



Original article

Prognostic value of AIMS65 score in cirrhotic patients with variceal bleeding

Trong Nguyen Dang Huynh^{a*}

^aDepartment of Gastroenterology and Hepatology, Cho Ray hospital, Ho Chi Minh City, Vietnam.

Received April 13, 2021; Revised October 22, 2021; Accepted November 2, 2021

Abstract: Background: In cirrhotic patients, variceal bleeding remains a major cause of death. After a variceal bleeding episode, mortality and rebleeding rates spike for the first 6 weeks before levelling off. We aimed to evaluate the performance of AIMS65 score in comparison with Child-Turcotte-Pugh (CTP) score and model for end-stage liver disease (MELD) score in predicting 6-week mortality and rebleeding in cirrhotic patients with variceal bleeding. **Method:** Data were collected prospectively from patients with cirrhosis and variceal bleeding at Gastroenterology and Hepatology Department of Cho Ray hospital from September 2016 to April 2017. The primary endpoint was 6-week mortality and rebleeding. The prognostic value of AIMS65, CTP, and MELD scoring systems for 6-week mortality and rebleeding was compared by receiver operating characteristics curves (ROC) and the area under the curve (AUC). **Results:** Among 80 patients, 15% rebled and 25% died during 6-week follow-up. AUCROC of AIMS65, CTP, and MELD scores in predicting 6-week rebleeding were 0.68, 0.54, and 0.48, respectively. AUCROC of AIMS65, CTP, and MELD scores in predicting 6-week mortality were 0.80, 0.74, and 0.64, respectively. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of AIMS65 score at the cut-off point of 2 were 95%, 55%, 41.3%, and 97%, respectively. **Conclusion:** AIMS65 score is a simple yet applicable tool for risk stratification in cirrhotic patients with variceal bleeding. We recommend using AIMS65 score with a cut-off point of 2 to identify patients at increased risk for 6-week mortality after variceal bleeding.

Keywords: variceal bleeding; AIMS65 score; liver cirrhosis.

1. INTRODUCTION

Variceal bleeding is a major cause of death in cirrhotic patients. Hemostasis can be achieved by endoscopic therapy in up to 80% to 90% of patients with active bleeding [1]. However, approximately one-third of patients with variceal bleeding experienced rebleeding within 6 weeks. Rebleeding risk is greatest during the first 5 days and returns to baseline after the sixth week. The 6-week mortality rate after variceal bleeding is 25% to 30% [2].

6-week mortality was proposed to be the primary treatment endpoint for variceal bleeding by the Baveno VI consensus [3]. Recent American Association for the Study of

Liver Diseases (AASLD) guidelines pointed out that risk stratification in variceal bleeding is essential [4]. Several prognostic models were developed to predict mortality and rebleeding risk including CTP score, MELD score, and hepatic venous pressure gradient (HVPG) [5-7]. Ideally, high-risk patients identified by these models receive more aggressive treatment. However, these tools have limited use in clinical practice for some reasons: HVPG measurements are not widely available [5], some components of CTP score have subjectivity [8], and MELD score can be difficult to calculate [8]. In 2011, Saltzman et al. developed a new score called AIMS65 to identify patients with a high risk of in-hospital mortality after upper gastrointestinal bleeding.

*Address correspondence to Trong Nguyen Dang Huynh at the Department of Gastroenterology and Hepatology, Cho Ray hospital, Ho Chi Minh City, Vietnam; E-mail: huynhnguyendangtrong@gmail.com

DOI: 10.32895/UMP.MPR.6.1.4

AIMS65 score is composed of: Albumin level < 3 g/dL (**A**), INR > 1.5 (**I**), Altered Mental Status (**M**), Systolic Blood Pressure ≤ 90 mmHg (**S**), and age > 65 years (**65**). A patient gained 1 point for each risk factor [9]. Serum albumin < 3.0 g/dL and INR > 1.5 are generally considered poor prognostic factors of cirrhosis. Hence, AIMS65 score could be a useful model for risk stratification in variceal bleeding. However, there is not enough data in the literature about the credibility of this scoring system.

This study aimed to evaluate the ability of AIMS65 score in predicting 6-week mortality and rebleeding in cirrhotic patients with variceal bleeding and to compare it with CTP and MELD scores.

