

Prediction of hospital mortality by MELD Na⁺ score for esophageal variceal bleeding

The success of the MELD Na⁺ score in predicting in-hospital mortality in patients with esophageal variceal bleeding

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Abstract

Aim: Esophageal variceal bleeding is one of the most serious complications resulting from portal hypertension. It is seen in approximately 50-60% of cirrhosis patients, and bleeding recurs within 24 hours of diagnosis in 60-75% of cases. The MELD score is a system used to reveal the severity of advanced liver disease. Its principal sphere of use is finding organs for liver transplantation, and it is also used to predict survival in patients with cirrhosis associated with infectious pathologies, esophageal variceal bleeding, fulminant hepatitis, and alcoholic cirrhosis.

Materials and Methods: Patients presenting with esophageal variceal bleeding were reviewed retrospectively. Sixty-four patients meeting the study criteria were included. The age, sex, etiological causes of esophageal varices, histories, laboratory values at the time of presentation, hospitalization status, endoscopy results, and outcomes of the patients were determined. MELD and MELD Na⁺ scores were calculated, and their success in predicting mortality was analyzed.

Results: Seventy-five percent of the cases were men, and patients' mean age was 60.91 ± 12.61 years. Sixty-three patients presented with bloody vomiting. Sixty-two of the 64 patients were hospitalized. Mortality was observed in 11 of the hospitalized patients. MELD score, MELD Na⁺ score, bilirubin and creatinine exhibited statistically significant correlation with mortality (pMELD =0.003, pMELD Na⁺<0.001, pbil=0.001 and pcre=0.007, respectively), while no relation was determined with hemoglobin, age, INR or serum Na⁺ (p>0.05).

Discussion: MELD Na⁺ score, bilirubin and creatinine values are important and significant parameters in determining in-hospital mortality in patients presenting with esophageal variceal bleeding and are more important than MELD scores. Emergency department and other physicians can more easily be alert to potential mortality using this easily calculated scoring.

Keywords

Bleeding; Cirrhosis; MELD Na⁺; Esophageal Varicose

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Introduction

Esophageal variceal bleeding (EVB) is one of the most serious complications resulting from portal hypertension (HT). It is seen in approximately 50-60% of cirrhosis patients, and bleeding recurs within 24 hours of diagnosis in 60-75% of cases. Portal HT developing due to cirrhosis leads to the formation of porto-systemic collaterals, the most important being esophageal and gastric varices. Although the etiopathogenesis of the bleeding is not fully understood, the most important agent is thought to be an increase in intraesophageal variceal pressure [1,2]. EVB is mainly diagnosed through history, physical examination, and upper gastrointestinal endoscopy. Stabilization and commencement of preparation for early intervention represent the basic therapeutic steps in patients presenting to the emergency department with EVB. Early intervention in these cases, with high mortality rates, and blood transfusion if required, are important cornerstones for EVB in the emergency department. Subsequent therapeutic modalities include balloon tamponade, endoscopic sclerotherapy, and band ligation. The recent addition to these treatments of vasoactive drugs has permitted good results to be achieved [3,4].

MELD is a scoring system used to reveal the severity of advanced liver disease. Its principal sphere of use is for finding organs for liver transplantation, and it is also used to determine survival in patients with cirrhosis associated with infectious pathologies, EVB, fulminant hepatitis, and alcoholic cirrhosis [5]. Studies have shown that the MELD Na⁺ score yields more accurate results with the addition of the patient's sodium levels. Although studies have evaluated the MELD score in predicting the prognosis of EVB in cirrhotic patients, few have investigated the use of the MELD Na⁺ score. The purpose of this study was to investigate whether there is any relation between the MELD Na⁺ score and mortality in patients presenting to our clinic with EVB and to compare the success of the MELD Na⁺ score obtained in predicting mortality compared to the MELD score.

Material and Methods

Study design

Data for consecutive cirrhotic patients aged over 18 years with suspected EVB due to hematemesis or melena and admitted to the Department of Emergency Medicine were collected retrospectively. The participants in the study were patients previously known to be cirrhotic and diagnosed with varices. Early in-hospital mortality rates were calculated using MELD Na⁺ scores at the initial examination.

Study Settings and Population

This study was planned in the emergency department of a training and research hospital with approximately 700 emergency presentations daily and 1100 bed capacity between January 1, 2014 and January 1, 2019. Patients presenting with EVB, with no deficient data, and with variceal bleeding confirmed by a specialist gastroenterologist were enrolled. The diagnosis of cirrhosis relied on previous liver biopsy findings, clinical assessment (signs of chronic hepatic disease), laboratory tests (serum albumin suppression, serum bilirubin elevation, or prolonged prothrombin time), or imaging findings suggestive of cirrhosis. The diagnosis of variceal bleeding was based on the evaluation

of gastroenterologists.

