PROGNOSTIC VALUE OF MELD SCORE IN CHILD PUGH C CIRRHOTIC PATIENTS

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Abstract

Background and aims: The Model for End Stage Liver Disease (MELD) is a scoring system used for the prioritization of patients waiting for liver transplantation. Patients with decompensated cirrhosis often have serious complications. The aims of this study were to evaluate the prognostic value of MELD score in relation to mortality complications and to acute variceal bleeding, spontaneous bacterial peritonitis, hepatoencephalopathy, hepatorenal syndrome of Child Pugh C Vietnamese cirrhotic patients in a period of six months after hospitalization. **Methods:** This prospective study includes 102 consecutive Child Pugh C cirrhotic patients who were admitted to the Gastrointestinal Department of Hue Central Hospital and the General Internal Medicine Department of Hue University of Medicine and Pharmacy Hospital, Vietnam, from April 2016 to February 2017. The MELD score of each patient was calculated at admission. All patients were then observed for 6 months to assess the following: acute variceal bleeding, spontaneous bacterial peritonitis, hepatoencephalopathy, hepatorenal syndrome and mortality. **Results:** The mean MELD score of all patients was 19.5 ± 7.1; of male patients was 19.7 ± 7.4; of female patients was 18.43 ± 4.4; of alcoholic patients was 19.5 ±7.5; and of non – alcoholic patients was 19.6 ± 5.9. The MELD score correlated with mortality during 6 months after hospitalization (with cut – off = 20; AUC = 0,69; sensitivity and specificity were 56.0% and 76.6%) and with hepatorenal syndrome (with cut – off = 25; AUC = 0.90; sensitivity = 83.3% and specificity = 85.4%). In this study, the MELD score did not correlated acute variceal bleeding, spontaneous bacterial peritonitis, hepatoencephalopathy during 6 months after hospitalization. **Conclusion:** MELD is a valuable prognostic score for mortality and hepatorenal syndrome in Child Pugh C cirrhotic patients in 6 months after hospitalization.

Key words: *MELD score, Child Pugh C cirrhotic patients*

1. BACKGROUND

Cirrhosis is the 12th most common cause of mortality worldwide and its etiology is multifactorial [15]. The serious clinical manifestations of cirrhosis occurs mainly in the decompensated stage with various complications: acute variceal bleeding (AVB), spontaneous bacterial peritonitis (SBP), hepatoencephalopathy (HE), hepatorenal syndrome (HRS) and death [4] [8] [9] [14] [18] [19]. The prognosis for cirrhosis in this stage plays an important role for clinicians in the decisions making for treatment and mornitoring of the patients during and after hospitalization [5] [6] [7] [17]. Both doctors and patients want to know what is waiting for them after 3 months and 6 months. The MELD score has three objective variables: serum bilirubin, serum creatinine and INR, and was initially developed from the data of patients who survivied after Transjugular Intrahepatic Portosystemic Shunt (TIPS). It was validated to anticipate the complications of cirrhosis in an American population dataset [13] [20]. Cirrhotic patients with Child Pugh C suffer a higher mortality prevalence than those with Child Pugh A and B [2]. Currently, there exists very little research which demonstrates the prognostic value of the MELD score for Vietnamese patients with monitoring during the next 6 months. Consequently, we have conducted this research to determine the prognostic value of MELD score for Child Pugh C cirrhotic patients. The research has two objectives: (1) To determine the MELD score in Child Pugh C cirrhotic patients and (2) To evaluate the value of MELD score in prognosis of patients within 6 months after hospilization.

2. PATIENTS AND METHODS

2.1. Patients

This prospective study was carried out in the Department of Gastroenterology of Hue Central Hospital and the Department of General Internal

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Medicine of Hospital of Hue University of Medicine and Pharmacy, Vietnam.

All cirrhosis patients who were admitted to the department from April 2016 to February 2017 were considered for this study. Those who fulfilled the inclusion and exclusion criteria were followed for 6 months after hospitalization.

Inclusion criteria

Patients who were diagnosed with Child Pugh C cirrhosis and agreed to participate in the research.