2. MATERIALS AND METHOD

2.1. Patient population

Data were collected prospectively at Gastroenterology and Hepatology Department of Cho Ray hospital, Ho Chi Minh City, Vietnam, from September 2016 to April 2017. Cho Ray hospital is a central-level hospital. It is the largest hospital in the South of Vietnam. All patients with cirrhosis and variceal bleeding were enrolled in the study. Cirrhosis was diagnosed based on past medical history, clinical assessment, laboratory tests, and imaging findings suggestive of liver cirrhosis. The source of bleeding was confirmed by endoscopy. Patients with stage D hepatocellular carcinoma (HCC), patients with variceal bleeding 6 weeks before admission, patients with incomplete records, and patients who lost contact before day 42 were excluded from this study. Patients with stage D HCC were excluded because of their high mortality rate (>60%) [5]. Informed consent was obtained from all subjects. The study protocol was approved

by the Board of Ethics in Biomedical Research of University and Pharmacy at Ho Chi Minh city (ID number: 216/DHYD-HD signed on July 19th, 2016).

2.2. Therapeutic interventions

Patients with variceal bleeding were treated with a combination of vasoactive drugs (octreotide or terlipressin), endoscopic band ligation (EVL), and antibiotic prophylaxis with ceftriaxone. Rescue therapy with Sengstaken–Blakemore balloon tamponade was applied in refractory bleeding. Secondary prophylaxis with propranolol was started and titrated to maximum tolerated dose if possible after the bleeding had been controlled. Time zero was the time of admission.

2.3. Methods

The primary endpoint of this study was 6-week mortality and rebleeding. Data regarding demographic, clinical, and laboratory information were collected from clinical records. AIMS65, CTP, and MELD scores were calculated from data obtained at initial presentation. Rebleeding was defined as new hematemesis or melena that occurred 24 hours after hemodynamic stability [10]. During hospitalization, clinical assessment was carried out every day for detecting symptoms of rebleeding. After discharge, telephone follow-up every 2 weeks was provided to collect information about rebleeding and mortality rate.

Calculation of the MELD score [11]: $MELD = 3.78 \times \log_e(\text{bilirubin [mg/dL]}) + 11.2 \times \log_e(\text{INR}) + 9.57 \times \log_e(\text{creatinine [mg/dL]}) + 6.43$

Calculation of the CTP score [12]:

Variables	1 point	2 points	3 points
Encephalopathy	None	Grade 1 – 2	Grade 3 – 4
Ascites	Absent	Mild to moderate	Severe
Bilirubin (mg/dL)	<2	2 – 3	>3
Bilirubin for PSC (mg/dL)	<4	4 – 10	>10
Albumin (g/dL)	>3.5	2.8 – 3.5	<2.8
Prothrombin (s prolonged)	< 4	4 – 6	>6
INR	<1.7	1.7 - 2.3	>2.3

2.4. Statistical analysis

The data analysis was performed by using SPSS 18 (SPSS Inc, Chicago). Continuous data were shown as mean ± standard deviation (SD). Categorical data were shown as frequencies. ROC curves with 95% confidence intervals (CI) were used to demonstrate the ability of AIMS65, CTP and MELD scores in predicting 6-week mortality and rebleeding. Comparison of AUCROCs was performed by Hanley & McNeil test using MedCalc Statistical Software version 19.8 (MedCalc Software Ltd, Ostend, Belgium). A *p*-value of < 0.05 was considered statistically significant. The predictive ability of AIMS65 score was analyzed based on sensitivity, specificity, PPV, and NPV. The optimal cut-off value was identified by Youden index analysis.