Patients with primary renal or blood disease, primary severe cardiovascular or pulmonary disease, malignant tumor including previous or current hepatocellular carcinoma, EVB associated with Budd-Chiari syndrome or portal venous malformation, endoscopic variceal ligation or receiving sclerotherapy injections in the three months prior to enrollment, non-variceal bleeding such as gastric or duodenal ulcer, started on treatment from external centers, receiving cardiopulmonary resuscitation, aged under 18, pregnant women, or whose study was unavailable were excluded. Patient data were retrieved from the hospital automation system and the patient record archive. In-hospital mortality was defined as that occurring within seven days after the presentation.

Study Protocol

Ethical committee approval was obtained prior to the collection of patient data (ethical committee no. 2019-GOKAE-0931). Patients with an EVB ICD diagnosis code and presenting to the emergency department were identified retrospectively from the patient data management system. These patients' age, sex, etiological causes of EVB, and outcomes (admission, discharge, death, etc.) were then retrieved from the hospital data management system. The serum creatinine, serum bilirubin, serum Na⁺ and INR values required to calculate MELD Na⁺ scores were obtained from the patient files. All data were recorded onto a pre-prepared study form.

Measurements

The following formula was used to calculate MELD Na⁺ scores [OPTN policy, January 2016];

$$\text{MELD}(1) = 0.957 \times (\text{creatinine value}) + 0.378 \times (\text{bilirubin}) + 1.120 \times (\text{INR}) + 0.643$$

If MELD (i) was >11 then the formula

$$\text{MELD Na}^+ = \text{MELD}(1) + 1.32 \times (137 - \text{Na}^+) - [0.033 \times \text{MELD}(i) \times (137 - \text{Na}^+)]$$

The following rules need to be observed during the calculation:

- The maximum creatinine value is taken as 4.0.
- If the creatinine and INR value is below 1.0 mg/dL, this is regarded as 1.0 mg/dL.
- If Na⁺ is below 125 mEq/dL then this is regarded as 125 mEq/dL, and if Na⁺ exceeds 137 mEq/dL then this is regarded as 137 mEq/dL in the formula [6-8].

Statistical analysis

SPSS (Statistical Package for Social Sciences) for Windows 20.0 software was used for the statistical analysis of all the data obtained. All data were summarized in tables during evaluation. The Mann-Whitney U test was used to compare the mean values of the data obtained, and the Pearson Chi-Square (and the Fisher's exact test when required) was used to compare non-parametric data.

Results were considered significant at $p < 0.05$, with a 95% confidence interval.

Results

Seventy-five percent (n=48) of the 64 patients in the study were men. The mean age of the cases was 60.91 ± 12.61 years. A history of hypertension (HT) was present in 7.8% of cases, diabetes mellitus (DM) in 18.8%, congestive heart failure in 4.7%, chronic kidney failure in 3.1%, malignancy in 7.8%, cor-

onary artery disease in 3.1%, and cerebrovascular disease in 1.6%. In terms of etiology, cirrhosis developed in association with hepatitis B in 10 cases, hepatitis C in 8 cases, hepatocellular carcinoma in four, chronic ethylism in 17, primary biliary cirrhosis in two, in association with drug use in three, and in association with other causes in 22 cases. Hematemesis was present in 61 cases.

Endoscopic imaging aimed at diagnosis and treatment was performed in all cases by a specialist gastroenterologist. Findings of active bleeding arising from varices were determined at endoscopy in all cases undergoing the procedure. Procedures aimed at the bleeding were performed on all patients during endoscopic imaging. Two patients included in the study were discharged from the emergency department, while 56 of the remaining 62 patients were admitted to the ward and six to the intensive care unit. Analysis of outcomes revealed that 53 patients were discharged at the end of clinical follow-up and treatment, while mortality occurred in 11 cases (four of the six patients admitted to the intensive care unit and seven of the 56 patients admitted to the ward).

No statistically significant relation was determined between hemoglobin (p=0.05), INR (p=0.206), serum Na⁺ (p=0.724) or age and mortality (p>0.05). However, serum bilirubin, creatinine, MELD score, and MELD Na⁺ score were significantly related to mortality (p<0.05) (Table 1).

Sensitivity and specificity values for MELD Na⁺, and serum bilirubin and creatinine values, identified as statistically significant, are shown in Figure 1 and Table 2.