The Child-Pugh score was calculated by following formulas: Child Pugh C: 10 – 15 points

Table 1. Child Pugh classification

Parameter	1	2	3
Ascites	Absent	Mild to moderate ascites	Tense ascites
Encephalopathy	None	Grade 1 to 2 hepatic encephalopathy	Grade 3 to 4 hepatic encephalopathy
PT (%) or INR	> 50 < 1.7	40 – 50 1.7 – 2.3	< 40 > 2.3
Albumin (g/l)	> 35	28 – 35	< 28
Bilirubin (µmol/l)	< 35	35 – 50	> 50

Exclusion criteria:

Patients with hepatocellular carcinoma due to liver disease, those were receiving hepatotoxic drugs or vitamin K antagonists drugs; or those with renal failure or blood disorders; or those with coma due to other causes such as: poison or stroke; or those who declined to participate the study; or those whose mortality from non medical cause such as trauma; and those who were lost to follow up for 6 months after hospitalization.

Methodology:

Personal information of patients (age, gender, occupation, liver disease history), sign and symptoms (anorexia, fatigue, palmar erythema, spider angioma, ascites, hepatomegaly, jaundice, icterus, edema, splenomegaly) were recorded. Laboratory tests were obtained (platelet, prothrombin ratio, INR, SGOT, SGPT, albumin, bilirubin, creatinine). Patients were then assessed for esophageal varices and portal hypertensive gastropathy.

The following formulas were used to calculate the MELD score: **M=3.78 x ln(bilirubin [mg/dL]) + 11.2 x ln(INR) + 9.57 x ln(creatinine [mg/dL]) + 6.43** [12]

All patients were observed for 6 months after hospitalization, either by direct examination at each hospital, through direct interviews with patients or their family, or through telephone interviews. They were interviewed at least once per month for complications such as: mortality, acute variceal bleeding, spontaneous bacterial peritonitis, hepatoencephalopathy, or hepatorenal syndrome.

Statistical methods

Participant's information was described by frequency and percentage of the classification variables; mean, standard deviation (SD), median, minimum value, maximum value for continuous variables.

The value of MELD score in predicting complications was estimated by ROC curve and survival analysis. The relationship between predictive value of MELD score and variables was estimated with X^2 test. All of these values were considered statistically significant if *p*-value was < 0.05. All statistical analyses were performed using SPSS Version 20 for Window, MedCalc 8.0.1.0.

3. RESULTS

From April 2016 to February 2017, a total of 102 cirrhosis patients were enrolled to the study. The rate of survival was 75.5%, mortality 24.5%; AVB 27.5% ; HE 11.8%; SBP 12% ; HRS 3.9%.

3.1. MELD score in Child Pugh C cirrhotic patients

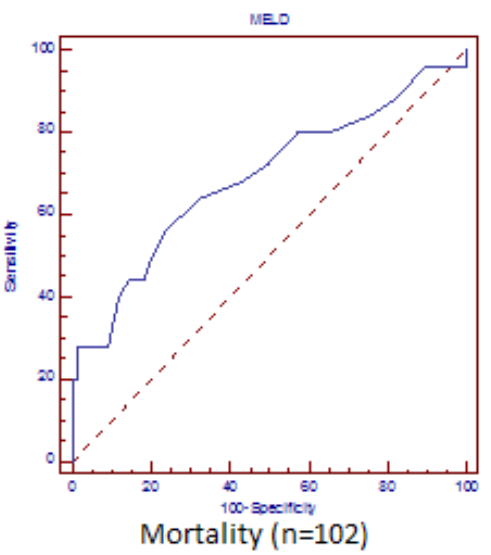
Table 2. Characteristics of patients

Patient characteristics		
	Male/female %	86.3/13.7
	Age; mean ± SD	55 ±11.1
	Alcohol/ HBV/HCV/ Autoimmune %	72.5/31.4/10.8/2.9