3. RESULTS

From September 2016 to April 2017, 84 patients were enrolled in the study. 2 patients lacked laboratory tests

required to calculate AIMS65 score (i.e albumin). 2 patients lost contact after discharge. Therefore, 80 out of the 84 patients had complete records. **Table 1** showed the clinical characteristics of these 80 patients. The majority of patients were male (80%). Alcoholic hepatitis was the most common cause of cirrhosis, followed by viral hepatitis. During the 6-week follow-up, the overall rebleeding and mortality rates were 15% and 25%, respectively. Timing of first rebleeding and death during 42-day follow-up was shown in **Figure 1** and **Figure 2**. 60% of patients rebled during the first 14 days. 75% of patients died during the first 14 days. **Table 2-4** showed rebleeding and mortality rate for each point of AIMS65, CTP, and MELD scores. 19/20 deceased patients had AIMS65 score of ≥ 2. AUCROCs for AIMS65, CTP, and MELD scores in predicting 6 – week rebleeding and mortality were shown in **Table 5** and **Table 6**. AIMS65, CTP, and MELD scores were not useful in predicting 6-week rebleeding. On the contrary, those 3 scores were shown to predict 6-week mortality. When comparing the AUROCs in

predicting 6-week mortality, we found that AIMS65 score performance was similar to CTP score ($p=0.26$), but was superior to MELD score ($p=0.02$) (Figure 3).

Table 1. Clinical features of the study population

Age, y	55.14 ± 10.06
Male sex, n(%)	64 (80%)
CTP score	8.82 ± 2.27
CTP class, n(%)	
A	31.2%
B	47.5%
C	21.3%
MELD score	15.9 ± 4.93
AIMS65 score	1.75 ± 1.15
Etiology of cirrhosis, n(%)	
Alcoholic	38 (47.5%)
Hepatitis B	22 (27.5%)
Hepatitis C	13 (16.25%)
Alcoholic and hepatitis B	4 (5%)
Alcoholic and hepatitis C	1 (1.25%)
Other*	2 (2.5%)
HCC, n(%)	15 (18.75%)
Endoscopic findings, n(%)	
Esophageal varices	65 (81.25%)
Gastric varices	15 (18.75%)
Blood transfusion at admission, n(%)	28 (35%)
Vasoactive drugs, n(%)	68 (85%)
Prophylaxis antibiotic, n(%)	80 (100%)
Sengstaken-Blakemore, n(%)	3 (3.75%)

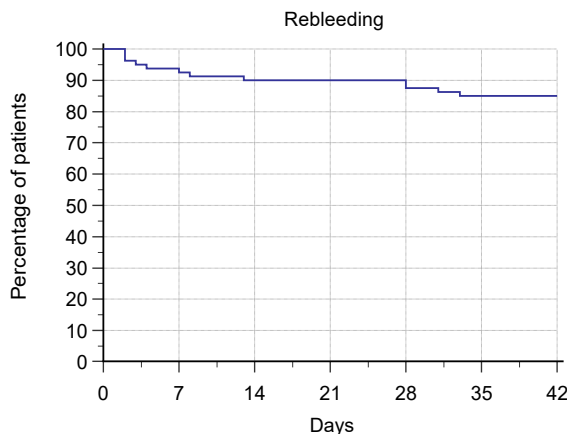


Figure 1. Kaplan-Meier survival curve outlining time to rebleeding in days

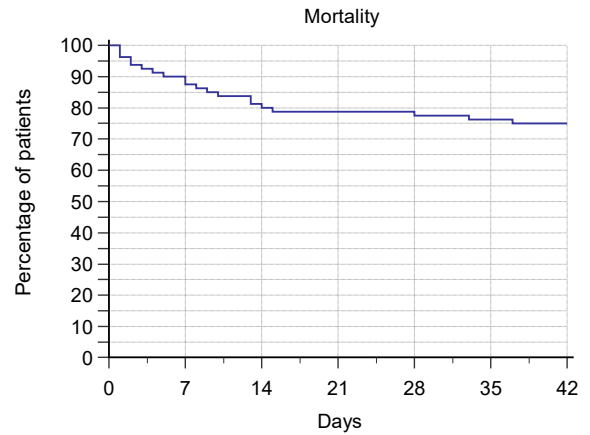


Figure 2. Kaplan-Meier survival curve outlining time to death in days

Table 2. Rebleeding and mortality rate by AIMS65 score

AIMS65 score	Rebleeding rate	Mortality rate
	n/N	n/N
0	1/14	0/14
1	0/20	1/20
2	5/21	6/21
3	6/22	12/22
4	0/3	1/3

