, MELD score > 18 ($p=0.0003$), APACHE II score > 14 ($p=0.0006$), SOFA score > 7 ($p=0.0001$) and AIMS65 score > 2 ($p=0.0001$).

By multivariate analysis we found that Higher age, presence of encephalopathy, rebleeding, and higher serum bilirubin were an independent factors for prediction of hospital mortality.

We analyze the prognostic risk stratification models in predicting hospital mortality; AIMS65 score and SOFA score found to have the largest area under the receiver operator curve (AUROC) was for followed by MELD score and APACHEII score then Child score, all of which achieved very good performance (AUROC > 0.8).

Pairwise comparison of (AUROC) showed no significant difference between AIMS65, MELD, SOFA, and APACHEII scores ($p < 0.05$). However, AIMS56 score was superior to with the best (AUROC) ($p > 0.05$). After evaluation of the performance of each model, AIMS 65 score has the best performance in prediction of mortality in patients with variceal bleeding, it has the higher sensitivity (100%), and negative predictive value (100%), but APACH II score has the highest specificity (98.2%), and positive predictive value (75.0%).

Discussion

In this study, we studied the factors associated with mortality in patients admitted to our hospital with AVH and liver cirrhosis and reported the outcome of those patients. Our in-hospital mortality (HM) rate of 7.67% is consistent with the experience from other centers. Although, this may be attributed to the relatively small sample size and including only patients who had an endoscopic intervention in our study. In 1998, Pauwels et al. [17] showed that in-hospital mortality in cirrhotic patients presented with acute variceal bleeding has decreased by 50% over the preceding 15 years. Chalasani et al. [18] in a large study over three years long reported that in-hospital mortality was 14.2%. In another large series of 403 cirrhotic patients and variceal bleeding, Del Olmo, et al. [19] reported a mortality rate of 7.4%.

In our study, older age was independently associated with hospital deaths following AVH this also previously reported by Das et al. [6] Du Cheyron et al. [20].

Our results revealed that increased serum bilirubin, presence of hepatic encephalopathy, and re-bleeding after endoscopy were independent predictors of mortality. These results are in line with Chojkier et al. [21] Afessa, et al. [22].

Magliocchetti et al. [23] further showed that Child-Pugh score, albumin level, encephalopathy, and GEV hemorrhage correlated with survival.

In our study, the type of endoscopic therapy (either band ligation, histoacryle injection, or both) and etiology of liver cirrhosis did not influence mortality and this correlates with findings of Hassanien et al. [24] However, presence of HCC and PVT were found also not to influence mortality and this does not correlate with this study.

In a large retrospective study of 403 cirrhotics with variceal bleed, renal failure with raised serum creatinine, post-gastroscopy re-bleeding, and presence of HCC and hepatic encephalopathy were found to be independent predictors of mortality [25]. The occurrence of rebleeding was significantly associated with mortality, a factor also reported in the series of Bamba et al. [5].

Portal vein thrombosis has no statistically significant difference between survivors and non-survivors in our study. These findings are in accordance with those of Moataz Hassanien et al. [24], although tumor infiltration to the portal vein seemed to increase the portal pressure and may increase the risk of uncontrolled bleeding.

Increased requirement of blood /blood product transfusion was significantly associated with mortality, this finding correlates with that of Al-Freah et al. [15]. Who reported that there was a 7% rise in hospital mortality with every unit increase in Packed RBCs transfusion on the day of admission. Increased requirements of blood transfusion was reported as a poor prognostic indicator with other researchers consistent with our finding [5,26].

We found that AIMS65 score is the best for predicting mortality among the mentioned 5 scores having the highest area under the curve. It was previously reported to be good predictor of outcome in patients with acute upper gastrointestinal hemorrhage by Nakamura et al. [27]. Moreover, Hyett et al. [28] found that AIMS65 score was better than Glasgow-Blatchford score for outcome prediction in those patients.

Also we found that SOFA score is superior to MELD score, APACHEII score, and Child's score in prediction of mortality with Child's (CP) score having the least area under the curve.

Cholongitas et al. [29] also reported that SOFA score had better predictive value compared to APACHE II and CP scores.

The child-pugh score had the worst performance, may be this is due to it doesn't include the kidney functions in its parameters [29]. However, this does not correlate with Afessa and Kubilis [21], who compared the prognostic performances of APACHE II and Child-Pugh score in 111 cirrhotic patients hospitalized for upper GI bleeding and did not find significant differences between the two scoring systems. In a single centre cohort of ICU admitted patients presented with acute upper gastrointestinal bleeding from varices Al-Freah et al. [15] found that MELD has the best performance as it could be best liver prognostic models and not significantly different from other ICU scoring models as predictors of outcome.

There are some limitations for this study including: First, it was performed in a single institution .Second, the relatively small sample size. Third, calculation of mortality was only during hospital admission, further follow up of the patients for 30 and 60 days was required. Finally, we only included patients who had an endoscopic intervention in our study.

Conclusion

Older age, presence of sepsis, serum bilirubin levels, presence of hepatic encephalopathy and re-bleeding after gastroscopy were independent predictors of mortality in our patients with liver cirrhosis and variceal bleeding. AIMS65 score was a simple and applicable scoring system to independently predict mortality in patients with variceal bleeding with high performance.

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