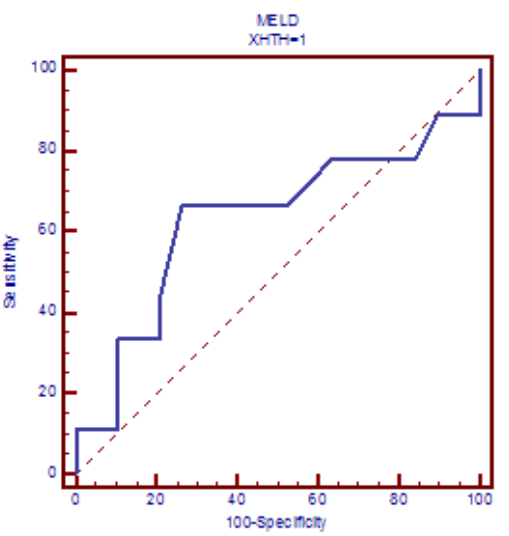
MELD score	Median (Min : Max)	18.5 (9 : 52)
	Mean	19.5 ± 7.1
Average MELD score	Male/female	19.7 ± 7.4/18.43 ± 4.4
	Alcohol/Non-Alcohol	19.5 ±7.5/19.6 ± 5.9

The survey of relation between the MELD score and complications occurring within 6 months after hospitalizing revealed that there was no significance difference between the MELD score of the mortality group 23.0 ± 10.5 as compared to the survival group 18.4 ± 5.2. In the mortality group, the mean creatinine and bilirubin was significant higher than survival group while the mean INR between the groups in the mortality group were insignificantly different. The mean MELD score in patients with acute variceal rebleeding (19.3 ± 5.3) was insignificant greater than the mean MELD score in non-variceal rebleeding (17.6 ± 6.5). The mean MELD score in AVB group (18.0 ± 6.1) was insignificant lower than non-acute variceal bleeding (20.1 ± 7.4). This is similar to Huo T.'s research comparing the cirrhosis prognostic value of 4 score (MELD, MELD-Na, iMELD and MESO): The mean MELD score in AVB group (14.5 ± 7.6) was insignificantly lower than non-acute variceal bleeding (15.4 ± 7.0) [11]. Overall, the MELD score was not associated with the prediction of gastrointestinal bleeding. This could be explained by the mechanism of variceal bleeding in which portal hypertension accompanied a blood clotting disorder in decompensated cirrhosis. Spontaneous bacterial peritonitis, hepatoencephalopathy, hepatorenal syndrome may appear more frequently in Child Pugh C cirrhotic patients than Child Pugh A or B ones, whereas variceal bleeding may occur commonly in Child Pugh A or B cirrhotic patients with compensated liver function. Besides, the mean MELD score in the SBP group (22.2 ± 6.1) was insignificant higher than the non - spontaneous bacterial peritonitis group (19.5 ± 7.4). The mean MELD score in the HE group (21.0 ± 7.8) was insignificant higher than the non - hepatoencephalopathy group (19.2 ± 6.9). The mean MELD score in the HRS group (29.8 ± 17.0) was insignificant higher than the non - hepatorenal syndrome (18.9 ± 5.6).

3.2. Predictive value of MELD score for complications occurring during 6 months after admission of Child Pugh C cirrhotic patients



Mortality (n=102)



Mortality due to AVB (n = 28)