Table 3. Rebleeding and mortality rate by CTP score

CTP score	Rebleeding rate	Mortality rate
	n/N	n/N
5	0/3	0/3
6	1/12	2/12
7	1/10	0/10
8	4/13	3/13
9	0/12	1/12
10	4/13	5/13
11	1/4	2/4
12	1/8	4/8
13	0/4	2/4
14	0/0	0/0
15	0/1	1/1

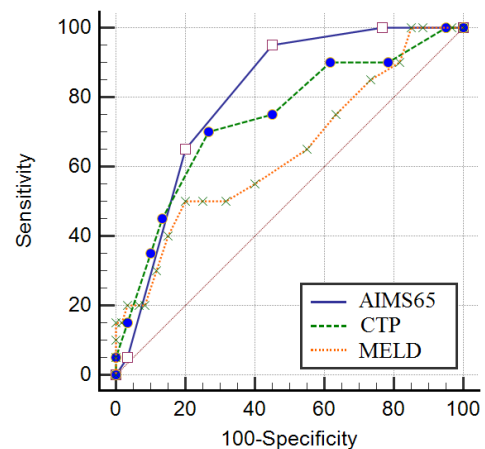


Figure 3. ROC curves demonstrating the ability of the three scoring systems in predicting 6 – week mortality

Table 4. Rebleeding and mortality rate by MELD score

MELD score	Rebleeding rate	Mortality rate
	n/N	n/N
8	1/2	0/2
9	0/5	0/5
10	0/2	0/2
11	2/4	2/4
12	1/6	1/6
13	1/8	2/8
14	1/7	2/7
15	1/11	2/11
16	0/6	1/6
17	0/4	0/4
18	0/3	0/3
19	1/5	2/5
20	2/4	2/4
21	1/4	2/4
22	0/1	0/1
23	0/2	0/2
24	1/2	1/2
25	0/1	0/1
26	0/0	0/0
27	0/1	1/1
28	0/0	0/0
29	0/0	0/0
30	0/1	1/1
31	0/0	0/0
32	0/0	0/0
33	0/1	1/1

Table 5. AUCROCs for AIMS65, CTP, and MELD scores in predicting 6 – week rebleeding

Score system	AUC	CI 95%
AIMS65	0.68	0.53 – 0.83
CTP	0.54	0.4 – 0.7
MELD	0.48	0.29 – 0.68

Table 6. AUCROCs for AIMS65, CTP, and MELD scores in predicting 6 – week mortality

Score system	AUC	CI 95%
AIMS65	0.8	0.7 – 0.9
CTP	0.74	0.6 – 0.86
MELD	0.64	0.5 – 0.79

Using Youden index analysis, we found that the optimal cut-off point was 2 for AIMS65 score in predicting 6-week mortality.

AIMS65 score was highly sensitive in predicting 6-week mortality rate after variceal bleeding.

Table 7. AIMS65 in predicting 6-week mortality using cut-off point of 2

	Death		
	Yes	No	
AIMS65 ≥2	19	27	PPV = 19/(19+27) = 41.3%
AIMS65 <2	1	33	NPV = 33/(33+1) = 97%
	Sens = 19/(19+1) = 95%		Spec = 33/(33+27) = 55%

4. DISCUSSION

Our study is the first prospective study evaluating the prognostic value of AIMS65 score in predicting 6-week mortality and rebleeding in cirrhotic patients with variceal bleeding in Vietnam. Current treatment guidelines aim to reduce mortality in this 6-week period [3]. The majority of previous studies evaluated the predictive value of AIMS65 score in a different population such as in upper gastrointestinal bleeding patients [14] or in a shorter period (i.e. in-hospital mortality) [15]. In these studies, AIMS65 showed promising prognostic value.

From this study, we found that AIMS65, CTP, and MELD scores were not useful in predicting 6-week rebleeding with AUCROCs of 0.68, 0.54, and 0.48, respectively. This is similar to the result from T. Cúrdia Gonçalves study, which showed that AIMS65 score could not predict rebleeding in patients with variceal bleeding [16].