Table 1. Distribution of laboratory results of cases and mean MELD score values

Parameters	Surviving cases n=53 (82.8%)	Exitus cases n=11 (17.2%)	P
Age (years) (mean)	60.79 ± 12.74	61.45 ± 12.54	.876
Male-Female	39-14	9-2	.716
Hemoglobin (mg/dL)	9.16 ± 2.01	7.83 ± 2.09	.050
Bilirubin (mg/dL)	2.26 ± 3.85	7.37 ± 10.53	.007
Creatinine	0.88 ± 0.42	1.57 ± 0.95	.000
INR	1.47 ± 0.39	1.64 ± 0.41	.206
Na ⁺	135.89 ± 4.76	136.45 ± 5.16	.724
MELD score	10.50 ± 2.67	14.45 ± 7.27	.003
MELD Na ⁺ score	14.39 ± 5.81	22.00 ± 9.21	.001

Table 2. Cut-off, sensitivity, and specificity values for MELD Na⁺ scores and parameters

Parameter	Bilirubin (95% CI)	Creatinine (95% CI)	MELD (95% CI)	MELD Na ⁺ (95% CI)
Cut-off value	2.59 mg/dL	1.12 mg/dL	10.50	8.20
Sensitivity (%)	54	72	90	54
Specificity (%)	83	87	54	33
Area under the curve (AUC)	.648	.748	.727	.762
Lower bound	.441	.557	.594	.604
Upper bound	.856	.939	.860	.921

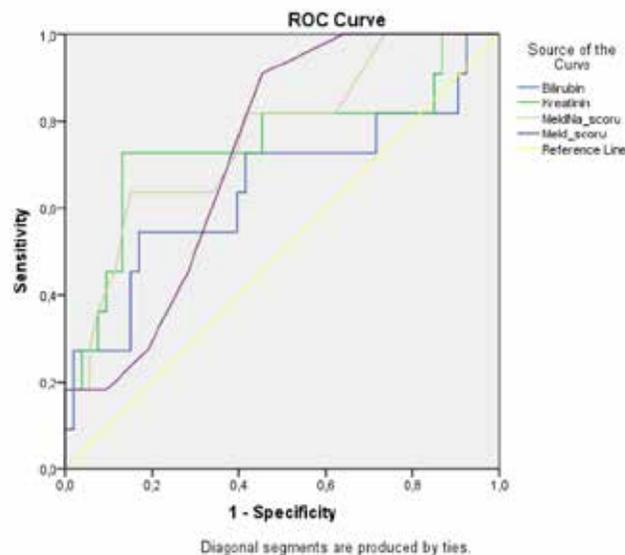


Figure 1. ROC analysis of MELD and MELD Na⁺ scores and parameters

Discussion

EVB is the most important complication of portal HT in cases of cirrhosis, and one of the severe causes of death resulting from hypotension and hypovolemic shock. First bleeding may be massive and unexpected, and this can also cause high mortality [9]. Emergency intervention is necessary in order to prevent this life-threatening bleeding. EVB is the second most common cause of upper gastrointestinal bleeding. Tuncer et al. reported that EVB is more common in men [10]. Men also represented 66% of cases in Kehribar et al.’s study [11]. In agreement with the literature, three-quarters of our patients were also men. Graham et al. reported mean ages of 48.1 ± 1.7 years for men and 49.2 ± 2.0 for women [9]. Onaca et al. determined a mean age of 50.5 years [13], and Wang et al. a mean age 48.9 ± 13.8 [14]. The mean age of the patients in our study was 60.91 ± 12.61 years. We think that the higher age in our study compared to the previous literature may derive from our low case number.

Several causes are involved in the etiology of cirrhosis. These include chronic ethylism, infectious causes (HBV, HCV and delta), autoimmune hepatitis, drugs and toxins, biliary system diseases, veno-occlusive diseases, metabolic diseases, and heart failure [14]. The most chronic etiological factor in our cases was chronic ethylism, followed by HBV. Tuncer et al. described HBV as the most common cause of cirrhosis in their EVB patients [10]. Yaraş et al. determined HCV as the most common cause of cirrhosis in cirrhotic patients with EVB in their study [15]. The low numbers of patients with EVB in the present and other studies may be responsible for the inconsistent results. In the study by Bambha et al., endoscopic imaging was performed 12 hours after admission in all cases except for one, the majority having esophageal varices only (81%), with gastric varices only in 6% and both gastric and esophageal varices in 13%. They reported active variceal bleeding at initial endoscopy in 71 patients (28%) [16]. Endoscopy was performed on all patients in the study by Reverter et al., with active variceal bleeding being seen in only 34% (n=60) [18]. All patients in our

study also underwent endoscopy, and active variceal bleeding was observed in 43.75% (n=28).

MELD is one of the scoring systems used in determining priority in patients requiring transplantation. It first began being used in 2002, being initially employed to predict prognosis in patients undergoing transjugular intrahepatic portosystemic shunt. It later became a reliable scoring system capable of yielding accurate results in predicting life span in cirrhotic patients [5]. The entry into the use of the MELD score led to decreases in patient losses occurring during the transplantation waiting period. The MELD score was previously used in determining post-transplantation mortality [18].