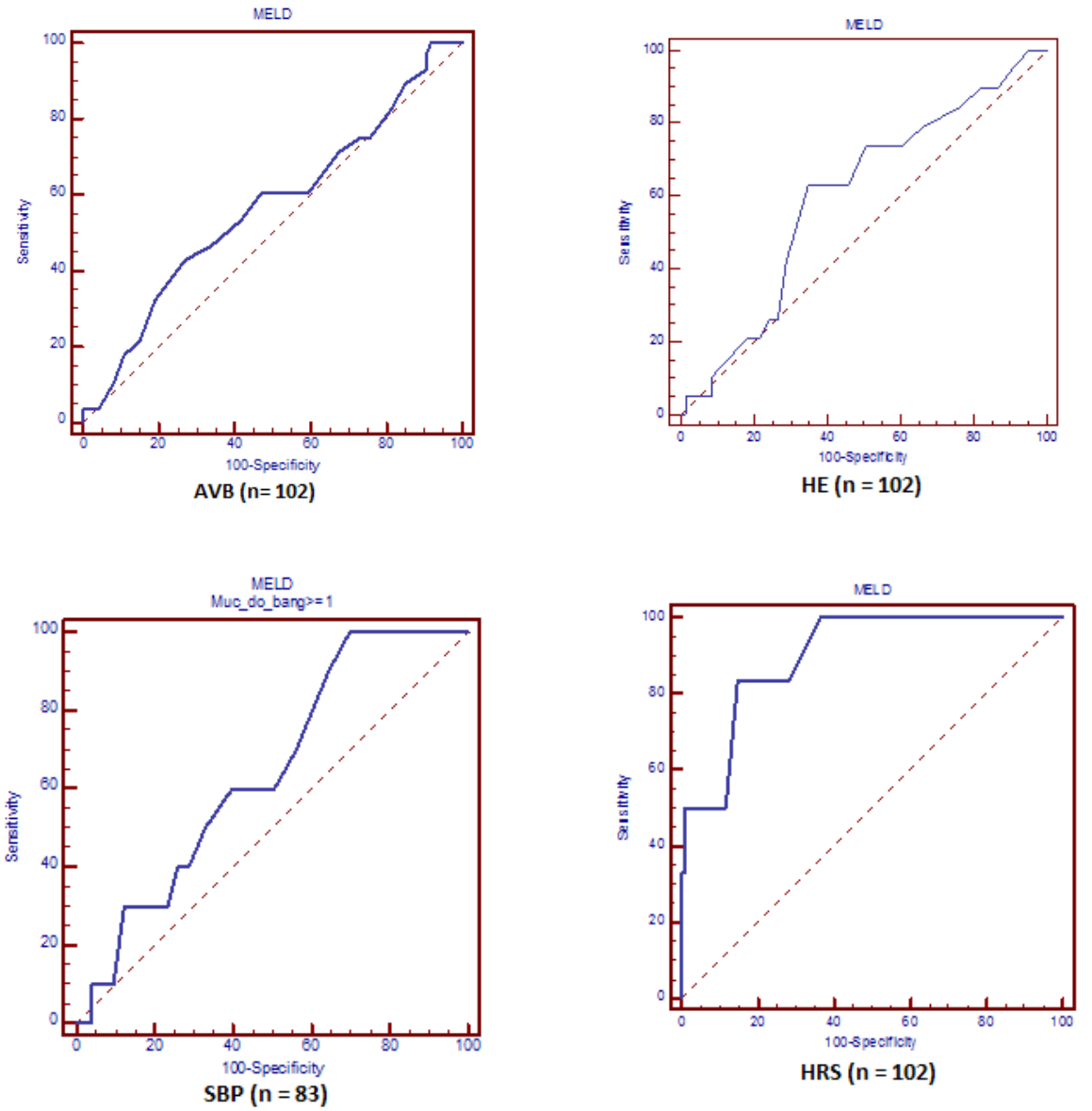
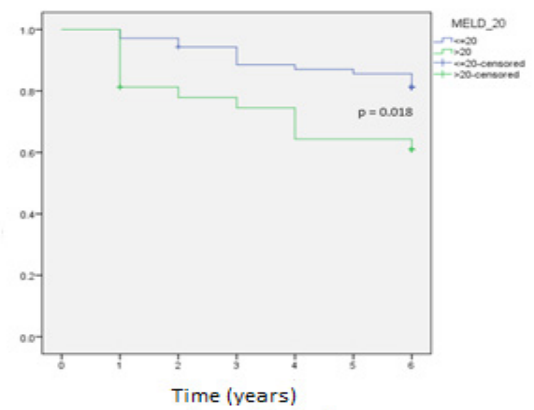


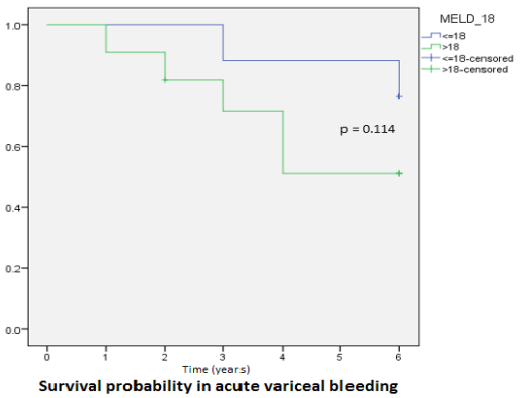
Figure 1. ROC curve of MELD score for predicting 6-months complications