Our study showed that AIMS65 score was useful in predicting 6-week mortality with AUCROC of 0.8. Its performance was similar to CTP score but was superior to MELD score. Recent studies support our findings. Wang et al. conducted a retrospective study involving 202 patients

with acute variceal bleeding and found that AIMS65 score (AUCROC: 0.8) was similar to MELD (AUCROC: 0.76), and CTP scores (AUCROC 0.74) in predicting 6-week mortality [17]. Marcus Robertson et al. evaluated the prognostic value of AIMS65 score in comparison with MELD and CTP scores in predicting 6-week mortality. The authors found that AIMS65 (AUROC: 0.8) was equivalent to MELD (AUCROC: 0.8) and CTP scores (AUCROC: 0.78) [18].

AIMS65 score with simple components can be calculated at the emergency department to stratify patients with variceal bleeding. Using a cut-off point of 2, AIMS65 could promptly identify patients at high risk of mortality. It should be noted that the cut-off point of AIMS65 score in this study was ≥ 2, different from that in previous studies. A retrospective study conducted by Miguel Motola-Kuba et al. in cirrhotic patients with acute variceal bleeding showed that the best cut-off value for predicting in-hospital mortality was AIMS65 ≥1. At this cut-off point, AIMS65 had a sensitivity of 85.7% and specificity of 57% [15]. Reducing the cut-off point to 1 would increase the sensitivity of AIMS65 in our study to 100% at the cost of reducing its specificity. The study conducted by Asmaa N. Mohammad et al showed the cut-off

point of AIMS65 > 2 had sensitivity and specificity of 100% and 93.8%, respectively in predicting in-hospital mortality [19]. These differences may be due to different end-point (6-week mortality in our study and in-hospital mortality in other studies) and pointed out the need for a more extensive validation.

A particular strength of this study was that all patients were prospectively followed up 6 weeks after variceal bleeding. Nonetheless, some limitations should be addressed. First, not all patients in our study received optimal therapy (85% of patients were treated with vasoactive drugs at admission). This may influence the mortality rate in our study. Further research with all patients who received optimal treatment according to Baveno VI consensus should be done to strengthen the result of this study. Another limitation is that comorbidities other than HCC were not addressed in this study. Comorbidities may contribute to the mortality rate and should be reported in future studies.

Conclusion

In conclusion, we found that the performance of AIMS65 score is similar to CTP score, but is superior to MELD score in predicting 6-week mortality. However, these scores are poor at predicting 6-week rebleeding. We recommend using AIMS65 in clinical practice as a simple yet accurate tool for risk stratification in cirrhotic patients with variceal bleeding. AIMS65 scores ≥ 2 predict patients at high risk for 6-week mortality.

FUNDING

The authors received no financial support for the research, authorship, and/or publication of this article.


CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ACKNOWLEDGEMENTS

We would like to thank Associate Professor Duc Trong Quach, Vice chair of the Department of Internal Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, and our colleagues at the Department of Gastroenterology and Hepatology, Cho Ray hospital, Ho Chi Minh City for their support.