Bambha et al. evaluated 368 EB patients in 16 centers. The principal finding of their research was that the MELD score is a clinically useful and objective predictor of short-term survival following acute variceal bleeding. The authors described the MELD score as a significant predictor of mortality in cirrhotic patients arriving with acute variceal bleeding, with every one-point increase resulting in mortality of 8-11% in a 5-6 week period [16]. Reverter et al. evaluated mortality in 178 EVB patients and compared MELD and other scoring systems, concluding that the MELD score was more effective [17]. In their multicenter retrospective study, Chalasani et al. reported that the MELD score predicted 83% of in-hospital mortality among 239 cirrhotic patients presenting with variceal bleeding (95% CI 0.74 and 0.92) and 78% of one-year mortality (95% CI 0.69 and 0.87) [19]. The MELD score was also a significant predictor of mortality in the present study.

Although studies have evaluated the MELD score in predicting the prognosis of EVB in cirrhotic patients, few have investigated the use of the MELD Na⁺ score. Na⁺ values have been observed to be associated with the prognosis of cirrhotic patients in recent years [14]. Previous studies have shown that the addition of serum sodium to the MELD score resulted in better accuracy compared to the MELD score alone in predicting mortality in patients with cirrhosis or end-stage liver disease [18]. Hyponatremia, a result of free water retention in the body, exhibits a positive correlation with the severity of portal HT [20]. Wang et al. reported that the MELD Na⁺ score successfully predicted three-month and one-year mortality following planning of endoscopic treatment in patients presenting with EVB [13]. It has therefore been suggested that the use of Na⁺ values in the MELD score will make the scoring more reliable. Both the MELD and MELD Na⁺ scores of the patients in our study were significantly correlated with mortality in cirrhotic patients with EVB, but the MELD Na⁺ score was more a significant predictor (pMELDNa⁺<0.001 and pMELD:0,003). MELD Na⁺ scores were higher in patients with a fatal disease course.

The cut-off value of the MELD score for mortality in EVB patients in the present study was 10.5 (sensitivity of 90% and specificity of 54%, lower bound 0.594, and upper bound 0.860 at 95% CI, AUC: 0.727), while the cut-off values for the MELD Na⁺ score for mortality in EVB patients was 8.20 (sensitivity of 54% and specificity of 33% were low, lower bound 0.604, and upper bound 0.921 at 95% CI, AUC: 0.762). Akdoğan et al. reported that a MELD score of 20 or more significantly shortened life span, and that two fatal cases post-transplantation cases had pre-transplantation MELD scores of 24 [21]. Onaca et al.

investigated predicting mortality using the MELD score in patients scheduled for transplantation. Higher mortality was determined in patients with MELD scores of 25-29 than in those with scores of 30 or above. However, the authors also stated that more extensive studies were needed to draw any clear conclusions [12]. It was also investigated whether MELD Na⁺ score parameters are associated with mortality or not, and a significant relation was observed with creatinine and bilirubin. Freeman et al. described serum bilirubin as an important parameter in predicting prognosis in portal HT-related portal gastrointestinal system bleeding [22]. Our study findings suggest that creatinine and bilirubin may be independent parameters in predicting mortality. However, this now needs to be supported with further, more extensive studies.

We determined no relation between mortality and INR, Na⁺ and hemoglobin globin levels in this study. Although Na⁺ has been reported to be associated with mortality in some studies, we determined no such relation [22].

Limitations

Our study has several limitations. First, because of the retrospective analysis method, deficient data were unavoidable. Patients who were lost to follow-up might have died in other hospitals.

Second, this was a single-center study, and our patient numbers were therefore low.

Third, patients with recurrent bleeding were not identified in our data.

Finally, physiological vital signs could not be used due to deficiencies in the records at the time of presentation. While the patient's physiological parameters represent the basis of the emergency department scoring system, comparison, the MELD Na⁺ score is calculated from laboratory parameters. Comparison of these two scoring systems would have made it possible to determine which one is more useful for emergency physicians.

Conclusion

EVB-related mortality is still a severe problem in Turkey and worldwide. Early diagnosis and treatment are of vital importance. Several studies have reported that EVB patients experience severe repeated bleeding soon after the initial bleed, and that two-thirds of EVB patients die within one year of the initial bleeding. Parameters or scoring systems predicting mortality for a clinical manifestation with such a high mortality rate are therefore needed. Our study shows that the MELD Na⁺ score and its parameters creatinine and bilirubin, which can be easily calculated in the emergency department, may be predictors of mortality in patients with EVB. We think that our study findings will be a useful guide for physicians and the literature, can assist physicians in terms of intensive care admission, and can contribute to the national economy by reducing mortality and morbidity.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical stan-

dards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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