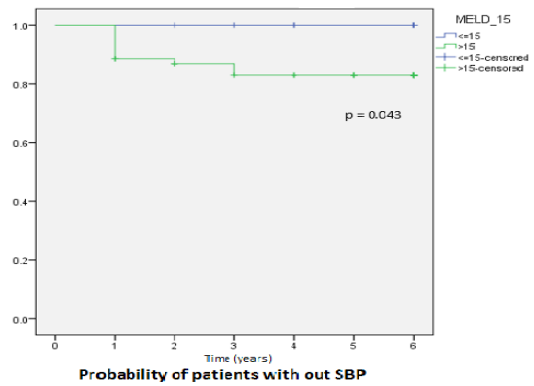
Complications	AUC	95% CI	Cut-off	Sensitive	Specificity	p
Mortality	0.69	0.60-0.78	20	56.0 (34.9-75.6)	76.6 (65.6-85.5)	0.005
Mortality after AVB	0.63	0.43-0.80	18	66.7 (29.9 – 92.5)	73.7 (48.8 – 90.9)	0.326
Variceal - Rebleeding	0.57	0.47-0.67	15	42.9 (24.6 – 62.8)	73.0 (61.4 – 82.6)	0.310

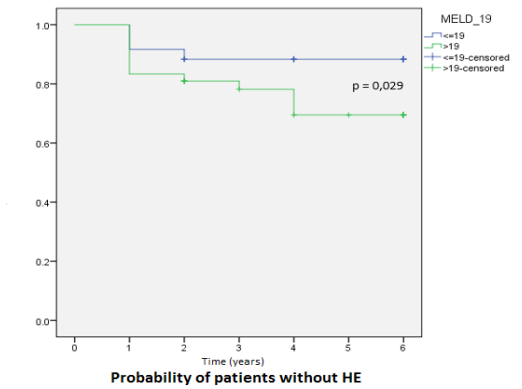
SBP	0.64	0.53 – 0.74	15	100 (69.2 - 100)	30,1 (19.9 – 42.0)	0.088
HE	0.60	0.50 – 0.70	19	63.2 (38.4 – 83.7)	65.1 (53.8 – 75.2)	0.160
HRS	0.90	0.83-0.95	25	83.3 (35.9-99.6)	85.4 (76.7 – 91.8)	< 0.0001

Table 3. AUC and cut - off of MELD score in predicting acute variceal bleeding, spontaneous bacterial peritonitis, hepatoencephalopathy, hepatorenal syndrome, mortality occurring during 6 months after hospitalization









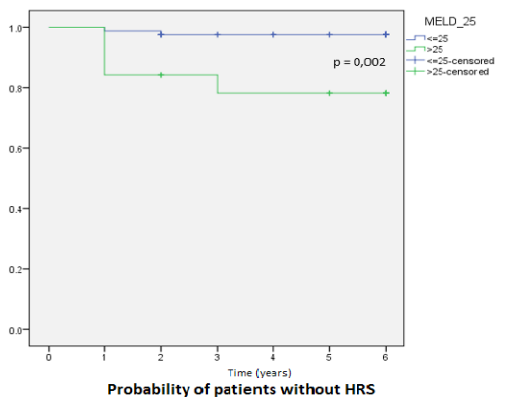


Figure 2. Probability of patients without complication occurring according to MELD score

4.DISCUSSION

The MELD scoring system has been widely applied in recent years and shown to predict complications across a broad spectrum of liver diseases. Accurate prognostic indicators for patient in Internal Medicine Department are important because it helps guide clinical decision making, talking to families of patients, and prescribing medication . This study showed that the cut-off score of 20 is useful to to predict mortality within 6 months since hospitalization; AUC 0.69; sensitivity 56.0%; specificity 76.6% (p = 0.005). With a similar result, the study of Attia K. A. (2007) revealed that value of cut - off for pronogsis of mortality in 6 months was 21; AUC 0.62; sensitivity 48.2%; specificity 69.5% [2]. According to a study by Mallaiyappan, the MELD score has a mortality predictable value for alcoholic cirrhosis with the cut – off 21 which was the highest sensitivity and specificity after 1 month, 3 months and 6 months in both retrospective and prospective validation [16]. The study of Cholongitas assessed for the MELD score in cirhotic patients admitted to ICU shows that MELD had high discriminiation (AUC = 0.81) almost the same as SOFA and superior to APACHE II [6]. In general, studies show that predictive value of MELD score ranges from medium to high for mortality in 6 months. The greater the MELD score is, the higher risk of mortality the patients have.