ORCID ID

Trong Nguyen Dang Huynh  <https://orcid.org/0000-0003-4534-255X>

REFERENCES

- Carbonell N, Pauwels A, Serfaty L, Fourdan O, Lévy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology*. 2004;40(3):652-9. Epub 2004/09/07. doi: 10.1002/hep.20339. PubMed PMID: 15349904.
- de Franchis R, Primignani M. Natural history of portal hypertension in patients with cirrhosis. *Clinics in liver disease*. 2001;5(3):645-63. PubMed PMID: 11565135.
- de Franchis R, Baveno VIF. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. *Journal of hepatology*. 2015;63(3):743-52. doi: 10.1016/j.jhep.2015.05.022. PubMed PMID: 26047908.
- Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017;65(1):310-35. doi: 10.1002/hep.28906. PubMed PMID: 27786365.
- Reverter E, Tandon P, Augustin S, Turon F, Casu S, Bastiampillai R, et al. A MELD-based model to determine risk of mortality among patients with acute variceal bleeding. *Gastroenterology*. 2014;146(2):412-19 e3. doi: 10.1053/j.gastro.2013.10.018. PubMed PMID: 24148622.
- D'Amico G, De Franchis R, Cooperative Study G. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology*. 2003;38(3):599-612. doi: 10.1053/jhep.2003.50385. PubMed PMID: 12939586.
- Moitinho E, Escorsell A, Bandi JC, Salmeron JM, Garcia-Pagan JC, Rodes J, et al. Prognostic value of early measurements of portal pressure in acute variceal bleeding. *Gastroenterology*. 1999;117(3):626-31. PubMed PMID: 10464138.
- Chalasan N, Kahi C, Francois F, Pinto A, Marathe A, Bini EJ, et al. Model for end-stage liver disease (MELD) for predicting mortality in patients with acute variceal bleeding. *Hepatology*. 2002;35(5):1282-4. doi: 10.1053/jhep.2002.32532. PubMed PMID: 11981782.
- Saltzman JR, Tabak YP, Hyett BH, Sun X, Travis AC, Johannes RS. A simple risk score accurately predicts in-hospital mortality, length of stay, and cost in acute upper GI bleeding. *Gastrointestinal endoscopy*. 2011;74(6):1215-24. doi: 10.1016/j.gie.2011.06.024. PubMed PMID: 21907980.
- de Franchis R. Developing consensus in portal hypertension. *Journal of hepatology*. 1996;25(3):390-4. Epub 1996/09/01. doi: 10.1016/s0168-8278(96)80127-9. PubMed PMID: 8895020.
- Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. *Gastroenterology*. 2003;124(1):91-6. Epub 2003/01/04. doi: 10.1053/gast.2003.50016. PubMed PMID: 12512033.
- Pugh RNH, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *British Journal of Surgery*. 2005;60(8):646-9. doi: 10.1002/bjs.1800600817.
- Frazier TH, Stocker AM, Kershner NA, Marsano LS, McClain CJ. Treatment of alcoholic liver disease. *Therapeutic advances in gastroenterology*. 2011;4(1):63-81. doi: 10.1177/1756283X10378925. PubMed PMID: 21317995.
- Thandassery RB, Sharma M, John AK, Al-Ejji KM, Wani H, Sultan K, et al. Clinical Application of AIMS65 Scores to Predict Outcomes in Patients with Upper Gastrointestinal Hemorrhage. *Clinical endoscopy*. 2015;48(5):380-4. Epub 2015/09/30. doi: 10.5946/ce.2015.48.5.380. PubMed PMID: 26473120.
- Motola-Kuba M, Escobedo-Arzate A, Tellez-Avila F, Altamirano J, Aguilar-Olivos N, González-Angulo A, et al. Validation of prognostic scores for clinical outcomes in cirrhotic patients with acute variceal bleeding. *Annals of hepatology*. 2016;15(6):895-901. Epub 2016/10/16. doi: 10.5604/16652681.1222107. PubMed PMID: 27740523.
- Cúrdia Gonçalves T, Barbosa M, Xavier S, Boal Carvalho P, Magalhães J, Marinho C, et al. AIMS65 score: a new prognostic tool to predict mortality in variceal bleeding. *Scandinavian journal of gastroenterology*. 2017;52(4):469-70. doi: 10.1080/00365521.2016.1260155.
- Wang F, Cui S, Wang F, Li F, Tang F, Zhang X, et al. Different scoring systems to predict 6-week mortality in cirrhosis patients with acute variceal bleeding: a retrospective analysis of 202 patients. *Scandinavian journal of gastroenterology*. 2018;53(7):885-90. Epub 2018/06/19. doi: 10.1080/00365521.2018.1481518. PubMed PMID: 29911438.
- Robertson M, Ng J, Abu Shawish W, Swaine A, Skardon G, Huynh A, et al. Risk stratification in acute variceal bleeding: Comparison of the AIMS65 score to established upper gastrointestinal bleeding and liver disease severity risk stratification scoring systems in predicting mortality and rebleeding. *Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society*. 2020;32(5):761-8. Epub 2019/12/22. doi: 10.1111/den.13577. PubMed PMID: 31863515.
- Mohammad AN, Morsy KH, Ali MA. Variceal bleeding in cirrhotic patients: What is the best prognostic score? *The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology*. 2016;27(5):464-9. Epub 2016/10/27. doi: 10.5152/tjg.2016.16250. PubMed PMID: 27782896.