Hepatorenal syndrome is a functional renal failure that frequently develops in patients with advanced cirrhosis and severe impairment in systemic circulatory function [3]. In our study, the cut - off to predict hepatorenal syndrome in the 6 months after hospitalization was 25; AUC 0.9; sensitivity and specificity was 83.3% and 85.4% (p < 0.0001). In a consecutive study with hepatorenal syndrome patients, the outcome of patients with cirrhosis and hepatorenal syndrome can be estimated by two available variables: hepatorenal syndrome type and MELD score. All type 1 hepatorenal syndrome patients had a MELD score ≥ 20 and an average survival time of 1 month. These factors points to the fact that the MELD score is significant to anticipate outcomes of hepatorenal syndrome [1]. It is useful for doctors and patients as hepatorenal syndrome requires close monitoring, careful differentiation from other disorders and treatment with specific medications.

In this study, we did not find a prognostic value of MELD for other complications: acute variceal bleeding, death after variceal bleeding, spontaneous bacterial peritonitis and hepatoencephalopathy.

Probability of patients being complication-free according to MELD score

In this study, the survival probability of patients whose MELD score > 20 was significant lower than those whose MELD score ≤ 20 (p = 0.018). After 6 months, the group of patients whose MELD score was > 20 included 61% alive patients as opposed to 81% for the group whose MELD score was ≤ 20. The study of Attia K. A. (2008) which aimed to compare Child Pugh and MELD score in prognosis the mortality of 172 black African cirrhotic patients followed up for 12 months concluded that the group with MELD score > 21 had a survival probability after 6 months of 66.1%; 95% CI ranged from 0.51 to 0.77. The survival probability of patients with a MELD > 21 was significant lower than those whose MELD score ≤ 21 (p = 0.002) [2]. This study revealed that, the survival probability in acute variceal bleeding patients with MELD > 18 was insignificant was lower than those whose MELD score ≤ 18 (p = 0.114). After 6 months, the group of MELD > 18 had 51% patients alive; meanwhile 77% patients whose MELD ≤ 18 alive. In Zhao's 2014 study on the risk factors at variceal rebleeding and mortality of variceal bleeding patients has shown that there was a worsening significantly of mortality at 7 weeks of 34% if their MELD score was ≥ 18 to 54% if their MELD score was < 18 [21]. The spontaneous bacterial peritonitis free probability of patients with a MELD score > 15 was significantly lower than those whose MELD score ≤ 15 (p = 0.043). The patients with a MELD score > 19 had lower rates of non-hepatoencephalopathy than those with a MELD score ≤ 19 (p = 0.029). After 6 months, the non- hepatorenal syndrome probability of patients with MELD > 25 was significant lower statistical significantly than those whose MELD score ≤ 25 (p = 0.002). According to the study of Heidemann, the Kaplan-Meier survival analysis of the patient cohort showed that mean short-term survival was significantly longer in patients with MELD score less than 27 compared with those having a MELD score ≥ 27: 28.5 days (95% CI 27.3–29.7) versus 25.4 days (95% CI 23.4–27.5) [10] .

5. CONCLUSION

This study has shown that MELD score is capable of predicting mortality when we use a cut - off of 20; AUC 0.69; sensitive 56% and specific 76.7%. The survival probability of patients whose MELD score > 20 is significant lower than those whose MELD score ≤ 20. Moreover, the MELD score allows predicting if the patients will develop hepatorenal syndrome by

6 months when we utilize a cut - off of 25; AUC 0,9; sensitivity = 83.3% and specificity = 85.4%. The non - hepatorenal syndrome probability of patients with MELD > 25 is significant lower than those whose MELD score ≤ 25. A prognostic value of MELD score for acute variceal bleeding, spontaneous bacterial peritonitis and hepatoencephalopathy within 6 months after hospitalization was not found in this study.

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